ANEXO II

TEMAS E ARTIGOS PARA A PROVA ESCRITA

TEMA DO ARTIGO 1:
Explorando fontes alternativas de proteína com foco nos mercados de alimentos

TEMA DO ARTIGO 2:
Aplicação de solventes verdes e novas técnicas ecológicas de extração compostos bioativos a partir de resíduos vegetais e associado a economia circular

TEMA DO ARTIGO 3:
Regulação ecológica integrada a sistemas alimentares saudáveis e sustentáveis em resposta ao aumento global de alimentos ultraprocessados

TEMA DO ARTIGO 4:
Corantes alimentares naturais: estabilidade e aplicações

TEMA DO ARTIGO 5:
Estratégia e perspectiva econômica da bioeconomia circular no setor agroalimentar.

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Review

Exploring alternative protein sources: Evidence from patents and articles focusing on food markets

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ABSTRACT

This review considers alternative protein sources through the analysis of food science literature and patents. Data collection was performed from scientific literature and patent documents using the Scopus and National Institute of Industrial Property databases, with a term combination “alternative protein source” and “source* AND protein* AND alternative*”. A total of 945 documents were analyzed. The scientific prospection showed that agricultural and biological science was the main application area. The food industry area had the highest number of filed patents. The annual evaluation of published documents demonstrated that this area had been investigated since the 1970s, and the number of articles was twice than that of filled patents. Although protein products are available for sale, animal and vegetable sources replace conventional protein products. Presently, alternative protein sources are already a worldwide trend in the food industry, enabling the development of new products to facilitate their insertion into the consumer market.

1. Introduction

Proteins are the main structural and functional constituents of food that develop biological (Adenekan et al., 2018) and technological functions for organism and food, respectively. They allow the body to maintain metabolic activities, such as maintenance, growth, and repair of cellular machinery (Akharume et al., 2021; Loveday, 2020). Proteins have diverse applications in the food industry because of their surface properties, such as the ability to form or stabilize emulsions, biological activity (enzymes), intermolecular interactions, and the ability to change the sensory properties of products (appearance, flavor, color, odor, and texture) (Małecki et al., 2021).

Previously, only animal (muscles, eggs, milk, and blood) and some vegetable proteins have been widely used. Most recently, due to the restrictive diets regarding the consumption of animal products, new market demands have been generated, and the search for new protein food sources has become necessary (Sá et al., 2019).

Unconventional proteins are gaining popularity worldwide because of their health benefits, environmental sustainability, and ethical merit (Akharume et al., 2021). The sources of these proteins are versatile and can be obtained from plants (cereals, edible seeds, pseudo-cereals, legumes, tubers, and oilseeds), unconventional alternative sources (e.g., agro-industrial by-products), microorganisms (fungi and bacteria), algae and microalgae, and insects (Loveday, 2020; Pojić et al., 2018). Microbial proteins derived from fungi and algae are also food ingredients of interest because of their high protein quantity and quality; however, there is no commercial food application for bacterial proteins (Boukid et al., 2021). Furthermore, using alternatively sourced food products contributes to lower environmental impact and offers a means to feed a growing world population. In contrast to many established proteins and protein fractions for which a substantial amount of knowledge has accumulated over the years, much less information is available regarding these emerging proteins (Grossmann & Weiss, 2021).

These new protein sources have already been recognized and are being used in diverse areas, including as animal feed for supplementation and improving protein intake in feed (Gałęcki et al., 2021; Gasco et al., 2020; Kusmayadi et al., 2021), for use in cosmetics and

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pharmaceuticals (Amorim et al., 2021; Coppola et al., 2020; Huang et al., 2021), and in the formulation of food products for human consumption (Botella-Martínez et al., 2021; Kotecka-Majchrzak et al., 2020; Zielińska et al., 2021), as well as their consumption *in natura* or preparations.

Concerns regarding food security allied to the challenge of increasing world population growth encourage the search for foods that provide micro-and mainly macronutrients, which are sustainable and environmentally viable. To meet consumer demands and individual food needs, the diversification of protein sources and functions is essential for food safety and product development and manufacturing, with animal, vegetable, and microbial proteins being vital to meet the world's supply needs of protein.

In addition to scientific studies in the area, understanding alternative protein sources in the patent scope is also an important tool to guide efforts to develop new technologies. Currently, this knowledge is fundamental for expanding anticipation capacity and stimulating the organization of innovation systems in the academic environment. The structure of the texts in scientific papers and patents is different because they are tools for the diffusion of scientific and technological knowledge, respectively (Hasner, Lima, and Winter, 2019). The analysis of both supports the purpose of this study, which is to map alternative protein sources through the analysis of articles and patents, focusing on food markets.

2. Methodological aspects

Data were collected from scientific papers and patent documents using the Scopus database in June 2021, with a term combination covering the proposed theme of this review ("alternative protein source"). The Scopus patent database describes information about the United States Patent and Trademark Office (UPSTO), European Patent Office (EPO), Japan Patent Office (JPO), and World Intellectual Property Organization (WIPO), known as Patentscope, and the United Kingdom Intellectual Property Office (IPO). Data collection from patent documents was also performed in the National Institute of Industrial Property (INPI) database using the ~~Portuguese~~ terms "source* AND protein* AND alternative*." The search was limited to the listed terms in the titles or abstracts of the papers and documents from the selected databases.

A total of 683 articles, 305 patent documents, and five patent documents were found in Scopus and INPI, respectively, but only 262 were available for download (Fig. S1). The results and discussion were divided into four parts: a) scientific prospection (application area, origin country, authors, and universities or research institutions); b) technological prospection (application area, International Patent Classification, origin country, inventors, and holders); c) scientific and technological prospection (annual evaluation); and d) trends in the global market.

In addition to investigating the articles and patent documents, the trends in the global market for alternative protein sources were also analyzed. The products available for sale were analyzed in August 2021 in online food markets and articles.

The results of this review are presented in tables and figures (produced by GraphPad Prism 7.0, Excel – Microsoft 365, PowerPoint – Microsoft 365, and VISME–www.visme.com). The term "patent document" includes both submitted and granted patents. The relevant information was found in each document, and the online market was extracted and discussed in this review.

3. Scientific prospection

3.1. Application area

After searching and studying the documents (articles and patents) from Scopus and the INPI databases, it was possible to determine the main application areas of the studies. For reports, most studies have been about alternative protein sources, of which 51.5% were related to the Agricultural and Biological Sciences, 8.1% were related to Biochemistry, Genetics, and Molecular Biology; 7.7% were related to Environmental Science, and 7.6% were related to veterinary studies. Other areas were identified, such as nursing (3.5%), engineering (4.7%), chemistry (2.7%), medicine (2.5%), and immunology, and microbiology (2.1%) (Fig. 1).

Table 1 shows the main articles related to alternative protein sources in the food industry. Insect protein was the most studied source, followed by vegetable sources (sesame, lupine, lentils) and microalgae. The purpose of all studies was to search for new protein sources to replace meat protein due to environmental and financial costs, or cultural reasons, considering that the world population is projected to reach 8.6 billion people in 2030. These findings contributed to the recommendation of the World Health Organization (2018) for increasing plant-based products in the diet. The changes in consumer patterns toward a more natural lifestyle with less animal-product consumption motivated industries and researchers to find new products. In this scenario, there was an increased incidence of the "plant-based" term, which can be understood as excluding animal-based products or reducing them, according to Aschemann-Witzel and Peschel (2019).

To ensure food security, it is necessary that the essential nutrients in the human diet occur. Among the macronutrients, we highlight proteins, which are indispensable, including essential amino acids for the proper functioning of organisms and maintenance of life. Amino acids are the main nitrogen-containing elements and protein structural compounds in the human body. Proteins present differences in their nutritional values and quality depending on their digestibility, bioavailability and the profile of their amino acids. Each amino acid plays an essential and different role in the functioning of our organism. Essential amino acids, namely threonine, leucine, isoleucine, lysine, phenylalanine, histidine, tryptophan and valine, methionine, cannot be synthesized in the human body and therefore the importance of being present in the diet. It is recommended that adults consume between 0.8 and 1.0 g of protein per body weight (kg) per day, with a limit of 0.66 g/kg/d being suggested to avoid deficiency. The amount of protein to be consumed and the pattern of amino acids needed are related to several factors such as age, genotype and phenotype, sex, body weight, lifestyle, physical exercise, health conditions and metabolic abilities (Sá et al., 2020).

Several plant proteins have balanced nutritional quality and high protein content as a potential supplier of this macronutrient to the human population as well as new possibilities for industrial applications. Vegetables are widely used as protein sources, mainly in soy. The amino acid profile, technological characteristics, water retention capacity, gel formation, and health benefits are some reasons for incorporating vegetable protein into food formulations. Pulses (beans, lentils, peas) have gained importance because of their hypoallergenic characteristics and nutritious and accessible proteins (Žugčić et al., 2018; Thavamani, Sferra, and Sankararaman 2020). Microalgae are nutritionally and bioactive in proteins, polysaccharides, and polyunsaturated fatty acids and have also been recognized for manufacturing nutraceuticals and supplements (Žugčić et al., 2018). Depending on the source, plant proteins may be deficient in some essential amino acids. Legumes have a deficiency in sulfur amino acids (methionine and cysteine) cereals usually contain low levels of lysine. However, pseudocereals (amaranth and quinoa) are good sources of lysine. Also, one should take into consideration that the same plant can vary in composition (macronutrients, such as protein, amino acid profile and oil content), according to differences of soil diversity and climatic, geographic localization, agricultural practices, precipitation levels and cultivars (Sá et al., 2020).

Studies in humans concerning the bioavailability and metabolic utilization of plant proteins are still lacking. Such studies can potentially provide the strongest evidence and give clear-cut answers with regard to the nutritional values of plant proteins (Pihlanto et al., 2017). The bioavailability of plant proteins and micronutrients can be increased

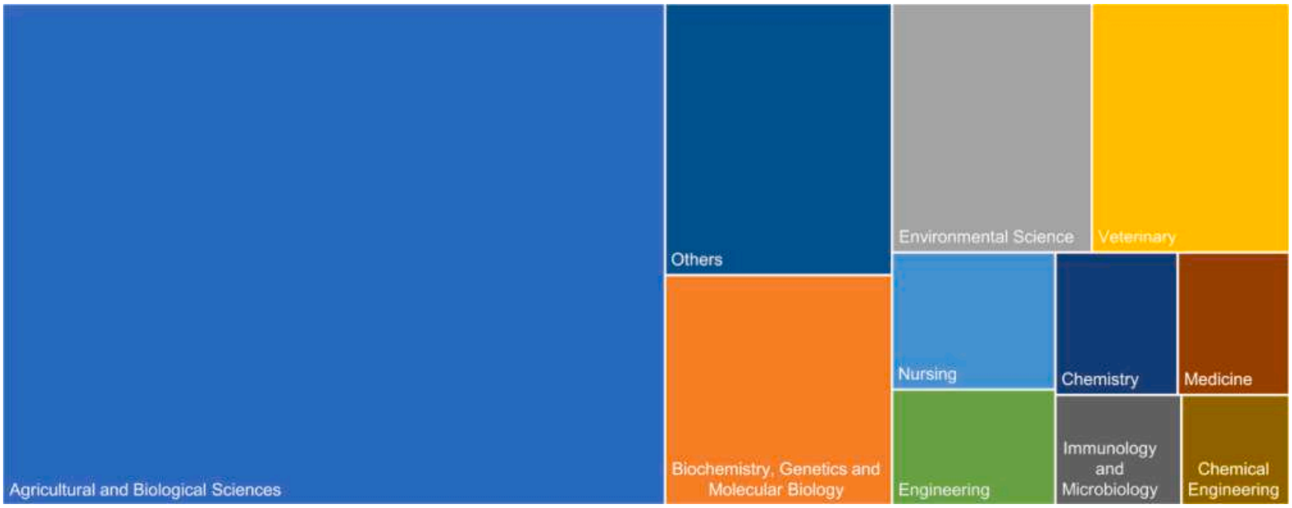

Fig. 1. Application areas of alternative protein sources from Scopus articles database.

through fermentation, which provides effective means to improve the nutritional quality of these foods. With regard to mineral solubility and protein digestibility in products based on legumes and cereals, it is possible to reduce the inhibitory activities of phytic acid and proteases through microbial fermentations as well as germination and/or addition of phytases. In addition, another strategy would be the combination of different fermented vegetable proteins to improve the amino acid profile of the final product (Kårlund et al., 2020).

Insects are not only nutritious and highly palatable, but can also be considered as an eco-friendly source of protein. Several studies have shown that the protein quality of insects is promising in terms of availability and digestibility compared to casein and soy, and can still be improved by removing chitin. Edible insects are excellent sources of minerals (copper, iron, magnesium, manganese, phosphorous, selenium, and zinc), fibers (chitin is the most important fiber found in insects), vitamins (riboflavin, niacin, pantothenic acid, biotin, and, in some cases, folic acid), fats (rich in polyunsaturated fatty acids: linoleic and α-linolenic acids) and proteins. The nutritional value of vegetable proteins is lower than that of animals due to deficient and/or unbalanced levels of essential amino acids. The protein content of an insect is quite significant (up to 77% on a dry matter basis), some insects are better protein sources compared to pork, poultry, beef and lamb. High values of amino acids (46%-96%) were found in insects, especially isoleucine, leucine, phenylalanine, tyrosine and glycine (Akhtar & Isman, 2018). Entomophagy is still not classified as a “plant-based” product; the use of insects is a new and sustainable source of protein for humans and animals, mainly because of their high nutritional value. Furthermore, the increasing number of studies on the use of insects for human food is related to very low-cost alternatives, high reproduction rates with low amounts of greenhouse gases, and good acceptability by consumers, as described by Akande et al. (2020).

3.2. Origin country

Most articles published on alternative proteins (Fig. S2) came from Asia (38.1%), with an emphasis on China (16.8%), Japan (13.6%), and India (8.9%) as the main countries with publications on the subject.

The geographic location of these countries, such as the Asian Pacific, suffers from extreme agro-climatic variations that affect agricultural production (Madan et al., 2018), combined with an increase in allergy cases to different foods consumed by the Asian population (Hossny et al., 2019), in addition to cultural identity, which has been gaining attention and recognition as a new food experience (Almansouri et al., 2021), they support innovative studies dealing with foods that meet these demands, which consequently gains attraction globally.

3.3. Authors and founders

The main authors were identified with scientific prospecting; L. Gasco (11) and G. Parisi (10) have the lead journal publications in alternative protein sources. The other authors indicated in Fig. S3A stand out with eight publications each.

Although the articles are mostly from Asia (Fig. S2), the top ten universities and research institutions (Fig. S3B) that publish the most are from Europe, representing 21% of all published articles. The Wageningen University & Research accounts for 37% of the publications in alternative protein source areas, mainly related to insects.

In 2013, the International Platform of Insects for Food and Feed (IPIFF) was founded, a non-profit organization representing the interests of the private fraction of the insect industry. IPIFF comprises 27 companies that operate through a network of collaboration in the insect value chain in 15 different countries, mainly in Europe, but also globally, promoting a sustainable eco-industry (PROteINSECT, 2016).

Among the largest founders for articles published on the subject under study (Fig. 3-B), it was observed that Universities (Wageningen University & Research, Universitá Degli Studi di Napoli Federico II, Tokyo University of Marine Science and Technology, among others) are the ones that most invest in publications followed by research centers (United States Department of Agriculture- USDA Agricultural Research Service, Consiglio Nazionale delle Ricerche, and the USDA), with Italy being the most represented country (Università degli Studi di Napoli Federico II, Università degli Studi di Firenze, Università degli Studi di Torino, and Università degli Studi di Bari) followed by the United States of America (USDA Agricultural Research Service and United States Department of Agriculture).

When extracting the results about the main authors and funding institutions/universities with specific publications for the use of alternative protein sources for human consumption, 100 articles (14.64%) were selected, being possible to highlight 3 main authors: Heidemann MS, Molento CFM and Reis GG, which together account for 4% of publications in the area. Among the funders of these articles, Universities stand out, being the University of Copenhagen (2%), Federal University of Paraná (1.33%) and University of São Paulo (1.33%), being the last two Brazilian Universities.

4. Technological prospection

4.1. Application area

Based on 271 patents recorded and analyzed in the Scopus database, 35.1% were involved in the food industry, 19.9% were involved in the

Table 1
Main articles found with alternative protein sources in food area.

Title	APS*	Purpose	Nutritional and functional aspects	Reference
Nutritional and anti-nutritional properties of lentil (*Lens culinaris*) protein isolates prepared by pilot-scale processing	Food (lentil)	Investigate the nutritional and antinutritional properties of lentil flour (*Lens culinaris*) from whole seeds (LF) in comparison with lentil protein (LPIs) prepared on a pilot scale by isoelectric independence (LPI-IEP) and ultrafiltration (LPI-UF).	Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols profiles showed significant reductions in total galacto-oligosaccharides contents by 58% and 91% in LPI–IEP and LPI–UF, respectively, compared to LF. Trypsin inhibitor activity levels based on dry protein mass were lowered by 81% in LPI–IEP and 87% in LPI–UF relative to LF. Depending on the stage of digestion, the in vitro protein digestibility of LPIs was improved by 35–53% compared to LF, with both products showing a similar long-term protein digestibility to that of bovine serum albumin.	Joehnke et al. 2021
Sesame seed as an alternative plant protein source: A comprehensive physicochemical characterization study for alkaline, salt and enzyme-assisted extracted samples	Food (sesame)	Produce sesame protein through three different techniques; alkaline, salt and enzyme-assisted extraction and a comprehensive physicochemical characterization of the extracts was performed.	–	Koysuren, Oztop, and Mazi 2021
School children cooking and eating insects as part of a teaching program – Effects of cooking, insect type, tasting order and food neophobia on hedonic response	Insects (locust and flour larvae)	Tactile interactions in the form of a cooking activity for the introduction of edible insects in children.	–	Chow et al. 2021
The Brazilians' Sensorial Perceptions for Novel Food – Cookies with Insect Protein	Insects - larvae (*Tenebrio molitor*)	Sensory perception of Brazilians through a sensory analysis of cookies made with flour larvae (*Tenebrio molitor*) flour.	–	Lucchese-Cheung et al. 2021
Use of alternative protein sources in the bakery industry	Plants (millet, hemp, alfalfa, and lupine flour)	Create a gluten-free flour mix, with higher protein content in bread and suitable for use in the bakery industry.	Biological value of proteins: alfalfa 0.74, hemp seed flour 0.67, lupine and millet flour (0.30–0.51); Millet is rich in methionine, cysteine, leucine and isoleucine, lupine has an outstanding content of lysine, leucine and threonine;	Jakab et al., 2020.
Harnessing microbes for sustainable development: Food fermentation as a tool for improving the nutritional quality of alternative protein sources	Plant (most important species of pulses, cereals, and pseudo-cereals in the agri-food sector)	Effects of fermentation on protein digestibility and micronutrient availability in plant-derived raw materials as alternative protein sources.	Low phytic acid, proteases inhibitors, MV peptides and tannins. High free amino acids phenolic compounds	Kårlund et al. 2020
Assessment of Mulberry Silkworm Pupae and African Palm Weevil larvae as alternative protein sources in snack fillings	Insects (mulberry worm pupae and African palm weevil larvae)	Mulberry worm pupae (MSP) and African palm weevil larvae (APW) as substitutes for conventional proteins in snack fillings and assesses consumer acceptability of the new products.	The chemical composition showed that MSP is higher in protein and soluble fiber contents while APW is higher in crude fat, crude fiber, zinc, manganese and calcium contents. The cooked edible insects were rich in both essential and non-essential amino acids.	Akande et al. 2020
Quality characteristics of protein-enriched brown rice flour and cake affected by Bombay locust (*Patanga succincta* L.) powder fortification	Insects - Bombay locust (*Patanga succincta* L.)	Physicochemical characteristics of whole rice flours enriched with proteins obtained by adding Bombay Locust Powder (BL) carob powder defatted at different levels.	The protein content of resulting mixed flours was effectively improved, especially at 30% replacement provided almost 4-fold increased (11–42%), compared with control (BRF without BL fortification) ($p \leq 0.05$). Protein-enriched cakes prepared using the mixed flours, showed the differences in their physicochemical properties, texture profiles, chemical composition and sensory characteristics, which were influenced by BL fortification level. The 20% replacement of brown rice flour by BL (20-MF) provided a protein-enriched cake (20.8% of protein) with liking score ranged from 7.0 to 7.4 for all attributes tested, indicating the good acceptability.	Indriani et al. 2020
Cricket powder (Gryllus assimilis) as a new alternative protein source for gluten-free breads	Insects - cricket (*Gryllus Assimilis.*)	Cricket (Gryllus Assimilis.) powder as a new protein source for gluten-free breads compared to the use of lentils and buckwheat flour.	Proximate chemical composition (g/100 g) of cricket (*Gryllus assimilis*) powder in dry basis is as follows: protein, 62.76 ± 1.12 (non-protein nitrogen, 0.75 ± 0.01); lipids, 20.96 ± 0.28; dietary fibers, 8.42 ± 0.75; ash, 3.19 ± 0.04 and moisture, 9.70 ± 0.06.	da Rosa Machado and Thys 2019
Insects as ingredients for bakery goods. A comparison study of *H. illucens, A. domestica* and *T. molitor* flours	Insects (*Hermetia illucens*, *Acheta domestica* and *Tenebrio molitor*)	Insect flour as a protein-rich ingredient to partially replace wheat flour in baked goods.	Nutritional composition: *Hermetia illucens*- Protein 45.09%, fat 35.82%, ash 4.25%, carbohydrates 14.84% and chitin 3.52%	González, Garzón, and Rosell 2019

(*continued on next page*)

Table 1 (*continued*)

Title	APS*	Purpose	Nutritional and functional aspects	Reference
			Acheta domestica- Protein 56.58%, fat 27.08%, ash 4.02%, carbohydrates 12.33% and chitin 4.46% *Tenebrio molitor*- Protein 48.82%, fat 30.69%, ash 4.25%, carbohydrates 16.24% and chitin 4.73%.	
Effects of pulses and microalgal proteins on quality traits of beef patties	Food (vegetable) and microalgae	Physicochemical parameters (pH, color and texture), proximate composition (moisture, protein, lipids and ash content), amino acid content and flavor profile of hamburgers made with soy (control), legumes (peas, lentils and beans) and microalgae (*Chlorella* and *Spirulina*) as alternative sources of protein.	The protein content of beef patties varied according to the protein source used: soy 18.25%, pea 17.84%,lentil 17.93%, bean 17.92%, *Spirulina* 18.06%, *Chlorella* 18.20%. The inclusion of bean and seaweed proteins increased the concentrations of all amino acids in beef patties, being glutamic acids, lysine and aspartic acid the predominant amino acids. *Chlorella* patties showed the highest content in the total hydrolyzed amino acids (22.98 g/100 g) followed by *Spirulina* patties (21.73 g/100 g) and bean patties (20.97 g/100 g), while pea patties exhibited the lowest (18.36 g/ 100 g) values.	Žugčić et al. 2018
Ingestion of insect protein isolate enhances blood amino acid concentrations like soy protein in a human trial	Insects (flour caterpillar)	Quality of alternative protein sources, such as insect protein, for which a comparison of the postprandial availability of amino acids (AA) and the profile of AA in the blood after ingestion of isolated protein was made, flour caterpillar, whey isolate and soy isolate.	Evaluation of AA profiles in the different types of protein supplements revealed total amino acid (TAA) content of 96.2%, 83.2% and 69.1% for whey, soy and insect respectively. We report that ingestion of whey, soy, and insect protein isolate increases blood concentrations of EAA, BCAA, and leucine over a 120 min period (whey > insect = soy). Insect protein induced blood AA concentrations similar to soy protein. However, a tendency towards higher blood AA concentrations at the end of the 120 min period post ingestion was observed for insect protein, which indicates that it can be considered a “slow” digestible protein source.	Vangsoe et al. 2018

*APS: Alternative protein sources.
- Data do not show.

agroindustry, and the areas food and agriculture produced the greatest number of patent documents (Fig. S1A).

In other areas, the use of protein has various applications in the biomedicine and biotechnology, veterinary, pharmaceutical, and chemical industries, such as the development of new expression vector systems to increase the production of recombinant proteins (US 20170101450 A1) (Scher and Harrington, 2015), pharmaceutical formulations (WO 2021127525 A1) (Freedholm, Bloomfield, & Glasspool, 2019), and surfactant formulations (US 20050245414 A1) (Baldridge & Podella, 2005). This depicts the variability of area applications and uses for proteins studied. Of all the patent documents studied, 31.7% used food as a source of alternative protein, 17.3% used plants as a protein source, and 25.5% of the patent documents did not mention the source (Fig. S1B).

The main food sources mentioned in the patent documents included cereals, such as rice, wheat, fruits, vegetables, and animal sources, such as whey, milk, and eggs. Lemna, *Spirodela polyrhiza*, *Fabaceae*, and *Asteraceae* are the most cited alternative protein sources in plants. Contrary to the previously mentioned document analysis, the use of insects as a protein source was observed in only 3.3% of patent documents. Most of them have been recently deposited (since 2018), suggesting that other patents should be filed in the next few years, which is consistent with the increased number of articles about insects as a protein source.

Table 2 lists the main patent documents related to food—most are patent documents associated with the development of methods for protein extraction and their use. Pickardt et al. (2010) and Gonzalez et al. (2016) (US 20110301074 A1 and US 20160345611 A1, respectively) were related to protein preparation produced from rapeseeds and rice. The development of new products is also the goal of patent documents, such as nutritional supplements (US 20140205710 A1) (Janow, 2014), protein-fortified flour (US 20160037808 A1) (Miller, 2015), and high protein beverages (US 20160262412 A1) (Pedersen & Tingleff, 2016).

The Codex Alimentarius (2021) found that seaweed, microalgae, edible insects, cell culture-based food products (meat, fish, dairy), plant-based protein alternatives and 3-D printed foods are the more prominent topics within new food sources and production systems and the Table 2 demonstrates that the alternative protein sources food products patents documents developed converge to this line.

Regarding the national and functional composition of the main patent documents involving alternative protein sources in the food area (Table 2), it was possible to observe a greater amount of protein ≥10% dry matter in most documents (16133619, 20140205710 A1, 20170196243 A1, 20160345611 A1). Furthermore, in two patent documents (20140205710 A1; 20160037808 A1) there was a concern regarding the amino acid profile of the products developed, where some of them such as alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine and valine were highlighted. Few brought information regarding the functional composition, being the fibers (GB2587048A) and the phenolic acid (20110301074 A1). These findings are relevant, as they demonstrate that the technologies being developed with alternative protein sources aim not only at the protein appeal, which would be a significant finding from the health point of view, but also at a functional and concern with the entire nutritional balance that involves the inventions.

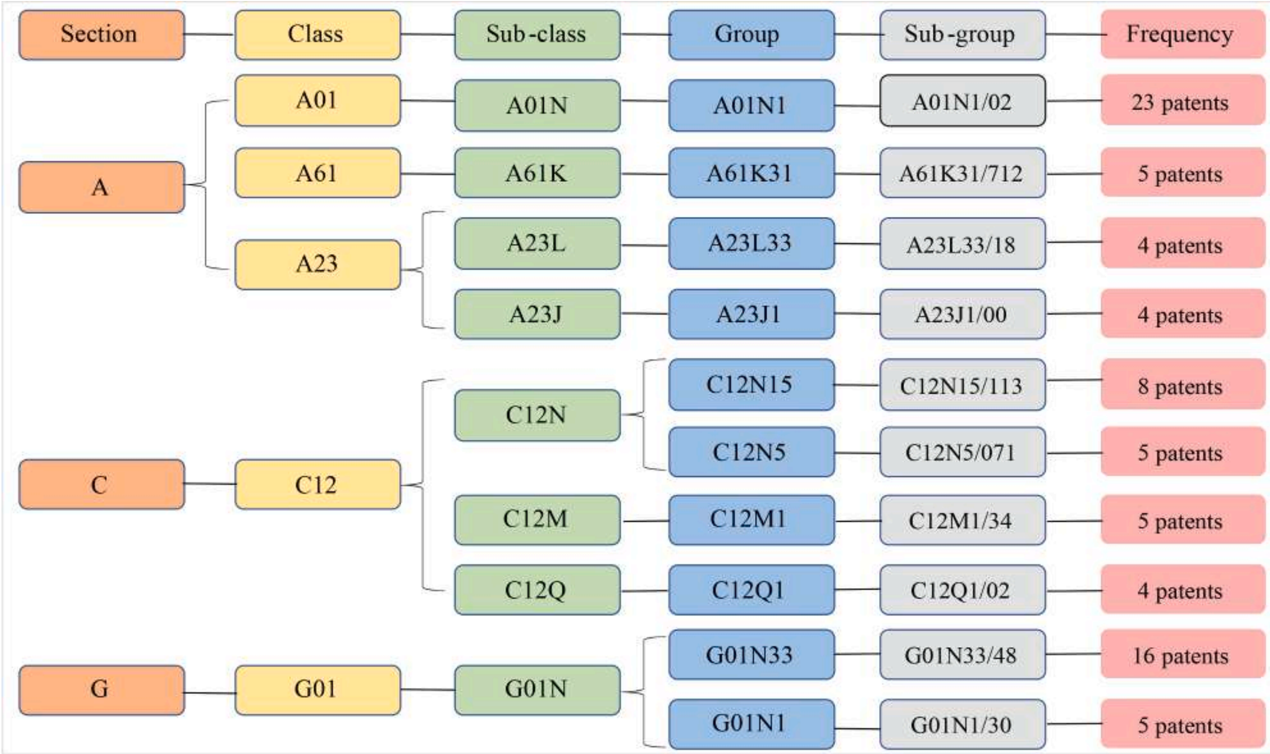

Fig. 2. Distribution of top IPC codes used by patent documents related to alternative protein source in the last 22 years (1998 –2020) found in Scopus and INPI patent databases.

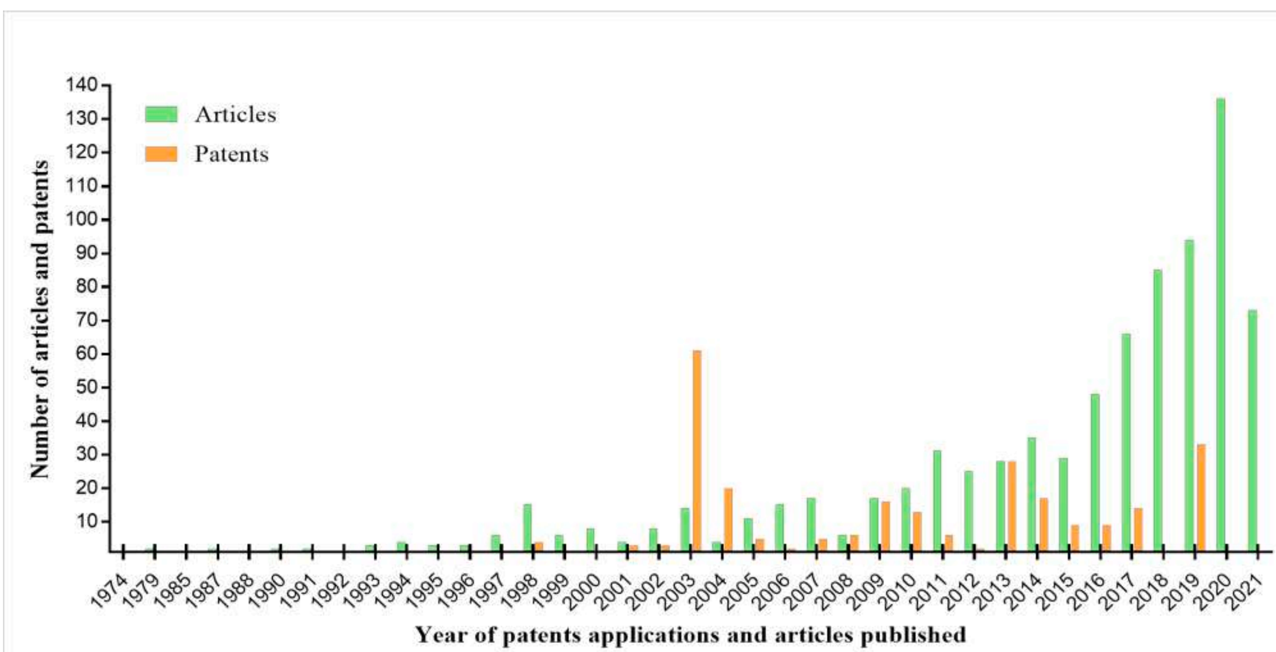

Fig. 3. Annual evolution of scientific articles and patent documents found in Scopus and INPI patent databases.

4.2. International patent classification (IPC)

Most IPC codes were classified in Section A (human necessities), C (chemistry, metallurgy), and G (physics) (Fig. 2). Among them, Section A had the highest frequency, with 36 patent documents. This section includes Class A01 (agriculture, forestry, animal husbandry, hunting, trapping, fishing), A61 (medical or veterinary science; hygiene), and A23 (foods or foodstuffs; their treatment, not covered by other classes). Although this result is slightly different from Figure 5, the three areas of greatest application of patent documents related to alternative protein sources (vegetable and animal sources, plants, and genetic material) were consistent with the most common IPC codes.

Patent examiners widely use patent classification systems to recover the state of art. The International Patent Classification System is one of

Table 2
Main patent documents found with alternative protein sources in food area.

Title	APS*	Purpose	Depositors/ Country	Nutritional and functional composition	Application number
Protein-Containing Composition	Yeast cells, plant-derived flour	Producing and compositions of single-cell food products.	Wild Earth, INC. / USA	Vegetable protein (>20% dry weight), intact yeast cells (>20% dry weight), plant-derived flour (20% − 70%), plant-derived starch selected from amylose, amylopectin and a combination thereof (>15%), a vegetable oil, and a nutritional supplement comprising a plurality of vitamins and a plurality of minerals, water (<30% weight) and the product is produced by heat expanded extrusion.	16,133,619
Food Product	Gluten, flaxseed, chia seed, soluble fiber, egg powder, and raising agent	A high protein bakery product containing low amounts of sugar and wheat flour, which may be gluten-free if required.	Direct Food Ingredients LTD/GB	Dry matter: gluten (15–25%), flaxseed (10% or less chia seed 3–20% soluble fiber), egg (>powder 5%), sugar (<5%).	GB2587048A
High protein, fruit flavored beverage; high protein, fruit, and vegetable preparation; and related methods and food products	Fruit and/or vegetable preparation	A new type of high protein, fruit-flavored beverage comprising fruit flavoring agents and high protein denatured whey protein compositions, and to a method of producing the beverage.	Arla Foods Amba/DE	Water, sweetener, protein (>4% w/w), a fruit flavoring agent (>5% w/w), food acid. pH (3.0–4.8).	US10729150
Rice protein supplement and methods of use thereof	Rice	A nutritional supplement comprising rice protein isolate and methods of use thereof.	Axiom Foods, INC/ USA	Each gram of the rice protein isolate comprises alanine (54 mg), arginine (77 mg), aspartic acid (87 mg), cysteine (21 mg), glutamic acid (174 mg), glycine (43 mg), histidine (22 mg), isoleucine (41 mg), leucine (80 mg), lysine (31 mg), methionine (28 mg), phenylalanine (53 mg), proline (45 mg), serine (49 mg), threonine (35 mg), tryptophan (14 mg), tyrosine (14 mg), valine (58 mg).	20,140,205,710 A1
Potato based protein mixtures and nutritional compositions comprising potato protein	soy protein, rice protein, wheat protein, legume protein, hydrolyzed, dairy protein	Nutritional compositions, including potato protein with other proteins.	Abbott Laboratories/ USA	Vegetable protein (10–100%), dairy protein (0–90%) by weight of the total amount of protein.	20,170,196,243 A1
Protein preparation produced from rape seeds	Rape seeds	A method to protein preparation produced from rape seeds.	Fraunhofer-Gesellschaft zur Forderung der angewandten Forschung e.V. - GE	Phytic acid (<10% dry matter), progoitrin (<1000 mg/kg), phenolic acid (<5% dry matter).	20,110,301,074 A1
Rice protein hydrolysate-based formulas and production thereof	Rice	A method(s) to producing rice protein hydrolysate.		Rice protein hydrolysate (>20%), carbohydrate, fat or lipid, emulsifier (octenyl succinic anhydride modified starch: 0.01–20%).	20,160,345,611 A1
Arthropod protein-fortified alimentary flour and methods of manufacture	Arthropod sources	Grain-free flour compositions fortified by arthropod-derived proteins.	Bitty Foods, LLC USA	Powderized arthropods and/or arthropod-derived compounds (10–50%), binding agent selected from the group of vegetable gums (1–5%), one density improving textural supplement selected from the group of extracted starches, (0–20%), moisture improving textural supplement selected from	20,160,037,808 A1

(continued on next page)

Table 2 (*continued*)

Title	APS*	Purpose	Depositors/ Country	Nutritional and functional composition	Application number
				the group of ground nuts (0–20%).	
Composition for replacing milk powder	Cereal	A milk powder substitute using cereal as protein source.	Cerestar Holding B.V. / US	Gluten (30% dry matter), alcalase (0.3%), neutrase (0.125%), starch slurry (30% dry matter), termamyl (0.135%), $CaCl_2$ (150 ppm), liquid lysine (3.06 parts), threonine (0.95 parts), trytrophane (0.16 parts), calcium hydroxide (2.7 parts), phosphoric acid (2.6 parts) .The complete mixture was dried in a ring dryer (air inlet 140 °C, air outlet 80 °C). The dry matter of the final product was 95%.	US 20,060,134,309 A1
Expression of human milk proteins in transgenic plants	Seeds of a transgenic plant	An infant formula comprising such as food supplement composition.	Ventria Bioscience / EP	Using at least 3% by total human protein milk with growth factor activity such as human lactoferrin, epidermal growth factor (EGF, IGF-1), albumin, casein and transferrin.	EP2294930 A2

the most established classification systems used to categorize patents in various technological fields according to technological content or function (Oliveira et al., 2021). Considering the alternative protein source definition, alternative proteins are produced from sources with a low environmental impact to replace established protein sources. They can also be obtained from animal husbandry with good animal welfare (Grossmann & Weiss, 2021); Hence, these IPC code results were expected because their conception covered food, agricultural and genetic areas.

In Section A, the most frequent sub-group was A01N1/02, with 23 patent documents. This was described according to the WIPO IPC codes as Section A (human necessities), Class A01 (agriculture, forestry, animal husbandry, hunting, trapping, and fishing), Sub-class A01N (preservation of bodies of humans, animals, plants, or parts thereof), Group A01N1 (biocides; pest repellants or attractants; plant growth regulators), and sub-group A01N1/02 (preservation of living features).

In Section C, the most frequent sub-group was C12N5/113, with eight patent documents. This was described according to the WIPO IPC codes as Section C (chemistry; metallurgy), Class C12 (biochemistry; beer; spirits; wine; vinegar; microbiology; enzymology; mutation or genetic engineering), subclass C12N (microorganisms or enzymes; compositions thereof; propagating, preserving, or maintaining microorganisms; mutation or genetic engineering; culture media), Group C12N15 (mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g., plasmids, or their isolation, preparation, or purification; use of hosts thereof), and sub-group C12N15/113 (non-coding nucleic acids modulating the expression of genes, e.g., antisense oligonucleotides).

In Section G, the most frequent sub-group was G01N33/48, with 16 patent documents. This was described according to the WIPO IPC codes as Section G (Physics), Class G01 (measuring; testing), Sub-class G01N (investigating or analyzing materials by determining their chemical or physical properties), Group G01N33 (Investigating or analyzing materials by specific methods not covered by groups) and Sub-group (G01N33/48 (biological material, e.g., blood, urine; hemocytometers (counting blood corpuscles distributed over a scanned surface).

4.3. Origin country

The food market has been considered an economic activity with the greatest prospect of success in recent years (Onwezen et al., 2021). Given this positive projection, a relevant issue for investors in the sector concerns granting patent documents in this area, as shown in Fig. S5.

In recent years, there has been a growing interest in alternative proteins as food sources. This fact drives studies and, consequently, patents with innovative ideas that aim to serve vegetarians, vegans, omnivores, and flexitarians who opt for plant-based diets (Karmaus & Jones, 2021).

Recently, there has been an increase in patents filed for alternative proteins, and North America stands out in this scenario, contributing to 70.1% of all patents. The United States holds 98.4% of the deposits, followed by Canada with 1.6%. In comparison, Europe represents 13.8% of the total number of patents found in this prospection, with the main filing countries being the United Kingdom (50%), Denmark (20%), and Germany (15%). Figure 7 shows Latin America lacks significant technologies in this field, contributing to <2% of all patents. These numbers mainly stem from the largest industries working in these fields (veterinary, enzymes, and surfactants, pharmaceutical), which are of US origin, holding large portions of the granted and filed patents.

The development of technological innovation has changed. China has made significant efforts in science and technology with high-impact reforms in this area, which have improved both research and development and higher education. Therefore, innovation in China plays an increasingly important role in its economy. Innovation is followed by research and international and international partnerships fostered by Chinese companies (de Freitas et al., 2021).

4.4. Inventors and holders

Companies hold 79.3% of all patent deposits, followed by independent inventors (17.6%) and universities, with the smallest share of deposits (3.1%) (Fig. S6A). Regarding technology foresight, we noticed that the biggest inventors were Gary Durack with over 65 patents, followed by Jeremy Hatcher, Niraj Nayak, Gary Vandre, Jeffrey Wallace, and Lon Westfall, with approximately 60 applied-for patents. Inventors with >25 patents include Muhammad Anzar, Jeffrey Graham, Cindy Ludwig, and Kathleen Crowley (Fig. S6B).

This study identified the top 10 companies investing the most in patents. Among them, only three are related to the food industry (Mars, AB Agri, and Axiom Foods), and most of them are in the United States

(Figure 8C). Inguran LLC is the company that invested most in patents (62) within the theme of alternative protein sources, followed by Warsaw Orthopedic (16 patents), Advanced Biocatalytics Corp. (14), Axiom Foods Inc. (10); the other companies provided five patents (Purina Animal Nutrition LLC, Mars Incorporated, and AB Agri Limited) or four (Dupont Nutrition Biosciences APS, Altmann Stossel Dick Patentanwalte Parg MBB and Abbott Laboratory).

Inguran LLC provides genetic improvement services to the livestock industry. It offers sexed semen to dairy and other livestock industries. Advanced BioCatalytics is a technology and product development company with production capacities in industrial biotechnology. It focuses on discovering protein surfactant complex (PSC)-based chemistry for use in cleaners, industrial and agricultural wetting agents, wastewater treatment, environmental remediation, and other applications. Axiom Foods is a leading supplier of hypoallergenic, whole grain brown rice ingredients and products through outstanding research, technology, quality control, and knowledge sharing. Most of the companies mentioned are from the USA and work with food, pharmaceutical, and health care products.

5. Scientific and technological prospection

5.1. Annual evaluation

Science and technology have been the subject of academic studies and research for decades. New technologies and scientific discoveries are publicly disclosed daily in non-patentable literature, such as studies described in technical and scientific journals, theses and dissertations, and conference proceedings, among others (Perez-Molina & Loizides, 2021). A topic attracting the scientific community's attention since the 1990s and has increased considerably as of 2015 is the use of alternative proteins in diverse areas, including the food industry.

Currently, we are living in a knowledge economy, the production and dissemination of further knowledge will be central to solving the problems of climate change and environmental sustainability, reducing poverty, and addressing other global issues. The search for alternative proteins is closely related to ecological issues since meat of animal origin, the main source of protein, is strongly related to negative environmental impacts (Godfray et al., 2018; Willett et al., 2019) and public health (Willett et al., 2019). Realizing this movement, several companies are directing resources to research and production of vegetable products analogous to eggs, milk, dairy, and fish. Focusing on the final experience of a larger group of consumers, along with the consequent abundance of investments that this generated, enabled a great advance in the technologies involved in producing alternative proteins over the years (Ismail et al., 2020). This is also reflected in Fig. 3, which shows the trend in the publication of patents and articles related to alternative protein sources from 1974 to 2021.

The patenting activity showed 259 existing patent documents with their first registrations in 1998, with four patents filed in the United States of America (USA). One of the pioneering patents (US 20120295329 A1) (Jones, Dickman, and Lloyd, 2012) protected a method that could be used in the food industry, where it was possible to produce chemically modified mutated serine hydrolases that catalyze transamination or a transpeptidation or a transesterification reaction.

Although the results do not show an increase in the number of publications per year, the use of alternative proteins as a food source is growing rapidly (Aschemann-Witzel & Peschel, 2019). Between 1998 and 2002, only 11 patent registrations were observed. However, in 2003, there was a higher quantitative expression for these records (61 documents), including a concentration of 23% of the total documents reaching the top of the temporal analysis. Many patent documents can also be observed in 2004 (20 documents), 2013 (28 documents), and 2019 (33 documents). The decline in the number of patent applications in 2020 may reflect the confidentiality period, which is necessary at the stage of obtaining patents. It should be noted that there is an 18 month confidentiality period for patents (counted from the filing date) and a time lag for documents to be indexed in the database (Oliveira et al., 2021).

Unlike patent documents, the first scientific articles related to alternative protein sources were dated from 1974, "Alternative sources of protein" by Andrews (Andrews, 1974). Since then, an increase in publications can only be seen from the year 1993 (three publications), and scientists have improved the technologies to produce meat-like products and the development of cooking with high moisture, allowing vegetable proteins to develop fibrous structures such as meat (Wild et al., 2014). A variable growth profile can be observed until 2015 (29 publications. Since then, a growing profile can be observed, reaching 136 articles published in the year 2020, the most notable year until the date of the prospection (73 publications in the year 2021).

In 2013, Mark Post of Maastricht University publicly presented the first hamburger product cultivated in a laboratory (Chiles, 2013). Since then, scientific interest has increased along with the growth of the food market. The twentieth century saw the emergence of companies such as Impossible Foods (2016) and Beyond Meat (2017), which produced the first hamburgers made with alternative protein sources capable of imitating real meat, contributing considerably to market growth (nine companies only in 2018) (Burton, 2019).

When comparing the number of scientific articles with the number of patent documents in 2003 and 2004, the number of published patents was higher than the number of articles (61 patents and 14 articles in 2003 and 20 patents and 4 articles in 2004). The number of patents and articles in 2008 and 2013 were equal, 6 and 28, respectively. Over the years, the number of scientific articles (683) was two times larger than the total number of patent documents (310) related to alternative protein sources. Thus, patent documents have become an important indicator of scientists' innovation and impact. Academic research with patentable potential is growing (Rasmussen et al., 2006). However, there are still some issues between patenting and publishing, such as how to market a patent developed within a university (Lissoni et al., 2013), and mainly, issues involving whether patents are filed under the name of the university or not (Fini et al., 2010; Lawson, 2013).

6. Technological-scientific advances and legal aspects of alternative proteins

Alternative proteins are associated with environmental and sustainable aspects, as well as health benefits and functional properties, as previously demonstrated. However, the protein obtention process is the frequently related to protein isolation difficulties and low recovery (Bleakley & Hayes, 2017; Tenorio et al., 2018), it became a challenge to industrial scale.

According to studies and patents analyzed, we observed that the alternative protein sources can be used in two ways, using the whole raw material, as mainly applied to insects and algae, and submitting the raw material to the protein extraction process and applying the protein as an ingredient in food formula, as occur to cereals and plants. The process is widely variable according to raw material.

The major of studies shown in Table 1 used the whole source in food formulation, without the process of protein extraction (Akande et al., 2020; Chow et al., 2021; González et al., 2019; Indriani et al., 2020; Lucchese-Cheung et al., 2021; Machado & Thys, 2019; Vangsoe et al., 2018). The studies developed by Žugčić et al. (2018), Jakab et al., (2020), and Vangsoe et al. (2018) were carried out with commercial protein isolates. Joehnke et al. (2021) and Koysuren et al. (2021) evaluated the extraction process.

The main techniques for protein extraction involve alkaline extraction (Joehnke et al., 2021; Koysuren et al., 2021), however novel techniques have been applied to improve protein recovery, such as ultrafiltration, microwave, pulsed electric field, extraction assisted by enzyme, etc (Bleakley & Hayes, 2017; Gençdağ et al., 2020; Joehnke et al., 2021; Koysuren et al., 2021; Prandi et al., 2021). The selection of the technique for protein extraction is very important for the efficiency of the process, and for the characteristics of the final product.

Koysuren et al. (2021) carried out sesame seed to alkaline, salt and enzyme-assisted protein extraction and concluded that the alkaline extraction had a lower yield of protein when compared with enzyme and salt extractions. The highest yield was obtained with enzyme extraction (over 45% protein yields). Prandi et al. (2021) achieved 69% and 43% for protein extraction yields from chickpeas, and 10% and 58% or protein extraction yields from peas, using direct aqueous extraction and enzyme assisted aqueous extraction, respectively. According to authors, the extraction efficiency is an important parameter to determine if the process is economically sustainable.

Patents documents (Table 2) rarely mentioned the extraction protein process, due to the reason that it showed little innovative activity, it became difficult the patent application process. The major of documents refer to applications in food products or features. Pickardt et al. (2010) carried out rape seeds to aqueous-alcoholic solutions (60–95%) to protein extraction, and after the extraction the alcohol is removed. The authors do not mention the yield of process.

Regarding legal aspects, in countries that market this protein source as an innovator, legislators must approve and consider safe before being consumed and be subject to the same regulatory requirements that apply to all types of food. Due to the recently recognized potential, regulations on insects are scarce or non-existent. Although local producers can easily sell their products in local markets, exports to industrialized countries remain a challenge. In the United States, the Food and Drug Administration (FDA) only mentions insects in the context of Food Defect Action Levels (FDAL), which defines the acceptable level of defects that a product can contain (Raheem et al., 2019).

From the elaboration of the report "Edible insects: future prospects for food and fed security" by the Food and Agriculture Organization of the United Nations (FAO) (Van Huis et al., 2013), insects have been considered as a possible source of food for the future. This fact is evidenced by a significant number of scientific articles published on the subject. However, the use of insects in human food is mainly influenced by the resistance of the population to the consumption of insects where this custom does not exist. In Western cultures, for example, the consumption of insects is not part of eating habits, causing neophobia, such as feelings of fear, repulsion, and rejection, demonstrating resistance to the consumption of unknown foods (Lucas, Menegon, & da Rocha, 2020). The emergence of products with insects in their composition also causes some reluctance in consumers due to the lack of knowledge related to entomophagy and food safety, as well as the advantages of using insects in food (Van Huis et al., 2013).

In technological terms, there are still some relevant hurdles for the consumption of insects as the lack of specific legislation on the subject. Recently, the European Food Safety Authority (EFSA) defined, after analyzing supporting data, that the dehydrated *Tenebrio molitor* larvae has the necessary requirements (Regulation EU 2015/2283) being considered, through Regulation EU 2021/882 (Commission of June 1, 2021) as a novel food. The insects were considered suitable for commercialization, in the powder form or dehydrated, being commercially safe. The regulation specifies the nutritional, physicochemical, heavy metals, mycotoxins, and microbiological parameters that must be respected to guarantee the safety of this new food (European Union Commission, 2021). More information about the required parameters and methodologies used is available in Turck et al. (2021). It is worth considering that, currently, only the European Union considers the consumption and trade of edible insects as a legal activity.

7. Trends in the global market

As the demand for proteins increases with growing populations, alternative proteins are emerging as a potential option for use as substitute food products (Botella-Martínez et al., 2021; Kotecka-Majchrzak et al., 2020; Zielińska et al., 2021), feed (Gałęcki et al., 2021; Gasco et al., 2020; Kusmayadi et al., 2021), cosmetics, and pharmaceuticals (Amorim et al., 2021; Coppola et al., 2020; Huang et al., 2021), among others. The protein market is a sector of the food industry that stands out for its expansion. It is expected to have a 9.1% growth rate from 2020 to 2027 (Ismail et al., 2020). Animals have been the major source of protein in developed markets for years. However, consumer behavior changes and interest in different protein sources have made way for growth in the alternative-proteins market.

A study developed by Joseph et al., 2020 shows that the US meat and poultry markets predominate in value and volume (305 billion USD and 45 million MT, in 2018), while meat alternatives represented<5% by weight and volume (1.35 billion USD and 121,143 MT).

Although industrial production of alternative proteins is nascent, the panorama already shows an area with great potential. Since 2010, the most popular food and beverage product searches have been vegan products (Bashi et al., 2019). The number of companies focused on plant-based products as alternatives to traditional meat, milk, eggs, and fish and using various alternative protein sources to enrich food products is increasing each day. Factors such as increasing sustainable production, combined with the conscious search to use green technologies and address environmental issues, which simultaneously lead to greater productivity and better product value, thus leading to growth in the research and development sector, will leverage the market for alternative proteins for applications with different purposes.

As already demonstrated (Fig. 1 and Fig. S4), the market analysis for companies involved with alternative proteins follows the same perspective as the articles and patents found in this study. It can be observed that companies developing alternative proteins are mostly in the food sector. Table 3 shows the major companies in the market that use alternative protein sources for human consumption.

In the last five years, scientific knowledge regarding insects as human food and animal feed has grown exponentially. The same is true for the industrial sector, which is increasingly engaged in the rearing, processing, and marketing of edible insects (van Huis, 2020). Edible insects have been promoted as an alternative sustainable food source because of their high protein content, which is the main component of their nutritional composition. They also contain significant amounts of other important nutrients, such as lipids, beneficial fatty acids, vitamins, minerals (Nowak et al., 2016; Sun-Waterhouse et al., 2016), and fiber, present in the form of chitin, in the exoskeleton of insects (Krishnan et al., 2014; Lucas et al., 2020).

Currently, the number of companies using insects as an alternative protein source is increasing. They are located all over the world, mainly in Europe and the United States. Among these is Jimini's. Located in Vaux-le-Pénil, near Melun, in Ile-de-France, Jumini emerged in 2021, and its stated mission is to make people love edible insects and enjoy the benefits they bring to daily life. Crickets and mealworms are obtained from European insect farms and are used mainly to enrich the nutrients in certain products, although whole insects are also used. Different products such as sweet and savory seasoned whole insects and sweet and savory grocery products such as granola, pasta, and protein bars made with insect powder are produced following European food regulations and guaranteeing food safety (FSSC 22 000).

The list of companies producing animal-free alternatives to traditional meat, milk, eggs, and fish or using alternative protein sources to enrich food products are also increasing each day. Some of these companies are plant-based, some use precision fermentation, and some use insects in different ways, but all of them contribute, in a way to protecting the environment.

8. Considerations and future perspectives

This study shows the alternative protein source analysis of articles and patents, focusing on the food market. This is the first review of this approach and perspectives for developing technologies and innovation in this area. The major application areas for scientific and technological

Table 3
Main companies in the market that use alternative protein sources in food area.

Product	APS*	Purpose	Company / Country	Reference
Pasta, oil, chili, tea, and flavored snacks	Insects	Food products fortified with insect protein powder	Thailand Unique / Thailand	https://www.thailandunique.com/
Snacks, protein bars, pasta, and granolas	Insects	Food products fortified with insect protein powder	Jimini's / France	https://www.jiminis.com/en/
Beer	Insects	Beer flavored with protein from insects	Belgium	https://www.beetlesbeer.be/en/
Nutritional yeast dietary supplement	Yeast	Nutritional yeast (flake) for use as a cheese replacement or to add flavor to vegetables and popcorn.	Amazon/ Product of Estonia Packaged in USA	https://www.amazon.com/stores/Revly/Homepage/page/9446DF01-C5BD-4950-B126-F140E8D34540
Meat-like compounds from a non-GMO organism	Red and green algae	Sustainable Plant-based protein uses non-GMO processes to produce a completely vegan plant protein made from red and green alga products.	Triton Algae Inovations / USA	https://www.tritonai.com/
Burgers, ground meat, sausage, meatballs, and beef	Peas, mung beans, faba beans and brown rice	Sustainable plant-based meats made combining expert innovation with simple, non-GMO ingredients.	Beyond Meat / USA	https://www.beyondmeat.com/

*APS: Alternative protein sources.

prospection were agricultural and biological sciences and the food industry (animal and vegetable sources; plants), respectively, and the main IPC code was A01N1/02. Asia and Europe generated the most published articles, and North America generated the most patent documents. While the main authors, universities, and research institutions were from Europe, the main inventors and patent holders were from North America, including stand-out companies such as Inguran LLC. The term "alternative protein sources" is recent and suggests a great potential for increasing sector growth, as demonstrated by the increase of article and patent publications over the years, which suggests new technological possibilities. The market has shown different food applications, such as hamburgers, beers, nutritional supplements, cereal bars, and pasta, from sources such as insets, yeast, algae, and grains. For future perspectives, it is expected that this field can be explored within the scope of the development of new food products in an innovative, economically viable, sustainable way with important nutritional potential. Furthermore, this study can serve as a starting point for companies and researchers who aim to develop or improve this technology in different areas, especially in the food sector.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.foodchem.2022.133486.

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Green solvent extraction and eco-friendly novel techniques of bioactive compounds from plant waste: Applications, future perspective and circular economy

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ABSTRACT

Agro-foodwaste is rich in bioactive compounds which has prompted the search for sustainable extraction technologies aligned with green technologies and circular economy principles. This review evaluates advanced eco-friendly extraction methods and green solvents for isolating valuable bioactives including polyphenols (flavonoids and tannins), alkaloids and terpenes from plant waste such as peels, leaves, and seeds. However, the use of green solvents with conventional extraction techniques, and green techniques such as ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and supercritical fluid extraction (SCF) can enhance yield, reduce solvent use, and preserve thermo-labile constituents. Green solvents such as ionic liquids, deep eutectic solvents (DESs), supercritical CO_2, bioethanol, and switchable water offer promising, low-toxicity alternatives to petroleum-based solvents, though challenges such as viscosity, mass transfer limitations, and solvent selectivity persist. This review highlights the pharmaceutical, nutraceutical, and food applications of bioactive compounds. Ultimately, green extraction technologies offer a path toward sustainable resource recovery, aligning economic, environmental, and health-related goals in a bio-circular-green economy paradigm.

1. Introduction

Global increase in plant-based waste products and residues (agro-industrial residues, agri-food by-products, plant biomass) all over the world is a challenging environmental and economic problem. Poorly handled disposal by landfills or burning leads to the emission of greenhouse gases in the form of methane and carbon dioxide, in addition to soil and water pollution. The conversion of such waste streams into useful products by extracting bioactive compounds is one of the efficient methods to reduce the ecological footprint and promote sustainable activities. Non-edible portions of many crops, such as peels, seeds, pomace, leaves, bark and husks contain many nutritional and bioactive compounds. These are dietary fiber, proteins, lipids, minerals, vitamins and especially secondary metabolites, including polyphenols, flavonoids, tannins, carotenoids, and terpenes (Oleszek et al., 2023; Lobo et al., 2018). For instance, the processing of pomegranates produces by-products which include ellagitannins, ellagic acid, and other enolics in very high concentrations compared to the ones in the edible juice or seeds (Ballistreri *et al.*, 2024). Similarly, citrus peels also contain flavanones, polymethoxylated flavones, and phenolic acids, which have significant antioxidative properties (Bekavac *et al.*, 2025). These are also known as antioxidants that exhibit antimicrobial, anti-inflammatory and cardioprotective effects and so, plant residues are not mere wastes but stores of potentially useful pharmacologically relevant molecules (Basile *et al.*, 2024).

Bioactive compounds are isolated by conventional methods such as maceration, Soxhlet extraction, and heat reflux typically in organic solvents, e.g. methanol, ethanol, acetone, or ethyl acetate traditionally. Although effective, these approaches are limited by disadvantages such as the consumption of a lot of solvents, a time-consuming extraction

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process, high power requirements, and thermal degradation of delicate bioactives. To overcome these shortcomings, a number of new extraction technologies have surfaced over the past few years. There are different new techniques such as ultrasound-assisted extraction, microwave-assisted extraction, enzyme-assisted extraction, pressurized liquid extraction, subcritical and supercritical fluid extraction, hydrodynamic cavitation, pulsed electric fields, and high-pressure (Wang *et al.*, 2023). These methods have some clear benefits, i.e, reduce the consumption of solvents, decrease the time of processing, decrease energy consumption, and improve yields without compromising the integrity of the compounds. However, the extraction of polyphenols in pomegranate by-products aided with ultrasound has been demonstrated to yield more results using less energy and time (Ballistreri *et al.*, 2024). In the same way, extraction of blueberry pomace with the help of microwaves enhanced the total yield of anthocyanin and phenolic compounds compared to the reflux method (Capaldi *et al.*, 2024). Enzyme-assisted extraction has also been proven to have greater efficiency, especially in releasing bound phenolics in the cell wall matrix, thereby creating extracts that possess increased antioxidant activity (Streimikyte et al., 2022).

In addition to the growth of technological inventions, the development of green solvents is a key development in the eco-friendly extraction methods. More traditional volatile organic solvents are being substituted by more eco-friendly solvents such as natural deep eutectic solvents (NADES), bio-designed ionic liquids, supercritical carbon dioxide, subcritical water, bioethanol, glycerol, GRAS solvents (water, ethanol) (Pimentel-Moral et al., 2020) and plant-based solvents such as limonene. These solvents are less toxic and less hazardous to the environment, but also more selective and stable extracted bioactives (Wang *et al.*, 2024). In another case, NADES have also been documented to form very high-antioxidant and antimicrobial polyphenol extracts compared to ethanol or water-based extracts (Zhou *et al.*, 2023). Even low concentrations of ethanol as a co-solvent in supercritical carbon dioxide have been reported to perform well in the recovery of phenolics and flavonoids with minimal amounts of solvent remaining and, thus reducing the cost of post-processing (Herzyk *et al.*, 2024). Subcritical water has additionally been employed extensively in extracting polar compounds such as flavonoids and phenolic acid in the extraction process, which has offered high extraction efficiency under mild and friendly environmental conditions (Aminzai *et al.*, 2025).

The synergies created by the combination of new methods of extraction and new green solvents bring to result the greatest efficiency and the minimal environmental damage. The combination of ultrasound with NADES does not only enhance the process of extracting phenolics in less time but also surpasses the limitation of viscosity of these solvents, thereby yielding an increased extraction process (Santos-Martín *et al.*, 2023). Similarly, the enzyme-assisted solvents with green solvents also improve the solubilization of bioactives and decrease the utilization of strong solvents or high temperatures (Streimikyte *et al.*, 2022). Ethanol co-solvent in supercritical carbon dioxide is maximized to produce similar or even better yields than the traditional methods and using significantly less energy and cleaner extracts (Decorti et al., 2014). These integrated approaches can be aligned with the goals of the circular economy by valorise waste and reduce resource utilisation. The high bioactivity, and high scalability can be achieved by optimal choice of solvent system and extraction methods.

In conclusionthe process of green solvent extraction along with the introduction of new, environmentally friendly methods of extraction, is a significant paradigm shift in the sphere of waste management and resource recovery. Besides helping to counter the present environmental issues, these methods offer a chance to recover bioactives that can be used in food, nutraceutical, pharmaceutical and cosmetic sectors. The inclusion of new approaches and green solvents can improve the efficiency and productivity of the process at the same time, decreasing pollution of the environment and strengthening the ideas of the circular economy. Moreover, the scalability of such technologies allows to achieve the best solvent recovery, life-cycle assessment, and respond to regulatory demands. As a result, these strategies can convert the waste in the plants into a sustainable innovation center.

The recent advancements in eco-friendly extraction technologies and green solvents for isolating bioactive compounds from plant waste, with a focus on their integration into circular economy models. It aims to critically analyze the efficiency, environmental impact, and scalability of modern extraction techniques, such as ultrasound-assisted extraction, microwave-assisted extraction, and supercritical fluid extraction, in comparison to conventional solvent-based methods. Furthermore, this study highlights the potential application of green solvents including ionic liquids, deep eutectic solvents, and bioethanol in achieving sustainable and high-yield extractions. The novelty of this article lies in its holistic approach that connects green chemistry principles with circular bioeconomy strategies, emphasizing how solvent innovation, process optimization, and sustainability assessment frameworks can collectively transform plant waste valorization into a viable industrial model.

2. Plant waste as a source of bioactive components

Plants waste that can affect the environment and human health includes peels, leaves, seeds, and stems. It produces billions of tonnes of waste at various stages of the food chain, such as production, handling, storage, processing, packing, distribution, marketing, and consumption. Therefore, it is necessary to create a novel process for turning these wastes into value added products. Generally theinedible parts of fruits (seeds, peel, and pomace) and vegetables (leaves, shells, stems, and seeds) as well as agri-food residues such as shells, seeds, straws, barks, and leaves are organic materials that are a significant source of bioactives (Prasad *et al.,* 2020; Haq *et al.,* 2021). On the basis of their composition, bioavailability, and dosage, bioactive chemicals have a positive physiological or cellular impact on a living creature. Quercetin, kaempferol, catechin, terpenes, carotenoids, polyphenols, tannins, gallic acid, and ascorbic acid are a few examples (Table 1).

A study has investigated the detection of various bioactive nanoparticles in bio-waste streams. It is important to note that "roots, cereals, tubers, fruits and vegetables" are some of the foods that spoil instantaneously. "The fruit and vegetable category is dominated by bananas, citrus, apples, watermelons, grapes, onions, cabbage, tomatoes, cucumber, potatoes, and carrots". A wide range of compounds, including "fatty acids, vitamin (A and E), anthocyanin, minerals, volatiles, and tannins," are included in the bioactive compounds that have been identified (Ben-Othman et al., 2020). However, other valuable components, such as "phytochemicals, sugars, fibers, organic acids, antimicrobial compounds, pigments, and enzymes," can be recovered from such wastes and used as food additives or supplements. Terpenoids, alkaloids, and phenolic chemicals are the three primary categories of secondary metabolites. Secondary metabolites are found abundantly in reproductive and vegetative structures, especially in specific tissues such as bark where are essential for protection (Yang *et al.,* 2020). Moreover, it has significant social and economic appeal and is used for medicinal purposes because of its antimicrobial, antitumor, anti-inflammatory, antidiarrheal and antioxidant activity. Tannins are classified as secondary metabolites. Because of their astringent flavor, are bioactive compounds that are crucial to plant life (Sousa et al., 2022; Bottamedi *et al.,* 2021). Bioactive compounds are present in notable quantities in sugarcane products, by-products, and the whole plant. Terpenoids and phenolic compounds (PCs) are two of the most studied bioactive compounds in the sugarcane industry.

Plant-derived waste materials such as peels, pomace, seeds, leaves, and stems are often discarded in massive quantities during agricultural processing, food manufacturing, and distribution chains. However, these residues are increasingly recognized as valuable sources of bioactive compounds that can be recovered for nutraceutical, pharmaceutical, and food applications. Among the numerous phytochemicals present in plant waste, four major groups phenolics, flavonoids,

Table 1
Bioactive compounds composition in plant waste.

Sources	Residues	Bioactive compounds	Outcome	References
Pistachio (*Pistacia vera*)	Leaves, twigs, seed coats, green, empty kernels	Gallic acid, anacardic acid, quercetin derivatives	The chemical compositions of pistachio were analysed using UPLC-DAD-ESI-MS/MS	Piñeiro et al., 2025
Tomato, potato from processing industry	Tomato pomace (TP), potato peel (PP)	Gallic acid, protocatechuic acid, 4-hydroxybenzoic acid, chlorogenic acid, vanillic acid, caffeic acid, syringic acid, vanillin, coumaric acid, ferulic acid	The assessment showed the recovery of bioactive compounds from Tomato pomace and potato peel	Almeida et al., 2025
Onion, tomato, pistachio from companies	Onion peels, tomato peels, pistachio green hulls	Protocatechuic acid, p-Cumaric acid, p-hydroxybenzoic acid, chlorogenic acid, rutin, myricetin, luteolin, kaempferol, naringenin, isorhamnetin	Onion peels are found to be rich in quercetin and its derivatives, and other flavonoids	Benito-Román et al., 2025
Granny Smith apples	Apple peel	Catechin, procyanidin, epicatechin, procyanidin tetramer, chlorogenic acid, quercetin-3-o-glucuronide, quercetin pentoxide, quercetin hexoxide, kaempferol-3-o-glucuronide	The biofortified apple peel can serve as a biofactory of phenolic compounds	Villamil-Galindo et al., 2025
Pineapple from fruit processing company	Core Waste	Phenolic compounds, antioxidant activity, carotenoids	Dry pineapple core (DPC) is considered a valuable source of natural antioxidants	Sanahuja et al., 2025
Sweet lime fruits	Sweet lime peels	Coumarin, ferulic acid, hesperidin, naringin, phloroglucinol, sinapinic acid, tangeritin, quinic acid	The study can lay the basis for utilizing SLP as a functional food ingredient due to its potential benefits	Thiruvalluvan et al., 2025
Navel variety orange	Orange peels	Methyl-protocatechuic acid-O-sulfate, narirutin, luteolin rutinoside, hesperidin, apigenin-7-O-(malonylapyosil)-hexoside	The membrane process investigates the purification and concentration of phenolic compounds from the orange extract	Alonso-Vázquez et al., 2025
Okra (*Abelmoschus esculentus*) agriculture by-product	Okra flowers	Anthocyanins, cyanin, cyanidin-3-rutinoside, and cyanidin-3-glucoside	The outcomes pave the way for utilizing okra flower byproducts as a sustainable source of bioactive anthocyanins	Pashazadeh et al., 2025
Brewer's spent grain (BSG) industry	Byproduct of the brewing	Ascorbic acid, gallic acid, catechol, ellagic acid, acetylsalicylic acid, vanillin	The results verified that BSG is a rich source of dietary fibers, phenolic acids and antioxidants	Chu et al., 2025
Lavender from pilot farm	Solid residues of lavender	Gallic, chlorogenic, syringic, vanillic, p-coumaric, ferulic, isoferulic acids, rutin, quercetin, luteolin, kaempferol	The solid waste of lavender represents a sustainable source of phenolic compounds	Barar & Bensebia, 2025
Sugar beet from sugar industry	Beet leaves	Phenolic compounds, vitexin	Ultrasound extraction proved to be an excellent method for extracting bioactive compounds	Dukić et al., 2025
Walnut waste	Walnut shell	Flavonoids, catechin, isoquercitrin, taxifolin, quercetin,	The green chemistry principle offers a sustainable strategy for the valorization of agro-industrial by-products	Erdem et al., 2025
Tobacco (*Nicotiana tabacum* L.) waste from industry	Tobacco leaves	Gallic acid, protocatechuic acid, vanillic acid, chlorogenic acid, caffeic acid, ferulic acid	The tobacco waste extracts showed antifungal activity	Liu et al., 2024
Malay jackfruit fruit from shop	Jackfruit peel	Ascorbic acid, quinic acid, chlorogenic acid, shikimic acid, glycyrrhetinic acid	Sequential Microwave-Ultrasonic Assisted Extraction coupled with Natural solvent (ChCl-LA) proved to be an efficient green technique for the extraction of phenolic compounds	Ly & Sothornvit, 2024
Celery from vegetable processing plant	Leaves and roots	Palmitic acid, succinic acid, 3-butylphthalide, sedanolide, scopoletin, tyrosol	The valorization of celery waste as a biostimulant source and crop protection tool	Motti et al., 2024

terpenoids, and alkaloids stand out due to their abundance, diversity, and proven biological activities. The valorization of these compounds not only addresses environmental concerns associated with organic waste accumulation but also contributes to resource efficiency within a circular economy framework (Chiocchio *et al.*, 2021).

Phenolic compounds are widely distributed in plant wastes and are considered one of the most abundant classes of secondary metabolites. It includes phenolic acids, tannins, lignans, and stilbenes, all of which are known for their antioxidant, antimicrobial, and anti-inflammatory activities. Grape pomace, a by-product of the wine industry, is especially rich in phenolics, with reported concentrations ranging from 20-60 mg gallic acid equivalents (GAE)/g dry weight (Pessoa *et al.*, 2019; Karastergiou *et al.*, 2024). Citrus peels are another significant source, containing up to 50 mg GAE/g dry matter, with hesperidin and naringin as dominant flavanones (Sorrenti et al., 2023). These compounds have been shown to scavenge free radicals, reduce oxidative stress, and provide cardiovascular benefits. Furthermore, phenolic-rich extracts from fruit and vegetable residues are being studied for their potential in functional foods and natural preservatives due to their strong antioxidant activity (Waseem *et al.*, 2023).

Flavonoids (subgroup of polyphenols) are among the most studied compounds in plant residues because of their diverse structures and biological activities. Onion and apple peels contain high concentrations of flavonoids such as quercetin, ranging between 10-25 mg/g dry weight (Parra-Pacheco *et al.*, 2024). Grape pomace provides not only anthocyanins responsible for red-purple pigmentation but also resveratrol, a stilbene with demonstrated cardioprotective properties (Gracia-Lomillo & Gonzalez-Sanjose, 2017). In addition, banana and mango peels are reported to contain significant amounts of catechins and proanthocyanidins, further broadening the spectrum of waste-derived flavonoids (Roy *et al.*, 2022). These compounds have been linked to reduced risks of chronic diseases such as diabetes, hypertension, and cancer, highlighting their potential for pharmaceutical and nutraceutical exploitation.

Terpenoids represent another vital group of secondary metabolites present in agricultural by-products, characterized by their structural diversity and bioactivity. Citrus peel residues are particularly rich in limonoids and carotenoids such as β-carotene, lutein, and zeaxanthin, with β-carotene levels reaching 3–6 mg/100 g dry matter. These terpenoids act as natural colorants and antioxidants, while also serving as precursors of vitamin A. Sugarcane bagasse and molasses contain diterpenes and triterpenes with notable antimicrobial and anti-inflammatory properties. Additionally, tomato peels and carrot pomace are well-documented sources of lycopene and carotenoids, widely used in nutraceuticals and functional foods. The recovery of terpenoids from such wastes not only adds economic value but also contributes to reducing the reliance on synthetic additives (Awuchi, 2020).

Although alkaloids are less abundant in common fruit residues compared to phenolics and flavonoids, are highly bioactive and valuable. For instance, potato peels contain glycoalkaloids such as α-solanine and α-chaconine in concentrations ranging from 1.5–2.5 mg/g dry weight, which are considered antinutritional at high levels but also exhibit potential pharmacological activities such as anticancer and antimicrobial effects (Roy *et al.*, 2022). Tea and coffee by-products are notable for their content of purine alkaloids like caffeine and theobromine, often exceeding 10–15 mg/g dry weight (Chiocchio *et al.*, 2021). These alkaloids are widely used in the food and beverage industry for their stimulant properties, while also being studied for metabolic and neuroprotective effects. In addition, alkaloid-rich wastes from medicinal plant residues are being investigated as potential sources of therapeutic agents, underscoring their economic and biomedical relevance.

In conclusion, plant waste streams constitute a diverse and renewable reservoir of phenolics, flavonoids, terpenoids, and alkaloids, each contributing unique health benefits and industrial applications. By quantifying their presence in agro-industrial residues and developing sustainable extraction methods, these bioactive compounds can be effectively valorized. This approach reduces waste, enhances resource efficiency, and contributes to the global movement toward a circular bioeconomy. Future research should focus on optimizing extraction techniques, ensuring scalability, and integrating waste-derived bioactive compounds into value chains ranging from pharmaceuticals to food systems (Parra-Pacheco *et al.*, 2024; Sorrenti *et al.*, 2023).

3. Extraction of bioactive compounds using green solvents

Green chemistry involves developing and applying chemical processes and products that aim to reduce or eliminate hazardous materials. Sustainable extraction of natural compounds can be achieved by designing methods that save energy, using environmentally friendly solvents, and recycle waste into co-products (Benvenutti *et al.*, 2019). Green solvents are characterized as biodegradable, recyclable, low in volatility or non-volatile, non-flammable, and safe to inhale, being non-toxic and non-carcinogenic. They also feature diverse physical and chemical properties, enabling their use across various extraction techniques (Winterton, 2021) (Fig. 1).

Supercritical carbon dioxide is widely used as a supercritical solvent due to its safety and renewability (Clarke *et al.*, 2018). These solvents typically exhibit high diffusion rates similar to gases. However, since pure supercritical carbon dioxide has very low polarity, co-solvents such as ethanol are often added to enhance the solubility of solid reagents and products (Clarke *et al.*, 2018).

Ionic liquids (ILs) are recognized as "green solvents" because maintain excellent thermal stability and exhibit minimal vapor pressure properties to support product recovery along with recycling and simplify containment method. Significant variances exist between various ionic liquids when examining their ability to mix with liquid molecules as well as their stability under moisture conditions. Ionic liquids serve as solvent solutions in the extraction of numerous natural bioactive compounds. According to Lei *et al.* (2017), ionic liquids are pure ionic compounds characterized by strong ion properties and rapid reaction rates in various industrial processes. Deep eutectic solvents (DESs) have emerged as a promising alternative to replace ionic liquids. Deep eutectic fluids are primarily made up of a neutral hydrogen bond donor

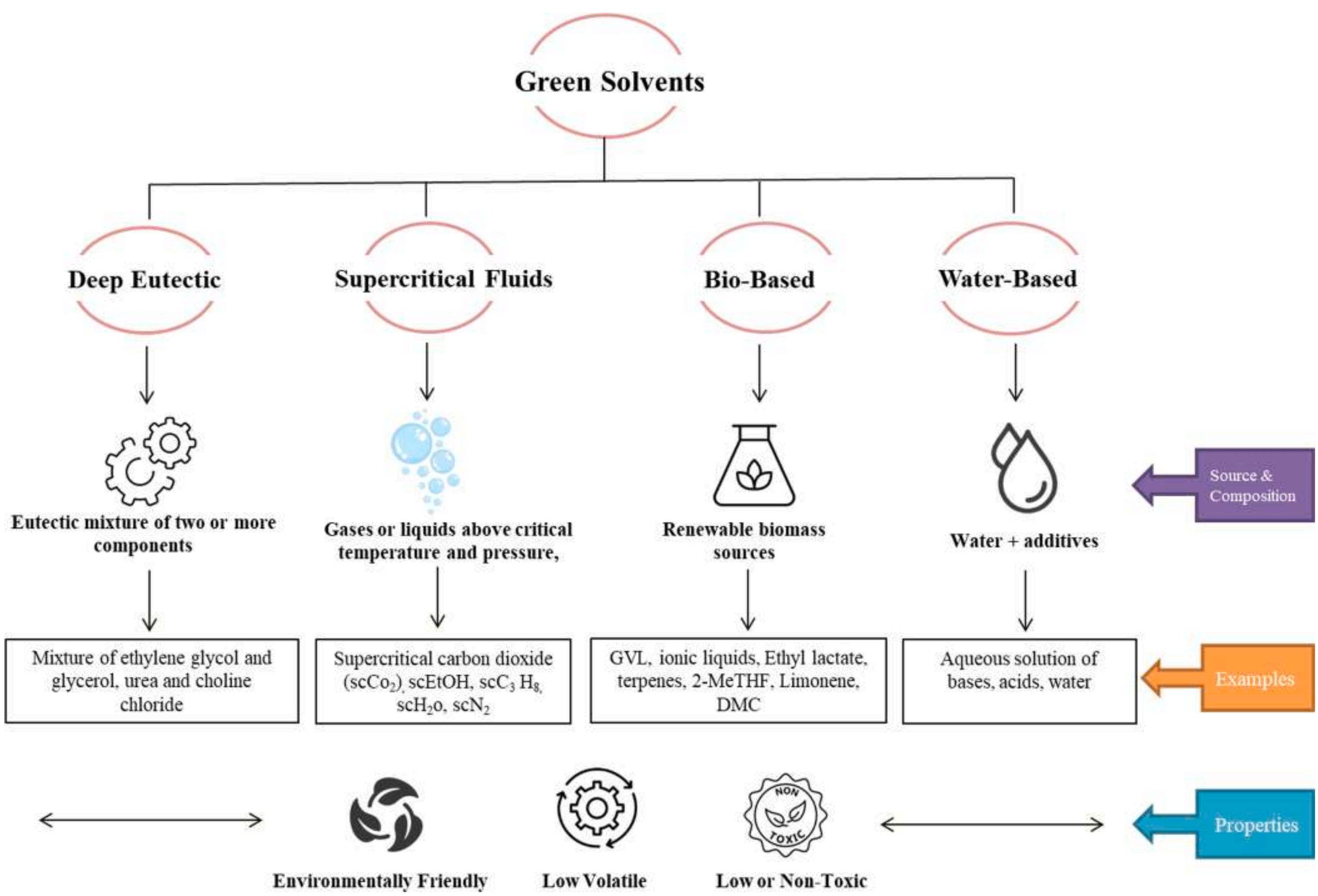

Fig. 1. Types of green solvents and their sources adopted from Usman et al. 2023.

that interacts with the halide, and a hydrogen bond acceptor that typically uses quaternary ammonium salt. The natural composition of deep eutectic solvents leads to cost-effectiveness and simpler production methods, as well as environmentally beneficial characteristics, compared to ionic liquids (ILs) (Yu *et al.,* 2021).

Researchers consider that water stands as the most environmentally friendly solvent available in chemical applications. Water ranks as the most natural solvent among all known chemical solvents. The scientific world discovered switchable water (ability of aqueous solution to alter its properties) techniques during recent decades. The production of switchable water occurs through the dissolution of base components like *N,N,N N*-tetramethylbutane 1,4-diamine. The use of "the switch" depends on CO_2 being added or removed to monitor ionic strength in an aqueous environment solution. A water solution becomes a preferred extraction solvent for polar compounds because its base component is removable to maintain safety and cleanliness (Lajoie et al., 2022).

Natural solvents represent environmentally friendly solvents obtained through regenerative biological sources like plants sugar and natural oils. These are natural substance-based solvents developed to replace fossil fuels. Which mainly include bioethanol, esters of natural organic acids like ethyl acetate and ethyl lactate, fatty acid esters, terpene compounds such as limonene and eucalyptol, glycerol derivatives, and isosorbide. These solvents are often called “green solvents” because they are environmentally safe and pose no threat to human health (Viñas-Ospino et al., 2023) (Table 2).

4. Green methods for extracting bioactive compounds

Vegetables, roots, nuts, herbs, fruits, and spices are a source of bioactive substances, primarily non-starch polysaccharides and polyphenols (Saeed *et al.,* 2021). The manufacture sector is seeking for environmentally novel technological advances to reduce the loss of bioactive chemical compounds because of their significance (Gomes-Araújo et al., 2021). These chemical compounds have properties that are anti-cancer, anti-diabetic, antioxidant, anti-depressive, and anti-inflammatory. (Ben-Othman et al., 2020). Development and manufacturing of functional and nutraceutical products are becoming significantly important in the food industry. This novel class of food products has garnered considerable attention in the food market due to growing consumer interest in “healthy” eating. As a result, the pharmaceutical and food industries are eager to find new natural bioactive compounds which can be used as nutraceuticals, additives, functional foods or pharmaceutical agents (Yusuf, 2017).

Various researchers have used modern methods to extract bioactive compounds. Such precious chemicals are obtained under various sources using a variety of extraction procedures. Commercial and novel techniques have been used to extract bioactive compounds in various natural sources (Moreira *et al.,* 2019; Mahmood *et al.,* 2019). The process of extraction must be optimal and minimise the contaminants whilst keeping its efficacy, safety, cost-effectiveness and environmental sustainability. The choice of a method of extraction depends on the substance, the amount of energy, and the mode of preparation (Zhang *et al.,* 2018).

Maceration is an old method of extraction that has been widely applied in the laboratory and industrial spheres to extract a range of chemical elements in different matrices (More *et al.,* 2022). To enable the transfer of mass and diffusion of the components of interest, the process could be separated into three steps: (1) fine particulates of the material are homogenised; (2) the pulverised solid should be immersed in a closed vessel whereby it will be fully saturated with the solvent and, in some cases, external heat may be applied; (3) the liquid extract may be separated in the form of a filtrate, and the solid that remains solid may be pressed (Bitwell *et al.,* 2023; Nirmal et al., 2023). Soxhlet extraction is also another traditional method used during the recovery of a wide variety of different compounds. In this technique, the plant material is standardised, dried using anhydrous substances, pulverised and the material weighing pre-extraction cycle is taken. After placing the sample in the thimble and wrapping it in filter paper, a suitable solvent is added to the round bottomed flask. Following heating to predetermine temperature, the solvent transition from the boiling state to the vapour state, travels by means of thimble, and eventually contacts the condenser, where it is once more liquefied. Typically, traditional extraction and separation methods rely heavily on large amounts of organic solvents, which are often toxic, time-consuming, highly volatile,

Table 2
Origin, commercial and typical functional uses of green solvents.

Green Solvent	Origin	Commercial Applications	Typical Functional Uses	References
Cyclopentyl Methyl Ether	Produced from methanol and cyclopentene, and biomass (sugars and lignin)	Bio-refineries and green synthesis	Bio-extractions, chromatographic separations, biotransformations	de Gonzalo et al., 2019; Azzen et al., 2019
Glycerol	Produce from *Jatropha* Shell	Cosmetics, food, and drug formulations, biodiesel production	Formation of green solvent	Habaki et al., 2019; Stettler et al., 2025
Limonene	Extracted from citrus peels (waste valorization)	Packaging, cosmetics, cleaners	Flavor, fragrance and green solvent	Ciriminna et al., 2014
Supercritical CO_2	CO_2 in its fluid state under pressure	Pharmaceuticals, polymer processing	Caffeine and oil extraction, clean tech applications	Tutek et al., 2021; Conde-Hernandez et al., 2017
Deep Eutectic Solvent (DES)	Made from hydrogen bond accepters and hydrogen bond donors	Biomass treatment, extraction, green catalysis	Alternative to ILs, excellent solvent for natural product extraction	Smith et al., 2014
Sulfolane	Synthesized from butadiene and sulfur dioxide	Industrial solvents	High-polarity solvent for specialty extractions	Kobarfard and Gorecki, 2023
Ethyl Lactate	Processing of corn	Agrochemicals and food processing	Cleaning, degreasing, and tape coatings	Dwivedi et al., 2021; Nikles et al., 2001: Xue et al., 2024
Ionic Liquids (ILs)	Engineered organic salts	Electronics, desulfurization, biomass conversion	Biocatalysis, carbon capture, reusable solvent systems	Yang and Pan, 2005; Torres-Valenzuela et al., 2020
Water	Naturally occurring, abundant	Food, petrochemical, and pharmaceutical industries	Universal solvent used in countless extractions and reactions	Breslow, 2010; Narayan et al., 2007
Bioethanol	Fermented from sugarcane or starch crops	Fuel, chemicals, pharma	Motor fuel, reaction medium, clean-burning solvent	Dwivedi et al., 2021; Wong & Sanggari, 2014
Dimethyl Carbonate (DMC)	Synthesized from methanol + CO + O_2	Paints, coatings, and polymer chemistry	Safe solvent for organic synthesis, phosgene alternative	Dwivedi et al., 2021; Pyo et al., 2017
n-Butane	Extracted from natural gas	Refining and chemical industries	Propellant in aerosols, fuel blending, extraction of aromas	Dwivedi et al., 2021; Rapinel et al., 2017
Ammonium	Emitted via urea breakdown and manure volatilization	Agriculture, fertilizers, textiles	Dyeing, pesticide formulation, textile auxiliaries	Melo et al., 2013; Gracia-Chavez et al., 2012
Plasma activated water (PAW)	Origin of reactive species present in PAW	Agriculture industry, microbial inactivation	Biotechnology applications, Water purification to biomedicine	Zhou et al., 2020; Guo et al., 2021; Thirumdas et al., 2018

and can damage heat-sensitive compounds. Therefore, developing new sustainable analytical techniques requires replacing these conventional solvents with safer alternatives.

Novel extraction methods based on "green" models that use energy and solvents efficiently have been proposed to address the many limitations of traditional extraction techniques (Putnik *et al.*, 2018). Modern methods of extraction of dietary fiber soluble in water (SDF) involve a wide range of different methods, including high-pressure processing, colloidal gas aphron (CGAs), ultrasound and microwave-assisted extraction (UMAE), accelerated solvent extraction (ASE), pulsed electric field (PEF), microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), and subcritical and supercritical fluid extraction (SCF). These modalities could be implemented either alone or interchangeably, which results in the high quality of products and at the same time, reduces operation costs. UAE is useful in the removal of thermally mobile constituents such as polyphenols. The method encourages the recovery of bioactive substances in a homogenized manner through increased heat transfer and mass flow, and in a paradigm that is environmentally sustainable sustainable (Marmol, 2021). MAE, SCF, and UAE are the most superior technologies of bioactive compound recovery.

Failure to follow proper extraction procedures will lead to incorrect data depiction and unwanted target compounds. In this regard, this paper examined the operational process and key elements affecting the three methods discussed above (UAE, SCF, and MAE) and explained their respective benefits and drawbacks in addition to establishing the potential optimization approaches. The purpose of the current study was to provide in-depth academic content along with practical advice and suggestions as well as to suggest new sources of extraction.

4.1. Ultrasound-assisted extraction (UAE)

Ultrasound assisted extraction (UAE) is a technique that utilizes ultrasonic waves to improve the yield of bioactive molecules in food matrices, botanical vegetables and pharmaceutical preparations. Over the past ten years, there is a significant amount of literature that examines UAE as a green, affordable option to the traditional methods of extraction. This approach can provide a more effective and cost-effective recovery of bioactive components and maintain the simplicity of operation and environmental sustainability (Ranjha *et al.*, 2021; Teixeira *et al.*, 2023). Ultrasound is a mechanical wave that spreads through media in changing states of compression and rarefaction. An important mechanism used in the process of increasing many food-processing processes is cavitation bubbles, which are formed and collapse when the acoustic energy in the liquid phase reaches critical value. These bubbles burst, and their bursts have shockwaves (Machado-Carvalho et al., 2023; Shekhar *et al.*, 2023). The major physical phenomenon, which underlies ultrasonography, is acoustic cavitation (Chauhan *et al.*, 2023). Cavitation can be either stable or transient; stable cavitation creates shear stresses due to micro-jets formed by the bursting of microbubbles along cellular structures, and transient cavitation produces strong temperature and pressure variations (Lavilla & Bendicho, 2017). The process enhances the lysis of the cell walls, increases the solvent permeation into plant tissues, and increases the rate of mass transfer, increasing the release and overall productivity of extractable bioactive constituents (Gueffai *et al.*, 2022).

The fundamental design features of the extraction process, such as the density of acoustic energy, ultrasonic intensity, ultrasound power, or operating mode (either pulsed or continuous), can be determined by UAE, which are important for the extraction process (Tiwari *et al.*, 2015). UAE can be applied either directly with an ultrasonic probe or indirectly with an ultrasonic bath. The focused effect of direct ultrasonic therapy in a specific location generally makes it more effective and powerful. In contrast, ultrasound transducers can be positioned on the sidewalls of the extraction tank, beneath the bottom, or in a separate transducer array box. They generate sonication in the ultrasound bath system. The distribution of sound pressure in the medium can be adjusted more easily by placing the transducer array box in any direction around the tank. Transducers in the ultrasonic bath system usually have a large surface area. At the same time, the transducer drive can be attached to the tank's sides or bottom, which are often larger than the transducer surface, to cause vibrations and produce sound waves in the tank's medium. These factors demonstrate that the sound energy comes from low-intensity, large surfaces.

Ultrasound-assisted extraction systems come in various forms, including (a) transducer-equipped ultrasonic bath on the side of the ship, (b) ultrasonic baths with transducer beneath the vessel's bottom, (c) transducer in a different array box net to an ultrasonic bath, (d) continuous ultrasonic horn-based extraction, and (e) ultrasonic horns. The efficiency of extraction is influenced by several variables, including the solvent type, extraction duration, solvent-to-solid ratio, temperature, pH, and ultrasonic amplitude, frequency, and power intensity during the UAE process (Dadi *et al.*, 2019; Rathnakumar *et al.*, 2017). Increased power or intensity/amplitude levels can enhance sonochemical effects. However, high amplitude can cause the ultrasonic transducer to deteriorate, increase depression, and lower cavitation levels. Therefore, increasing cavitation and process efficiency does not require large amplitudes. Since high viscosity can significantly reduce effects such as micro-turbulence, moderate agitation, micro-jet, and cavitation caused by mechanical movements of UAE devices (ultrasound probe), the amplitude should be increased when working with high-viscosity samples. The cavitation level of the extractant decreases as ultrasonic frequency increases. Furthermore, the UAE technique is versatile and can be used with both non-polar and polar solvents at various temperatures to increase phytochemical yield while reducing extraction time (Nikolić et al., 2023; Machado-Carvalho et al., 2023). Additionally, ultrasound can be combined with other extraction methods, such as heat, high pressure, vacuum, enzymes, pressurized liquids, microwave, pulsed electric field, and others, to improve the recovery efficiency of bioactive compounds from plant-based materials (Viganó et al., 2020; Sharif *et al.*, 2023).

The separation of various chemicals from multiple plant sources has been achieved through UAE (Setyaningsih *et al.*, 2019; Sharayei *et al.*, 2019). The use of UAE has become a standard method for extracting bioactive compounds from fresh produce and their processing waste materials. Researchers studied pomegranate peel UAE while comparing the yields obtained to conventional extraction outcomes. During pulsed and continuous UAE operations, the extraction process achieved higher antioxidant output levels than traditional methods by 24% and 22%, respectively, while completing extractions 90% and 87% faster compared to traditional processes. The research showed that pulsed UAE, combined with continuous UAE, boosted antioxidant production levels by 24% and 22%, respectively, while reducing extraction times by 90% and 87% compared to conventional methods. Traditional extraction methods should be replaced by UAE since it decreases extraction time and energy usage while improving antioxidant yield. UAE technology extracts bioactive compounds from oleaginous seeds, herbs, spices, fruits, and vegetables (Jacoted-Navarro *et al.*, 2015). The caraway seed aromas are treated with UAE. The outcomes demonstrated that seeds treated with ultrasound achieved better carvone and limonene recovery rates than untreated seed materials. Several studies have demonstrated the successful extraction of bioactive compounds through UAE from different plant sources, including banana peels by Vu *et al.* (2017), waste products of tangerine, lime, and orange by Razola-Díaz et al. (2021), Morus alba leaves by Garcia-Vaquero et al. (2020), Ficaria kochii flowers by Shahidi (2022), peaches and pumpkins by Altemimi *et al.* (2016), green tea leaves by Bindes *et al.* (2019), and hibiscus sabdariffa calyces (Paraiso *et al.*, 2019).

4.2. Microwave-assisted extraction (MAE)

Another extraction method called microwave-assisted extraction

(MAE) utilizes microwave energy to extract various phytochemicals. MAE is a rapid extraction rate BCs as compare to conventional methods. The extraction of bioactive ingredients from complicated herb mixtures uses MAE as an essential green technological solution. Numerous studies have utilized MAE during the last few decades to extract bioactive components, particularly from plant materials (Rodsamran and Sothornvit, 2019; Kaderides *et al.,* 2019). Materials inside microwaves that operate at 300 MHz to 300 GHz connect to heating through the processes of ionic conduction and dipole movement (Horikoshi *et al.,* 2018). A microwave system contains two fields running perpendicular to one another: electric and magnetic fields. A microwave device operates with four essential parts including the waveguide, applicator (for containing the sample), circulator, and magnetron. MAE devices can be contain as single-mode or multimode systems, depending on the microwave intensity applied during the sample extraction process. The multimode system ensures consistent sample treatment through its use of microwave radiation that spreads throughout the entire space. Single-mode systems efficiently extract samples due to direct access to the sample.

Microwave heating, which raises the extraction temperature and speeds up mass transfer, is the main mechanism behind MAE (Kaderides *et al.,* 2019). Microwaves can generate direct or bulk heating within the solvent and sample due to interact with polar components and can penetrate certain materials to a specific depth. Water, with its high dielectric constant, absorbs and emits microwave radiation, increasing the temperature needed for quicker extraction. This direct and bulk heating shortens the time required to heat the solvent and samples, especially in large-scale extractors. The degree of microwave-induced heating depends on the dielectric properties of the solvent and sample, influenced by factors like temperature, microwave frequency, solvent makeup, and sample type. Additionally, the direct heating penetrates the matrix and, together with increased local temperature and pressure during MAE, can push target components out of the matrix into the solvent. This process enhances solvent penetration and facilitates the transfer of target substances. The primary role of microwave heating in MAE is on the sample matrix content. As moisture evaporates, pressure inside plant cells increases, causing swelling and eventual cell rupture. This process exposes cell contents to the solvent, boosting solvent penetration (Zhi *et al.,* 2017).

In conventional extraction methods, heat transfer occurs from the heating medium to the inside of the cells, while solute mass transfer happens in the opposite direction. In microwave-assisted extraction (MAE), heat and mass gradients work together to improve the extraction process by encouraging the flow of target chemicals from inside the cells to the solvent. This dynamic reduces overall extraction time and helps extract valuable chemicals (Picot-Allain et al., 2021).

Various factors can influence MAE, including irradiation duration, microwave power, moisture content, frequency, sample particle size, solvent type and composition, temperature, solid-to-liquid ratio, number of extraction cycles, and pressure. MAE effectively isolates a broad spectrum of phytochemicals (Belwal *et al.,* 2017; Hu *et al.,* 2021). Pectin, an essential functional ingredient in the food industry for gelling, thickening, and stabilization (Lasunon *et al.,* 2022), can be extracted using MAE combined with an acidic solution, yielding 31.58% pectin from tomato pomace (Lasunon *et al.,* 2022). Vu *et al.* (2019) demonstrated that MAE with water can recover phenolic compounds from banana peels. Microalgae are another source of bioactive compounds like lipids and polysaccharides, with MAE significantly enhancing lipid extraction efficiency. The effectiveness of this method varies depending on the specific microalgae species targeted (Zhou *et al.,* 2022; Yao *et al.,* 2018). It is important to note that MAE relies on microwave energy to heat the biomass and disrupt cell walls; however, this can pose limitations when extracting heat-sensitive chemicals (Zhou *et al.,* 2022).

Numerous benefits of microwave-assisted extraction have been documented, including increased extraction yield, lower temperature gradients, faster heating, and smaller equipment size. As a result, MAE offers several advantages over conventional extraction methods, such as a higher extraction rate, quality products at a lower cost, shorter extraction times, and reduced solvent use (Vinatoru., 2017; Marić *et al.,* 2018).

4.3. Supercritical fluid extraction (SCF)

The process that occurs when material (such as carbon dioxide) approaches its point of critical mass, where the difference between its gas and liquid phases becomes indistinguishable, is called supercritical fluid extraction (SCF) (Chen *et al.,* 2022). A supercritical fluid combines physical properties of both a gas and a liquid at critical point (Chen *et al.,* 2022). These specific characteristics allow supercritical fluids to perform extraction tasks efficiently by separating and dissolving extractable substances (Bitwell *et al.,* 2023). Because supercritical fluid extraction uses a renewable solvent, it is widely recognized as an environmentally sustainable technology. The fluid exhibits properties of both a gas and a liquid, which is the main advantage of using a solvent in the supercritical state. Since CO_2 is non-polar, adding a small amount of polar solvent can significantly increase the overall yield of the extraction (Wrona *et al.,* 2017).

A solvent that dissolves the targeted compounds in the sample is employed in the super critical fluid procedure. The target compounds are subsequently extracted by the solvent's interaction with the sample while it is being pumped through packed bed. The solvent is eventually released from the extraction jar. The pressure and temperature fluctuate when the solvent departs, prompting the pressure to fall and temperature to rise. The extracted chemicals remain in a solvents-free state after the solvent recovers to a gaseous state, on the other hand results can be fluctuated (Bitwell *et al.,* 2023).

Carbon dioxide is used as a fluid in supercritical fluid extraction, and it becomes supercritical at pressures of (7380 KPa)and higher temperatures (31.1°C). Supercritical carbon dioxide has powerful solvation capacity for phytochemicals that are non-polar, which is the primary reason for its numerous benefits when used in extraction procedures. Polarized phytochemicals, however, frequently demonstrate poor solubility in supercritical carbon dioxide extraction. Various co-solvents including water, ethyl acetate, ethyl alcohol, acetonitrile and methanol enhance the soluble capacity of polar phytochemicals in supercritical carbon dioxide extraction procedures. These modifications lead to more efficient phytochemical production. Superficial carbon dioxide serves different industries such as pharmaceuticals cosmetics and food due to its scalable features and versatile nature. Supercritical carbon dioxide finds industrial use for extracting fatty acids, aromas, carotenoids, triglycerides and various low molecular weight weakly polar substances (Belo *et al.,* 2019; Rosas-Quina & Mejía-Nova, 2021).

The commercial extraction of natural resources mainly depends on supercritical carbon dioxide extraction process. Precise management of pressure and temperature settings during extraction is vital for maximizing the production of unmodified biological substances. Thermo labile compounds require careful handling in extraction processes although the solubility of carbon dioxide increases with temperature elevation. To successfully separate thermo labile phytochemicals at high efficiency without quality reduction, use elevated pressure along with low temperature and ensure the sample is dry (Ferrentino *et al.,* 2020).

Monoterpene content correlates directly with pressure, likely due to increased density. Elevated temperatures allow analytes to release vapor pressure, easing the sequential extraction of compounds with different densities. In the case of tocopherol extraction from apple seed oil using supercritical carbon dioxide, higher pressures were found to be beneficial, but yields decreased as temperatures rose (Montanes *et al.,* 2018). Pavlić et al., 2018 utilized supercritical fluid extraction to examine how pressure and temperature affect the separation of monoterpenes from sage herbal dust. Additionally, Kitrytė *et al.* (2020) optimized extraction variables such as duration, pressure, and temperature to isolate the non-polar components of elderberry pomace.

Rosas-Quina and Mejía-Nova (2021) investigated the extraction of bioactive compounds from onion waste using a co-solvent of supercritical carbon dioxide and ethanol. The findings identified five primary components, primarily 7,4-diglucosdie, kaempferol, quercetin 3, 4-diglucoside, quercetin 4-glucoside, and quercetin. Quercetin 3, 4-diglucoside was the compound with the highest flavonoid content, accounting for 45.19% of the total. The main components of onion peal extracts that have antioxidant effects, like quercetin and kaempferol reported 39.94% and 1.27% respectively. The extraction of phytochemicals from tomato peels using supercritical extraction techniques and hydrogen-rich water was assessed by Stefou *et al.* (2019). Hydrogen-rich water extracts showed higher levels of total phenolic and flavonoid contents, as well as increased total anthocyanin and antioxidant activity. However, Lajoie *et al.* (2022) demonstrated that supercritical procedures extract more than twice the amount of lycopene (1016.94 mg/100g extract) compared to Soxhlet extraction with ethyl acetate (454.54 mg/100g extract). Other kinds of bio-compounds, like bioactive pigments, can also be extracted via supercritical fluid extraction (Sanzo *et al.,* 2018). Astaxanthin was extracted from *Haematococcus pluvialis* by Sanzo *et al.* (2018) using supercritical extraction, yielding 98.6%. Astaxanthin is a highly desired carotenoid with an enormous market position. This carotenoid is used in different industrial sectors, including natural medicine, nutraceuticals, pharmaceuticals, cosmetics, and functional foods, because of its purported anti-inflammatory and antioxidant qualities (Molino *et al.,* 2018).

5. Applications of natural solvent produced extracts

Natural chemical molecules that occur in trace amounts in food, plants, and other biological sources and have physiological effects that may support good health are referred to as bioactive compounds. There are many different fields in which they might be used. For most animals, including humans, tocopherol and food-based carotenoids are the main sources of vitamin E and A respectively (Shahidi & de Camargo, 2016; Rodriguez-Concepcion *et al.,* 2018). As an auxiliary pigment in photosynthesis, carotenoids are vital for fruits because they absorb energy and protect against photo-oxidation. Additionally, some carotenoids are converted into vitamin A, which plays an important nutritional role. Other benefits include a lower risk of coronary heart disease, prevention of contact diseases, aging-related macular degeneration, and reduced risk of degenerative conditions.

The functional qualities such as the presence of bioactive substances in fruits with antioxidant activity, which may have extra physiological effects even in tiny amounts, are linked to increased fruit consumption. Consistent intake of vegetables, grains, and fruits that contain antioxidants including phenolic compounds, vitamin C, and carotenoids has been associated with certain health benefits (Pieniz *et al.,* 2009). Phenolic compounds are naturally occurring bioactive compounds mainly found in plant tissues. These compounds show interesting bioactivities such as antibacterial, anti-inflammatory, antiproliferative, and antioxidant effects. Tannins are high-molecular-weight phenolic chemicals present in plants that precipitate proteins, especially salivary proteins, from the mouth cavity (Brandao *et al.,* 2017). The market value of cosmetic products is greatly influenced by natural ingredients, particularly terpenes and terpenols. These ingredients help improve attractiveness by making skin wrinkle-free, healthy, and youthful. Carotenoids, and selected other terpenes are increasingly popular as ingredients in skin care cosmetics. Due to their antioxidant properties,

Table 3
Application of produced bioactive compounds in food and pharmaceuticals.

Residue/ Source	Green extraction	Bioactive compounds type	Product	Application	References
Fig peels and blackthorn fruits	Ultrasound assisted extraction (UAE)	Anthocyanin	Confectionery products	Improved antioxidant and antimicrobial activities	Backes et al., 2020
Pumpkin seeds and rinds	–	Dietary fiber	Bakery product	High fiber bakery product	Nyam et al., 2013
Peel of camu-camu fruit	–	Phenolic compounds	Yogurt	Yogurt fortification	Conceição et al., 2019
Apple pomace	Ultrasound assisted natural deep eutectic solvent extraction	Polyphenols	Bakery product	Innovative gluten-free product	Rashid et al., 2023; Gumul et al., 2021
Apple pomace	Boiling water with 1% acetic acid	Polyphenols	Yogurt	Supplemented yogurt	Fernandes et al., 2019
Apple pomace	NADES	Phenolic compounds	–	Natural antimicrobial agents in the food industry	Han et al., 2024
Waste broccoli leaves	Ultrasound-assisted deep eutectic solvent	Phenolic compounds	–	Antimicrobial effects	Cao et al., 2023
Michelia alba	NADES-UAE	Polyphenols	Pharmacology	Biological activity	Wang et al., 2024
Mango peels	Ultrasound-assisted natural deep eutectic solvent	Polyphenols	Food, pharmaceutical, and cosmetic	Natural antioxidants	Lanjekar et al., 2022
Moringa leaves	Water in a Soxhlet extractor	Total phenolics and flavonoids	Goat meat patties	Protect cooked patties against lipid oxidation	Das et al., 2012
Origanum vulgare leaves	Conventional	Antioxidant-rich bioactive	Chevon Meat	Novel natural antioxidants in chevon emulsion	Jagtap et al., 2020
Jabuticaba residue	Water	Anthocyanin	Fresh sausage	Low-cost natural pigment	Baldin et al., 2016
Pomegranate, tomato, grape and olive pomaces	Water	Antioxidant potential	Lamb patties	Reduced microbial counts	Andrés et al., 2017
Pumpkin peel	Supercritical fluid extraction (SFE) and subcritical water extraction (SWE)	Phenolic and carotenoid contents	Edible oils	Natural antioxidant in edible oils	Salami et al., 2020
Pomelo peel	Distilled water	Pomelo peel sponge layer insoluble dietary fibre	Dough and bread	PP-IDF great potential for the development of innovative bread	Sang et al., 2023
Spent coffee grounds	Deep eutectic solvent	Chlorogenic acids (CGAs)	Nutraceutical	Alternative approach for the extraction of nutraceutical	Fanali et al., 2020
Saffron flowers	Natural deep eutectic solvents with UAE	Antioxidant as (poly) phenols	Novel hydrogels	Use for food or cosmetic	Cerdá-Bernad et al., 2023
Raw propolis	Ultrasound-Assisted Extraction with NADES	Naringenin and apigenin	Cosmetic cream	High antioxidant base cream	Tzani et al., 2022
Fresh laurel leaves	Microwave NADES Extraction	Antioxidant and antimicrobial activities	cosmetic and pharmaceutical ingredient	Effective antimicrobial activity against different Gram-positive	Caviglia et al., 2025

which protect against pigmentation, UV damage to skin cells, and aging, they are commonly used in cosmetics. Recognizing their benefits and commercial potential, researchers have explored the role of different carotenoids, such as astaxanthin, fucoxanthin, and β-carotene, in maintaining youthful, healthy skin cells (Sathasivam & Ki, 2018). Besides skin health, carotenoids, vitamin E, and other terpenes like squalene, and carnosic acid are also used in functional foods (Table 3).

5.1. Role of natural solvents produced bioactive in food applications

Natural ingredients with biological activity and, occasionally, nutritional value are known as food bioactive substances. In addition to minimizing the risk of disease, they play crucial parts in the growth and development of humans, which make them valuable to the safety and well-being of communities. The primary goal of developing functional foods is to incorporate them into everyday foods. By introducing bioactive substances to food products, it is feasible to manufacture goods with unique biological qualities, which substantially increase consumer acceptance (Table 3).

Certain natural sources provide natural bioactive chemicals. There are two kinds of these naturally occurring bioactive substances. First flavor enhancer, antioxidants, colorants, stabilizers, and antimicrobials are substances that have functional effects in food systems. Second, anti-inflammatory, antihypertensive, antioxidant, and anti-diabetic chemicals are that have functional effects in consumers. Both spoilage microorganisms and pathogenic can be effectively controlled by certain natural antimicrobials (Kaur, 2021). The extracts of plants and essential oils have been utilized to extend the oxidative and microbiological shelf-life of foods (Domínguez et al., 2020; Munekata *et al.,* 2020). Food products are protected from oxidative processes by natural bioactive substances (Dominguez *et al.,* 2019). Furthermore, a promising tactic to reduce the usage of artificial dyes in the pharmaceuticals and food industries is the encapsulation of organic colorants. Therefore, in order to deliver consumers, the required therapeutic effects natural functional medicinal chemicals are either used directly or integrated into food systems (Ghosh *et al.,* 2022).

Natural polymers such as gelatin, gummi arabicum, and apple pectin were utilized to encapsulate the essential oil extracted from savory leaves (*Satureja hortensis* L.). For every polymer, a greater encapsulation efficiency was observed. This led to an increase in tomato and amaranth herbicidal activity efficiency (Taban *et al.,* 2020). Pepper oil is another active oil that has been evaluated over time to prevent bacterial oxidation. Such oil was encapsulated by gummi arabicum which had an inhibitor impact on *Staphylococcus aureus, Enterococcus faecali*, and *Pseudomonas aeruginosa*. These polymers served to increase pepper oil's resistance to oxidation while it was being stored (Karaaslan *et al.,* 2021).

Due to high nutrient and dietary fiber content, bread and bakery goods have grown in importance in the human diet. For superior nutritional advantages, bakery goods made with ordinary wheat flour must be fortified with enriched wheat flour, as they have a poor antioxidant capacity. Colored wheat bran can be utilized in various industrial processes to recover bioactive components that function as antioxidants selectively (Zanoletti *et al.,* 2017). A wide variety of bioactive compounds found in moringa trees can be extracted from various vegetative structures, including pod husks, seeds, stems, and leaves. Multiple food products can be formulated with bioactive components. Functional peptides, carbohydrates, proteins, oils, fatty acids, and phenolic compounds make up the bioactive components of food.

Several by-products are produced during the eating and processing of many fruits, including apples, grapes, citrus, and mangos. These by-products often include a high concentration of beneficial bioactive components. Fruit pomace is one of the most significant by-products of fruit processing. Fruit pomace is an inexpensive, low-calorie bulking agent that can be used in food products to partially replace fat, sugar, or flour. By improving the stability of emulsion and water and oil retention, it typically enhances food functionality (Iqbal *et al.,* 2021). As with baked goods, a number of studies have also reported the use of fruit pomace in meat products, fruit pomace has been added to many meat products to raise their dietary fiber content. Apple pomace in the meat, for instance, might compensate for out diet's deficiency in fiber. Researchers have developed a beef alternative, using 2-8% apple pomace (Younis *et al.,* 2018). Dairy products can also occasionally use fruit pomaces as an organic stabilizer and texturizer. Among the most extensively cultivated crops, citrus fruits (grapefruit, lemon, mandarin, and orange) yield a vast amount of by-products, including pulp and peel. Citrus by-products contain both soluble and insoluble dietary fiber, which are excellent source of dietary fiber. By-products of citrus can be utilized to replace fat in meat dishes or to boost the amount of nutritional fiber.

The most significant class of molecules with antimicrobial action are bioactive substances notably phenolics, which include isoflavonoids, anthocyanin, and terpenes. Proanthocyanidins and other phenolic chemicals are abundant in grape seed extracts, which are by-products of grape juice or winemaking. *Salmonella* sp., *Campylobacters* sp., *Staphylococcus aureus*, and *Listeria monocytogens* were among the foodborne pathogens whose development was inhibited by grape seed extracts (Filocamo *et al.,* 2015). Citrus peel is rich in a variety of nutrients that act as antibacterial and functional substances, depending on their constitution. Secondary metabolites include flavonoids, carotenoids, terpenoids and furanocoumarins. Especially flavones and polyethoxylated flavones are present in these by-products. Apple and orange juice spoilage bacteria have been found to be affected by the addition of citrus oil and moderate heat treatment (de Souza Pedrosa et al., 2019).

5.2. Pharmaceutical applications

The anti-inflammatory and antioxidant bioactive substances are promoting health include terpenoids together with polyphenols and alkaloids and other nitrogen-containing components. The introduction of plant-derived nutraceuticals and dietary supplements into functional foods has occurred recently because these supplements contain elements that benefit health while improving human well-being. All nutritional formulae consisting of dietary supplements and functional meals carry bioactive compounds which deliver medical advantages together with their essential nutrients. Scientific research demonstrates the presence of naringenin and hesperidin flavonoids in citrus peels which exhibit strong anti-inflammatory and vasoprotective properties (Sachdeva *et al.,* 2020). Potent antioxidant properties exist in bioactive compounds found within the peels of citrus and bananas and pomegranate fruits as well as vegetable scraps made from carrot tops and onion skins and plant leaves. These substances protect against heart disease and cancer as well as neurological outcomes through free radical neutralization and decreased oxidative stress that prevents cellular damage (Ravindran & Jaiswal, 2016).

Apple pomace alongside grape skins serves as sources of polyphenols which experts use for producing functional foods while offering high doses of antioxidants. Grape pomace which emerges during fresh grapes processing primarily finds application as a basis for wines and liquids. The polyphenol capabilities for capturing free radicals exist strongly in both grape pomace and olive mill waste material. Anti-oxidative species in antioxidants eliminate reactive oxygen species to reduce oxidative stress that leads to diabetes and neurodegenerative diseases and cancer. Research shows that Alzheimer's disease models demonstrate neuroprotective qualities through active compounds such as oleuropein and resveratrol. *In vivo* tests have demonstrated these positive impacts on blood pressure levels together with cholesterol and cardiometabolic indicators among human consumers even though numerous studies defining polyphenol medical value were performed using *in vitro* chemical measures (dos Santos Lima *et al.,* 2022). New research connects frequent or prescribed intake of these articles with alterations in inflammatory pathways which results in NF-κB signal restraint along with cytokine suppressing effects. Grape pomace extract (GPE) demonstrates robust anti-inflammatory action through its direct inhibition of NF-κB signaling combined with cytokine suppression especially targeting IL-6 and MCP-1. Studies indicate that GPE exhibits therapeutic potential against bowel inflammation because it dramatically lowers inflammatory actions in intestinal epithelial and endothelial cells (Calabriso *et al.,* 2022). Research indicated that processed grape waste reduces intestinal inflammation and blocks NF-κB pathway activation to help prevent colorectal cancer developing alongside inflammatory bowel illness (Abi Rached, 2025).

Secondary metabolites derived from food waste such as grape skin resveratrol and turmeric peel curcumin have experienced thorough research for both anti-inflammatory capabilities and anti-cancer properties. Secondary metabolites from food waste serve as therapeutic agents for cancer and chronic inflammatory conditions by promoting apoptosis of cancer cells as well as blocking inflammatory pathway activation (NF-κB, COX-2) (Sharma *et al.,* 2022). Scientific studies validate that chemical substances from waste materials possess effective antiviral and antibacterial properties. The antibacterial qualities of bacteria such as *Escherichia coli* and *Staphylococcus aureus* are reached by potent fluoroids and limonene found in citrus peel extracts. Garlic and onion peel waste provides two valuable compounds namely allicin and quercetin which demonstrate effectiveness in fighting both antibiotic-resistant bacteria and viral infections (El Mashad *et al.,* 2019). Bioactive substances can be included in nanocarriers when developing targeted drug delivery systems. Medical research demonstrates the use of fruit waste-derived flavonoids within liposomes or nanoparticles to boost drug availability and achieve target-specific release during cancer treatments (Saini *et al.,* 2024).

Aloe vera leaf extracts combined with banana peel and mango skin extracts resulted in the development of ointments and gels which bring antibacterial and tissue-regenerative properties together with anti-inflammatory benefits for wound healing. The combination of these ingredients helps wounds heal faster by reducing visible scars. The therapeutic effects of phytochemicals present in mangos (*Mangifera indica* L.) are proven to be potent. The main chemical components in mangos consist of polyphenols that contain three groups of compounds: flavonoids together with mangiferin and tannin as reported by Al-Naymi et al. (2024). Among all polyphenols in mangoes mangiferin stands out as the most abundant compound because it exhibits strong tissue defense properties alongside potent antibacterial capability against Gram-positive and Gram-negative bacteria. Food waste bioactives demonstrate usefulness in metabolic disease management such as diabetes and obesity because they contain the vitamins C and A found in mangiferin which fosters wound healing. The combination of citrus pulp with wheat and rice bran wastes plus dietary fibers and polyphenols affects both lipid profiles and glucose metabolism for possible diabetes management (Chauhan *et al.,* 2023).

Recent scientific research demonstrates that rice bran substances act as protective agents against metabolic disruptions and oxidative stress. The bioactive chemical compounds found in rice bran water extract from milling processes consist of γ-oryzanol in combination with vitamins E as tocotrienols and tocopherols along with phenolic compounds. Bioactive substances present in rice bran products show protective qualities against type 2 diabetes and vascular disease and cancer. Patients who consumed rice bran oil supplemented with γ-oryzanol showed lower levels of cholesterol and LDL-C in clinical tests. The data indicates that adding γ-oryzanol to rice bran oil can help decrease risk factors associated with cardiovascular disease. The antioxidant and anticancer properties emerge from various phenolic compounds and vitamin E which are present within rice bran (Tan et al., 2023). Scientific studies show that peptides derived from rice bran proteins work more effectively to control hypertension in human body systems. The research shows that angiotensin-converting enzyme (ACE) inhibition occurs with rice bran protein hydro lysates that have molecular weights below 3kDa (Piotrowicz et al., 2020).

The biologically active substances in wheat bran demonstrate multiple effects on the human body which include improved lipid control together with glucose regulation and cancer protection capabilities. Research findings provide backing to this potential. A clinical study established wheat bran supplements beneficial for type 2 diabetes patients by reducing both fasting blood sugar and serum cholesterol levels (Budhwar et al., 2020). Research confirms that wheat bran acts as a dependable shield against colon cancer development. The anticarcinogenic activation in colon cells results from butyrate microbial metabolites cooperating with alkylresorcinol C21 found in bran.

Scientific research examined the combined effect of alkylresorcinol (AR) C21, and butyrate on human colon cancer cell suppression. The results showed that C21 and butyrate together reduced the growth of human colon cancer cells. Further mechanistic studies revealed that cotreatment with C21 and butyrate significantly increased the expression of cytochrome C, the lipid-conjugated membrane-bound form of microtubule-associated protein 1A/1B-light chain 3 (LC3-II), cleaved poly (ADP-ribose) polymerase (PARP), cleaved caspase 3, p53 upregulated modulator of apoptosis (PUMA), and C/EBP homologous protein (CHOP). These findings suggest a link between the activation of apoptosis, autophagy, and ER stress pathways, and the dual anticancer effects of C21 and butyrate. In mice given human-like C21 doses, large intestine C21 concentrations ranged from 0.86 to 1.78 μmol/g, based on laboratory experiments, indicating that a wheat gluten (WG) wheat diet may produce these intracellular levels. These findings open new possibilities for cancer treatment and functional food development using wheat bran (Zhao et al., 2019).

6. Circular economy in green solvent extraction of bioactive compounds

Circular economy functions as a resource management system that minimizes waste through recycling methods which convert unused materials into usable components. Under the circular method companies design recycling and reuse solutions instead of continuing their standard practices of "take-make-dispose." The circular nature of plant waste benefits arises from its composition of peels alongside leaves and seeds. People typically discard plant leftovers that contain extractable bioactive compounds which should be made useful rather than discarded. Along with sustainability, the circular economy is becoming an effective plan for worldwide industries to respond to challenges and remain stable. Under plant waste conditions, circular economy frameworks use agri-food waste to produce valuable bioactive materials. It is significant that plant-based by-products have a high amount of phenolic acids, flavonoids, alkaloids, saponins and terpenoids. These molecules are useful in medicines, dietary, health fields and cosmetics (Mungwari *et al.,* 2024). Accomplishing circular economy principles guides us toward lower environmental impacts from plant waste operations while building sustainable outcomes and establishing economic benefits. Through the development of plant-derived residue value, society both tackles important ecological problems and supports economic transformation to more resource-efficient systems. The circular economy operates through methods which reduce waste production to extract materials better while maintaining product durability and sustainably drive economic activities (Romero-Hernández & Romero, 2018). Green solvent extraction is critical to promoting circular economy goals by employing green solvents and new technologies to extract valuable bioactive compounds from plant residues. Green technique is a less risky with respect to sustainable methodology against the use of conventional extraction methods relying immensely on volatile organic solvents dangerous to human life and environment harm. The extraction techniques use water as well as bio-based fluids and supercritical fluids which successfully extract compounds without creating environmental harm. Circular economy systems become sustainable through the integration of green solvent extraction because they transform waste elements into valuable products while minimizing dependence on original resources and maintaining environmental cleanliness. Developing environment-friendly solvents together with advanced extraction technology must become the top priority to enhance the principles of circular economy and achieve a progressive sustainable model. The successful implementation of circular economy extraction methods for bioactive compounds demands the reduction of both solvents and energy consumption in extraction procedures. These methods enhance operational efficiency and establish them as planning tools for waste management which helps achieve sustainability targets (Akinade *et al.,* 2020). Bioactive compound extraction approaches using multiple methods generate optimal combinations between sustainable natural product preservation and environmentally friendly methods. Multiple important extraction conditions like temperature, pressure and the solvent-to-solid ratio can reduce energy requirements yet enhance overall process performance. The combination of prevalent low-cost plant waste materials and energy-efficient extraction methods makes production procedures more cost-effective. A proper waste management solution contains organized operational methods to extract valuable assets from waste plant streams during collection phases and treatment operations. In a circular economy framework their joint application enables the efficient utilization of resources while minimizing environmental impact throughout high-value bioactive compound sustainable production (Obiuto *et al.,* 2024).

The marketplace need for sustainable technologies and health-promoting foods containing high levels of bioactive substances provides the main driving force for circular economy principles in plant waste valorization. People are now more conscious about food-related health and environmental impacts hence they increasingly seek sustainable products that support their health needs. Eco-friendly customers drive the food sector toward the adoption of circular economy principles. The new approach supports plant by-product utilization through innovative uses of extracts along with fresh peels and dehydrated materials and complete waste residues for maximizing resource availability. The transformation of plant waste into valuable marketable products helps reduce waste production while establishing a stronger sustainable food system. Bioactive compound extraction that integrates circular economy principles leads to enhanced sustainability and economic advantage for the food industry (Liu *et al.,* 2023). In recent time, high value nutraceuticals are being produced using bioactives obtained from citrus peel, tomato skins, pomegranate husks and seeds from tropical fruits. These support circular economy and also address issues such as crowded landfills, excess greenhouse gas emission and the shortage of natural resources (Fidelis et al., 2019). The circular economy produces functional and nutraceuticals products from plant waste materials to fulfill consumer needs for healthy sustainable foods. Customers are choosing functional and nutraceuticals food over traditional health foods because these products provide additional value beyond basic nutrition. Plant waste contains valuable bioactive compounds although these resources fail to achieve their maximum functional food and nutraceuticals development along with market innovation. The industry possesses the ability to maximize its economic potential and preserve the environment by adding value to plant waste materials that support consumer preferences. Sustainable food industry advancement through product development based on circular economy principles generates dual benefits of environmental sustainability and market competitiveness and innovation (Kover *et al.,* 2022).

7. Safety and regulatory aspects of extracts derived from waste

Food waste valorisation enables a circular bioeconomy and improves resource efficiency, offering a sustainable solution to the world's waste problems (Arvelli *et al.*, 2025). The recycling and upgrading of food waste and by-products in line with the European Bioeconomy Strategy and the EU Circular Economy Action Plan is of great interest these days (Beltr an-Medina *et al.*, 2020; Ribeiro *et al.*, 2020). Modified or newly created foodstuffs based on valorised products should also adhere to the EU's laws governing food safety for human consumption. This includes those aimed at animal feed (European Parliament & the Council of the EU, 2002) and those that are based on the production of non-toxic goods suitable for human consumption (European Parliament & Council, 2002).

Other considerations, such as product safety, influence the ultimate choice of methodology, yield of the technologies are crucial for the industrialization of recovery processes. These factors are crucial when it comes to developing technologies since they may be overly complex in relation to the yield boost. However, safety considerations primarily address the unknowable consequences of cutting-edge technologies rather than the established harm to customers. Conventional methods like concentration, centrifugation, or microfiltration are typically thought to be safe for the macroscopic pre-treatment stage since they have been widely used in several food industry sectors and are associated with matching materials (Galanakis, 2012).

Despite being authorized for use in food in many countries, synthetic bioactive chemicals are losing favour with consumers. As a result, there is growing interest in using natural bioactive molecules to replace these artificial ones. These organic substances can be employed as food additives to preserve food quality, safety, and appeal, or as nutraceuticals or food supplements to maintain appropriate nutrient intake, address nutritional deficiencies, or support physiological processes. From the time a bioactive compound's potentialities are demonstrated until it reaches the end user, it may have to overcome toxicity and safety issues along the way to be valued (Vilas-Boas *et al.*, 2021). According to Mateos-Aparicio and Matias (2019), food losses and waste (FLW) are an excellent source of bioactive compounds, including phenolic compounds, flavonoids, anthocyanins or carotenoids, pectin, dietary fiber, proteins, and enzymes. Food by-products include significant actions like antioxidants, anti-inflammatory, anti-proliferative, antidiabetic, as well as antibacterial and antiviral properties, because of this abundance in various bioactive compounds. Biological instability, possible pathogenic contaminations, high water activity, the possibility of rapid auto-oxidation, and high levels of active enzymes are some of the issues that can compromise product safety when using those compounds recovered from food wastes (Devkota *et al.*, 2017).

The quality of the finished product may be harmed by some of the methods (heat treatment or ionising radiation) used to get rid of bacterial contamination and manage mycotoxins. Monitoring and preventing contaminations at an earlier stage of processing or at the raw material itself, avoiding their entry into the food processing system, are some examples of mitigation measures that can be taken (Lai *et al.*, 2017). The prevention of fungal growth and mycotoxin formation is the most efficient method of controlling the presence of mycotoxins and ensuring the safety of food supplements. According to Lai *et al.* (2017), they require the implementation of good agricultural practices (GAP) in the field, such as managing harvesting and storage conditions enhanced by technological innovations like controlled atmospheres and managing other physical techniques like cleaning, milling, etc. According to Cinar & Onbaşı, 2020, the use of HACCP is a successful technique for the prevention, control, and periodic monitoring of mycotoxin at every stage, from the field to the consumer.

8. Policy and regulatory frameworks

The government needs to develop essential policies and regulations that drive circular economy practice development in bioactive compound extraction from plant residues. The adoption of environmentally responsible extraction methods like using green solvents by industry sectors become more likely through strategic monetary incentives such as tax credits or subsidies and grants. Systemic reform can be induced by implementing policies that ban conventional extraction techniques which harm the environment. When governments promote enabling policies, they help develop sustainable extraction practices by building equal innovation conditions which reduce environmental pressures together with fostering industrial adoption across the board

(Aït-Kaddour *et al.,* 2024). They can also lead to new jobs in the green economy, encourage creative ideas in the community and help everyone in society. When public and private stakeholders make it known how many benefits the circular economy provides, it encourages everyone to come together and agree on circular economy policies. The development of global norms in conjunction with worldwide collaboration enables the speeding up of the application of circular economy measures together with environmentally friendly extraction and processing technologies globally. Information and technology sharing as well as best practices enable regulatory frameworks to harmonize and makes the implementation standardized across various geographic boundaries. The clear demonstration of circular economy advantages which generate social benefits together with environmental benefits accelerates the implementation process. The initiatives will simultaneously create green employment opportunities and promote equal opportunities for society. Explicit statements of these advantages by stakeholders will propel their collective movement towards sustainable and equitable global circular economy development (Jimenez-Lopez et al., 2020). Moreover, important infrastructure projects supported by the government, as well as public-private partnerships, can aid in increasing the scale of green technology used to extract minerals. As an example, launching national research centers focused on green biological systems and biorefinery may help promote the growth of new ideas and rules (Lim & Rashidi, 2023). The adoption of strict benchmarks and standards for bioactive green extracts by manufacturers motivates them to use sustainable methods and compete effectively in the market. Consideration of LCA (life cycle assessment) and TEA (techno-economic analysis) during policy making ensures that issues of the environment and economy are always included in reviewing and selecting new extraction methods (Vettorazzi *et al.,* 2020).

9. Challenges and future perspective

Green solvent extraction and eco-friendly novel techniques face challenges such as scalability, solvent recovery, and high initial costs that limit industrial adoption. Optimization of process parameters and solvent recyclability remains crucial for efficiency and sustainability. Future research should focus on integrating green solvents with advanced technologies like ultrasound, microwave, and supercritical fluids. Developing multifunctional, cost-effective systems can revolutionize large-scale recovery of bioactives from plant waste toward a circular bioeconomy. The focus on sustainable development and circular bioeconomy has led to increased research in green solvent extraction and eco-friendly technologies for plant waste. Despite significant advances, numerous technical, environmental, economic, and regulatory restrictions remain.

9.1. Challenges

The high capital cost, scalability, selecting an effective solvent, proper framework of eco-friendly extraction units and green solvent procurement remain recurring challenges. System-level evaluations need to be conducted to establish practical implementation of green extraction techniques, which should focus on industrial-scale circular economy models.

9.1.1. Difficult to select an effective solvent

Green solvents such as supercritical CO_2, ionic liquids (ILs), and natural deep eutectic solvents (NADES) form the foundation of environmentally friendly solutions extraction. However, it remains challenging to find a solvent that is both effective at extracting compounds and safe for the environment. In particular, NADES offer adjustable polarity and biocompatibility, but their high viscosity often restricts mass transfer and limits large-scale production (Ristivojévic *et al.,* 2024; Panzella *et al.,* 2020). Furthermore, the efficacy of these solvents differs greatly depending on the target phytochemicals (flavonoids, alkaloids, phenolics, etc.) and the plant matrix. This requires case-specific optimization, which is resource-intensive and restricts the widespread adoption of standardized practices.

9.1.2. Scalability of green extraction methods

Several green extraction methods, including ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and pressurized liquid extraction (PLE), demonstrate promise in laboratory settings scale. However, scalability remains a significant challenge. The use of these technologies often requires customization to accommodate the complex feedstock compositions of plant waste, as well as variable particle sizes and moisture content (Usman *et al.,* 2023). Furthermore, heat sensitive chemicals can degrade during thermal processing, and it is technically challenging to maintain consistent energy distribution at industrial levels. This leads to inconsistent product quality and reduced extraction efficiency.

9.1.3. High capital cost

The high capital cost of eco-friendly extraction units and green solvent procurement remains a recurring challenge. While green technologies offer long-term cost benefits through waste minimization and product diversification, their initial financial stability may be limited, particularly for small and medium-sized businesses. Market uncertainties and the lack of strong financial incentives limit the switch from traditional to sustainable methods (Yadav *et al.,* 2024). Additionally, business models that build a circular economy need to establish processes for waste production, resource retrieval, and product recycling within value networks. This research field lacks adequate funding and has minimal exploration.

9.1.4. Lack of proper regulatory frameworks

Green solvents and innovative extraction procedures lack a proper regulatory network that restricts standardization and safety approval. The European Food Safety Authority (EFSA) as well as Food and Drug administration (FDA), alongside other regulatory agencies, lack established standards for validating new solvent residues, process verification, and waste-derived phytochemical extract limits. The lack of standardized regulatory frameworks prevents their use in functional food as well as nutraceutical and cosmetic industries (Roselli *et al.,* 2024). The adaptation of Life Cycle Assessment (LCA) and Techno-economic Assessment (TEA) approaches for green extractions remain in its early stages of advancement. The lack of standardization comparison frameworks of new technologies and solvent restricts industrial adoption and regulatory approvals.

9.2. Future perspective

Plant waste consists of various substrates that differ in cellulose, hemicellulose, lignin content, and bioactive phytochemical concentrations. This natural variability of plant waste material leads to variations in yield and purity regardless of similar processing conditions. Different pretreatment methods involving drying and grinding and storage affect chemical stability while altering solvent penetration (Ivanović *et al.,* 2020).

9.2.1. Development of robust extraction methods

The development of robust extraction methods that manage diverse variations of feedstock with a high extraction yield while using minimal energy and solvents. The implementation of extraction methods with green sustainability characteristics remains under development within existing circular bioeconomy models. Few research studies investigate the contribution of these processes to reduce greenhouse gas (GHG) emissions and enhance resource circularity and nutrient cycling. System-level evaluations need to be conducted for establishing practical implementation of green extraction techniques, which should focus on industrial-scale circular economy models (Amran *et al.,* 2021).

9.2.2. Sustainability

The growing interest in environmental protection and sustainability makes green solvent extraction and eco-innovative technologies for recovering bioactive chemicals from plant waste more appealing for the future. The future economy requires the scientific development of green extraction technologies, which must integrate with circular economy designs and biorefinery infrastructure at the global sustainability goals.

9.2.3. Extraction rate enhancement

Development to enhance extraction rates, reaction specificity, and environmental performance will depend on green solvents, such as low-viscosity NADES, ionic liquids (ILs), and bio-derived solvents. The combination of COSMO-RS (Conductor-like Screening Model for Realistic Solvation) computational modeling with molecular dynamics simulations proves useful for predicting solute-solvent interactions while reducing experimental time (Ristivojević *et al.,* 2024). The future investigation will examine the use of solvent-free extraction methods like enzyme-assisted extraction and pulsed electric field as alternative procedures removing the need for chemical additives.

9.2.4. Artificial intelligence

Artificial intelligence (AI), together with machine learning and sensor-based automation, will make it possible to perform real-time monitoring and optimization of eco-extraction processes. The systems will use an automated approach to control factors such as solvent concentration, duration, temperature, and pH to ensure yield consistency and quality of extract from various waste materials. The adoption of "smart biorefineries" shows strong potential for becoming widespread in future operations (Usman *et al.,* 2023).

9.2.5. Zero-waste initiatives

Future extraction techniques will integrate cascade extraction models to recover various bioactive compounds (polyphenols, dietary fibers, and essential oils) from a single waste matrix. The method enhances resource preservation and meets the standards of zero-waste initiatives. Food, pharmaceutical companies, cosmetic manufacturers, and bioenergy industries will benefit from this approach through considerable opportunities for co-product development (Yadav *et al.,* 2024).

The adoption of green extraction technologies depends heavily on regulatory frameworks establishing sustainability goals, circularity rules, and biowaste recycling principles. Worldwide collaboration of academic, industrial, and governmental bodies is essential to establish safety regulations, green product identification practices, and lifecycle assessment systems (Roselli *et al.,* 2024).

9.2.6. Lowering landfill burden

Green extraction technologies play an essential part in the development of the bio-circular-green (BCG) economic model. The idea focuses on sustainable recycling of biomass resources while decreasing environmental effects and creating valuable products from waste materials. Green extraction acts as a main component to transform agri-food waste into functional compounds while benefiting local economies and lowering landfill burden (Amran *et al.,* 2021).

10. Conclusion

The review emphasizes the crucial importance of green solvent extraction and eco-friendly methods in the sustainable recovery of bioactive compounds from plant residues. The bio-residues, which contain high levels of secondary metabolites such as polyphenols, flavonoids, alkaloids, and terpenes, represent a rich yet underexploited resource for nutraceuticals and pharmaceuticals. However, green methods, including UAE, MAE, and SCF, which are more modern, represent environmentally friendly alternatives that follow green chemistry and circular economy principles. Technologies can improves extraction yield, preserves compound integrity, lowers operational expenditure, and reduces solvent dependence.

Additionally, innovation in solvents, such as use of NADES or natural product-derived solvents, is facing challenges related to viscosity, efficiency in mass transfer, and in phytochemical selectivity. To fully realize the potential of green extraction in a circular bioeconomy, future research should focus on solvent design, process optimization using artificial intelligence-based technologies, and integration into existing biorefinery infrastructure. Ultimately, transitioning towards a future of sustainable production of bioactive compounds from plant waste requires collaboration among academia, industries, and policy-making systems to create robust, cost-efficient, and environmentally friendly extraction systems.

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CRediT authorship contribution statement

Muhammad Shahbaz: Writing – review & editing, Writing – original draft, Visualization. **Mahreen Riaz:** Writing – review & editing, Validation, Data curation. **Ushna Momal:** Writing – review & editing, Writing – original draft, Validation. **Izza Faiz Ul Rasool:** Writing – review & editing, Writing – original draft, Validation, Software, Data curation. **Hammad Naeem:** Writing – review & editing, Writing – original draft. **Nighat Raza:** Writing – review & editing, Writing – original draft. **Andres Moreno:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Data curation. **Waseem Khalid:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Resources, Investigation, Data curation, Conceptualization. **Tuba Esatbeyoglu:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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No data was used for the research described in the article.

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Ecological regulation for healthy and sustainable food systems: responding to the global rise of ultra-processed foods

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Abstract
Many are calling for transformative food systems changes to promote population and planetary health. Yet there is a lack of research that considers whether current food policy frameworks and regulatory approaches are suited to tackle whole of food systems challenges. One such challenge is responding to the rise of ultra-processed foods (UPF) in human diets, and the related harms to population and planetary health. This paper presents a narrative review and synthesis of academic articles and international reports to critically examine whether current food policy frameworks and regulatory approaches are sufficiently equipped to drive the transformative food systems changes needed to halt the rise of UPFs, reduce consumption and minimise harm. We draw on systems science approaches to conceptualise the UPF problem as an emergent property of complex adaptive food systems shaped by capitalist values and logics. Our findings reveal that current food policy frameworks often adjust or reform isolated aspects of food systems (e.g., prices, labels, food composition), but under-emphasise the deeper paradigms, goals and structures that underlie the rise of UPFs as a systems phenomenon, and its socio-ecological implications. We propose that a 'leverage points' framework illuminates *where* to intervene in food systems to generate multi-level changes, while the theory of ecological regulation highlights *how* to respond to complex multi-factorial problems, like the rise of UPFs, in diverse ways that respect planetary boundaries. More research is needed to better understand the transformative potential of ecological regulation to advance food systems transformation and attenuate whole of food systems challenges.

Keywords Ultra-processed foods · Food systems · Complex adaptive systems · Leverage points · Food policy · Food regulation

Abbreviations

FAO	Food and Agriculture Organization of the United Nations
HLPE	High Level Panel of Experts on Food Security and Nutrition
ILF	Intervention Level Framework
NCDs	Non-communicable diseases
SSB	Sugar-sweetened beverages
UPFs	Ultra-processed foods
WHO	World Health Organization

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Introduction

Today's food systems are contributing to multiple, intersecting health and ecological crises (Development Initiatives 2021; Swinburn et al. 2019). Malnutrition in all its forms – including childhood stunting and wasting, micronutrient deficiencies, overweight and obesity, and diet-related non-communicable diseases (NCDs) – affects billions of people, and unhealthy diets are the leading contributor to the global burden of disease (FAO et al. 2021; Murray et al. 2020; Willett et al. 2019). Global food system practices are driving biodiversity losses and greenhouse gas emissions (Benton et al. 2021; Leite et al. 2022; Tubiello et al. 2021), contributing to climate change and threatening population nutrition and food security (HLPE 2020; Myers et al. 2017). Recognising these challenges, many authoritative international bodies, including the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO), and independent expert groups, are calling for food systems transformations to promote health and sustainability (FAO 2018; HLPE 2017; Swinburn et al. 2019; WHO and FAO 2018; Willett et al. 2019).

Governments play a vital role in the response to food systems challenges, including through developing policy, legislation and various forms of regulation to facilitate good governance and effective interventions (HLPE 2020; Willett et al. 2019). While food and nutrition policy frameworks (from hereon 'food policy frameworks') exist to inform policy actions (Diaz-Bonilla et al. 2020), there is a lack of research that considers whether these frameworks are equipped to drive the system-wide changes needed to address today's food systems challenges (Lee et al. 2020). There is also insufficient scrutiny of current regulatory approaches to see if they are up to the task of food systems transformation, or preference incremental modifications and reforms that may generate some change but do not disrupt the status quo (Lawrence et al. 2015). Given the role of today's food systems in current health and ecological crises, some propose that food policy and regulation must focus on truly transforming the orientation of food systems as a whole, rather than making incremental or reformative adjustments to minor system parameters (Lawrence et al. 2015; Parker et al. 2018; Slater et al. 2022; Webb et al. 2020).

The rise of ultra-processed foods (UPFs) in human diets is an illustrative example of a major current food systems challenge, requiring a "unified and impactful" policy response (Popkin et al. 2021, p. 462). The term 'UPF' is derived from the NOVA food classification system introduced in 2009 (Monteiro 2009), defined as "formulations of ingredients, mostly of exclusive industrial use, that result from a series of industrial processes (hence 'ultra-processed')" (Monteiro et al. 2019b). UPFs include many different food products: for example, carbonated soft drinks; confectionery; mass-produced packaged bread, pastries, biscuits and cakes; sweetened breakfast cereals; ready-to-eat shelf-stable or frozen meals; chicken and fish 'nuggets' and 'sticks'; packaged 'instant' noodles, soups and desserts; and margarines and other spreads (Monteiro et al. 2019a). They typically contain little, if any, whole foods, and are manufactured using ingredients rarely found in kitchens, including cosmetic additives like flavourings, colourings and thickeners designed to enhance the product's sensory properties (Monteiro et al. 2018). UPFs now dominate the food supply of high-income countries, such as the USA, Canada, the UK and Australia, and are rising rapidly in many highly-populated middle-income countries in all regions (Baker et al. 2020; Monteiro et al. 2019a; Popkin and Ng 2022).

The rise of UPFs in human diets raises serious concern for global health, given dietary exposure to UPFs associates with poor diet quality and multiple adverse health outcomes, including obesity, type-2 diabetes, cardiovascular disease, depression, all-cause mortality and potentially cancer (Askari et al. 2020; Chen et al. 2020; Elizabeth et al. 2020; Lane et al. 2021; Meneguelli et al. 2020). These outcomes can be explained not only by the unbalanced nutrient profile of UPFs and the dietary displacement of minimally processed foods, but also by the novel physical and chemical properties that result from industrial processing. Proposed mechanisms include, for example, higher glycaemic load and reduced gut-brain satiety signalling linked with food matrix degradation, inflammation resulting from food additives and gut microflora dysbiosis, and endocrine disruption from chemical plasticisers used in packaging (Baker et al. 2020; Fardet and Rock 2019; Kliemann et al. 2022; Zinöcker and Lindseth 2018). Commercial supply chains provisioning UPFs also generate significant environmental harms (da Silva et al. 2021; Fardet and Rock 2020; Hadjikakou and Baker 2019; Seferidi et al. 2020). Among high-income countries, these include an estimated 36–45% of diet-related biodiversity loss, up to one-quarter of total diet-related water-use, and up to one-third of diet-related greenhouse gas emissions, land use and food waste (Anastasiou et al. 2022; Hadjikakou 2017). Such impacts are especially remarkable considering that UPFs are unsuitable for healthy diets and superfluous to human need.

The rise of UPFs in human diets reflects major transformations in food systems, which have accelerated in recent decades, although with wide variations between regions, countries and contexts (Baker et al. 2020). Agricultural industrialisation has enabled the production of cheap commodity ingredients for global supply chains, rapid urbanisation and income growth in middle-income countries has created new markets of aspirational consumers, and the globalisation of transnational food corporations – including their supply chains, marketing practices and corporate political activities – have acted as vectors for the spread of UPFs between and within countries (Baker et al. 2020; HLPE 2017; Monteiro and Cannon 2012; Moodie et al. 2021; Swinburn et al. 2019). The complex, global-scale and multi-layered nature of such 'ultra-processed food systems', calls for food policy frameworks and regulatory approaches that can drive the whole of food systems changes needed to halt the rise of UPFs, reduce consumption and minimise harm. At the same time, there is no single, uniform 'global food system', but a diversity of food systems types across regional, national and local levels, cultures and contexts, suggesting the need for adaptive and responsive policy action (Fanzo and Davis 2021).

Systems science approaches are useful in understanding the interrelated drivers of complex systems problems

(Carey et al. 2015; Meadows and Wright 2009). The systems science concept of 'leverage points' can help identify the places to intervene in a system based on the potential impact for systems transformation (Abson et al. 2017; Fischer and Riechers 2019; Meadows 1999). Expert reports have called for innovative approaches and holistic models, such as diversified agroecological systems, to guide transitions across food systems that provide alternatives to the dominant practices, rules, institutions, structures and paradigms of industrial agriculture, and contribute to food systems transformation (HLPE 2019; IPES-Food 2016). While current food policy frameworks present various policy options related to different aspects of food systems, it is unclear whether they are up to the task of generating whole of food systems change. Some have suggested that a current influential food policy framework, the NOURISHING framework, could be expanded to include more policy actions in key areas related to food systems, such as environmental sustainability, governance mechanisms, and comprehensive food and nutrition monitoring and surveillance systems (Lee et al. 2020). However, few studies have turned to the systems science literature to consider whether current food policy frameworks are sufficiently equipped to generate truly transformative food systems change.

From a regulatory standpoint, the dominant 'instrumental' approach to regulation tends to use isolated regulatory tools to respond to one specific harm or risk at a time, rather than coordinated strategies to tackle cumulative harms to human and planetary health (Parker and Haines 2018). Noting the limitations of current regulatory approaches, Parker and Haines (2018) have proposed an ecological approach to regulation to address challenges that cut across many regulatory domains. Ecological regulation emphasises the need for a diverse range of interacting regulatory strategies that work together, like a natural ecosystem, to respond to multi-dimensional and interconnected problems in ways that respect planetary boundaries. While some have examined the regulatory studies literature to determine what forms of regulation may work best for public health problems (Magnusson and Reeve 2014; Voon et al. 2014), there is limited research that directly considers the regulatory approaches best suited to addressing the many factors that drive the rise of UPFs in human diets (Parker et al. 2018; Parker and Johnson 2019).

This review aims to critically examine whether current food policy frameworks and regulatory approaches are equipped to drive the transformative food systems changes needed to halt the rise, reduce consumption and minimise the harms of UPFs. This review has three objectives: first, to characterise the nature of the UPF problem by reviewing the literature that considers the rise of UPFs as a food systems phenomena; second, to review existing food policy frameworks and ascertain whether the recommended policy actions can adequately address the whole of food systems determinants of the UPF problem; and third, to examine the potential combination of systems science concepts and regulatory approaches to best inform future responses to the UPF problem.

Methods

Given the complexity of the topic and the need to draw from diverse literature sources and disciplines, we adopted a narrative review and synthesis method (Grant and Booth 2009; Green et al. 2006). This involved three steps: first, a semi-systematic search for academic and grey literature; second, analysis of included literature; and third, synthesis of the results.

Search process

In consultation with an academic librarian, we developed search strings based on the main concepts in the objectives of the review: ultra-processed foods and food systems, food policy frameworks, and systems science concepts and regulatory approaches (Table 1). We used the EBSCOHost research platform to search six selected academic databases from relevant fields (Academic Search Complete, Health Policy Reference Center, Legal Source, MEDLINE Complete, Political Science Complete, SocINDEX with Full Text). We also searched the websites of global public health

Table 1 Search categories and search strings used in the review

Search categories	Search strings
Ultra-processed foods and food systems	"Ultraprocessed food*" OR "ultra-processed food*" OR "ultra processed food*" OR "processed food*" OR "packaged food*" OR "food system*"
	AND
Systems concepts	"Systems science" OR "systems approach*" OR "systems thinking" OR "leverage points" OR lever OR ecolog* OR holistic OR multisector OR multi-sector
	AND
Policy frameworks and regulatory approaches	Policy OR policies OR regulat* OR legislat* OR law OR legal OR rule* OR intervention* OR framework*

nutrition bodies, such as the WHO, the FAO, the Pan American Health Organization (PAHO) and the International Panel of Experts on Sustainable Food Systems (IPES-Food), to obtain relevant documents. To supplement the structured searches, we hand-searched the reference lists of key articles to locate other relevant sources and conducted additional searches to consider emerging lines of enquiry.

Documents were included if published in English between 2000 and 2021 in a peer-reviewed journal or by an international organisation mandated to address nutrition, and outlined a food policy framework or regulatory approach relevant to public health nutrition at the global or national level. We limited the dates of search results to between 2000 and 2021 as initial preliminary searches revealed that most relevant publications were published from 2000 onwards. Given the broad scope of this review, we excluded documents that focused narrowly on interventions targeting specific settings, like schools, hospitals, workplaces, or individual behaviour change. To develop a feasible and relevant inclusion criteria, our search process excluded various other documents, such as sources in languages other than English, broader books on food policy or food systems, or reports from civil society organisations, social movements or global corporate organisations. This limits the scope of the analysis and conclusions presented in the review to the range of documents considered.

For the purposes of the second objective of the review, we limited our analysis to food policy frameworks that identify policy actions to address public health nutrition issues relevant to food systems and the UPF problem. Food policy frameworks were included if they presented clear policy options related to multiple policy areas at the national level, applicable to different countries and contexts. We excluded country-specific food policy frameworks, such as the FOOD-PRICE framework in the USA (Gerald J. and Dorothy R. Friedman School of Nutrition Science and Policy at Tufts University 2019), or frameworks focused on a particular policy area or issue, like the WHO framework for implementing the recommendations on the marketing of foods and non-alcoholic beverages to children (2012). We also excluded reports that contained high-level policy guidance and broad recommendations on food systems approaches, or decision-making tools to assist policymakers to implement policy actions under policy frameworks (Fanzo et al. 2020; Global Panel on Agriculture and Food Systems for Nutrition 2021).

Analysis and synthesis

Full documents were obtained from the relevant academic databases and stored electronically. Each document was reviewed by the lead author to identify and code themes relevant to the aim and three objectives of this review. We conducted an iterative process of constant comparative analysis to organise the qualitative data, uncover nuances in the literature and code sub-themes as the themes evolved. This involved developing, integrating and adding to the coded themes and sub-themes over a number of iterations of coding the documents (Corbin and Strauss 2008). Given the large number of sources included and the complexity of the topic, we did not use multiple-coders nor assess coder reliability. The results were synthesised to present a textual account of the findings that emerged from the literature and interpreted to report on key points for discussion.

Results

The included literature spans multiple disciplines and fields, including public health, food policy, systems science and regulatory studies. In the results section below, we present a synthesis of the main findings, organised by the three objectives of the review.

The whole of food systems determinants of the global rise of UPFs

In this section, which addresses the first objective of the review, we outline a whole of food systems approach to the global rise of UPFs and the nature of the policy and regulatory challenge. We consider the components and drivers of the UPF problem to understand the policy issues and determine possible places for regulation to intervene in food systems, in order to generate transformative change.

Food systems are complex adaptive systems

The broad term ‘food systems’ encapsulates the variety of food systems that exist in different regions and contexts worldwide (Fanzo and Davis 2021). The High Level Panel of Experts on Food Security and Nutrition (HLPE) identifies three core components of food systems: ‘food supply chains’, which consist of the various actors and activities that take food from its production to consumption and disposal of waste; ‘food environments’, referring to the broader context in which people interact with the food system and make food choices; and ‘consumer behaviour’, which reflects people’s decisions about the foods they acquire, prepare and eat (HLPE 2017). The HLPE also describes a range of drivers of food systems: for example, political and economic drivers, like globalisation and trade; or demographic drivers, such as population growth and urbanisation (HLPE 2017). Combined, the components and drivers of food systems make up the ‘whole of food systems determinants’ (discussed below) of human diets, that influence nutrition and health outcomes, and impact the economy, society and the environment (FAO 2018; HLPE 2017; Ingram 2011; WHO and FAO 2018).

The components and drivers of food systems do not operate in isolation, but intersect to produce the system's behaviours, properties and outcomes (IPES-Food, 2015). In this respect, food systems are 'complex adaptive systems' that are dynamic, non-linear and contain interdependent elements (Ericksen 2008; Guptill and Peine 2021; Hammond and Dubé 2012; Hill 2011; Leeuwis et al. 2021). Complex adaptive systems have common features, such as feedback loops that deliver information about the outcome of an action back to the source, and time delays in the availability of information about the state of the system relative to the rate of change. They also display 'emergent properties', phenomena that form in the system as a result of dynamic interactions within the system, and not just the sum of its separate parts. Such emergence may be desired or undesired, intentional or unintentional, depending on the perspectives and interests of different food systems stakeholders. Others have described various food systems phenomena as emergent, including obesity (Hammond 2009; Nobles et al. 2021; Swinburn et al. 2019), NCDs (Knai et al. 2018), dietary inequities (Sawyer et al. 2021), and broader phenomena like malnutrition, environmental harms, food insecurity and poverty (Leeuwis et al. 2021).

Food systems, are also 'adaptive' in that a change in one part of the system can affect other parts of the system (Hammond 2009; Hill 2011; Swinburn et al. 2019). This creates challenges for policymakers and regulators because a particular policy or regulatory measure may have broader effects that counteract the regulator's intention, even if the outcome may be desirable from the perspective of other actors in the system, such as commercial actors (Hammond and Dubé 2012; Nobles et al. 2021). For example, policies to regulate artificial trans-fats in some countries have in part precipitated the rise of palm oils, another cheap and versatile UPF ingredient that can harm human and planetary health (Freudenberg 2021). Similarly, policy actions that seek to reduce added sugar consumption may lead to the increased use of non-nutritive sweeteners in UPFs, a substitution that on its own does little to shift the quality of the food supply or promote healthy dietary patterns (Russell et al. 2022). Food systems also intersect with other systems; for example, food standards to protect public health and safety relate to both the food system and the health system (Fanzo and Davis 2021; FAO 2018). This can mean that policy actions in other systems may have ripple effects on food systems. For example, a policy to promote more biofuel in the energy system will also impact food systems due to the need for crops, seen in the strong demand for agricultural inputs to produce biofuel that in part contributed to the global food price crisis of 2007–2008 (FAO 2009, 2018).

The global rise of UPFs as a systems phenomenon

We build on the literature presented above to conceptualise the global rise of UPFs in human diets as an emergent property of today's unhealthy and unsustainable food systems. While the complexity and diversity of food systems cannot be fully captured by general categories, experts have developed various food systems 'typologies' to illustrate shared characteristics at the country level, highlight patterns in outcomes and guide policy action (Fanzo et al. 2020; HLPE 2017; Nugent et al. 2015). For example, one typology demonstrates that different types of food systems associate with different levels of UPF consumption, and indicates that UPFs are most abundant in 'industrial food systems' in urbanised countries, yet the rate of the rise in UPF consumption is most rapid in countries that have transitioning and rural food systems (Nugent et al. 2015). There are also other terms used to differentiate food systems from dominant capitalist-industrial models, such as 'alternative food system' approaches, movements and practices that arise from concepts of social justice and equality and draw on local and indigenous forms of knowledge (Baker et al. 2021).

Changes in national economies and population demographics are linked to various factors that drive UPF consumption (Béné et al. 2020; Ingram 2011; Popkin 2001, 2006). As economies grow, associated rises in per capita income tend to lead to increased expenditure on food, particularly ultra-processed relative to minimally processed foods, and also on items that facilitate UPF consumption, like microwaves and refrigerators (Baker et al. 2020; HLPE 2017). Urbanisation also influences UPF consumption, as it increases access to major supermarket chains and exposure to mass media channels promoting UPF products (Baker and Friel 2016). Lifestyle and employment changes in urbanised societies, such as the shift to dual-worker households, also enable UPF manufacturers and retailers to capitalise on the convenience of UPFs that ease the time and skills demands of sourcing food and preparing meals (Béné et al. 2020). These factors can also displace freshly prepared meals and traditional foods in the diet and undermine food cultures (Juul and Hemmingsson 2015; Monteiro et al. 2011; Moubarac et al. 2014; PAHO 2015).

The global integration of food supply chains further supports the expansion of UPF markets (Baker et al. 2020; Popkin 2001, 2006; Qaim 2017). Dominant industrial productivist agricultural policies and practices facilitate increased and efficient production on a large-scale for maximum profit (Gordon et al. 2022; Parker and Johnson 2019). For example, food production policies such as agricultural subsidies and export measures can incentivise the mass, often surplus, production of commodity ingredients used in UPF manufacturing, like maize, soy and wheat, at low cost (IPES-Food, 2016; Schiavo et al. 2021; Swinburn et al. 2019). These commodity crops comprise the basic inputs for the production of industrial ingredients, such as high fructose corn syrup or soy protein isolate, predominantly used to manufacture an array of UPF products (Béné et al. 2020; Lock et al. 2009). Global food distribution networks are ideally suited to facilitate the transport of non-perishable food products, such as UPFs, over vast distances (Monteiro et al. 2013, 2019a; Moodie et al. 2021). Food retailers, particularly transnational grocery chains and regional supermarket oligopolies, also influence UPF sales and consumption, in part due to marketing techniques such as price discounts, promotions and product placement in prominent locations, like the end of the aisle or near the checkout, that suit shelf-stable and branded UPF items (Baker et al. 2020; Hawkes 2008; Machado et al. 2017).

Political and economic forces also drive the rise of UPFs. Trade and investment liberalisation has supported the global expansion of transnational UPF corporations into new markets, mainly through the acquisition of domestic competitors and the establishment of new production facilities and distribution networks (Baker et al. 2014, 2020; Hawkes 2005). Large transnational UPF corporations hold substantial material power in the form of assets and monetary resources, which can be used to support corporate political activities to delay or defeat proposed regulations that compromise their commercial interests (Baker et al. 2018; Clapp and Scrinis 2017; Moodie et al. 2013; Swinburn and Wood 2013; Wood et al. 2021). This includes, for example, lobbying politicians, establishing front groups, making political donations, self-regulation to avert government intervention, and public relations campaigns that present the UPF industry as 'part of the solution' (IPES-Food 2017; Lacy-Nichols and Williams 2021; Lauber et al. 2020; Mialon et al. 2020a; Mialon et al. 2020b).

The rise of UPFs is also linked to the rising power of financial actors within food systems, and an increasingly liberal global financial regime that features a rapid increase in marketised securities and greater monetary exchange freedoms (Clapp 2019; Hawkes 2010). This 'financialisation' provides UPF corporations with greater access to capital for ongoing expansion, helps to offset risks associated with sourcing large volumes of commodity ingredients on volatile global markets, and encourages more aggressive modes of profit-seeking to generate shareholder returns (Baker et al. 2020; Clapp 2019). The rising power of transnational corporations in a globalised economy can also feed the UPF problem, when governments provide tax or regulatory concessions to corporations in response to the implied or real threat of relocating jobs and investment (Baker et al. 2014). Similarly, trade liberalisation under rules governing international trade, investment and property rights can limit the capacity or desire of governments to regulate UPF corporations due to fear of a costly trade dispute or formal sanctions, sometimes called 'regulatory chill' (Friel et al. 2020; Hawkes 2010; Reeve and Gostin 2019).

Current nutrition policies and regulations reflect the material and ideological systems that permeate broader society. Global industrialised food systems are shaped by prevailing neo-liberal capitalist systems that organise political and economic activity in pursuit of capital accumulation and prioritise economic growth, market competition and individual responsibility (Baker et al. 2021; Lencucha and Thow 2019; Rose 2021; Schram and Goldman 2020). This dominant ideology supports voluntary industry self-regulation, such as food industry pledges on responsible marketing to children, and influences political preferences for market-oriented and multi-stakeholder hybrid governance approaches, including public-private partnerships (Cullerton et al. 2016; Lawrence et al. 2019; Russell et al. 2020; Shill et al. 2012). The presence of the UPF industry in food policy and governance often leads to an emphasis on nutrient-based responses, like reformulation, that diverts attention from the commercial determinants of unhealthy diets, such as UPF availability and intensive marketing (Clapp and Scrinis 2017; Ngqangashe et al. 2021a). Instead, many national nutrition policy actions focus on providing information to influence individual lifestyle-behaviour change, like nutrition labelling and education campaigns (Capacci et al. 2012; I et al. 2020; Lee et al. 2020; Mason-D'Croz et al. 2019; Mazzocchi 2017; Mozaffarian et al. 2018; WHO 2018a).

In the last decade, more countries, particularly in Latin America, have taken steps to regulate unhealthy foods. This includes legislated front-of-pack (FOP) warning labels, restrictions on food marketing to children, and constraints on foods for sale or promoted in schools (Corvalán et al. 2013; Popkin et al. 2021; Reyes et al. 2019). There has also been an increase in national taxes on sugar-sweetened beverages (SSB), introduced in over 50 countries (Sacks et al. 2021; Thow et al. 2022). Far fewer countries have enacted comprehensive and coordinated regulations to tackle unhealthy diets (Popkin et al. 2021; Swinburn et al. 2019). A notable example is Chile's Law of Food Labelling and Advertising, which combines mandatory FOP warning labels for packaged foods and drinks that exceed threshold nutrient amounts, restrictions on marketing these products to children, plus a ban on their sale or promotion in schools (Popkin et al. 2021; Taillie et al. 2021). However, such regulatory measures generally identify unhealthy foods based on nutrient profiling systems. Although UPFs are generally high in added sugars, sodium and unhealthy fats and usually contain relatively low levels of other nutrients, the UPF definition is not based on a food's nutrient profile but instead focuses on the use of industrial ingredients and processes (Machado et al. 2022; Monteiro et al. 2019a; PAHO 2019; Soil Association 2020). Aside from the recognition of the UPF concept in the national dietary guidelines of several countries (Koios et al. 2022; Monteiro et al. 2019a; PAHO 2019), the UPF category is yet to attract direct or comprehensive policy attention at the country level.

A nutrient-centric approach to nutrition science influences the design of evidence synthesis methods and informs nutrition policy reference standards, such as dietary guidelines (Ridgway et al. 2019; Scrinis 2013). This reductionist approach underlies how synthesised evidence is translated into nutrition policy actions, like food labelling, and also how food standards agencies interpret their primary objective to protect public health and safety using a risk analysis framework that assesses risk primarily in terms of acute food safety concerns, rather than chronic public health nutrition outcomes or environmental sustainability (Independent Panel for the Review of Food Labelling Law and Policy 2011; Lawrence et al. 2019). The emphasis on nutrients in policy design arguably generates unintended emergent challenges for public health. It can incentivise UPF reformulation to achieve commercially desirable outcomes; for example, to attract higher 'healthiness' ratings under nutrient-centric schemes, meet the criteria for nutrient content claims, or fall under nutrient thresholds that trigger the application of mandatory warning labels or advertising restrictions (Sambra et al. 2020). Reductionist policy actions to 'correct' unhealthy foods may give UPFs a 'health halo' that operates to displace minimally processed foods from the diet (Dickie et al. 2018, 2020). It can also devalue traditional understandings of healthy and sustainable diets implicit in cultural practices and dietary patterns (Monteiro et al. 2015). In addition, there is a broader opportunity cost for more comprehensive and holistic policies that seek to transform entire food systems to promote human and planetary health (Russell et al. 2022).

Can existing food policy frameworks adequately respond to the rise of UPFs as a systems phenomenon?

The prior section presented the UPF problem as an emergent food systems phenomenon with multiple determinants, and anchored to neo-liberal capitalist values and logics. From a policy perspective, the nature and scope of the UPF problem suggests that transformative action to tackle the rise of UPFs will entail a wide range of interventions at many different places in food systems.

Various food policy frameworks have been developed to classify and inform nutrition policy actions (Diaz-Bonilla et al. 2020). This section, which addresses the second objective of the review, will examine three influential food policy frameworks focused on the promotion of healthy diets and relevant to the UPF problem: the NOURISHING framework, the Healthy Food Environment Policy Index (Food-EPI) and the WHO Global Action Plan for the Prevention and Control of NCDs 2013–2020 (WHO Action Plan). These frameworks have been widely cited in nutrition policy analyses worldwide (Allen et al. 2018; Bakhtiari et al. 2020; Guariguata et al. 2021; I et al. 2020; Laar et al. 2020; Lee et al. 2020; Mason-D'Croz et al. 2019; Nieto et al. 2019; Vanderlee et al. 2019; Vandevijvere et al. 2019b; Yamaguchi et al. 2021). While each framework is presented and used as a distinct policy tool, they are interrelated documents and broadly consistent in content. In this section, we provide a summary of the frameworks (Table 2) and consider whether they adequately address the whole of food systems determinants of unhealthy diets in today's food systems, illustrated by the UPF problem.

Our review of these frameworks identified some key themes. First, such frameworks tend to propose that a 'menu' or 'package' of listed policy actions is the foundation for a policy response to unhealthy diets. This approach is useful to delineate tangible policy areas and actions, however it risks discounting the intangible and dynamic qualities of food systems. By their nature, complex adaptive systems cannot be fully understood as the sum of their parts because they feature interdependent components and adaptive responses (Holmes et al. 2012). A list of policy options may also under-emphasise the importance of interactions among policy actions. For example, while NOURISHING recommends multiple actions across policy domains, it does not specifically contemplate the ways that policy actions may interact to generate synergistic effects (Hawkes et al. 2013). Another example is the concept of cost-effective 'best buy' interventions in the WHO Action Plan (Allen et al. 2018; WHO 2017). While it is strategic to unite health impact and economic benefits, this approach may not be sufficiently sensitive to the broader impacts of a particular intervention on population nutrition and health outcomes, or society and the environment.

Second, while these food policy frameworks offer substantial guidance on policy actions to change isolated parts of food systems, they do not fully consider the deeper drivers that shape how the system works. Food policy frameworks tend to adopt the current reductionist approach to nutrition science and focus on exposures to risk nutrients, like added sugars, sodium and unhealthy fats. For instance, listed policy actions related to food composition generally focus on nutrient targets or reformulation strategies (Hawkes et al. 2013; Swinburn et al. 2013; WHO 2017). The emphasis on examining the presence or absence of amounts of nutrients in foods can detract from the burdens that reformulated UPFs still place on human health and the planet (Askari et al.

Table 2 Summary of food policy frameworks considered in the review

Food policy framework	Author	Description	Relevance to other frameworks
WHO Action Plan	WHO	• The WHO Action Plan outlines a 'road map and menu of policy options' for member states to implement collectively in order to attain nine global NCD targets for the prevention and control of NCDs by 2025 (WHO 2013). • The menu of policy options includes policies relevant to unhealthy diet (e.g., 'replace trans fats with unsaturated fats', 'manage food taxes and subsidies to promote healthy diet'). The Action Plan also specifies examples of multi-sectoral action on unhealthy diet (e.g., reduced amounts of salt, saturated fat and sugars in processed foods', 'controlled advertising of unhealthy food to children'). • The WHO Action Plan discusses governance structures (under Objective 4) and recommends that states set up a national multi-sectoral mechanism to implement coherent 'health-in-all-policies' and 'whole-of-government' approaches. It also affirms that an effective policy response must engage multiple actors (e.g., state, civil society, industry, organisations) and sectors, and be protected from the undue influence of any vested interests. • A 2017 update to the WHO Action Plan set out a list of policy options called 'best buys' that are cost-effective and feasible to implement (WHO 2018b, 2017). Best buys related to unhealthy diet focus on reducing salt intake in food products. Other effective and recommended interventions include legislation to ban the use of industrial trans-fats, SSB taxation and nutrition labelling.	• The WHO Action Plan is foundational to the development of both the NOURISHING and Food-EPI frameworks, which are described as consistent with the WHO Action Plan (see below).

Table 2 (continued)

Food policy framework	Author	Description	Relevance to other frameworks
NOURISHING	World Cancer Research Fund International	• NOURISHING aims to provide global recommendations for a 'comprehensive policy package' to promote healthy diets and prevent obesity and NCDs. It also seeks to establish a framework for reporting, categorising and monitoring policy actions worldwide (Hawkes et al. 2013). • NOURISHING presents three policy domains: food environment, food system, and behaviour change communication (World Cancer Research Fund International). There are ten policy areas (e.g., 'Nutrition label standards and regulations on the use of claims and implied claims on foods', 'Give nutrition education and skills'). Each domain lists related policy options (e.g., 'Nutrient lists on food packages', 'Health literacy programmes'). • The food system domain attaches to one policy area, 'Harness the supply chain and actions across sectors to ensure coherence with health' and lists related policy actions (e.g., 'Supply-chain incentives for production, public procurement through 'short' chains, health-in-all policies, governance structures for multi-sectoral engagement') (Hawkes et al. 2013).	• NOURISHING formalises the list of policy options set out in the WHO Global Action Plan for the Prevention and Control of NCDs 2013–2020 (WHO Action Plan) (Hawkes et al. 2013).

Table 2 (continued)

Food policy framework	Author	Description	Relevance to other frameworks
Food-EPI	International Network for Food and Obesity / NCDs Research, Monitoring and Action Support (INFORMAS)	• The Food-EPI aims to measure and benchmark the implementation of recommended policy actions at the country level compared to international best practices, and to propose and prioritise country-specific policy actions to fill identified gaps (Swinburn et al. 2013; Vandevijvere et al. 2019a). • The Food-EPI has two components: Policies and Infrastructure Support. The Policies component contains domains related to food environments: food composition, food labelling, food promotion, food provision, food retail, food prices, and food trade and investment. The Infrastructure Support component contains domains relevant to policy development and implementation: political leadership, governance, monitoring and surveillance, funding, platforms for interaction and health-in-all policies (Swinburn et al. 2013; von Philipsborn et al. 2022). • Each domain corresponds to good practice indicators used to rate the country's progress and identify the policy actions needed to create healthier food environments (Harrington et al. 2020; Djojosoeparto et al. 2021).	• The FOOD-EPI is consistent with the WHO Action Plan and also the NOURISHING framework (Harrington et al. 2020).

2020; Chen et al. 2020; Elizabeth et al. 2020; Hall et al. 2019; Meneguelli et al. 2020).

Third, these frameworks often recommend separate regulatory tools to address specific issues, a narrow conceptualisation that may limit the potential for regulation to tackle systems problems (Lawrence et al. 2015). For example, taxes are often described as a way to incentivise the purchase of healthy foods or reduce consumption of a risk nutrient, such as SSB taxes to reduce sugar consumption (Fischer and Riechers 2019; Meadows 1999). Based on these policy objectives, a SSB tax may be considered a policy 'success' if more products are reformulated to contain less sugar, even if excess UPF production and consumption continues (Ng et al. 2021; Pell et al. 2021; Russell et al. 2021). Given the scope and objectives of current food policy frameworks, single policy actions to address specific issues can contribute to beneficial public health outcomes. However, a focus on reductionist approaches to food policy issues may obscure the range of other options available to tackle the underpinning socio-ecological determinants.

In contrast, a broader perspective creates new possibilities for more holistically conceptualised policy actions to promote whole of food systems transformation; for example, using fiscal measures to redistribute profits from UPF corporations and fund social and health services, or more innovative options like taxes on advertising (Parker et al. 2018). Similarly, food policy frameworks often propose food labelling policies to help consumers make healthier choices (Hawkes et al. 2013; Swinburn et al. 2013). Yet in practice, labelling schemes often reflect dominant market-based and nutrient-centric approaches that can operate to benefit UPF corporations, by misrepresenting the healthiness of UPF products and potentially misleading consumers. For example, evidence suggests that the UPF industry is 'gaming' the nutrient profile algorithm used in Australia's voluntary Health Star Rating FOP labelling tool to generate higher ratings (Dickie et al. 2018, 2020). If considered as a mechanism for food systems transformation, new food labelling measures could synergise with other regulatory strategies to shift power away from UPF corporations and towards other systems actors and more sustainable alternatives (Parker et al. 2020).

While current food policy frameworks do contain some policy options and objectives that consider food systems, such as recommendations for multi-sectoral 'health-in-all-policies' and 'whole-of-government' approaches, these considerations are presented as aspects of the policy framework (Hawkes et al. 2013; Swinburn et al. 2013; WHO 2013). Yet many of the policy actions focus on diet-related interventions or changes to food environments to achieve human health outcomes, rather than broader strategies to address the social, commercial, political and environmental dimensions of today's food systems problems. Some scholars have proposed that the NOURISHING 'food systems' domain could be expanded to better encompass the health and sustainability dimensions of food systems, and in particular to feature interventions on environmental sustainability, multisector and inclusive governance structures and coordination mechanisms, and foundational tools for population-level monitoring and surveillance systems to inform policy action (Lee et al. 2020).

The potential of systems science concepts and regulatory approaches to inform responses to the UPF problem

In this section, which addresses the third objective of the review, we consider the systems science literature to better understand the places to intervene in a complex adaptive system to fundamentally change it. We also look to the field of regulatory studies to examine whether current approaches to regulation are equipped for food systems transformation, and investigate the potential for ecological regulation to reorient food systems to health and sustainability and inform responses to the UPF problem.

Leverage points and levels to intervene in complex adaptive systems

Systems science approaches seek to identify the drivers of complex systems problems and the places to intervene for maximum transformative impact (Bolton et al. 2022; Carey et al. 2015; Meadows and Wright 2009). They use 'systems thinking' to examine the interactions across a system that create its properties and outcomes (Clifford Astbury et al. 2021; Knai et al. 2018; Meadows and Wright 2009). Systems science approaches have been applied to analyse various public health problems, such as obesity prevention (Johnston et al. 2014), the social determinants of health (Carey and Crammond 2015), and food insecurity (Jiren et al. 2021).

An influential example of a systems science approach is Meadows' 'leverage points' framework (1999) that sets out 12 places to intervene in a system, in order of the potential impact on systems change (Fig. 1). It proposes that interventions to modify the system's 'parameters' – the isolated, existing parts of the system – have a low potential impact on systems change. Adjustments to parameters are sometimes described as 'shallow' interventions as they tackle issues one-by-one and rarely lead to radical systemic shifts (Abson et al. 2017; Fischer and Riechers 2019). In contrast, interventions to change the system's paradigms and goals – the 'mindset' and objectives that underlie the system – have a high potential impact on systems change. They are referred to as 'deeper' interventions because they can fundamentally alter the system's core beliefs and business-as-usual objectives (Meadows and Wright 2009; Nobles et al. 2021).

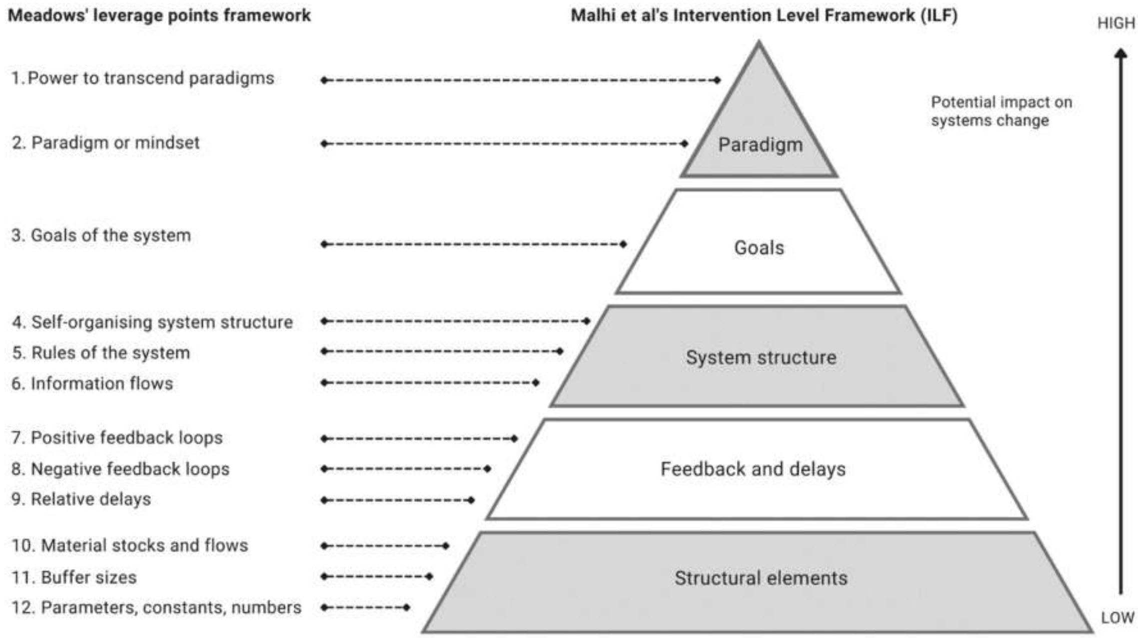

Fig. 1 Adaptation of Meadows' 12 leverage points (1999) mapped to Malhi et al's Intervention Level Framework (2009) in order of potential impact, building on McIsaac et al's presentation of the ILF (2019)

One prominent adaptation of Meadows' framework is Malhi et al's Intervention Level Framework (ILF) (2009), first developed in the context of food systems and later applied to other public health phenomena (Carey and Crammond 2015; Durham et al. 2018; Johnston et al. 2014; McIsaac et al. 2019). The ILF simplifies Meadows' 12 leverage points into five levels of intervention for systems transformation (Fig. 1). The lowest level comprises the 'structural elements' of the system, a similar concept to parameters. The ILF then lists 'feedback and delays', and 'system structure' as levels that have more impact. It describes the goals and ultimately the paradigms of the system as the levels of interventions likely to have the most transformative impact (Johnston et al. 2014; Malhi et al. 2009). In Tables 3, we summarise the levels of intervention and build on prior studies to present examples of possible policy actions related to the UPF problem.

Leverage points frameworks present a hierarchy of places to intervene in ascending order of the potential impact on systems transformation, which corresponds to how 'difficult' it is to intervene at that level (Meadows 1999). This hierarchy of interventions relative to impact and difficulty usefully emphasises that "tinkering at the margins" of the system is insufficient to fix systemic problems (Meadows and Wright 2009, p. 112). However, leverage points analyses also demonstrate that multiple, complementary actions at different levels can interact to increase their collective impact (Jiren et al. 2021; Leventon et al. 2021; Nobles et al. 2021). For example, a study on transformative approaches to gender equality in Ethiopia found that gender-aware policy reforms (a relatively 'deep' leverage point), prompted tangible rule changes to permit women to save money or take out a loan (relatively 'shallow' leverage points) (Manlosa et al. 2019). In turn, this legitimised formal opportunities for women to engage in work and public life, creating the enabling conditions for a shift in social norms and attitudes around gender (a deep leverage point). Some have theorised that interventions can be joined into multi-level 'chains of leverage' that create momentum for change and sometimes spark the conditions for a new paradigm to flourish (Fischer and Riechers 2019).

Current regulatory approaches to food systems problems

Law and regulation can be important policy tools to help achieve public health nutrition goals at the population level, such as reducing unhealthy food consumption (Gostin 2004, 2007; Liberman 2014; MacKay 2011; Magnusson 2008a, b; Reeve and Gostin 2015; Voon et al. 2014). In this section, we look to the regulatory studies literature to analyse how three different approaches to regulation inform the choice of regulatory tools used to intervene in food systems: instrumental, responsive and ecological (Parker and Haines 2018). We highlight the transformative potential of an ecological approach to regulation to address the UPF problem.

'Regulation' includes legal mechanisms (such as food standards and labelling laws) but can also be used more broadly to refer to any mechanism that influences behaviour

Table 3 Levels of intervention as proposed by Malhi et al. (2009), their relationship to the 12 leverage points originally developed by Meadows (1999) and policy examples

Intervention Level (ILF)	Leverage points (Meadows)	Description of level of intervention	Examples of policy actions related to the UPF problem
1. Paradigms	1. The power to transcend paradigms. 2. The mindset or paradigm out of which the system arises.	• The system's 'mindset', deepest beliefs and shared ideas.	• Human rights approaches to food systems, based on principles of participation, accountability and non-discrimination, and 'Food as Commons' ideas that decommodify food and prioritise its non-market value over the economic orientation of the dominant neo-liberal capitalist model (Anderson 2008; Baker et al. 2021; HLPE 2020; Rose 2021; Weber et al. 2020). • Food movements and discourses that depart from industrialised productivist agricultural models and focus on alternative approaches, like regenerative agriculture and agroecology, which adopt and apply ecological concepts, principles and practices to design and manage socially just and sustainable food systems (Gordon et al. 2022; HLPE 2019, 2020; IPES-Food 2016). • Holistic, ecological approaches to nutritional science that see a food's health potential as more than the sum of nutrients and consider the whole food matrix (Fardet and Rock 2019; Lawrence 2021; Lawrence et al. 2019).
2. Goals	3. The goals of the system.	• The targets that the system seeks to achieve.	• Unified policy goals to transform foods systems and ensure healthy and sustainable diets (e.g., to promote healthier diets and protect public and planetary health as a co-benefit of targeting the rise in UPF production and consumption) (Baker et al. 2020; Popkin et al. 2021). • Food policy targets that facilitate an agroecological transition (e.g., goals that seek to shift diets towards minimally processed foods and away from UPFs, balance specialisation and diversification in agricultural production, and support diet quality as a primary policy outcome) (Global Panel on Agriculture and Food Systems for Nutrition 2016; Schiavo et al. 2021; Wezel et al. 2020). • Policy targets that seek to achieve a balance of power across the food supply chain (e.g., goals that support farm diversity rather than consolidation, and promote agroecological systems that will generate more equitable power relations) (IPES-Food 2016; Malhi et al. 2009).

Table 3 (continued)

Intervention Level (ILF)	Leverage points (Meadows)	Description of level of intervention	Examples of policy actions related to the UPF problem
3. Systems structure	4. The power to add, change, evolve, or self-organise system structure. 5. The rules of the system. 6. The structure of information flows.	• The interconnections between the elements of the system (e.g., actors, activities, sub-systems). • This includes the flow of information among system actors.	• Multi-sector policy actions that target the multiple dimensions of the UPF problem (e.g., health, agriculture, trade, consumer protection) and engage many different actors (e.g., the state, commercial entities, civil society) to foster collaborations that support healthy and sustainable food systems (Carey and Crammond 2015; Malhi et al. 2009; Popkin et al. 2021). • Robust governance structures for public health dialogues and decisions (e.g., democratic and participatory structures that include local stakeholders and citizens, such as Food Policy Councils) (Baker et al. 2021; López Cifuentes and Gugerell 2021; Weber et al. 2020). • Social finance initiatives that redirect capital to a diversity of food systems actors and help break up corporate concentration in the food supply chain (Stephens 2021). • Rules around transparency in policy processes to prevent or mitigate conflicts of interest related to the role of private sector actors, such as UPF corporations (Baker et al. 2018; Mozaffarian et al. 2018; Swinburn et al. 2019).
4. Feedback and delays	7. The gain around driving positive feedback loops. 8. The strength of negative feedback loops, relative to the impacts they try to correct against. 9. The length of delays, relative to the rate of systems change.	• The mechanisms that allow the system to self-regulate. • This includes chains of causal connections that enable a system to deliver information about the outcome of an action back to the source of that action (called *feedback loops*) and delays in information about the state of the system, relative to the rate of system change (described as *time delays*).	• Evaluation of food policy actions to assess the impact on UPF markets and UPF dietary patterns over time (e.g., evaluate the impact of SSB taxes on sales and consumption patterns; evaluate the connections between crop prices, food choices, food availability and food consumption) (Johnston et al. 2014; Malhi et al. 2009). • Legislation that prescribes key variables to be measured, monitored and benchmarked across corporate performance and in turn facilitates collection of this data (e.g., corporations required to report on environmental and social performance metrics) (Swinburn et al. 2019). • Measures to assess the impact of policies across different sectors on healthy and sustainable food systems (e.g., the impact of social welfare policies or employment policies on UPF consumption) (Carey and Crammond 2015).

Table 3 (continued)

Intervention Level (ILF)	Leverage points (Meadows)	Description of level of intervention	Examples of policy actions related to the UPF problem
5. Structural elements	10. The structure of material stocks and flows. 11. The size of buffers and other stabilising stocks, relative to their flows. 12. Parameters, constants, numbers.	• The specific physical elements that exist in the system (e.g., actors, activities, sub-systems, parameters).	• Restrictions on the activities of food systems actors (e.g., legislation to restrict UPF marketing to children) (Hawkes and Lobstein 2011). • Regulation of information provision to consumers (e.g., food labelling schemes; food standards that regulate nutrient content claims related to UPF products) (Malhi et al. 2009). • Fiscal policies that dis/incentivise certain consumer behaviours or commercial practices (e.g., SSB taxes; redirecting agricultural subsidies to support local and regional food markets that provide whole foods, rather than large monocultural agricultural corporations that produce monocrops and commodity UPF ingredients) (Johnston et al. 2014; Swinburn et al. 2019).

– including formal but not non-legally binding rules or 'soft law' (such as industry and technical standards, codes of conduct and transnational laws that lack legal enforceability), informal social norms (such as norms for eating healthy invoked by expert and civil society campaigns against 'junk food'), market forces (such as retail price or investor expectations) and other contextual factors (such as a food environment that requires shelf-stable foods capable of travel through shipping and long supply chains) (Black 2001; Parker and Braithwaite 2012). In this respect, regulation can incorporate a range of potential tools for intervention, not just formal legal regulatory measures.

Formal legal regulation often takes an 'instrumental' approach to regulate the harms generated by business activities – often called market failures or 'externalities' – one at a time (Haines and Parker 2017; Parker and Haines 2018). An instrumental conception of regulation is premised on neoliberal capitalist assumptions about the fundamental benefits of a competitive market, and prefers regulation that places as little burden on businesses as possible. Therefore, instrumental regulatory tools are designed narrowly to address specific harms or risks, such as excess sodium intake or single nutrient deficiencies. In some instances, this can be useful to resolve identified and often acute harms, such as to respond to toxicity issues and contribute to a safer food supply. However, instrumental regulation alone cannot address the multi-faceted and dynamic harms that arise from complex adaptive systems, like socio-cultural or environmental harms (Parker et al. 2020; Parker and Johnson 2019). It often creates a fragmented regulatory landscape that is not attuned to considerations of social and ecological wellbeing (Black 2001; Parker and Johnson 2019).

Instrumental regulation tends to benefit larger corporations who have the power to lobby to influence regulations to suit their interests, and the resources to demonstrate regulatory compliance (even if only on the surface) or fight alleged non-compliance in legal proceedings (Haines and Parker 2017). In contrast, instrumental rules create barriers to entry for smaller companies that cannot easily meet the regulatory constraints placed on their business practices (Parker and Haines 2018; Parker and Johnson 2019). An instrumental solution to one policy problem can also be counter-productive for other problems. For example, food safety requirements may indirectly incentivise the production and consumption of airtight sealed and packaged shelf-stable UPFs for catering in institutional settings.

An alternative approach, responsive regulation, proposes that governments should be 'responsive' to the conduct of the actors they seek to regulate, and take more coercive measures only if 'softer' methods to encourage voluntary compliance fail (Ayres and Braithwaite 1992). Responsive regulation approaches recognise that regulation can take many forms, and that different actors – state, markets and civil society – 'regulate' one another (Black 2002; Braithwaite and Drahos 2000; Eberlein et al. 2014; Scott 2001; Steurer 2013). Yet in practice, regulatory spaces are often influenced by economic and political interests, and tend to amplify the loudest voices in political and public spheres, such as transnational UPF corporations, and sideline others, like workers, animals and environments (Parker and Haines 2018). The dominant economic logic inscribed in regulations can limit the scope for regulatory actors to be responsive to non-economic, ecological values and issues (Besselink and Yesilkagit 2021). Some have noted that responsive regulation can be limited in the absence of policy goals to achieve public health outcomes and sanctions to inform and enforce effective self-regulation (Magnusson and Reeve 2014; Ngqangashe et al. 2021b; Reeve 2011). Additionally, while responsive regulatory approaches recognise the need for multiple regulatory measures to meet policy objectives, they under-emphasise the cumulative effect of different regulations to address complex system problems, and may not look at the synergies and trade-offs across entire food systems (Ingram 2011). Responsive regulatory theories also inadequately attend to the social and environmental boundaries for safe, fair and sustainable human activities, including the regulatory system itself (Parker and Haines 2018).

Ecological regulation: an approach to whole of food systems problems

Parker and Haines' theory of ecological regulation (2018) challenges policymakers to reorient the regulatory toolkit to support socio-ecological goals and attend to the social, economic, political and environmental dimensions of complex systems challenges. Inspired by natural ecosystems, ecological regulation seeks to design a 'regulatory ecosystem' of legal and governance tools across multiple substantive regulatory domains, to facilitate a sustainable solution to diverse problems (Johnson 2021; Parker and Haines 2018; Parker and Johnson 2019). It also emphasises that regulations must be embedded in local and planetary ecosystems to ensure that human and business activities operate within ecological limits (Parker et al. 2020). Ecological regulation recognises that regulatory measures interact to generate a cumulative impact greater than the impact of any one action alone. It equips regulators to consider policy actions holistically to identify the synergies and trade-offs within and across systems.

An ecological approach to regulation includes a broad base of actors, issues and interests – not just dominant corporate voices, but also the voices of marginalised groups, other living species and natural ecologies. In this respect, ecological regulation itself encompasses multiple regulatory strategies that reflect diverse values and worldviews to support a sustainable system, rather than many discrete regulatory regimes that share capitalistic beliefs, values and practices and assume the benefits of competitive markets (Haines and Parker 2017). Ecological regulation recognises that corporate actors 'regulate' the food system using various measures; for example, formalised co-regulatory measures like industry standards of practice, corporate marketing practices that regulate individual behaviour, or lobbying in the political sphere (Parker and Haines 2018; Parker and Johnson 2019). Ecological regulation is also attuned to the ways that corporate actors develop adaptive responses to regulatory interventions to maintain the status quo and favour their commercial interests, or adopt strategies to nudge the market in another direction as markets change (Parker and Haines 2018).

Parker and Johnson (2019) have proposed that ecological regulation can be applied to facilitate a deeper analysis of the regulations needed for food systems transformation. Subsequent studies have considered the application of ecological regulation to food systems problems. For example, a study on the potential of ecological regulation to respond to the problem of intensive meat production and consumption suggested that regulatory tools may include eliminating government subsidies that benefit intensive and unsustainable meat production, strict regulation of health, safety and labor conditions in meat production facilities, and innovative options like a universal basic income or taxes on advertising to challenge the neo-liberal values and logics that perpetuate the problems of intensive meat (Parker et al. 2018). Another study on ecological regulation proposes that food labelling schemes can contribute to sustainable food systems if connected to a range of regulatory measures that generate the conditions for creating a system that produces good consumer choices, such as recognising citizens' rights to social support and restricting unfair and unsafe labour practices (Parker et al. 2020).

Ecological regulation embraces "diversity and plurality" in policy actions and regulatory strategies (and equally in food production and consumption practices) because, like in natural ecosystems, these characteristics contribute to adaptability and resilience in food systems and food policies (Parker et al. 2020, p. 925). This emphasis on diversity, a key component of sustainable ecologies, is particularly salient in the context of food systems transformation. Expert reports have explored the need to dismantle the dominance of uniformity and monocultures in industrial agriculture and restore diversity as the imperative of agroecological systems (HLPE 2019; IPES-Food 2016). An ecological approach to regulation is important to help facilitate this paradigmatic transition as it invites regulators to pay attention to how regulatory regimes themselves may reinforce existing power structures or valorise single 'monocultural' solutions that stifle local initiatives and undermine different approaches better suited to tackle context-specific problems (Parker et al. 2018).

Connecting ecological regulation to leverage points frameworks

The literature suggests that ecological regulation and leverage points frameworks are conceptually compatible approaches that have the potential to inform holistic interventions in today's food systems to promote health and sustainability. Ecological regulation and leverage points frameworks share a common emphasis on the need for nuanced and multi-level approaches to transform complex adaptive systems, such as today's food systems, and tackle multi-faceted systems phenomena, like the rise of UPFs. They also attend to the multiple yet interrelated health, social, commercial, political and ecological dimensions of modern food system challenges.

Ecological regulation and leverage points frameworks have some differences. For example, leverage points frameworks, such as the ILF, include all kinds of interventions (e.g., programs, policy, informal social agreements) (Meadows 1999), and do not specify the nature or form of the regulatory tools used to shift the system in a particular direction. Also, the hierarchical depiction of the levels for intervention based on impact and difficulty may discount the importance of diversity in regulatory strategies, and undermine the potential significance and practical challenges of certain interventions to change the system's structural elements. For example, a policy action to eliminate the agricultural subsidies for grains such as corn, wheat and rice, monocrops that form the basis of most UPF products, would amount to an intervention at the 'shallow' level of structural elements, classified in the ILF as low impact and relatively 'easy', despite the deep potential impact and political intractability of redirecting the substantial subsidies that benefit large monocultural agricultural corporations (Swinburn et al. 2019). However, both approaches encourage the strategic use of many different yet synergistic interventions that interact to catalyse systems change. This is reflected in the concepts of a 'regulatory ecosystem', central to ecological regulation, and the empirical findings and theoretical work on multi-level chains of leverage, described in leverage points analyses.

We propose that while leverage points frameworks illuminate the spectrum of places to intervene in a system, an ecological approach to regulation highlights the need for a diversity of regulatory tools that interact to transform it (Parker et al. 2017). Leverage points frameworks, such as the ILF, seek to understand how a complex system works, and direct attention to the multiple levels for interventions. In this respect, the ILF provides useful guiding principles for holistic and strategic policy design that considers *where* to intervene to transform a system (Meadows 1999). It offers a general framework that can help policymakers to identify and coordinate interventions across multiple leverage points to respond to complex public health problems in a way that moves the system in a new direction. Consistent with this, ecological regulation elaborates on *how* to use regulatory tools to intervene for socio-ecological outcomes, a reorientation that is fundamental to tackle the UPF problem and the associated harms to human health and the environment. We provide a general summary of this combined approach in Table 4. From a regulatory perspective, the theory of ecological regulation adds nuance as it specifically examines how regulatory strategies could operate to advance systems transformation. The normative element of ecological regulation also highlights the need for regulatory strategies to be responsive to ecological values and perspectives. In other words, what is needed is not just regulatory interventions, but regulatory interventions designed to respect the ecological boundaries around food systems and contribute to socio-ecological goals.

Discussion

This review aimed to critically examine whether current food policy frameworks and regulatory approaches are equipped to respond to today's food systems problems, illustrated by the global rise of UPFs in human diets. Our findings address three key objectives and offer insights on the transformative potential of policy and regulation to drive food systems changes that tackle the UPF problem.

Table 4 Summary of a combined approach that draws on the ILF and ecological regulation

	ILF ('Where')	Ecological regulation ('How')
Scope	• System in its entirety	• Diversity of actors, issues and interests in food systems
Focus	• Leverage points / levels	• Regulatory toolkit
Interventions	• Interventions at multiple leverage points / levels	• 'Regulatory ecosystem' of legal and governance tools across multiple substantive policy domains
Orientation	• Organising structure for policy actions to help reconfigure the system	• Ecological by design • Supports socio-ecological goals to help generate the conditions for healthy, sustainable and equitable food systems

First, the rise of UPFs is not just a dietary harm, but an emergent property of today's commercialised and commodified food systems. Current industrial food systems operate in a neo-liberal capitalist paradigm that values economic productivity and perpetuates a culture of consumption, with little respect for human and planetary health (Freudenberg 2021; Parker and Johnson 2019). Dominant market-oriented and nutrient-centric ideologies permeate food environments, food and nutrition policies, and the corporate political activities of UPF corporations, reinforcing the status quo in today's food systems and driving current systems phenomena, like the rise of UPFs (Leeuwis et al. 2021; Lencucha and Thow 2019; Nestle 2022).

The prevailing neo-liberalist capitalist paradigm results in a market-based approach to regulation that responsibilises individuals to make healthier choices, entrusts the UPF industry to take a leading role in food policy processes and regulatory governance, and limits the transformative potential of regulatory interventions. This demands the application of a holistic regulatory theory to extend the conceptual parameters of what it means to regulate to promote healthy and sustainable food systems. It also underscores the need for a range of regulatory responses that generate other changes and exert a cascading influence on the entire system and related systems, rather than make multiple, minor indentations in delineated food policy domains.

Second, current food policy frameworks are not sufficiently equipped to address the whole of food systems determinants of the UPF problem. Our findings suggest that these frameworks under-emphasise key systems characteristics. In particular, these frameworks predominantly consider the structural elements of food systems, such as prices, labels or food composition, rather than tackling the deeper levels that shape food systems. They do not directly confront the neo-liberal capitalist or nutrient-centric ideologies that anchor today's industrial food systems to business-as-usual goals and structures, industrial food production practices and financial flows that are ecologically unsustainable.

Current food policy frameworks pay insufficient attention to the possibilities for 'deeper' interventions at the levels of the system's paradigms, goals and systems structures, and how such measures may complement and catalyse other changes across the system as a whole. They tend to present lists of separate policy options classified into distinct policy domains, a format that does not reflect the multiple dimensions or dynamic interactions that characterise today's food systems problems, such as the rise of UPFs (Parker and Johnson 2018). From a systems standpoint, isolated policy actions to adjust or nudge the structural elements of food systems are not commensurate to the systems nature of the UPF industrial complex or up to the task of entire systems transformation (Lawrence et al. 2015).

While current food policy frameworks do consider food systems, they present food systems as one part of the framework rather than the foundation for it. A stand-alone 'food systems' policy domain or a specific policy option that recommends food systems approaches may detract from the need for *all* food policy actions to contribute to a whole of food systems response that has a unified and transformative impact. This raises a key question: is it enough to extend a food systems domain situated in an existing food policy framework, if that framework itself is not oriented to the socio-ecological dimensions of food systems? Given that the limitations of current frameworks relate to a weak line of systems thinking and insufficient elevation of the socio-ecological dimensions of food systems regulation, there is potential to draw on ecological approaches to regulation and systems frameworks to examine how to use regulation more effectively to intervene for whole of food systems change.

Third, the systems science concept of leverage points and an ecological theory of regulation have the potential to illuminate *where* and *how* to intervene in current food systems to advance transformative change and attenuate the rise of UPFs. Leverage points frameworks, in particular the ILF, provide a general structure that helps to organise the range of places to intervene in food systems to spark transformation (Johnston et al. 2014; Malhi et al. 2009). Ecological regulation then turns attention to the regulatory toolkit available to tackle multi-dimensional systems problems, such as the UPF problem (Parker and Haines 2018). It also shifts the focus of regulation from economics as the basis for action to ecosystems, and starts from the premise that regulation itself must respect the socio-ecological boundaries that need to remain intact for healthy and sustainable food systems – and all human activities more broadly – to flourish (Parker and Johnson 2019). This holistic approach to regulation reflects and supports the broader landscape of international movements, community initiatives and expert reports that are already challenging the dominant market-based orientation and industrial scale of food systems, and calling for joined-up policy changes to collectively move towards a fundamentally different paradigm of diversified agroecological food systems (IPES-Food 2016; Leeuwis et al. 2021).

We propose that a united conceptual lens incorporating the multi-level structure of leverage points frameworks and an ecological approach to regulation offers the principles and the tools to contribute to transformative food systems change. A combined approach has the potential to facilitate the design of a diverse set of synergistic regulatory strategies that interact with one another – and with various elements of food systems themselves – to catalyse systems transformation.

Strengths and limitations

This review draws on systems science concepts and regulatory approaches to highlight the possibilities for policy and regulation in food systems transformation. Given the complexity of today's food systems problems, this multidisciplinary perspective is useful to understand where and how to intervene in these systems for transformative impact. This review has some limitations. Due to the broad nature and scope of this topic, our search strategy focused on academic articles and official technical or policy reports, limited to English sources and often global in scope. This may have omitted other relevant literature, such as reports from civil society organisations or corporations, which could have affected the narrative and synthesis presented. However, the search process used collected a broad range of documents across different disciplines, relevant to the review's three objectives. It also identified key articles from the fields of systems science and regulatory studies that did not necessarily mention UPFs or food systems but contained relevant insights on systems change or regulatory approaches.

This review presents the rise of UPFs as an illustrative example of a current global food systems problem that demands a policy response and regulatory strategies to attenuate the harms to human and planetary health. A limitation of this orientation is the lack of discussion of more healthful and sustainable food systems that exist on local or regional levels, or 'alternative' food systems movements. The review also mainly focuses on the role of governments to use law and regulation in food systems transformation, particularly to address the 'harms' of UPFs, as distinct from using regulation to promote 'goods' such as healthy diets. This is not intended to suggest that governments alone have the capacity to transform food systems. As this review highlights, there are many actors that regulate food systems, and our emphasis on national interventions does not detract from the important roles of the private sector, which includes a diversity of corporate actors that are not part of the UPF industry, civil society and public interest groups. Finally, we acknowledge that the narrative review and synthesis method necessarily involves some degree of author subjectivity to interpret and synthesise complex concepts from multiple disciplines. Therefore, the results and discussion of this review are inherently subject to author bias and subjective socio-cultural interpretations. To minimise these biases, we have integrated semi-systematic search processes and described the concepts, theories and frameworks considered before presenting a critical synthesis that contributes to the literature.

Conclusion

This article has examined whether current food policy frameworks and regulatory approaches are equipped to respond to the rise of UPFs in human diets and generate food systems transformation. Despite recent calls to action in the international policy sphere, the whole of food systems determinants of the UPF problem are not holistically considered under current food policy frameworks. While these frameworks adjust certain important parts of today's food systems, they do not adequately address the deeper drivers that underlie and permeate food systems from their foundation. This limits the capacity of current frameworks to tackle today's food systems problems, such as the UPF problem, which present substantial threats to human and planetary health.

To divert the current course and reroute in the direction of health and sustainability, a whole of food systems approach that addresses the many, interacting determinants of the UPF problem is required. This calls for an ecosystem of integrated and synergistic interventions that work at multiple points across a variety of sectors (e.g., health, agriculture, trade, environment, consumer protection) to support healthy and sustainable food systems. While a variety of coordinated and multi-level interventions are needed, rather than any one intervention in isolation, some policy examples include democratic and participatory governance structures to facilitate public health dialogues and decisions inclusive of multiple stakeholders and citizens, actions that seek to redistribute power across the food supply chain, and specific measures that adopt and apply agroecological concepts, principles and practices for population and planetary health.

Our review finds that system science concepts and an ecological approach to regulation can inform holistic policy design and regulatory tools to help drive food systems transformation, attenuate the UPF problem and reduce related harms. Leverage points frameworks, such as the ILF, provide useful organising principles to guide policy action on the places to intervene in complex adaptive food systems. To extend this line of systems thinking into regulatory policy and practice, ecological regulation emphasises how to regulate for sustainable solutions to multi-dimensional problems, like the rise of UPFs. Given the magnitude of current socio-ecological crises, there is substantial scope for future research that develops our understanding of how to use ecological regulation to respond to the UPF problem and promote global food systems transformation. A unified conceptual lens that combines a leverage points analysis and an ecological regulatory approach has the transformative potential to highlight *where* and *how* to intervene to create holistic systems changes that collectively support a healthier and more sustainable future for global food systems.

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Review

Betalains from vegetable peels: Extraction methods, stability, and applications as natural food colorants

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A B S T R A C T

Betalains are hydrophilic pigments naturally present in a limited number of plants and fungi. In addition to providing pigmentation, ranging from yellow to red, they show potential for replacing artificial food colorings. Betalains can be obtained from agri-food waste like vegetable peels through conventional and emerging extraction methods; however, they are susceptible to chemical changes due to various degradation factors, such as the presence of oxygen, light, and increased temperature. In this context, encapsulation can be used as a strategy to stabilize and reduce the pigment degradation rate for later industrial application in processed foods. This study reviews data from the last five years on the production and relevance of valuing agri-food waste, in addition to research carried out on betalains obtained from vegetable peels, such as extraction methods, encapsulation as a method of controlling stability and applications as colorant in food matrices, highlighting news insights for the field of pigments from plant sources. This review shows that encapsulation techniques using mixtures of wall materials offer superior protection than isolated materials. Despite advances in applicability, gaps still persist regarding stability in food matrices, especially on an industrial scale. However, future investigations should focus on filling the gaps regarding the maintenance of the properties of betalains for application in food industries as natural food coloring based on the precepts of circular economy and sustainable technology.

1. Introduction

Around 34 million tons of waste from food systems are wasted worldwide and inappropriately discarded annually, which, in addition to being rich in nutrients, significantly impact the environment due to emissions of harmful greenhouse gases (FAO, 2023). With them, the vegetable processing industry generate 16.5 to 20.5 million tons of waste, including peels that are rich in bioactive compounds and show attested health benefits (such as preventing chronic diseases). These effects are frequently associated with natural antioxidants, corroborating the inhibition of oxidative stress (Jha & Sit, 2021). Vegetable peels may configure the raw materials for extracting natural pigments to produce natural colorants. Recovering pigments from wastes adds value to these by-products (More et al., 2022) and enables their reinsertion into the production cycle, contributing to the concepts of sustainable development and circular economy (Sarkar et al., 2023).

Betalains consist of natural pigments that occur in a few selected vegetal peels. They are water-soluble pigments composed of betacyanins (red to violet color) and betaxanthins (yellow to orange color). In addition to presenting several functional properties, betalains have been explored as natural food colorants (Carreón-Hidalgo et al., 2022). However, its application as natural pigment is often limited by its limited stability due to the influence of environmental factors such as high temperature and water activity and exposure to light and oxygen,

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which may change the biological and functional properties of betalains (Jiang et al., 2021).

The limited stability of betalains has fostered research for alternative extraction methods that involve mild extraction conditions to maintain the pigment properties and ensure more eco-friendly solvents (such as water), leading to reduced environmental impacts. Non-thermal physical technologies may offer future natural pigment extraction alternatives as they prevent adverse effects on structural integrity and bioactivity of target compounds, which usually undergo the influence of the high temperatures of conventional extraction techniques. Additionally, their shorter procedure time can provide higher yields (Tzanova et al., 2024; Zhang et al., 2024). The selection of the appropriate conditions for each extraction technique also follows the composition of the vegetal matrix, such as its lignocellulosic content. Overall, vegetable peels exploited for betalains extraction—such as beet, pitaya, and prickly pear—contain less lignin (5–9 %) than other parts of the vegetable (i.e., stems), facilitating pigment extraction (Hernández-Carranza et al., 2019; del Amo-Mateos et al., 2023; Taharuddin et al., 2023) and demanding easier extraction conditions. The literature contains recent reviews that have taken a general approach to the various sources of betalains, including those from agri-food wastes (Sharma et al., 2021; Benucci et al., 2022; Calva-Estrada et al., 2022). Despite these facts and the expressive amount of found in betalains-source vegetables (Jalgaonkar et al., 2022; Manzur-Valdespino et al., 2022; Shakir & Simone, 2024), the literature still lacks reviews on extraction and encapsulation strategies for betalains, especially from vegetable peels.

Thus, this study has gathered recent information from studies that have been published in the last five years on the extraction and application of betalains as natural colorants in foods. This study particularly focused on extraction of betalains from vegetable peels by conventional and non-conventional methods and encapsulation procedures to improve stability. The final portion of this review discussed the challenges related to the use of betalains as natural pigments and new perspectives for their extraction, encapsulation, and application in food products. To the best of our knowledge, this is the first review to focus only the extraction, encapsulation, and application of betalains that had been exclusively extracted from vegetable peels.

2. Agri-food waste: Source of natural pigments

According to the Food and Agriculture Organization of the United Nations (FAO), around one billion tons of vegetables have been produced worldwide in the last five years (FAO, 2023). Therefore, investment in studies has increased to prove the beneficial effects of the new trend of plant-based foods, and which bioactive phytochemical compounds promoter the most positive biological effects associated with health (Alcorta et al., 2021).

Waste from agri-food systems occurs throughout the supply chain, ranging from harvesting to consumption, wasting varying amounts, depending on the phase and food product, contributing to food insecurity and negatively impacts the United Nations (UN) sustainable development goals (SDGs): good health (SDG 3), green and affordable energy (SDG 7), efficient consumption and production (SDG 12), climate change (SDG 13) and life land (SDG 15) (Kour et al., 2023).

When inappropriately disposed of in the environment, these potentially valuable resources cause environmental problems, such as loss of biodiversity and increased carbon footprint. Its effective reuse is based on the concept of circular economy. Thus, the added value of these agro-industrial byproducts by converting them into diversified products can impact both the economy and the environment and guarantee sustainability (Kour et al., 2023; Sarker et al., 2024).

This segment includes fruits, which, the latest FAO data on global production (including the total of primary and citrus fruits) estimates at over 900 billion tons. In parallel, the fruit processing industry expands. Moreover, the expansion of the fruit processing industry remains constant. Thus, the production of by-products (totaling around nine discarded billion tons) obtains one of the leading international concerns as it affects the environment, especially due to greenhouse gas emissions. (Fao, 2023; Leong et al., 2022; Ray et al., 2023).

Fruit pulping usually discards a considerable mass of seeds, peels, leaves, stalks, and pomace that remains undervalued (Ben-Othman et al., 2020). As the edible parts of fruits, waste offers a source of natural pigments that can be recovered and explored as ingredients in functional foods (Ghissing et al., 2021). To reduce the inappropriate disposal of this fruit waste, several studies in the last decade have been conducted to reduce negative impacts on nature, offering alternatives to add value to by-products and existing products in the market (Sharma et al., 2021).

Aiming at sustainability, focused on three central elements, environmental, economic, and social, recently, the valorization of agri-food waste has been a goal to fulfill one of the UN SDGs, which meets the fundamental principles of the green circular economy (SDG 12). This model promotes the conversion of a linear chain into a closed circuit and focuses on the efficient consumption of resources and balanced costs of the three central elements. Thus, the exploration of pigments with bioactive potential from vegetable waste can collaborate with the principles of sustainable development (Sharma et al., 2022).

The development of processes to produce pigments from natural sources constitutes a global interest. This interest has mainly stemmed from consumers who worry about insecurity and adverse health effects from synthetic dyes—which are widely used in food processing industries (Choo & Saik, 2021). Therefore, sustainability necessitates the viable development of pigments with bioactive properties to produce natural dyes from vegetable-derived waste.

3. Natural vegetable pigments

A main factor consumers consider when evaluating the acceptability and quality of a product is its color, which denotes freshness, safety, and adequate sensory qualities (Nabi et al., 2023). Regarding this, the primary source of color in products of plant origin is natural pigments, which mainly derive from plant secondary metabolites. Due to increasing global awareness of their nature, food safety, and their health benefits, potential applications of natural pigments in food have been recently investigated (Lu et al., 2021).

However, artificial colorings remain the most used in the food industries for their advantages in production cost (chemical synthesis), excellent stability, comprehensive range of application, and coloring potential (Mohammad Azmin et al., 2022).

However, its excessive consumption by people who are sensitive to artificial colors has been associated with adverse effects on human health, such as brain disorders (Hosieny et al., 2021), skin rashes (Sadowska et al., 2022), stimulation of the production of cells with carcinogenic potential (Monisha et al., 2023), and the environment, as they are non-biodegradable and cause undesirable toxic effects (Olas et al., 2020; Yadav et al., 2023), such as changes in biochemical parameters, as creatine and urea, increased levels of leukocytes and platelet count, and reduction in hemoglobin and red blood cell counts (Reza et al., 2019).

Therefore, due to growing consumers' concern about the adverse effects of synthetic dyes, natural pigments from plant sources tend to be used as substitutes. This, in addition to the demand for more natural safe foods with health-promoting properties (Mohammad et al., 2022), corroborates the clean-label marketing strategy carried out by the food industries.

Pigments provide intense and uniform color, preserve nutrients, and increase the acceptability of food product. Their use contributes to sustainability (Pailliè-Jiménez et al., 2020). Vegetables are essential to achieve a balanced and healthy diet, being sources of bioactive constituents with significant antioxidant activities that are associated with promising health benefits, such as anti-inflammatory, antimicrobial, and even anticancer effects (Ghosh et al., 2023); reducing oxidative stress, inhibiting DNA damage, regulating genes, and preventing lipid peroxidation (Fu et al., 2020; Carrillo et al., 2022).

Nonetheless, natural plant pigments have higher costs than synthetic ones. Furthermore, its availability decreases due to seasonality and variability in the quality of the raw material under the influence of geographic origin (Bora et al., 2019). Another challenge arose from red beetroot and radish having undesirable aromas and flavors due to substances such as geosmin and pyrazines, as evidenced by previous studies (Chaudhary & Singh, 2021). Faced with these questions, recent research has explored vegetable by-products as promising sources of natural pigments for industrial application in food products. This approach seeks to overcome limitations associated with flavor alteration and to offer a broad spectrum of colors (Sharma et al., 2021).

Pigments are also susceptible to degradation due to environmental conditions, such as the incidence of oxygen and light and variations in pH and temperature, which affect their stability (Ranaweera et al., 2020). Natural pigments generally occur in vegetables (which constitute part of the population's diet), thus including betalains (Nabi et al., 2023), a group of hydrophilic pigments that are more stable over a wide range of pH than anthocyanins (Echegaray et al., 2023).

4. General aspects and biological properties of betalains

Betalains are nitrogenous pigments that provide a broad spectrum of colors depending on composition and concentration range, and are found in edible parts of plants, such as fruits, flowers, leaves, and stems and in some fungi (Zannou et al. 2023). Pigments derived from betalains are restricted to plants of the order *Centrospermae*, of the species of *Caryophyllales*, but also occur in *Cactaceae* and some mushrooms (*Amanita, Hygrocybe* e *Hygroplhorus*). Regarding their chemical structure, betalains are classified in two structural subgroups, betacyanins and betaxanthins, which are derived from the basic structure of betalamic acid (Fig. 1).

Betacyanins have a red-violet color tone with a maximum absorbance close to 550 nm. Their chemical structures result from the condensation of betalamic acid by the aromatic nucleus *cyclo*-Dopa (*cyclo*-3,4-dihydroxyphenylalanine). Betaxanthins have a yellow-orange pigmentation with a maximum light absorption around 485 nm and are formed by condensing betalamic acid with amino compounds (amino acids, amines, or derivatives) (Rodriguez-Amaya, 2019). The type of condensation of the basic structure of betalains is related to the characteristics of pigmentation and the part of the plant studied with the proportion of the found composition of betacyanins and betaxanthins (Calva-Estrada et al., 2022).

Betalains occur in different climates and geographic regions of the planet, are soluble in water, exhibit stability in the pH range from 3 and 7, and have several favorable biological properties associated with health, such as antioxidant (Gómez-Maqueo et al., 2021), anti-inflammatory (Smeriglio et al., 2021), antimicrobial (Wijesinghe & Choo, 2022), antifungal properties (Luu et al., 2021), and contribute to preventing and possibly operating a therapeutic effect on specific diseases chronic diseases such as hypertension, dyslipidemia, diabetes, cardiovascular diseases, and cancer (Calvi et al., 2022).

Betalains have antioxidant properties due to their phenolic and cyclic amines, which are influential electron donors. The antioxidant and antiradical activities of betanin have been explained based on its ability to donate electrons, bond dissociation energy, and ionization potential. The resonance between the secondary amine group and the hydroxyl group, which participates in the keto-enol tautomeric equilibrium, facilitates the removal of an electron from the phenolic oxygen of betacyanins. The betacyanin radicals formed are stabilized by delocalizing the unpaired electron by an aromatic ring. The connection of the betalain electron resonance system to the aromatic ring increases the Trolox equivalent antioxidant capacity of betalains by 0.4 mol/mol (Sadowska et al., 2022).

Betalains effectively protect against oxidative damage, inflammation, and chronic diseases, modulating several signaling pathways that protect organs in pathological conditions. They activate the nuclear factor erythroid 2-related factor 2 (Nrf2) and antioxidant response element pathway, increasing the expression of antioxidant enzymes such as glutathione peroxidase, superoxide dismutase, and catalase. In addition to their antioxidant properties, betalains regulate inflammatory processes, decreasing pro-inflammatory cytokines and stimulating anti-inflammatory mediators, such as the regulation of nuclear factor kappa B. Studies indicate that betalains can reduce inflammation and improve the function of several organs, including the heart, intestine, kidneys, lungs, liver, and reproductive organs. This suggests that betalains and their derivatives play a significant role in protecting organs in disease situations by regulating antioxidant and anti-inflammatory processes (Nirmal et al., 2023).

Despite the availability of a range of colors, betalains have limitations regarding synthetic pigments—especially when applied to food—such as low stability due to degradation at high temperatures, exposure to a specific pH range (<3 and > 7) and high production levels, such as the need for extra steps in the process for isolation (Gahlawat, 2019; Ghosh et al., 2022; Nabi et al., 2023). Its physiological disadvantages include its low bioaccessibility and bioavailability related to the characteristics of the food matrix and its transformations during digestion and absorption. More in-depth discussions on the bioaccessibility and bioavailability aspects of betalains can be consulted in reviews available in the literature (Madadi et al., 2020; Sadowska-Bartosz & Bartosz, 2021; Martínez-Rodríguez et al., 2022). This necessitates further systematic research on new sources of pigment extraction and more effective methods to improve its stability and expand its applications in food.

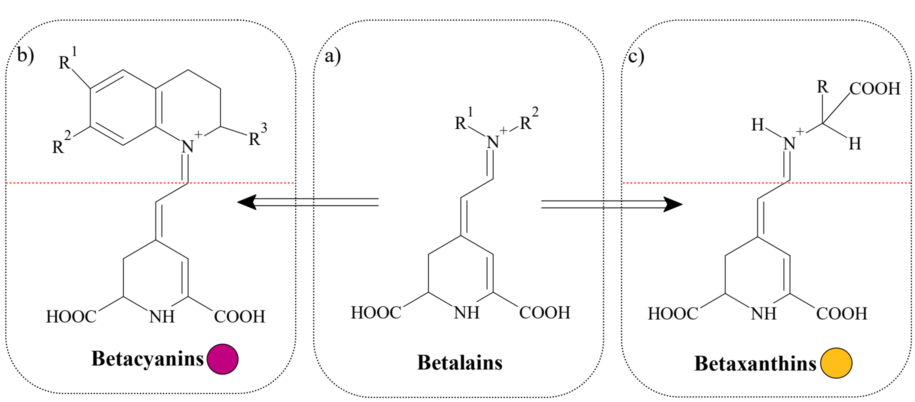

Fig. 1. General chemical structure of betalains (a): betacyanins (b) and betaxanthins (c).

5. Conventional and unconventional methods for extracting betalains

Betalains can be extracted using several techniques, usually after dehydrating and grinding the plant material. From this, the solvent is defined according to the selected extraction technique, which can be conventional or unconventional (Yadav et al., 2023). Furthermore, the choice of the extraction method will depend on the definition of the part of the plant to be studied or the extract to be obtained.

Conventional extraction methods involve mixing and macerating plant material with a solvent to solubilize betalains, remove lignocellulosic material, and produce extracts rich in natural pigment. In contrast, unconventional or emerging methods, following the principles of green chemistry, employ less aggressive thermal technologies. These methods aim to achieve high yields, decreased extraction times, and minimal use of solvents or chemical agents, also reducing the presence of harmful substances and simplifying the extraction and isolation process (Zin et al., 2020a; Carrillo et al., 2022). Table 1 shows the most evident relevance and limitations in the main conventional and non-conventional methods that have been recently used to extract betalains in vegetable waste. The subsequent sections detail the primary methodologies, process parameters, and extraction yield.

5.1. Conventional methods to extract betalains from vegetable peels

Conventional extraction methods only become advantageous when compared to new techniques due to their low capital investment and easy procedure execution (More et al., 2022). As they do not require sophisticated equipment, maceration and hydrodistillation remain the most used processes to extract natural pigments (Sharma et al., 2021).

Even so, they show several limitations as time constraints, temperature sensitivity, and the excessive use of toxic organic solvents, which lead to time-consuming, inefficient, unsustainable, and hazardous extractions (Lazăr et al., 2021; Carrillo et al., 2022). Still, Castro-Enríquez et al. (2020) consider that combining conventional and modern methods may offer an alternative to improve extraction process without intervening in the natural properties of betalains. Table 2 summarizes conventional techniques to extract betalains from vegetable peel residues.

5.2. Unconventional methods to extract betalains from vegetable peels

Emerging techniques, generally called unconventional forms, receive this name because they remain little used in the industrial sector (Carrillo et al., 2022). They arose from the need to overcome the disadvantages of traditional techniques, being more advantageous about short extraction time and high yield and lower impact on thermal degradation, qualitative damage to pigments (Wani et al., 2021), and impact on the environmental due to its of ecologically correct solvents. Table 3 shows some studies using vegetable peels as raw material to extract betalains from non-conventional green extraction methods.

The studies in Table 3, which apply unconventional techniques for extracting betalains from vegetable peels—in correlation with bibliometric analysis by Marinho et al. (2023) —confirm that beetroot (*Beta vulgaris*), from the *Amaranthaceae* family, remains the prevalent plant species in contemporary research. The most studied species in the *Cactaceae* family refer to *Opuntia*, *Hylocereus*, and *Stenocereus*, in that order.

Šeremet et al. (2020) emphasize that the maximum recovery of betalains during extraction from beetroot (*Beta vulgaris*) peels depends on the appropriate choice of technique. They also state that their study was the first to explore innovative methods to extract betalains from beet peels. According to the same authors, of the applied techniques, ultrasound-assisted extraction (UAE) yields one of the highest contents of betalains in dry weight—including total betacyanins (3.87 mg betanin/g) and betaxanthins (8.61 mg vulgaxanthin/g), showing that time and temperature constitute the factors that most significantly impact the total betalain content.

The research conducted by Zin & Bánvölgyi (2021), using the microwave-assisted extraction (MAE) method, showed lower betalain than Šeremet et al. (2020). However, it found that, of the four solvents used in extractions (pure water, acidified water, ethanol–water, and acidified ethanol–water), pure water showed the best absorption capacity with the used technique, emerging as the most effective condition among the evaluated ones. It specifically showed of 1.1589 mg/g, 0.8621 mg/g, and 2.0208 mg/g total levels for betacyanins, betaxanthins, and betalains, expressed in dry extract, respectively. Rodríguez-Félix et al. (2022) extracted betalains from beetroot bagasse for application in zein films and reported low yield values obtained through the UAE extraction process. The levels of betacyanins, betaxanthins, and total betalains—expressed in the dry extract—totaling 1.38 mg of

Table 1
Central relevance and limitations of conventional and unconventional extraction methods applied to recover betalains in agri-food waste.

Methods		Main relevance	Main limitations	Reference
Conventional	Maceration	Simple and low-cost extraction process	Long extraction time, low yield, and use of large amounts of organic solvents	(Castro-Enríquez et al., 2020; Manzoor et al., 2021)
	Hydrodistillation	Absence of organic solvent	Extraction in high time and temperature with high energy consumption	(Castro-Enríquez et al., 2020; Wani et al., 2021)
Unconventional	UAE	Higher yield and reduced extraction time	Degradation of the compound of interest and formation of free radicals	(Martínez-Olivo et al., 2023; Das et al., 2022)
	MAE	Absence of organic solvent	Overheating and manipulation of betalains	(Manzoor et al., 2021; Miranda et al., 2021)
	PLE	Low temperatures prevent the degradation of thermolabile pigments, short extraction time, and lower solvent consumption	High equipment cost	(Benucci et al., 2022; Rodríguez-Mena et al, 2023)
	PEF	Extraction at low temperatures, with fast mass transfer, change in the structure of the cell membrane and high compound selectivity	High equipment cost	(Moreira et al., 2019; Zhang et al., 2019; Saldaña et al., 2021; Yu et al., 2023)
	SFE	No degradation of thermolabile compounds, short extraction time with the use of non-toxic fluids, and easy separation and reuse	High equipment cost. Requires additional purification	(Ray et al., 2023)
	EAE	Greater extraction yield and maintenance of heat-sensitive pigments. Possible enzyme recovery and absence of organic solvents	High cost of enzymes and recovery	(Benucci et al., 2022)

UAE – Ultrasound-assisted extraction; MAE – Microwave assisted extraction; PLE – Pressurized liquid extraction; PEF – Pulsed electric field; SFE – Supercritical fluid extraction; EAE – Enzyme-assisted extraction.

Table 2
Content of betalains obtained from vegetable peel residues by conventional extraction methods.

Vegetal	Species	Extraction technique	Solvent (mass/solvent ratio)	Time and temperature	Total betalain content (mg/g dry weight) *	Prevalence betalain group (mg/g dry weight) *	Reference
 Beet peel	*Beta vulgaris*	Water bath	Aqueous ethanol 15 % (5:3, w/v)	1 h/20 °C	1.39	Betacyanins (0.82)	(Zin et al., 2020b)
	Beta vulgaris	Infusion	Distilled water (1:20, w/v)	30 min/80 °C	18.21	Betacyanins (9.80)	(Šeremet et al., 2020)
	Beta vulgaris	Maceration in an orbital shaker	Ethanol and citric acid (1:10, w/v)	49,9 min/ 52,52 °C	1.20	n.d.	(Lazăr et al., 2021)
	Beta vulgaris	Shaker	Distilled water (1:20, w/v)	1 h/25 °C	535	n.d.	(El-Beltagi et al., 2022)
	Beta vulgaris	Orbital shaker	Ethanol (1:35, w/v)	90 min/45 °C	577.08	Betaxanthins (368.28)	(Chaari et al., 2022)
 Pitaya peel	*Hylocereus polyrhizus*	Maceration in a waring blender	Deionized water (1:9, w/v)	30 s/25 °C	0.28	Betacyanins (0.21)	(Chew et al., 2019)
	Hylocereus polyrhizus	Maceration in a blender	Ethanol (3:8, w/v)	15 min/4 °C	n.d.	Betacyanins (175)	(Qin et al., 2020)
	Hylocereus polyrhizus	Maceration in shaker	Water (1:50, w/v)	n.d./25 °C	59.90	n.d.	(Putthawan et al., 2021)
	Hylocereus polyrhizus	Maceration in a blender	Ethanol (1:1, w/v)	60 min/40 °C	2.09	n.d.	(Tran et al., 2022)
	Hylocereus polyrhizus	Maceration in a high-speed blender	Ethanol 60 % (1:6, w/v)	20 min/25 °C	0.03	Betacyanins (0.02)	(Li et al., 2022)
	Hylocereus polyrhizus	Maceration in magnetic stirrer	Water (75:25 %, w/v)	12 min/30 °C	n.d.	Betacyanins (0.05)	(Thuy et al., 2022)
	Hylocereus undatus	Cold maceration	Methane with 0.01 % hydrochloric acid (1:2, w/v)	24 h/n.d.	n.d.	Betacyanins (95)	(Dey et al., 2022)

n.d.: Data not available.
* Total betalain content and the content of the predominant groups were equated to the same unit for better correlation.

Table 3
Content of betalains obtained from vegetable peel residues by non-conventional extraction methods.

Vegetable	Specie	Unconventional extraction method	Solvents (mass/ solvent ratio)	Time and temperature	Total betalain content (mg/g dry weight) *	Prevalence betalain group (mg/g dry weight) *	Reference
 Beet peel	*Beta vulgaris*	UAE	Distilled water (1:20, w/v)	30 and 60 min/ n.d.	12.48	Betaxanthins (8.61)	(Šeremet et al., 2020)
	Beta vulgaris	MAE	Pure water, acidified water, ethanol (0,1–0,2 w/v)	30–150 s/ n.d	2.02	Betacyanins (1.16)	(Zin & Bánvölgyi 2021)
	Beta vulgaris	UAE	Distilled water (1:15 w/v)	10 min/ n.d	1.84	Betacyanins (1.38)	(Rodríguez-Félix et al., 2022)
 Prickly peel	*Opuntia engelmannii*	PLE	Water and ethanol (1:40, w/v)	5, 17.5 and 30 min/ambient	–	Betaxanthins (0.26)	(Castro et al., 2019)
	Opuntia engelmannii	UAE	Water (1:9, w/v)	0.5–2.5 min/ 3–35 °C	201.6	Betacyanins (197.51)	(Melgar et al., 2019)
	Opuntia ficus-indica	PLE	Water (1:3, w/v)	5–15 min/ 40–100 °C	–	Betacyanins (11.85)	(Shen et al., 2019)
 Pitaya peel	*Hylocereus undatus*	PLE	Water (1:3, w/v)	5–15 min/ 40–100 °C	–	Betacyanins (2.18)	(Shen et al., 2019)
	Stenocereus queretaroensis	UAE	*Opuntia ficus-indica* mucilage (1:2, w/v)	10 min/ambient	3.2	–	(Soto-Castro & Castellanos 2022)
	Hylocereus polyrhizus	SFE	Ethanol (1:10, w/v)	25 h/40 °C	0.31	Betacyanins (0.28)	(Yu et al., 2023)

UAE – Ultrasound-assisted extraction; MAE – Microwave assisted extraction; PLE – Pressurized liquid extraction; SFE – Supercritical fluid extraction.
n.d.: Data not available.
* Total betalain content and the content of the predominant groups were equated to the same unit for better correlation.

betanin/g, 0.46 mg of indicaxanthin/g, and 1.84 mg of total betalains/g.

Castro et al. (2019), extracting betalains from *Opuntia bark*, only quantified betalains from the betaxanthin group by pressurized liquid extraction (PLE), with a maximum yield of 0.26 mg indicaxanthin/g of dry extract. Unlike Zin & Bánvölgyi (2021), who found that extraction using 40 % ethanol showed a 14 % higher yield than extractions with water alone. Another relevant factor refers to the increase in pressure from 0.1 MPa to 300 MPa. To recover betalains and other bioactive compounds in an environmentally friendly manner, Melgar et al. (2019) used the UAE method on *Opuntia* fruit peels and achieved higher yields depending on the extraction conditions, time (1.5 min) and temperature (20 °C), obtaining a total betacyanin content of 197.51 mg/g of dry extract. They also found that the higher the percentage of water in methanol, the better the extraction performance, confirming that betalains are more soluble in polar solvents.

Intending to extract betacyanins from by-products of the agri-food system, Shen et al. (2019) investigated the fruit peels of the cacti *Opuntia ficus-indica* and *Hylocereus undatus*, based on optimization in PLE about the water/solid ratio (6.0 and 10.9 mL/g), time (9.0 and 7.5 min), temperature (56.9 and 70.1 °C) and pressure (6.7 and 9.2 MPa) and reported significant yields with 11.85 mg betanin/g and 2.18 mg betanin/g, in the dry extracts, respectively. Furthermore, the authors show that the extraction technique can recover betacyanins, possibly producing ingredients rich in this pigment for subsequent food applications.

In turn, Soto-Castro & Castellanos (2022), studying UAE processes for betalains in pitaya (*Stenocereus queretaroensis*) peel, concluded that 2.25 MHz constituted the optimal ultrasonic frequency in the extraction yield of betalains (3.2 mg/g of dry weight), evincing the negative interference of higher values. They also emphasize that the power must be specific for each process, aiming to optimize the extraction of bioactive compounds and the applied temperature, making prior knowledge of the plant matrix essential to investigate. Yu et al. (2023) reported results with lower betalains concentrations by supercritical fluid extraction (SFE) and the application of fractionation technology with the solvent supercritical carbon dioxide, conducted at a pressure of 25 MPa. Even with a low betalain content in other studies, the authors describe that the high-intensity fractionation enables the isolation and recovery of natural compounds to further application as food colorant, thus offering the possibility of contributing to reducing environmental pollution and attribute added value to fruit peel waste.

Enzyme-assisted extraction (EAE) remains poorly explored on plant residues in general, as per the review by Lombardelli et al. (2022) which shows only a few recent studies for recovery of betalains. Therefore, applying EAE constitutes a promising field technique for betalains specifically from vegetable peels.

6. Factors affecting the stability of extracted betalains

As for other natural pigments, betalain degradation relates to intrinsic and extrinsic factors, which interfere with their chemical properties. Intrinsic ones include the chemical structure, pH, water activity, enzymes, and metals present in plant tissues, whereas the extrinsic ones refer to temperature, incidence of light, and presence of oxygen (Carreón-Hidalgo et al., 2022).

Temperature is a critical factor for the stability of betalains during food processing and storage, although they are more stable at low temperatures. Betalains are heat-sensitive pigments; temperatures above 50 °C cause their thermal degradation by cleavage, making their applicability as a natural dye unfeasible (Rodríguez-Mena et al., 2023). High temperatures and long exposure times can also cause isomerization and decarboxylation reactions in betalains (Rodríguez-Mena et al., 2023). Therefore, these factors must be considered mainly during the pigment extraction process.

The synchronous combination of temperature and light factors also degrades betalains, especially in temperatures above 40 °C. The simultaneous effect negatively impacts the color during processing and storage, and, ultimately, the quality of the final product. Betacyanins are less stable than betaxanthins under these conditions (Lombardelli et al., 2021).

Regarding pH, betalains remain stable from 3 to 7. pH values above 7 causes degradation and hydrolysis reactions, releasing betalamic acid, *cyclo*-dopa (Fig. 2. a), betalamic acid plus amino acids, or amines for betaxanthins (Fig. 2. b) (Qin et al., 2020), with betanidine and indicaxanthin prevailing in the two existing subgroups. In acidic media and high temperatures, betalains are subject to epimerization, i.e., forming compounds with the opposite absolute configuration or isomers with the oxidative decarboxylation reaction.

Water activity levels above 0.60 negatively interfere with the stability of betalains, whereas lower levels reduce degradation rates (Albuquerque et al., 2021). Other parameters, such as exposure to ambient light, also affect color stability (more specifically the L^* and $+a^*$ values), with color varying from purple-violet to yellowish brown due to pigment degradation (Kayin et al., 2019). Oxygen sensitivity is another critical factor related to betalain stability, which typically follows first-order kinetics for betalain loss.

The presence of enzymes also limits the stability of betalains due to oxidative degradation. After mechanical injuries to vegetables, enzymatic browning of the betalain source may occur due to the enzyme polyphenoloxidase (Dey et al., 2022), which can be inactivated by thermal pretreatment at a maximum temperature of 50 °C. On the other hand, betalains also undergo degradation by interaction with some metal ions, such as Al^{3+}, Ni^{2+}, Fe^{2+}, and Cu^{2+}, as these ions act as catalysts during the oxidation process, thus causing a color change (Kumorkiewicz et al., 2019; Sadowska-Bartosz & Bartosz, 2021).

Thus, several methods aim to improve the stability of betalains, such as intra- and intermolecular pigmentation, which consists of the interaction of other bioactive compounds, such as phenolic pigments (Saberian & Noghabi, 2021), or even with other betalains molecules. Structural modification of food matrix can enhance batalains stability, as the incorporation of a more rigid food matrix hinder the rotations of specific bonds and thus positively interfere with fluorescence quantum yields (He et al., 2019). Other strategies as the use of additives such as antioxidants, chelators or β-cyclodextrin have been explored. The interaction of charged nitrogen with antioxidants and chelators neutralizes the electrophilic center of betalains, whereas β-cyclodextrin acts as a protective layer by forming inclusion complexes with betanin (Carreón-Hidalgo et al., 2022).

Betalain degradation factors are synchronous in their stability, occurring in different conventional and non-conventional extraction methods. These factors can cause damage from their molecular chemical structures to changes in the original color. Therefore, knowledge and control of these factors can constitute an excellent strategy to reducing the impacts of processes on loss of stability during extraction and storage until application. Techniques such as encapsulation may usefully increase betalain stability for future industrial applications.

However, this work focuses only on reviewing the encapsulation methods applied to betalains extracted exclusively from vegetable peels. Encapsulation of betalains extracted from various sources of food waste, can be found in the work of Zannou et al. (2023).

7. Encapsulation as a preservation technique of betalains extracted from vegetable peels

Numerous encapsulation methods have been recently explored to preserve the characteristics of betalains (Fig. 3) and expand their use as food colorings.

Encapsulation has been used to increase the stability of betalains, extend the shelf life, and maintain the biological properties of these pigments (Lan et al., 2023). Encapsulation can be conducted using different physical, physicochemical, and chemical technologies (Rodríguez-Mena et al., 2023). Drying methods (spraying and freeze-

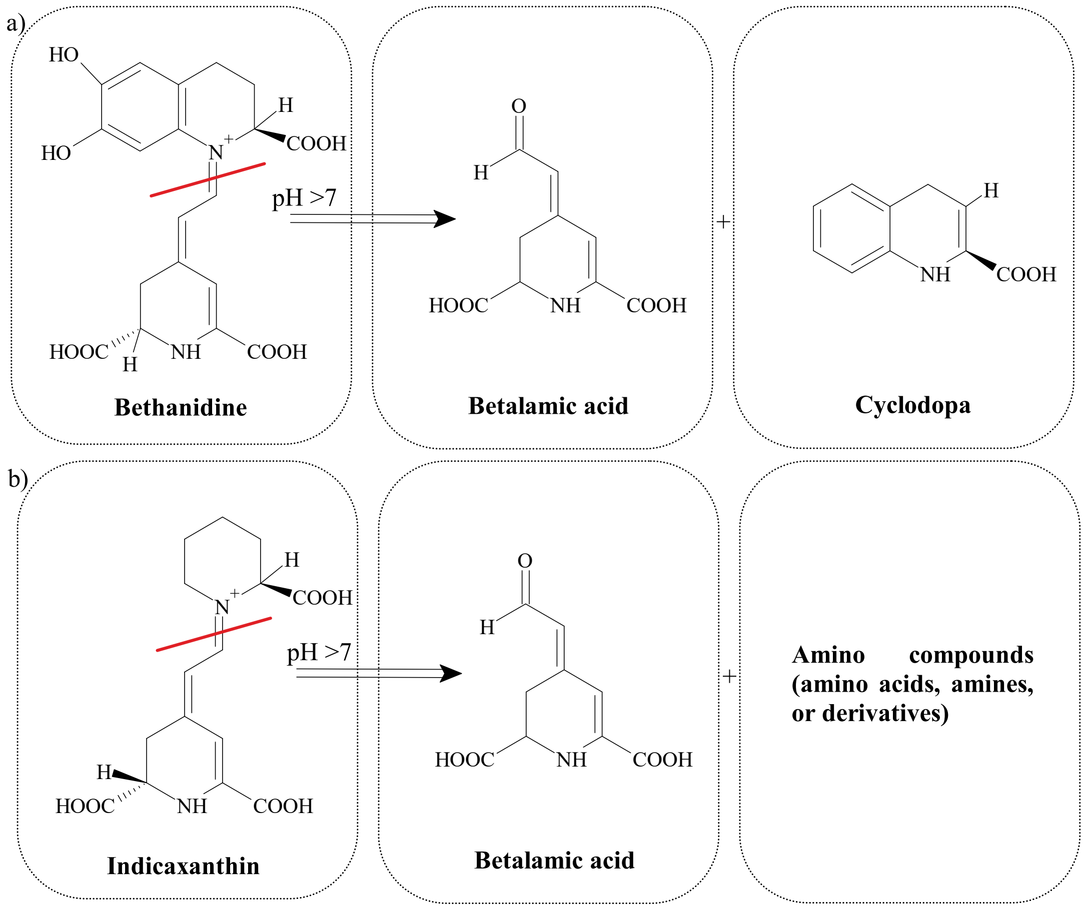

Fig. 2. Degradation reaction of the main betalains of the betacyanin (a) and betaxanthin (b) subgroups extracted from vegetable peels.

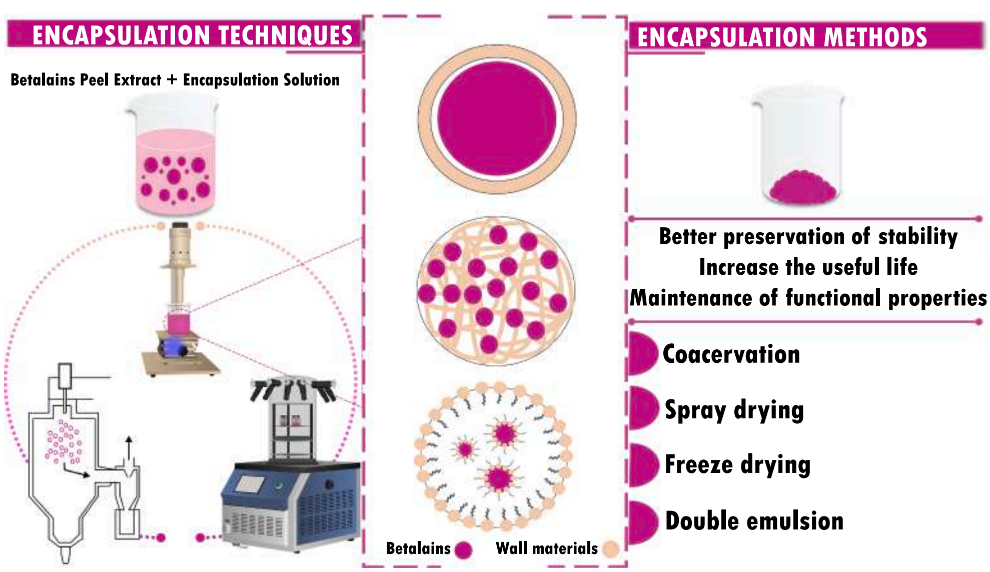

Fig. 3. Main encapsulation techniques to preserve betalains extracted from vegetable peels.

drying) are the most often applied techniques to encapsulate betalains from vegetable peels, the latter being better to preserve the characteristics of the pigment (Shofinita et al., 2023). Table 4 lists recently investigated encapsulation technologies for betalains obtained from vegetable peels, detailing the applied methods.

Raj & Dash (2022) studied the encapsulation of betacyanins from pitaya peels by the coacervation method. They found that binary mixtures of gum arabic and sodium alginate showed a greater encapsulation efficiency than maltodextrin alone and 12.72 % higher than particles formed with gelatin and sodium alginate. Dang-Bao & Tran (2023) evaluated the encapsulation by freeze drying of betalains extracted from red pitaya skins with microcrystalline cellulose and maltodextrin. The systems were incorporated to jellies, conferring high stability to betalains, even when stored at room temperature for 60 days.

Table 4
Recent studies have shown that the most common encapsulation techniques to control the stability of betalains stemmed from vegetable peels.

Vegetable	Specie	Encapsulation technology	Core material	Wall Material	Maximum encapsulation efficiency (%)	Reference
 Pitaya peel	*Hylocereus undatus*	Coacervation (spray drying)	Betacyanin	Maltodextrin, gum arabic, xanthan gum, and gelatin were mixed with sodium alginate	92.27	(Raj & Dash 2022)
	Hylocereus monacanthus	Freeze drying (ultrasonic)	Total betalains	Maltodextrin	79.88	(Li et al., 2022)
	Hylocereus polyrhizus	Freeze drying (ultrasonic)	Total betalains	Microcrystalline cellulose and maltodextrin	93	(Tran et al., 2022)
	Hylocereus polyrhizus	Freeze drying (ultrasonic)	Total betalains	Microcrystalline cellulose	98	(Dang-Bao & Tran 2023)
 Prickly peel	*Opuntia stricta* var. *dillenii*	Double emulsion	Total betalains	Gelatine, guar gum, gum arabic and caseinate	98	(Parralejo-Sanz et al., 2023)

Tran et al. (2022) analyzed different wall materials to encapsulate betalains extracted from pitaya peel. The systems formed by microcrystalline cellulose and pectin (obtained from the pitaya peel) were stable in the pH range from 3.6 to 7.4, proving to be an effective binary matrix for the encapsulation of betalains.

Table 4 highlights the extensive use of ultrasound to encapsulate betalains derived from pitaya peels. Li et al. (2022) used this technique, also with red pitaya peel, and showed that increasing ultrasound power and time resulted in particles with greater encapsulation efficiencies from 51.6 to 79.88 %. The authors concluded that this encapsulation technique maximizes pigment stability. Parralejo-Sanz et al. (2023) encapsulated betalains in double emulsions, finding that casein formulations achieved the highest encapsulation efficiencies, ranging from 73.7 to 98 %. Adding to this, the study attributed that the combined use of casein and gelatin to the stability of the target compound. The process of preparing the aqueous phase of the double emulsion includes the gelation, a mechanism that benefits the encapsulation of betalains from prickly pear.

Nanoencapsulation is another technique widely used to encapsulate natural pigments, including betalains (Ghosh et al., 2021). Kumar et al. (2020) encapsulated Basella rubra betalains in lecithin nanoliposomes. They observed an improvement in the stability of the extracted betalains during a maximum storage of 40 days at a temperature of 5 °C. Figueroa-Enriquez et al. (2023) evaluated the encapsulation of betalains from the pulp of *Stenocereus thurberi* by coaxial electrospraying to obtain nanoparticles. They reported that the gelatin-betalains nanoparticles were stable against temperatures above 100 °C.

However, the recent literature lacks report on nanoencapsulation of betalains extracted exclusively from vegetable peels in nanostructures. This encapsulation technology opens new horizons for exploring betalains from vegetable peels, potentially improving stability and expanding their application in foods. Toxicity studies are also necessary since scale reduction can intensify properties and confer toxicity to compounds that are originally non-toxic on a macro scale.

Ultrasonic encapsulation techniques, such as spraying, freeze-drying, and double emulsion, have shown excellent shelf life and thermal stability of betalains derived from fruit peels, including pitaya and prickly. Notably, the formation of new mixtures for the interaction of different encapsulating agents such as microcrystalline cellulose has been investigated, with proven efficacy in reducing the degradation of betalains.

Therefore, new combinations of agents with the potential to be used as wall materials are recommended to optimize encapsulation toward greater stability for betalains from vegetable peel residues.

8. Applications of betalains extracted from vegetable peels in the food industry

Several natural pigments are applied to food products (Shen et al., 2023). Compared to those extracted from food waste, such as those recovered from vegetable by-products, these can give enriched foods identity and functional appeal and favor sensory characteristics and nutritional quality (Wani et al., 2021).

At a global level, the main regulatory bodies for food additives are the European Food Safety Authority (EFSA) and the United States Food and Drug Administration (FDA), as for the application of natural coloring, such as betalains, with authorized use in foods and identified on labels as E162 and 73.40, for the European continent and the United States, respectively. However, the use of food coloring varies from country to country, as it must be in line with the specific legislation of each region (Bennuci et al., 2022). In the European Union, red betanin extracted from beetroot (*Beta vulgaris*) has a maximum limit of 200 mg/kg only for breakfast cereals flavored with fruit, whereas in the United States still has no established maximum limits (*quantum sattis*) (Thomsen et al., 2023), showing guidelines regarding its combined use with nitrite.

In recent years, to find new plant sources of betalains, studies with other vegetables, including those from the *Cactaceae* family, have been carried out given peculiar nutritional and technological properties that may present the potential for application in various food matrices, especially as natural dyes (Zin et al., 2020a).

Furthermore, it can contribute to sensory quality by pigmentation, and at the same time, it has bioactivity, which is associated with beneficial effects on human health. Betalains are one of the groups of natural pigments that have the potential to be added or supplemented in food (Prieto-Santiago et al., 2020). However, the major bottleneck is maintaining its stability in the face of environmental factors—specifically, during the processing and storage of enriched products—its use as a natural additive in processed foods has remained a challenge to date (Calva-Estrada et al., 2022).

As observed in the selected studies, beetroot, although it is the primary source for extracting betalains, shows a disadvantage for application in food as it contains substances, geosmin, and pyrazines, responsible for off-flavors (Chaudhary & Singh, 2021).

Putthawan et al. (2022) evaluated the stability of extracts obtained from *Hylocereus polyrhizus* after extraction with water observed that betalains showed greater stability at pH 7 (neutral) under the studied temperature conditions (50, 70, and 90 °C). These authors indicated the feasibility of incorporating betalains as food coloring in products with pH ranges close to 7 or slightly acidic, such as ice creams, drinks, as well as jellies, and with pH values of 2 (acidic) and 12 (alkaline) destabilize the pigment.

At the same time, Utpott et al. (2020) added pitaya betacyanin extract, microencapsulated with gelatin, maltodextrin, and pitaya peel mucilage to commercial natural yogurt. The extracted pigments showed potential as natural dyes because they maintained their color during storage when compared to the liquid extract, showing less degradation of betacyanin at 5 °C for 28 days. They also concluded that several food matrices, such as candies, soft drinks, ice cream, and bakery products, can be colored naturally by the microcapsules of the obtained extracts.

The use of betalains, recovered from vegetable peels, in foods, is predominantly used as food coloring, with a natural appeal. However, despite the technological evidence, studies show limitations regarding the stability of the powder color after application in food matrices, mainly about the determined time. Challenges include the need to use high quantities of extracts containing the pigment stands out to match the color stability of model formulations enriched with synthetic dyes, although high encapsulation efficiencies are evident (Dias et al., 2020). This assumption turns encapsulation into an ally toward protecting the application of natural pigments (Ghosh et al., 2022), including betalains. Therefore, further research must be carried out to predict the maximum time required to preserve the initial quality of betalains extracted from vegetable peels to achieve scalable yields, enabling economically viable exploitation for industry as a natural dye food.

9. Conclusion and future perspectives

Food waste, such as vegetable peelings, are co-products that contain high concentrations of natural pigments, such as betalains. Extracts from these by-products are alternatives to synthetic dyes, if they are extracted and used under controlled conditions regarding factors inherent to stability. The superiority of green extraction methods is emphasized, as they offer bioactive and functional properties, while being ecologically sustainable, avoiding the use of toxic solvents with environmental impact. The encapsulation technique is effective in reducing the degradation of betalains; however, the selection of protective matrices depends on the final product into which the particles will be incorporated.

Therefore, the appropriate selection of wall materials leads to maximum stability and better color quality. Despite recent evidence that betalains recovered from vegetable peels have high potential for application as natural food colorings, to date, the present review shows that studies are still limited, especially at industrial levels.

Therefore, additional systematic studies are necessary to establish suitable methods or in combination for the recovery and stabilization of betalains derived from vegetable peels, to achieve equivalent yields for application in the food industries. Future investigations should focus on industrial application in food matrices, simultaneously considering the concepts of sustainability, economic viability, and the maintenance of the bioactive properties of betalains.

CRediT authorship contribution statement

Ingryd Rodrigues Martins: Writing – review & editing, Writing – original draft, Conceptualization. **Luiza Helena da Silva Martins:** Writing – review & editing, Validation, Supervision, Conceptualization. **Renan Campos Chisté:** Writing – review & editing, Validation, Supervision, Conceptualization. **Carolina Siqueira Franco Picone:** Writing – review & editing, Validation, Supervision, Funding acquisition. **Maria Regina Sarkis Peixoto Joele:** Writing – review & editing, Validation, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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An economic perspective of the circular bioeconomy in the food and agricultural sector

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Transforming the agri-food system from a "take-make-waste", or linear production system, to a circular bioeconomy that reduces, recycles, recovers, reuses, and regenerates wastes and transitions from fossil to biobased fuels and products is being hailed as critical for meeting a growing population's food and fuel needs in environmentally sustainable ways. While a transformation towards a circular bioeconomy is an appealing strategy to achieve multiple environmental goals, we argue that this strategy needs to go beyond a techno-centric focus and adopt an economic value-based lens to balance the desire for circularity with its costs, benefits, and distributional effects on society. This perspective analyzes the mechanisms that sustain the existing linear economy and proposes a novel social cost-benefit framework to determine the optimal level and path to circularity. We present five critical pathways to achieve a sustainable circular bioeconomy in a market economy consisting of decentralized decision-makers.

Global food production has tripled since the mid-20th century, growing faster than human population and agricultural land. Technological advances, primarily induced by the objectives of enhancing productivity and profitability, have driven this intensification of agriculture. However, a large portion of inputs, including irrigation water, nutrients, and herbicides, that are applied for crop production are not taken up by the crop; this low input use efficiency results in environmental contamination and runoff that degrades soil and water quality[1–4]. Agricultural processing firms release additional nutrients into wastewater streams as they convert agricultural commodities into consumer goods. Much of the agricultural biomass produced with these inputs is wasted. Of the biomass that is consumable, losses during pre-harvest, post-harvest, and post-consumer stages add to organic waste[5]. Managing agricultural wastes is a challenge for both developed economies and developing countries, as it is often burnt or landfilled, contributing to GHG emissions and air pollution[6,7]. Agricultural pollution is the largest cause of degradation of surface and groundwater quality, loss of soil health, hypoxic zones, and biodiversity loss. Agriculture, forestry, and land use contributed to 22% of global emissions in 2019[8], 30% of energy consumption, 70% of groundwater extraction, and 75% of deforestation[9].

This existing agri-food production system is referred to as linear because it relies on a one-directional process of using extracted inputs, producing outputs and generating residues that become polluting wastes. Recognizing the limitations of relying on this approach to meet growing demands for agri-food products[2,10] has led to a call for a paradigm shift towards a circular bioeconomy[11,12]. Definitions of a circular bioeconomy vary across studies but have a common emphasis on reducing the use of virgin materials, recycling and reusing materials, restoring, and regenerating natural systems, and converting the unavoidable wastes and other biological resources into bioenergy or bioproducts to substitute for fossil fuels[13–17].

There are various existing and emerging technological pathways to enable the transition of the agri-food sector to circularity for any product supply chain and across the multitude of products in an economy (Fig. 1a). These include scientific developments in digital precision farming and artificial intelligence technologies for crop management which can reduce nutrient loss on the field, nutrient recovery and recycling at the edge of the field[18,19]. Similarly, there are multiple types of applications of synthetic biology, gene editing and biotechnology, and precision fermentation to convert and upcycle agricultural wastes and perennial energy crops to plant-based proteins, bioproducts, and bioenergy, that are substitutes for chemical and fossil energy-based products[20] (Fig. 1b). Other examples, include redesigning landscapes to include leguminous crops that necessitate fewer chemical treatments, pasture for grass-fed animals, converting organic waste generated at all stages ranging from crop residues to food scraps into compost and biochar for nutrient-rich soil amendments or into renewable natural gas can improve soil health and crop productivity and reduce need for fossil fuels[21,22].

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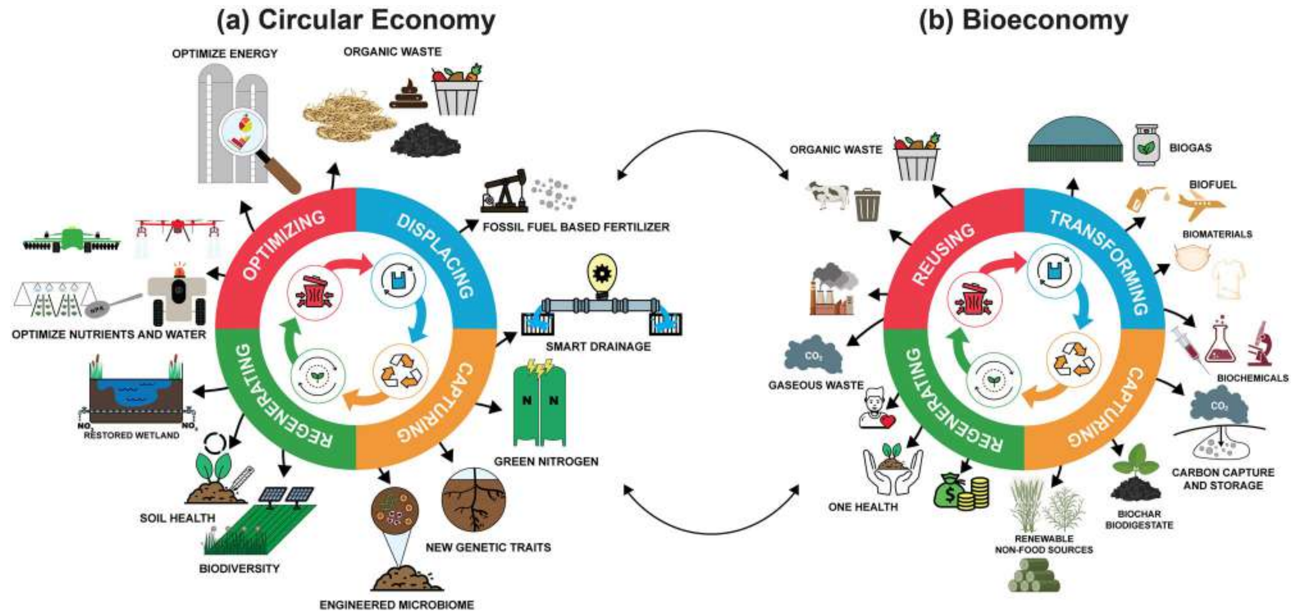

Fig. 1 | Multiple pathways to a circular bioeconomy. a represents multiple pathways to reduce, recyle and reuse waste in a circular economy; **b** represents multiple pathways to produce inputs, food and energy products in a bioeconomy. Together, the two panels show the interconnections among the pathways to reduce, recycle and reuse waste and to convert unavoidable waste and other biological resources to bioproducts that displace fossil fuels.

These pathways may vary in their environmental outcomes and impacts on GHG emissions, water quality, biodiversity, and land use, which may be synergistic or conflicting. These technologies can differ in their costs, pollution-reduction effectiveness, and impacts on productivity and trade-offs. A key complexity in charting a path to a circular bioeconomy is selecting the mix of technologies and the desired extent of circularity to be achieved with this transition; this will affect the costs of achieving a circular bioeconomy and other societal outcomes. The availability of technologies is necessary–but not sufficient–to guarantee a transition to a circular bioeconomy. Consumers and businesses throughout the agrifood supply chain make decentralized decisions guided by their private objectives. Even technologies with high readiness for deployment are often not adopted for economic, behavioral, and social reasons. Thus, a strategy for the transformation to a circular bioeconomy needs to combine technology availability with market-driven mechanisms, regulations, and other incentives for guiding individual consumer and producer choices among the various potential pathways.

Interest in a circular bioeconomy started primarily in environmental, agricultural, and biological engineering and the ecological sciences. There is a large literature on the imperative for transitioning to a circular bioeconomy across developed and developing countries[3,8], identifying barriers, opportunities, and recommendations for the transition and describing the technological pathways for specific sectors[23]. The concept of a circular bioeconomy has not drawn much attention from economists, who are largely unfamiliar with this terminology[24]. Economists have contributed to analyzing the economics of non-point pollution control and other agri-environmental policies[25], designing incentives for technology adoption[26], and developing approaches for quantifying food loss and waste[27] and the environmental impact of reducing food waste[5,28]. They have also noted the need for bundling technical innovations with policies, knowledge, social institutions, and cultural norms to reduce the land and water footprint of agri-food systems[29]. However, there has been no holistic analysis of the economics of transitioning to a circular economy, the optimal mix of the various dimensions of reducing, recycling, recovering, and reusing wastes to displace fossil fuels and the design of mechanisms for incentivizing a circular bioeconomy.

This perspective aims to present an economic lens to determine the optimal level of circularity, the mix of circular strategies, the optimal amount of waste disposal, and the acceptable trade-offs between higher economic costs for consumers and producers and the societal benefits from avoided environmental costs. Economics provides a framework to identify optimal strategies that balance private and social objectives while recognizing that resources are scarce and that trade-offs need to be made. This framework can be applied to design incentives and science-based regulations that price externalities and put a value on public goods to achieve the optimal balance between competing objectives. We describe the institutional, regulatory, and market structures that sustain the existing linear economic system and the need for their transformation to create a demand-pull for the technological advances for a circular bioeconomy.

Determining this optimal choice of pathways and the mix of carrots and sticks policy approaches to achieve it requires sound interdisciplinary collaborations among economists, other social and environmental scientists, biologists, engineers, and others. In addition to economic drivers, the transition to a circular bioeconomy will also depend on social norms and cultural barriers and have implications for social justice that need to be considered. We conclude by presenting five critical pathways to achieve a circular bioeconomy that is sustainable in a market economy consisting of decentralized consumers and producers.

Concept of a circular bioeconomy: its appeal and limitations

The concept of a circular bioeconomy unites two complementary alternatives to the existing linear agricultural production system. The first is the notion of circularity in resource use that emphasizes reducing, recycling, and reusing chemical and other inputs to increase resource use efficiency, maintain products, materials, and resources as long as possible, and minimize the amount of polluting waste released to the environment (Fig. 1a). The second is the concept of a bioeconomy, which consists of sectors of the economy that produce goods and services using renewable natural resources and biological resources as inputs (Fig. 1b)[30]. Bioeconomy can be viewed broadly as encompassing the use of biotechnology and biological resources from various sources to create an economic system in which bio-based products displace fossil fuel-based value chains. These two concepts are highly interconnected and emphasize waste reduction and re-use of wastes and other biological resources to displace fossil fuels.

The notion of a circular bioeconomy is appealing for various reasons. First, it recognizes that a key source of pollution and environmental degradation is waste generation during production, which typically does not use inputs efficiently, both technically and economically. Second, it emphasizes the importance of reducing waste generation at the source, recycling and reusing waste, and converting waste into useful final products to meet consumer demand. Third, it draws attention to the role that biological resources can play in displacing fossil fuels and mitigating changing climate. Lastly, a circular bioeconomy provides an operational and techno-centric path to environmental sustainability.

However, a techno-centric approach to sustainability may not be economically or socially sustainable, particularly if it views zero waste and replacement of fossil fuels as end goals rather than a means to an end which is improved human well-being. By itself, the circular economy framework does not provide a mechanism to determine the optimal level of circularity for a product supply chain, sector, or economy, as discussed below and shown in Fig. 2. Higher levels of circularity are likely to increase the cost of production and create trade-offs between the economic costs of circularity, environmental benefits, and social justice. Transitioning to a circular bioeconomy will involve movement along a continuum from a linear economy towards one that is more circular. Solutions that balance a mix of approaches that reduce, recycle, reuse, and dispose of waste with the costs for producers and consumers may enhance environmental and economic well-being.

The concept of a circular bioeconomy sets a single-minded goal of waste minimization and conversion to bio-based products. It does not consider the interconnected role that economic conditions, equitable distribution of resources, and environmental protection jointly play in the well-being of individuals and societies. More specifically, the vision for a circular bioeconomy does not articulate a mechanism for considering questions such as: What is the optimal level of waste and the mix of reducing, recycling, reusing and disposing it? How large are the costs of circularity, and how do they compare to the environmental benefits it leads to? Who pays for a and who benefits from a circular bioeconomy? Can we rely on voluntary approaches and corporate social responsibility to achieve the optimal level of circularity? What types of policy incentives are needed to achieve this optimal level cost-effectively and equitably?

Furthermore, the articulated vision of a circular bioeconomy is based on the implicit belief of "build it and they will come" and that the availability of technologies that reduce waste and increase resource efficiency will naturally make them desirable to adopt by producers. However, the availability of existing and emerging biological and technological solutions is insufficient to transform into a circular bioeconomy unless farmers, businesses, and consumers adopt them. Explicit and hidden costs of adopting circular technologies can limit incentives for adoption and one may need regulatory and market-based incentives to induce the optimal level of a circular bioeconomy.

This technology-push view must be supplemented with a "demand-pull" perspective that recognizes the need to incentivize farmers, businesses, and consumers to adopt circular practices, processes, and products. Lastly, the technology-centric approach to a circular bioeconomy overlooks the need for demand-side conservation efforts as another approach to

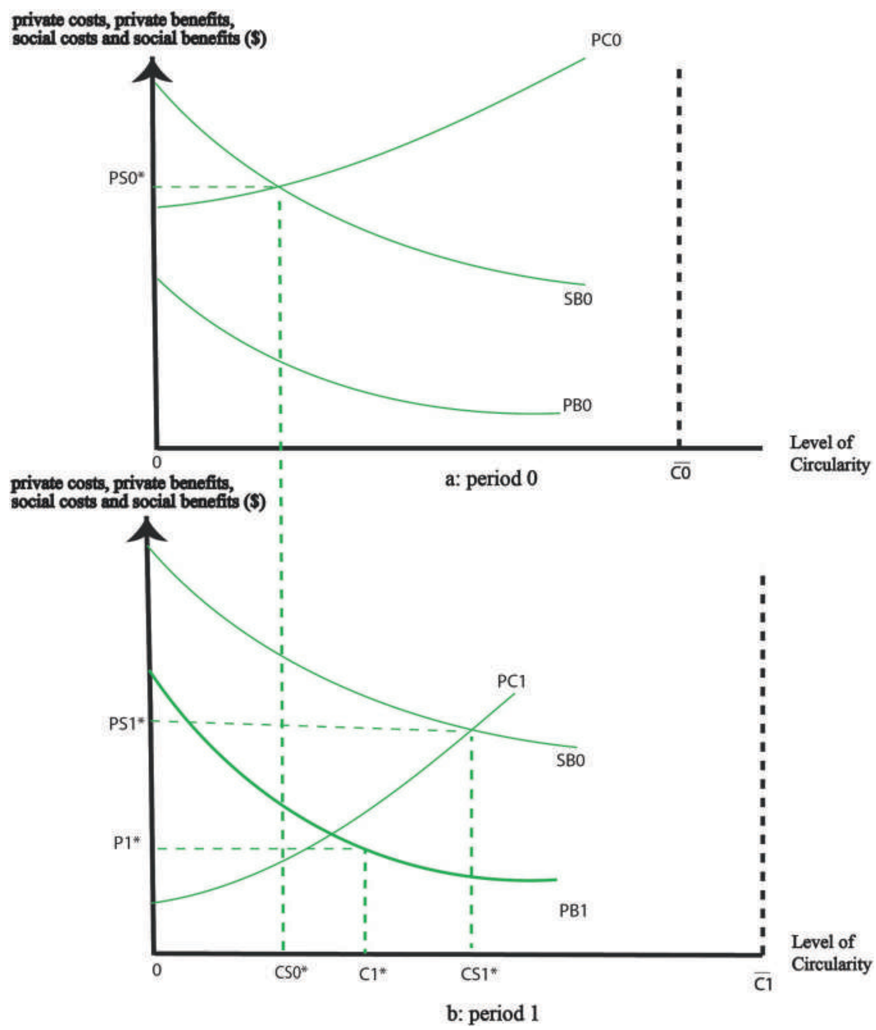

Fig. 2 | A social cost-benefit approach to determining the optimal level of circularity. Panel (**a**): A privately optimal linear economy; Panel (**b**): Private and socially optimal levels of circular economy.

environmental sustainability. Overconsumption of products that generate pollution arises because pollution damage is not included in the price of these products.

To design a sustainable circular bioeconomy, policymakers, government and non-government organizations and national and international development agencies need to adopt a normative, nuanced, and systems-view of the circular economy and an approach to determine the sustainable level of circularity – based on consideration of the synergies and trade-offs among costs and benefits of a circular bioeconomy along with the value of environmental benefits obtained and their incidence across society. These organizations frequently rely on cost benefit analysis and environmental impact analysis to examine if a policy or project is financially and environmentally sound.

Why do linear systems persist?

A common linear approach for crop production relies on tillage and nutrient intensive, monoculture crop production practices, and results in post-harvest crop losses, unused crop residues after harvest, and animal waste that could be converted to energy through anaerobic digestion, lack of recycling and reuse of chemicals during the production process, reliance on fossil fuels, single-use plastics, other disposable products as well as post-consumer food loss and waste. There is a large literature examining the factors that prevent the adoption of technologies that could be considered win-win because they are efficiency-enhancing, waste-reducing, and re-using technologies, which should save input costs while reducing nutrient loss, improving soil health, and increasing yield[31]. Despite the potential savings from reducing and reusing waste, circular and bio-based technologies may have higher costs (capital, labor, learning, and search costs), risks, uncertainties, and inconvenience, which can adversely affect the private economic well-being of producers and consumers[32]. Reluctance to implement circular methods may also arise due to a lack of infrastructure, disruption to existing jobs, limited scalability, and uncertainty about government policies[33]. Constraints on financing, access to credit and a short planning horizon (or high discount rates) limit investment in technologies that may take a few years to generate a payback through regeneration of soil health, savings in input costs, and development of markets for circular products[34–36]. Institutional factors, such as declining number of owner-operators on the farmland and lack of crop insurance for new agricultural practices, lack of extension services, technical assistance and infrastructure as well as behavioral drivers, such as attitudes, information, peers, and networks, affect producers' adoption of technologies[37,38].

In a decentralized market-based economy, individual consumers and producers make production and consumption choices based on self-interest. Individual decision-makers have minimal incentives to engage in costly activities to prevent problems such as climate change, hypoxia, and groundwater depletion; products such as certified organics that provide both private and public benefits are likely to be adopted voluntarily to the extent of their perceived private benefits but to levels that may be socially sub-optimal (as discussed below and shown in Fig. 2). Lack of awareness or education about the planetary benefits of circular products can lead to an unwillingness to pay a premium for such products, which can limit markets for these products. Most agricultural lands produce annual commodities like corn, soybean, wheat, and rice, which have long supply chains as feed for livestock and processed ingredients for food products.

Differentiating these commodities for the final consumer, based on the circularity of the methods used to produce them, is challenging due to the current supply chain infrastructure and technology that is designed to blend grain from millions of farms and transport them to wholesale markets and consumer packaged goods (CPG) companies. It is, therefore, difficult to credibly differentiate products sold to consumers based on their methods of production and charge premium prices from environmentally conscious consumers willing to pay for products with lower environmental impacts. CPG companies, however, can have vertically integrated supply chains that are circular for their products and differentiate their brand to appeal to environmentally conscious consumers. While buyers benefit from the availability of a variety or products to serve their differing preferences, product differentiation can become a source of market power. This can lead to increasingly concentrated sectors and affect the market efficiency of agri-food systems. This can affect market prices and social welfare and shift economic surplus from consumers to CPGs[39].

Pollution generated at various stages of the agri-food production process differs in its potential to be measured, monitored, attributed to a polluter, and verified at a reasonable cost; this has implications for the type of policy and behavioral interventions needed to induce circularity[40]. Pollution generated on the farm and food waste is non-point source while pollution generated by processing and CPG firms is point-source pollution. On-farm agricultural pollution is rarely subject to the polluter-pay principle and has not been directly priced. Instead, efforts to reduce pollution generated on the farm have taken the form of conservation programs that offer payments to farmers who voluntarily agree to adopt conservation practices that reduce pollution. These programs offer uniform payments that are practice-based rather than performance-(pollution-outcome)-based because of the non-point nature of agricultural pollution and challenges with measuring, tracking, and attributing pollution to sources at a reasonable cost. The voluntary, practice-based conservation payments approach to pollution control has had limited effectiveness at reducing major environmental problems such as hypoxic zones, impaired water quality in water bodies, groundwater depletion and contamination, and rising costs of waste-water treatment. Current approaches for inducing the adoption of environmentally friendly practices by farmers through conservation payments are limited by fiscal budget constraints, the inability to target participation by farmers that are causing the greatest environmental harm, and to link payments to the extent of ecosystem services provided. Agrifood processing firms are typically subjected to command-and-control air and water quality regulations which require end-of-pipe pollution control technologies and do not incentivize pollution prevention, recycling, or reuse of pollution. Food waste at the retail and household level is not directly priced or taxed and, in part due to lack of data and quantitative information on where it is being generated, stakeholder resistance to approaches that would raise the cost of food and the potential for illegal dumping.

Despite evidence of the potential of modern biotechnology to increase agricultural and biofuel yields, reduce chemical and land use, and thereby reduce biodiversity loss[41,42], public sentiment towards a bioeconomy has been mixed. Concerns about genetically modified crops' environmental and health impacts have led several countries to ban or restrict their production and use. Agricultural biotechnologies are widely used for fiber and animal feed production and less for food. The capacity of agricultural biotechnologies is expanding with innovations like CRISPR[43] and there is a need for regulatory reform for biotechnology to reach its potential. Early efforts at relying on food crops to produce biofuels in the US and EU and the accompanying spike in commodity prices have created a perception of competition between the traditional agricultural economy and the bioeconomy because they rely on the same land base. Concerns about the implications of a bioeconomy for converting non-cropland to crop production with adverse implications for carbon stocks in that land and for biodiversity have led to public skepticism about the net benefits of a bioeconomy. Efforts at switching from food crops to non-food dedicated energy crops that diversify agriculture, reduce nutrient leaching and regenerate soil organic matter have been hampered by high costs of producing advanced biofuels and bioproducts and lack of adequate incentives for investment and commercial-scale production.

Numerous alternatives to linear-based production methods exist, as described above. However, there are several failures in current markets, including subsidies, exerting downward pressure on prices for inputs (such as energy and water) and distorting incentives in production. Government subsidies have been a major form of policy support for agriculture and amounted to $817 billion per year worldwide in the 2019–2021 period[44]. While some forms of subsidies have boosted agricultural productivity, they have also raised serious concerns about introducing distortions and exacerbating the adverse environmental impacts of agri-food systems[45].

Many large farming operations and major agricultural corporations dealing in seeds, fertilizers, herbicides, pesticides, and large CPGs, are hesitant to embrace these alternatives due to concerns about reduced profit margins that could negatively impact shareholder returns. An increasing number of large corporations have voluntarily established net zero carbon, net zero waste and other sustainability goals to reduce waste to landfills, to water bodies and to increase efficiency, reuse, and recycling. The efforts are effective under restrictive conditions, in which firms set numerical goals, timelines for achieving them and their performance can be monitored, measured and tracked with public disclosure of environmental information[46]. While efforts such as private sustainability standards and information disclosure requirements are growing and can help improve the sustainability of production processes under certain conditions, these efforts are often difficult to scale and are not widely prevalent[47]. Moreover, the use of different methodologies and information reporting requirements can lead to a lack of clarity and credibility in the signals to consumers and producers[48].

Agricultural lobbying efforts by large conglomerates and farm associations significantly sway political decisions, hindering reforms to the prevailing systems and preserving the status quo, including crop insurance programs, policy support for production instead of conservation and biofuel mandates that incentivize the use of food crops for biofuel, from which they benefit substantially. The structure of institutions shapes the constituents whose interests are served by policymakers and constrains the potential for reforming agricultural support policies to lead to a more circular and diversified cropping and agri-food system. There are several explanations for the observed technology lock-in and persistence in agri-food systems even when preferred alternatives exist; the entrenchment of skills and knowledge with existing crops and technologies, policy and institutional settings that support the use of these technologies and the infrastructure and production systems that build around them and create reinforcing forces that favor their continued use[49,50].

Public concerns about climate change and environmental degradation have not led to legislation in most countries due to a lack of political will to implement policies that will impose immediate costs but would improve the well-being of the people, land, and the planet in the long run. Despite awareness of the benefits of preventing problems rather than fixing them later, governments with short time horizons fail to take preventive actions that impose short-term economic costs but provide long-term environmental benefits. The presence of multiple and diverse interest groups that vary in their gains and losses contributes to the complexity and challenges of crafting effective environmental regulations.

We now describe a framework to guide the transition to a circular bioeconomy that is sustainable in a market economy.

A framework for transitioning to a circular bioeconomy

Welfare economics offers a conceptual, social cost-benefit framework that determines optimal choices of consumption, production, and technology, and also the prices of market goods and non-market environmental goods that would maximize net benefits (for consumers and producers net of the environmental damages caused by those choices). A stylized representation of this framework is shown in Fig. 2, with circularity represented on the horizontal axis by a scale from 0 to $\bar{C}_0$<1, with *0* representing no efforts at waste reduction beyond what is in the private interests of producers in the absence of any market or regulatory incentives and $\bar{C}_0$ representing a technologically feasible extent (less than 100%) to which waste disposed to the environment can be reduced in the initial time period (Fig. 2a). This level is expected to shift to the right, with technological development, as shown by $\bar{C}_1$ (Fig. 2b). The incremental private cost of reducing waste is expected to be upward-sloping but could be linear, non-linear, or U-shaped. The high fixed costs of scaling up technology could initially result in declining incremental costs due to economies of scale. It is expected to increase, possibly at an increasing rate, as the marginal cost of waste reduction increases and becomes steeper as the theoretical maximum is approached. Monetized values of the benefits of reducing the multiple environmental externalities caused by human activities (based on individual willingness to pay for reducing environmental damages) represent a "demand" for circularity. This is expected to decline as circularity increases but may have an inverted U-shape as the marginal benefits of the first few units of waste reduction can be expected to be low and to increase as waste reduction increases up to a point after which there could be diminishing marginal returns to waste reduction. For simplicity, we represent the private marginal cost of circularity by PC_0 and the private marginal benefit of circularity by the PB_o at time $t = 0$. The social marginal benefit of circularity is represented by SB_o; it can also be considered as the inverse of the social cost of waste generation. Based on economic theory, the privately optimal level of circularity is the point where $PB_o = PC_o$, while the socially optimal level of circularity is represented by the point where $SB_o = PC_o$.

Figure 2(a) represents the case where the private demand for circularity PB_0 is low (because the environment has a large capacity to absorb waste, public awareness of the damages due to a linear economy is low, and incomes are low leading to low demand for environmental quality). In contrast, the incremental cost of circularity represented by curve PC_o is high. In the absence of political will and environmental regulations that price waste or set standards to reduce waste to C_{so}^*, the level of circularity chosen by a market economy is zero (representing a linear economy), because there is no intersection between the PC_o and PB_o curves in Fig. 2a. The socially optimal level of circularity is represented by C_{so}^* with an implicit social cost of waste of P_{so}* (Fig. 2a).

Over time, as environmental damage increases with growing economic activity and the private value placed on environmental quality grows, the private benefits to producers of being socially responsible increase. Suppose that the private demand for circularity shifts to the right to PB_1, at a future time period, $t = 1$ (Fig. 2b). At the same time, technological change reduces the private cost of increasing circularity and shifts the supply of circularity to PC_1. The privately optimal level of circularity is now C_1* with an implicit willingness to price waste at P_1^*. This represents the effects of corporate socially responsible efforts by large firms, such as CPGs, to reduce waste and increase efficiency through their supply chains that can also lead to on-farm efforts to adopt low carbon intensity practices, increasing nutrient use efficiency and soil carbon sequestration. Although, the level of circularity achieved through the socially responsible efforts of producers and consumers is higher than before but still likely to be less than the socially optimal level C_{s1}* with full internalization of externalities by consumers and producers.

With self-interested decision makers, government intervention in the form of penalties for waste generation (such as a carbon or pollution tax) or subsidies for waste removal, recycling, or carbon credits, priced at the social cost of waste, P_{s1}*, or regulatory limits on waste are needed to move towards a socially optimal level of circularity. The magnitude of these taxes will decrease with the availability of low-cost circular technologies and increase as the urgency, magnitude, and value of environmental damages increases. Further shifts in the demand for circularity to the right and reduction in the private cost of circularity, which shift the supply to the right, can result in higher levels of circularity becoming optimal over time.

This framework takes a systems view of the economy. It defines a linear economy as generating a significant amount of waste because it does not internalize the environmental damages from human activities. It recognizes the dynamic nature of technological innovation and evolution of consumer preferences for environmental quality that make a higher level of circularity optimal over time. By incorporating environmental damages in the accounting of social welfare, this framework can determine the optimal mix of technologies, pollution reduction, recycling, reuse, and disposal, and the extent of circularity that maximizes social net benefits. This framework can be extended to consider the social costs of the multiple environmental impacts and trade-offs involved in transitioning from a linear economy to a circular bioeconomy.

Figure 2 shows that the transition to a circular bioeconomy will involve imposing a social cost of waste on the production and consumption of agri-food products. This is expected to raise costs and prices of these products for producers and consumers. This social cost may decrease over time with technological improvements and a greater willingness to internalize the environmental damages of production and consumption decisions. The costs of efforts towards circularity may be disproportionately borne by smaller, low-income producers who cannot bear the costs of participation in sustainability certification program, and lack access to credit, insurance, and technical assistance. While the transition to a circular bioeconomy is socially optimal, this transition does not imply that it will result in a Pareto superior outcome for all, in fact, it may have notable adverse impacts on equity outcomes.

The framework described here can provide the price of various pollutants that need to be imposed, either in the form of pollution taxes or pollution reduction subsidies on carbon emissions, nutrient losses, and other pollutants, to achieve the optimal extent of transformation to a circular bioeconomy in a market economy. The application of this conceptual framework to a product supply chain, sector, or region to determine the optimal level and pathways to circularity requires interdisciplinary collaborations to develop a range of empirical analyses to quantify the costs and benefits of circularity under various technological, market and demand conditions. Economic and social science frameworks need to be integrated with agricultural, biological, and environmental engineering to understand the technological options for reducing, recycling, recovering, and reusing waste generation at each stage of the product from the cradle to the grave for each agri-food commodity. They also need to be integrated with environmental sciences to assess the impacts of alternative pathways for multiple environmental outcomes[51]. To incentivize applied economists and other social scientists to collaborate with agricultural scientists in interdisciplinary research, academic institutions should value publications in interdisciplinary journals, editors of mainstream interdisciplinary journals should prioritize publications that include social scientists, professional social science associations should showcase interdisciplinary research and funding agencies should emphasize interdisciplinary research with social scientists in their allocation decisions. Transition to a circular economy can be expected to involve trade-offs with low costs of food, energy, and water, at least in the short run, till low-cost alternatives to fossil fuels, plastics, and synthetic chemicals are available at scale. Reducing food loss and waste can also have food safety risks that need to be considered. These trade-offs are expected to be mitigated in the long run with technological advances and regulatory incentives that induce innovation. In the near term, the transition to a circular bioeconomy could have a negative consequence for equity within and across countries by raising prices of sustainably produced and differentiated agri-food products and leading to higher costs of energy and clean water to prevent waste. As a result, while the transition to a circular economy may increase the sum of welfare to all groups, it may not be "win-win" for each group. Equity considerations need to be incorporated in the design of policy incentives to mitigate the adverse impacts of a circular bioeconomy on the socially vulnerable groups and to wider acceptance of this transition.

This framework suggests that transforming a linear economy to a circular bioeconomy will depend on the following five pathways that can mitigate trade-offs between competing objectives and strengthen synergies.

Pathways to transition to a circular bioeconomy

Technological advances through investment in research and development are crucial for lowering the costs of circular and bio-based technologies[52]. Public investment in research and development from basic science to commercialization is key to making such technologies commercially available and competitive with conventional technologies, increasing their effectiveness, and thereby mitigating the trade-offs between private economic well-being and social benefits associated with this transition[53]. Emerging digital twin and artificial intelligence technological advances combined with high temporal and spatial resolution data that the field equipment will automatically gather has the potential to convert agriculture from a source of nonpoint pollution to a point source by documenting management practices implemented by farmers, lowering the cost of monitoring practices and using digital twin technology to determine the impact of those practices on the environment and enabling individualized agriculture and supply chain traceability[54,55]. These advances can enable causal attribution of the impacts of production systems on environmental outcomes[56]. This is critical for incentivizing a market-based transformation of the existing linear systems to a circular bioeconomy and implementing performance-based, "polluter pays" policies in the agri-food sector.

Regulatory incentives and institutional change

These transformations require regulatory changes that go beyond the existing voluntary conservation programs for farmers, technology mandates, and command-and-control regulations on businesses to market-based policies that price waste generation, processes, and products based on their social costs of production which include their external (environmental effects) and consumer valuation of those environmental damages. Market-based policies, such as a carbon tax, nitrate taxes, or nonpoint pollution trading schemes, provide the flexibility that is needed for the optimal mix of technologies, demand side conservation, and combination of reduce, recycle, reuse, and regenerate strategies to emerge. A circular bioeconomy also requires institutional transformations that reduce the riskiness of circular production practices through crop insurance programs, loan guarantee programs, environmental reporting, disclosure, and labeling requirements, and reducing regulatory barriers to developing new bio-based technologies.

Markets for circular products

Demand for circular products and processes can emerge voluntarily to some extent from socially responsible firms, investors, and environmentally conscious consumers. Voluntary markets for circular products can align private with social well-being. Credible certification of products and processes, branding and labeling of commodities as circular and bio-based will be needed to enable differentiated pricing of products. To measure and certify the level and impact of circular bioeconomy practices, a comprehensive framework which includes measurable indicators and certification standards is necessary. These indicators help track the effectiveness of circular practices in increasing resource use efficiency, reducing waste, enhancing biodiversity, regenerating natural systems and increasing profits. Verifying the adoption of circular practices in agriculture is essential for enhancing credibility and trust among consumers, investors, and regulators and for inducing environmentally conscious consumers to pay a premium for sustainably produced goods. This financial incentive encourages businesses to adopt and maintain circular practices. Emerging digital twin and blockchain technologies would allow practices to be benchmarked against best case scenarios and evaluate potential improvements to be implemented as well as offer a state-of-the-art method to verify and demonstrate compliance with sustainability standards effectively[57] This digital approach is crucial for meeting regulatory requirements, enhancing market access, improving operational efficiencies, and promoting sustainability. By leveraging advanced technologies, we can ensure more transparent, traceable practices which are aligned with the principles of the circular bioeconomy.

Public education and awareness

The environmental impacts of linear economic systems are often not immediate (as in the case of climate change) or felt by those contributing to those impacts (as in the case of water quality impacts on downstream waterbodies) through their production and consumption decisions. Educating consumers about the ecosystem services provided by circular bioeconomy products can lead to a change in their preferences and a higher willingness to pay, create a market for circular products, and generate political support, making circularity more sustainable in the long run.

Equity considerations

The regulatory, market and institutional transformations that accompany the transition to a sustainable circular bioeconomy are expected to have political economy implications since they are likely to create winners and losers. Higher production costs across the supply chain are likely to be borne partly by producers, consumers, and the government. Prices of circular agri-food products may also be higher due to market power induced by differentiation of products by CPGs. Anti-trust standards and efforts at increasing free entry by firms can play a critical role in preserving competition in differentiated product markets and prevent prices rising above competitive levels. Incorporating equity considerations into processes that support a sustainable and circular bioeconomy is crucial for ensuring that the benefits of such an economy are distributed fairly among all stakeholders, including marginalized and vulnerable communities. Aggregated measures of well-being such as social welfare, GDP, and the social cost of pollution hide the distributional impacts of the transition to a circular economy and who benefits and who would bear the transition costs. An equitable circular bioeconomy requires the governance and decision-making processes guiding the transition to be inclusive, involve diverse stakeholders, and consider ways to mitigate adverse consequences for vulnerable sections of society[58]. To compensate those that may lose from the transition to a circular bioeconomy, governments should establish compensation mechanisms including safety nets, income redistribution programs and workforce reskilling and upskilling programs.

Conclusion

The notion of a circular bioeconomy is appealing because it embodies eliminating waste, reducing environmental contamination, and converting waste into bioproducts that displace fossil fuels. However, the concept needs to provide a framework for transforming a linear economy into a circular bioeconomy that can be sustainable in a market-based system and design mechanisms to achieve that. The transition to a circular bioeconomy is expected to inevitably involve trade-offs between profits for producers, low-cost goods for consumers, and lower environmental impacts. Investment in research, improvement in scientific knowledge, and introduction and adoption of solutions that take advantage of this new knowledge and are enabled by sound regulation and policies will allow improvement of the set of trade-offs that society must make in the long run. The transition toward a circular bioeconomy will require political will to provide the needed policy changes (incentives or taxations) and investments to expand the research agenda to develop novel technological solutions to address major economic, market, and current policy challenges. It also requires private-sector partnerships to induce the adoption of new technologies and consumer acceptance of them. These significant changes in public and private sector choices can only be done with policy changes, that price waste and fossil fuel emissions and create incentives for industry and consumers to adopt these new technologies. We must formulate comprehensive strategies to smoothly transition between sunrise and sunset technologies, products, and practices and favor an overall reduction in societal consumption. The design of the mechanisms to enable a circular bioeconomy should be based on interdisciplinary science. Economics offers a social cost-benefit framework that together with life-cycle environmental impact accounting, engineering solutions for recycling and reusing waste, and agronomic and soil science knowledge of the causes of pollution on the farm can provide a systems approach to developing a circular bioeconomy. Sound economic thinking may result in more circular outcomes but not necessarily fully circular. Furthermore, the transition to a circular bioeconomy will likely be gradual and must adjust to political economic considerations. It is a diffusion process that occurs gradually due to heterogeneity among producers and regions. It benefits from learning and innovation, making circular approaches more attractive to larger fractions of the population over time. Depending on their social preferences, different societies may pursue policies varying in their tradeoffs between economic welfare and the extent of circularity.

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M.K. and D.Z. conceived of the paper; All authors contributed ideas and text; B.B. and G.H. contributed the figures; M.K. was the lead writer.

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The authors declare no competing interests.

Additional information

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