Journal of Functional Foods 109 (2023) 105793

Contents lists available at ScienceDirect

Journal of Functional Foods

journal homepage: www.elsevier.com/locate/jff

Sustainability, nutrition, and scientific advances of functional foods under the new EU and global legislation initiatives

Daniel Granato [a,b,c,1,*], Ioannis Zabetakis [a,b,c,1], Anastasios Koidis [d,1]

[a] Department of Biological Sciences, Faculty of Science and Engineering, School of Natural Sciences, University of Limerick, V94 T9PX Limerick, Ireland
[b] Bernal Institute, University of Limerick, V94 T9PX Limerick, Ireland
[c] Health Research Institute, University of Limerick, V94 T9PX Limerick, Ireland
[d] Institute for Global Food Security, Queen's University Belfast, 19 Chlorine Gardens, Belfast BT9 5DJ, United Kingdom

ARTICLE INFO

Keywords:
Food innovation
Circular economy
Food technology
Food safety
Chronic diseases

ABSTRACT

The health of the general population is one of the various factors at stake in the 2020′s generation: food security, safety, nutrition, and responsible, sustainable production and consumption are also part of the priorities of governments and enterprises. Under that prism, the new EU legislation (Green Deal – Farm to Fork) building on the top of the UN's Sustainable Development Goals groundwork has brought about a revamped focus on sustainability in the food industry, emphasising reducing food production's environmental impact and promoting sustainable food systems. Here, an integrative approach between scientific and technological advancement, policymakers, consumers, and society, to design sustainable, functional foods is presented, focusing on food innovation for developing bioactive-rich ingredients and tackling non-communicable diseases (NCD). We also critically analyse how these findings fit within the new policy frameworks of the EU and the UN under the common goal of achieving global food security and sustainable growth.

1. Background

Sustainability in the agri-food industry refers to meeting current and future food needs while maintaining the integrity of natural resources and ecosystems (Muscio, & Sisto, 2020). This includes reducing CO2 footprint, protecting water and soil quality, and conserving biodiversity (Veldkamp et al., 2022). It should be viewed, however, from a broader perspective that includes people, the planet, and industry/profit (Arayess & de Boer, 2022).

Considering the slow progress of the recent United Nations climate change conferences (COP25, 26, 27) policy agreements (Clément, 2022) and greenhouse gas (GHG) emission targets, global food security and agricultural production systems are at risk (Zurek et al., 2022) The recent pandemic has also revealed that the current food production systems are fragile and unsustainable (Galanakis et al., 2022). Promoting sustainable agri-food systems can help reduce GHG emissions and balance that with the need to produce more due to the reported population increase (Crippa et al., 2021). On the policy level, there is an opportunity to create a substantial difference and bridge the gap. Policies such as the United Nations Sustainable Development Goals (UN SDGs) (United Nations, 2022) and the European Green Deal (European Commission, 2021) are essential pressure points to world decision centres to mitigate the anthropogenic climate change crisis. Although the two policies have slightly different focuses and goals, they have synergy: they share a joint commitment to promote sustainable agri-food systems and protect the environment (Kuc-Czarnecka et al., 2023).

The legislative framework for sustainable food systems (FSFS) is at the core of the EU's Farm to Fork Strategy. It will unite the policy initiatives (food labelling, sustainable farming etc) under one common vector, raise sustainability in the public forum and promote the strengthening of the resilience of food systems at the EU level and member state level (European Commission, 2021). If implemented considerably, the new legislation presents a unique opportunity for the food industry to move towards more sustainable and nutritious food systems. Apart from allowing policies to, this requires scientific innovation(Cole et al., 2018) and attention to people, the planet, and economic factors (Arayess & de Boer, 2022). Research can help identify the most effective and sustainable food production practices and the

* Corresponding author at: Department of Biological Sciences, Faculty of Science and Engineering, School of Natural Sciences, University of Limerick, V94 T9PX Limerick, Ireland.
E-mail address: daniel.granato@ul.ie (D. Granato).
[1] Contributed equally to the work.

https://doi.org/10.1016/j.jff.2023.105793
Received 22 April 2023; Received in revised form 30 July 2023; Accepted 7 September 2023
Available online 14 September 2023

potential risks and unintended consequences of different policy options. Science can also help to develop new technologies and innovations that can improve the sustainability and resilience of food systems. One of these is the development of health-promoting foods. Health-promoting foods can be essential in the campaign for sustainable food systems (Ferraboschi et al., 2022). However, the challenge for science is developing functional ingredients, such as prebiotics, probiotics, and antioxidants, that have been shown to have health-promoting properties, such as antihyperlipidemic, gut microbiota-modulating, antidiabetic, heart-protecting, and antihypertensive effects (Alshehri, 2022; Fossi et al., 2022; Leite et al., 2023; Topal & Gulcin, 2022). These can be from various sources on the playbook of the circular economy. These ingredients can be incorporated into a range of food products, including snacks, beverages, spreads, emulsion-based formulations (e.g., ice creams, popsicles, mayonnaise, processed cheeses, and meats), and ready-to-eat meals to provide additional health benefits. Apart from improved public health, this change could provide economic development for smallholder farmers and local food systems through the cycle economy avenue (Muscio & Sisto, 2020).

Considering sustainable food production and consumption (e.g., Goal 12 from UN SDG), the good health and wellbeing of consumers (e.g., Goal 3 from UNSDG), and the need to innovate on food technology, the design of functional foods is pivotal and timely. In 2007, Lang (Lang, 2007) described functional foods as "nutraceuticals" or "designer foods" that enhance human health and prevent illnesses. As foods cannot be mistakenly taken as medicines, a regulatory framework controls the authorisation of health claims, which varies significantly from country to country. Policymakers have focused on introducing regulations to define health claims (i.e., functional effects in humans) based on clinical trials and scientific-based evidence on bioactivity (Alongi & Anese, 2021; Brown et al., 2018). After much scientific research on the topic, functional foods can be defined as industrially processed or natural foods that, when regularly consumed within a diverse diet at efficacious levels, have potentially positive effects on health beyond essential nutrition (Granato et al., 2017). According to the current European regulation (EC 1924/2006), any health claim should be supported by evidence from human interventions, such as clinical trials. Health claims approved by governmental health agencies (e.g. European Food Safety Authority, EFSA) are perceived as trustworthy by consumers, increase transparency, and ensure a high level of consumer protection against misleading, non-scientific-based information, especially those contained on the product's label and marketing campaigns (Nystrand & Olsen, 2020).

Different ingredients and food formulations could be designed and manufactured globally, and considering the local availability of raw materials, consumers would have many options to adopt in their regular diet. Products that are health-focused or have a health halo (e.g., vegan proteins are key focus areas for functional foods since health-minded consumers are already looking to these products to boost health (Temple, 2022). Functional foods that are clinically effective in decreasing the risk of chronic NCD are central to promoting healthy ageing and circularity In food systems, with an Impact on public health in the long run (Lie-Piang et al., 2022).

The current state-of-the-art on functional foods is associated with the use of food side streams to recover nutrients and bioactive compounds, such as proteins, phenolics, fibres, and oils (Alves et al., 2021; Gohara-Beirigo et al., 2022; Munialo et al., 2022; Othman et al., 2022). However, from a more comprehensive standpoint, functional food design can only be applicable when food processors adopt a sustainable and health-oriented focus to develop new ingredients and formulations. This is why in this paper, using a sustainability lens and a holistic perspective, we review the latest innovations in discovering functional ingredients from natural agri-food sources, focusing on human health and NCD. We also critically analyse how these findings fit within the new policy frameworks of the EU "green deal – farm to fork" era and the UN SDGs under the common goal to achieve global food security and sustainable growth.

2. Functional foods in the green Deal and 'Farm to Fork' era

2.1. Functional foods: From old definitions to current trends

In the 1980 s, the term 'functional food' was introduced in Japan to define foods with alleged benefits that improve human health and increase the well-being of the general population.

As the scientific definition of functional foods mentions, both industrialised and natural foods can be regarded as functional, depending on the health benefits it provides. For example, (Ruscica et al., 2018) used a randomised, parallel, single-centre controlled study for 12 weeks, where 26 individuals with metabolic syndrome consumed 30 g of soy protein/day. The nutritional intervention was able to modulate the lipid profile by decreasing the low-density lipoprotein (LDL), total cholesterol (TC), and body mass index (BMI), thus improving biomarkers associated with cardiometabolic risk. In a similar trend, Kaczmarek et al. (Kaczmarek et al., 2019) studied the effect of broccoli (200 g/day) in a controlled feeding, randomized, crossover study consisting of two 18-day treatment periods separated by a 24-day washout was conducted in healthy adults ($n = 18$). The consumption of broccoli improved energy metabolism and increased the pathways involved in the functions of the endocrine system, transport, and catabolism, modulating the profile and abundance of the gastrointestinal microbiota. In a double-blind, randomised, and controlled cross-over clinical trial, Davis et al. (Davis et al., 2020) analysed the beneficial effects of 20 g of chocolate (960 mg of polyphenols) after 6 h of consumption of a high-fat diet. Chocolate consumption increased HDL and decreased TC and LDL with the pro-inflammatory cytokine (e.g., IL-18). The authors concluded that chocolate, a processed polyphenol-rich food, improved postprandial dyslipidaemia and inflammation following a high-fat diet in diabetic patients.

As consumers are more aware of the relationship between food choices, eating and living habits, and the onset of chronic non-transmissible diseases, food companies are trying to boost sales by providing healthier, more sustainable, and more natural food options (Repar & Bogue, 2023). To deliver these foods and satisfy consumers' demands and expectations, multiple studies have been conducted to prototype foods that can be deemed healthy, and sensorially accepted (Genovese et al., 2022; Hossain et al., 2020; Jiang et al., 2022; Jing et al., 2022). Among conventional functional foods, those containing dietary fibres and complex carbohydrates (e.g. resistant starch, arabinoxylan, hydroxypropyl methylcellulose, glucomannan, β-glucans, and chitosan), functional lipids (e.g. docosahexaenoic acid, eicosapentaenoic acid, α-linolenic acid, linoleic acid, oleic acid, plant sterols, and stanols), polyphenols (e.g. resveratrol, quercetin, anthocyanins, and tea /cocoa flavanols), and carotenoids (β-carotene, lycopene, astaxanthin, and lutein) were the epicentre of attention from the 1980 s to 2010 (Abdul-Hamid & Luan, 2000; Agboola et al., 2010; Farré & Macaya, 2006; Jenkins et al., 2008; Moughan, 2008; Rakić et al., 2006). Current trends show a tremendous industrial interest in bioactive polar lipids (Redfern et al., 2021), food-derived peptides (Rivero-Pino, 2022), edible flowers (Ahmed et al., 2022; Wang et al., 2022), novel tea beverages (Ma et al., 2020), naturally-sources bioactive-rich extracts (Granato, Reshamwala, et al., 2022; Oliveira et al., 2022), and terpenoids, such as cucurbitacins (Zhong et al., 2020).

With the development of analytical techniques (e.g. spectroscopy-based techniques, high-resolution liquid chromatography-mass spectrometry, and biomolecular techniques) and computational software (e.g. online libraries, *in silico* and network pharmacology studies), the discovery of novel compounds and the analysis of their effects on human metabolism and specific pathways (e.g. inflammatory- or oxidative-driven diseases), either via simulated *in vitro* conditions or via *in vivo* studies, have made impressive headway for functional food design (Azevedo et al., 2022; Peredo-Lovillo et al., 2021; Tabassum et al., 2022;

Wang et al., 2022; Xia et al., 2022; Yi et al., 2022). Enterprise-driven research and collaborative studies between food/nutrition companies and research centres are paramount to make the research more translational. This means developing a functional food or ingredient should rely on its effectiveness. This was demonstrated by cell-based and test tube-based assays, animal models and human interventions, as shown in Fig. 1A. Notwithstanding, primary research data should be adopted by clinical practitioners after approval of independent scientific authority for food safety and governmental recommendations, as illustrated in Fig. 1B. Functional food is a broad discipline that should be translational and cross-sectional. For this reason, a multitask team should encompass professionals from different fields, such as biology, medicine, food science and technology, mathematics and statistics, nutrition, and pharmacology.

Today's needs and regulatory requirements demand evidence of the effects of food consumption on one or some physiological functions. The proof of concept (e.g. functional effect) can be obtained through human interventions, where the efficacy of the bioactive-rich food is assessed in relation to a placebo (e.g. no functional effect), and, where applicable, a dose-dependency on the impact can also be evaluated. Randomised-controlled trials are gold standards because they may bring about the cause (e.g., food consumption) and effect (e.g., efficacy, health benefit) (Granato et al., 2020).

Considering the technological and analytical advances and the regulatory requirements to ascertain health claims of potentially functional foods, some trends should be highlighted: A) the development of functional ingredients using agro-industrial side streams and by-products as raw materials, b) the isolation and testing of chemical compounds from natural resources to as ingredients added in foods and beverages, c) the creation of novel chemical molecules from well-known compounds, and d) the development of edible delivery systems for bioactive-rich extracts and compounds to enhance their bioavailability. The latter term includes both bioaccessibility and bioactivity *in vivo*. Some examples of research around these trends are: Gomez-Garcia *et al.* (Gómez-García et al., 2021) extracted bioactive compounds (e.g. dietary fibres, polyphenols, and carotenoids) from melon peels and found that the extracts showed antioxidant effects toward biologically-relevant free radicals. Various *Citrus* species are used as foods worldwide, and Gao et al. (Gao et al., 2022) isolated feruloylagmatine, haploside C, sagittatin A, linderagalactone C and koparin-2′-methyl ether from C. aurantium decoction. Crude and purified extracts containing a high content of the isolated compounds showed anti-colon cancer activity, showing potential to be used as food ingredients. Similarly, (Grau et al., 2023) synthesised novel resveratrol derivatives by alkylation or acylation of hydroxyl groups to increase human bioavailability and promote their use in different food and pharmaceutical applications. The authors have shown that the novel compounds had anti-angiogenesis activity and cytotoxicity in human colon carcinoma (HT-29) and human pancreatic adenocarcinoma cells (MIA PaCa-2) higher than those of (*E*)-resveratrol. Not only the recovery and synthesis of bioactive compounds are the focus, Lyu et al. (Lyu et al., 2022) designed edible self-microemulsions containing tocopherol polyethylene glycol to deliver highly bioavailable dihydromyricetin. The consumption of the bioactive emulsion was able to inhibit the increase of body weight and fat mass and prevent non-alcoholic fatty liver disease in a high-fat mice model. These examples clearly show that the path to a better understanding of functional foods is on the right track. Still, developments in other arenas are necessary, such as personalised nutrition, tailor-made foods, and sustainable, functional food production.

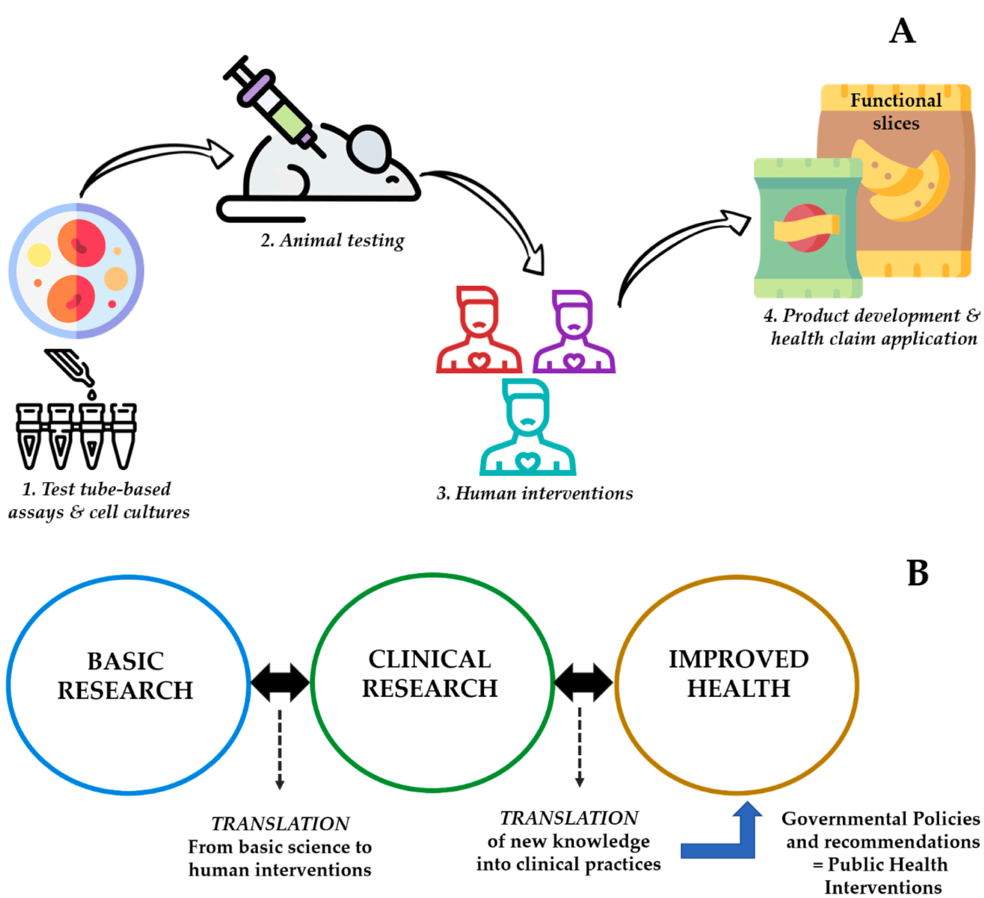

Fig. 1. Functional food development by design: basic research from *in vitro* testing to prototyping food models (A), and the translational pathway from basic research to public health interventions (B).

2.2. Sustainable sources and novel molecules for functional food design: Innovations and circularity of food processing

Approximately 32% of deaths globally (17.9 million in 2019) are caused by cardiovascular diseases (CVD). CVD can be prevented by adopting healthy eating and life habits (World Health Organization, 2021). Therefore, developing functional foods and nutraceuticals to counteract the harmful effects of oxidative stress and inflammation in overweight and obese individuals is paramount and has been incentivised (Granato, 2022).

Apart from functionality against inflammation, there is a need to apply, in food processing, the concepts of circular economy to recover bioactive-rich fractions (Granato, Carocho, et al., 2022; Kurniawan et al., 2022; Lugo et al., 2022). In many cases, these fractions have shown interesting nutritional profiles and bioactivities that should be explored more by the food and pharmaceutical sectors.

Considering circular economy concepts and targeting the UN SDGs, some examples can be described "from farm to fork": in primary production (i.e. agricultural practices to produce foods), using fertilisers is a common practice, but the nutrient shortage is a reality in some countries. (Kurniawan et al., 2022) identified ways to recover nutrients (e.g., P and N) from landfill leachate, decreasing waste and greenhouse gas generation. Similarly, (Papadaki et al., 2022) recovered milk whey proteins from cheese production and developed natural and edible biopolymers (i.e. packaging films) reinforced with bacterial cellulose nano-whiskers obtained from the fermentation of orange peels to reduce water vapour permeability and increase the film's tensile strength. Recently, (Pap et al., 2021) screened the bioactive compounds of Finnish agro-industrial side streams (e.g. sea buckthorn leaves, blackcurrant press cake, Norway spruce bark, and Scots pine bark) and found that the aqueous extracts, rich in different polyphenols, had antimicrobial effects and were able to scavenge hydroxyl radical, showed antioxidant effects in human cell lines, and decreased reactive oxygen species generation in THP-1 (monocytes) cells. (Ferreira et al., 2021) used ionic liquid ultrasound-assisted extraction to recover bioactive compounds from red guava coproduct and found that the extracts had antioxidant capacity using multiple test tube-based assays. Future work should implement the comprehensive principles of the EU Fusions Project (EU Fusion Projects, 2016). In trying to find new alternatives to reuse fruit pomace, (Costa et al., 2021) recovered the bioactive compounds from purple grape pomace and encapsulated the powder into alginate/chitosan capsules. Capsules were added to coconut water to produce a novel, potentially functional beverage source of total phenolics and anthocyanins. The authors observed antimicrobial activity against intestinal pathogens after *in vitro* static digestion simulation.

3. Functional foods against non-communicable diseases

The scientists working on the interface of sustainable production systems and functional foods face today is two-dimensional. On the one hand, we need to make more sustainable the production systems (e.g., reduce the use of pesticides and water, and valorise side streams of agriculture and food industries), and on the other hand, we need to make sure that the food produced has strong bioactivities against non-communicable diseases (NCD), i.e., cardiovascular diseases (CVD), diabetes, obesity, stroke etc. CVD are the number one killer diseases today worldwide, causing the death of 17.9 M annually. The underlying cause of most NCD is low-grade inflammation (Tsoupras et al., 2018). As reported (Zabetakis, 2013), the scientific challenges are demanding and urgent. We must re-evaluate the food production systems to make them more sustainable and efficient. Still, we would need to do so while ensuring that foods' functional properties against NCD remain strong (Zabetakis et al., 2022).

3.1. Inflammation should be the critical target

The bottom-line biochemical phenomenon causing NCD is inflammation. Therefore, we should focus on producing foods with potent anti-inflammatory properties. Dietary cholesterol and serum cholesterol have somehow been demonised, and statins have come into play as cholesterol has been wrongly suggested as the target molecule to combat chronic diseases. However, it is inflammation that causes NCD and not cholesterol (Tsoupras et al., 2018).

Since 2019, with the emergence of COVID-19, the focal point of inflammation has become ever more apparent. In March 2020, World Health Organization (WHO) issued guidelines highlighting that people suffering from NCD may be more susceptible to developing COVID-19 (World Health Organisation, 2020). Given these guidelines, much research since then has focused on inflammation. The virus causes acute inflammation, whereas people suffering from NCD have chronic inflammation, so people with NCD are more susceptible than those without NCD. The role of a healthy diet and lifestyle choices has been further highlighted since a nutritious diet, rich in anti-inflammatory nutrients, can reduce both types of inflammation (Zabetakis et al., 2020).

This research topic has attracted much interest from several research groups worldwide. Clinical trials have focused on assessing the impact of food consumption on several inflammation-related biomarkers. A recent review of related clinical trials reported that Brazil nut (BN) consumption improved lipid metabolism markers in healthy subjects but also in diabetes-bearing individuals with type 2 diabetes and mild cognitive impairment (da Silva et al., 2022). In a blind, randomized, controlled trial, the effects of data seeds on inflammation and oxidative stress were studied. It was found that the consumption of date seed can decrease oxidative stress, inflammation, and muscle pain (Moslemi et al., 2022). In a randomized double-blinded clinical trial on the effects of *Spirulina* sauce, it was found that this functional food can improve the fatty liver grade by modifying the enzymatic activities of liver enzymes, reducing oxidative stress, and improving lipid profiles (Mazloomi et al., 2022).

In a scoping review on the effects of consumption of *Moringa oleifera* Lam (MO) on cardiac and vascular dysfunctions, it was found that phytochemical compounds of MO, such as quercetin and N,α-L-rhhamnopyranosyl vincosamide, have antioxidant, anti-inflammatory and anti-apoptosis strong bioactivities (Deng et al., 2020).

3.2. Functional foods, the gut microbiome, and valorisation of side streams

Another essential aspect that future research should focus on is the role of a healthy gut microbiome in reducing inflammation. Daily intake of dietary fibre (DF) is substantially decreased today. Additionally, inflammatory bowel disease (IBD), allergies, and other auto-immune diseases are on the rise, especially in high-income countries; this pattern is a worrying one as it shows that our dietary patterns have deteriorated despite the abundance of food in these countries. How can we address this problem? The best way forward is to study further the role of food nutrients (i.e., the fibre in this case) in relation to gut microbiota composition and function (Zhang et al., 2022).

The gut microbiome has a fundamental role against the development of NCD while exerting critical functions within the human body. Our diet is probably the most powerful modulator of gut microbiota functions and composition (Rinninella et al., 2023). A recent article (Bhatt & Gupta, 2023) thoroughly explains the concept of valorising side food streams. Short-chain fatty acids (SCFAs) were emphasised in regulating epithelial barrier function and inflammation. The DF in side streams can control various mechanisms of inflammation and reduce IBD, and the gut microbiome produces several SCFAs that reduce inflammation.

Major emphasis has been put on valorising the by-products generated during fruits and vegetables (F&V) processing. These organic wastes include seeds, pulp, skin, rinds, etc.; they are collectively named "fruit pomaces" and are good sources of bioactive nutrients with several health promoting activities. A recent article describes various emerging technologies for extracting these bioactive nutrients from pomaces (Pattnaik et al., 2021).

Our group has been working on fruit pomaces for several years, focusing on olive and apple pomaces, which are rich in phenolic compounds, especially flavonoids and phenolic acids, such as rutin, phloretin, phlorizin, luteolin-7-glucoside, nüzhenide, oleuropein, and ligstroside. We have shown several anti-inflammatory activities in these side stream products, and we have suggested using them to produce sustainable animal and fish feeds (Nasopoulou et al., 2018). Much emphasis is given in the literature on prebiotics. It has been identified that carbohydrate-based substrates possess promising prebiotic activity (Flint et al., 2012; Peled & Livney, 2021; Yan et al., 2018). If the interactions between dietary fibre and the gut microbiota are studied, a more tailored approach to simulate gut commensals can be devised. This can be accelerated if computational machine-learning tools are used (Sabater et al., 2021). Using computational tools fed by structural, functional, and genomic data), there is the potential to identify substrates that may selectively stimulate organisms.

3.3. Sustainably produced nutraceuticals: Some examples and trends

To address environmental degradation, environmental pollution, and biodiversity loss driven by food and feed-intensive production, immediate action is required to preserve natural resources (Lacirignola et al., 2014). In this regard, research on different topics has emerged to tackle this issue: from sustainable production of ingredients using agro-industrial by-products to primary and secondary packaging materials (Calcio Gaudino et al., 2020) Therefore, focus on food production, including the circular use and reuse of by-products and emerging production and extraction techniques, should be emphasised to decrease waste generation and comply with the Agenda 2030 concepts (Viñas-Ospino et al., 2023).

We should highlight a problem concerning over-utilising a natural resource (fish oil) in producing nutraceuticals combatting CVD. For quite several years, it was thought that omega-3 fatty acids (OM3FA) (present in fish oil) could reduce the cardiovascular risk (CR) and hence the incidence of CVD. However, the current practice of supplementing esters of these OM3FA could be more effective, as recently discussed by Goff and Nissen (Goff & Nissen, 2022). In their work, they reviewed the two most large-scale trials on the efficacy of OM3FA to reduce CV (namely, REDUCE-IT and STRENGTH). They highlighted that an increased incidence of atrial fibrillation was observed in both trials. They concluded that the routine use of OM3FA outweighs any possible reduction of CV.

How can we address this issue? The answer is that it is the chemical nature of OM3FA that renders them ineffective. The esters of these acids are not water soluble and, therefore, not labile in the human body. Thus, much research has been carried out on discovering new ways to produce functional foods and nutraceuticals from marine sources that reduce CR. Following this concept, our group has been working on the role of polar lipids (PL) in inhibiting the Platelet Activating Factor (PAF) and reducing platelet aggregation and inflammation (Harishkumar et al., 2022). PAF is a potent lipid mediator related to platelet aggregation and thrombosis and its structure is similar to the ones of PL; PL compete with PAF for the PAF receptor (PAF-R), and in this way, they exhibit anti-platelet and anti-thrombotic activities (Fig. 2). Platelet aggregation and CR can be reduced by inhibiting the binding of PAF to its receptor (PAF-R). Research has shown that polyphenols and PL can affect the binding of PAF to PAF-R in a favourable way. Following this school of thought, we have produced a novel food-grade extract from salmon fillets with strong anti-thrombotic activities (Tsoupras et al., 2019). Other approaches could focus on valorising various side streams of food production systems. Some examples include olive pomace (Nasopoulou et al., 2018)(a side product of the olive oil industry) and other fruit pomaces (Coelho et al., 2022). The underlying principle in these studies is that pomaces are rich in anti-inflammatory compounds. They can be valorised in two ways: firstly, by rendering production processes more efficient and environmentally friendly, and secondly, by incorporating them into food production systems, the novel foods have more potent anti-inflammatory bioactivities.

Another avenue to contribute to sustainable nutrition is the development of food supplements from functional ingredients derived from sustainable sources. As an example, polyphenol-rich sources such as the grape pomegranate pomace and berries (bilberries, red currants) showed high concentrations of anthocyanins, gallotannins and gallagyl derivatives (Pérez-Ramírez et al., 2018) and other simple phenols such as rutin, chlorogenic acid and quercitrin (Frum et al., 2022). The polyphenol forms are stable and can be formulated into a dietary supplement. However, in a clinical study using the grape pomegranate pomace supplement that was previously characterised, the intake did not yield

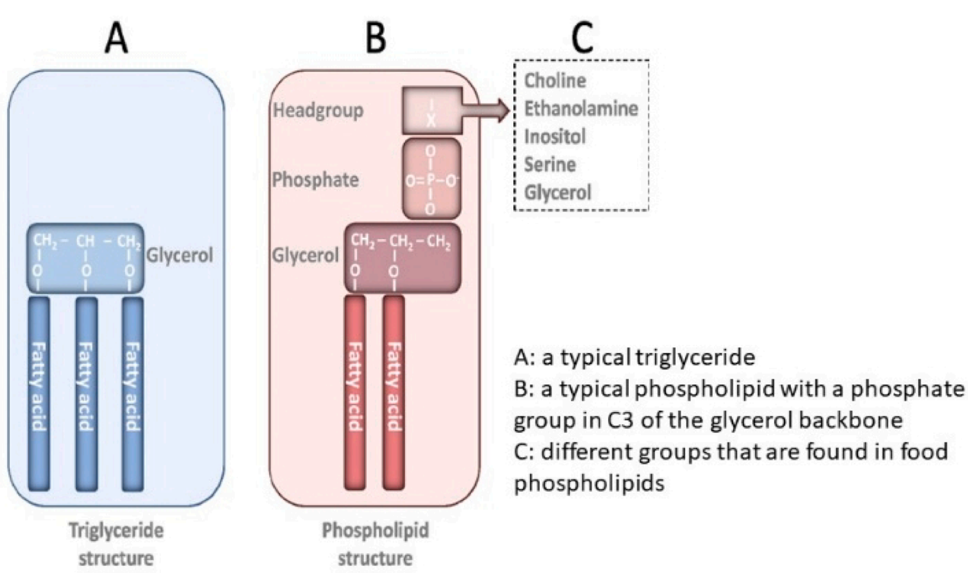

Fig. 2. Typical structures of non-polar and polar triglycerides. OM3FA are esters of A, whereas the PLs are esters of B. The phosphate group renders the phospholipids water soluble and, therefore, more labile once they enter the human body.
Source: (Lordan et al., 2017).

improvement in glucose metabolism and oxidative stress in adults with abdominal obesity (Pérez-Ramírez et al., 2020). Nevertheless, research in the area is ongoing and clinical trials with food supplements containing functional ingredients should be conducted to ensure the effectiveness of functional supplements.

4. Integrative concept to align science, technology, policymakers, and society

Sustainable food systems is still a concept that only few food companies worldwide have fully implemented in their daily routines, as multiple challenges should be addressed. According to (Araújo et al., 2023), environmental, economic, health, social, and agricultural impacts, value chain actors and the supply chain play a central role in sustainability. The adverse effects of agri-food practices should be minimised to avoid the disruption of natural resources, and, for this reason, policymakers and other stakeholders have been forced to make provisions and create basis and conditions to implement policies to strengthen the resilience of food systems and re-create plausible future scenarios under different contexts at different spatio-temporal levels (Agyemang et al., 2022). To accomplish this challenging and necessary outcome, setting strategic research, innovation, education (e.g. consumers and enterprises in the food chain), and a science-policy agenda is a reasonable and evidence-based goal (de Vries, 2023). The SDGs, societal, environmental, nutritional, and economic dimension indicators can be used to monitor the progress of actions taken to tackle the challenges in each phase of the implementation of actions (Carvalho et al., 2021).

Considering the overall challenges, the consumers' needs, the state-of-the-art technology and science-based approaches, it is evident that an interconnection should be actively present for the development, adoption, and success of sustainable, functional foods (Fig. 3). Goals and tasks should be drafted to inform consumers about the health aspects, ingredients, and the underlying technology used to develop these foods (Siegrist & Hartmann, 2020). In addition, scientific and technological breakthroughs should be financed so new processes and disruptive technologies can become available worldwide for large-scale processes, ensuring food security and the nutritional quality of foods. For food manufacturing, the rational use of natural resources, including energy use, testing and implementation of green technologies, should become a reality to reduce industrial side streams and by-products (Boyacı-Gündüz et al., 2021; Galanakis et al., 2022).

Finally, governmental bodies and independent scientific authority for food safety worldwide should keep up with scientific and technological advances by upgrading and drafting directives to assess the feasibility of implementing new technologies and ingredients in food production (Tweeten, 1999). Policymakers should also encourage the scientific development of technologies and ingredients by facilitating and funding research based on Research and Innovation Action (RIA) and Innovation Actions (IA) (European Commission Directorate-General for Research Innovation, 2021). This will enhance the technology readiness level (TRL) of projects from the technology concept (TRL 2) to actual technology completed and qualified through test and demonstration (TRL 8). For reference, TRL is an established scale to assess the maturity level of a particular technology ranging from concept to successful production successful operation (Innovation, 2022). These actions should be prioritised so new processes, food/nutraceutical products, and ingredients can reach the market.

5. Ethics statement

This research did not use animals or humans, so no ethical permission was sought.

CRediT authorship contribution statement

Daniel Granato: Conceptualization, Writing – original draft, Writing – review & editing. **Ioannis Zabetakis:** Conceptualization, Writing - original draft, Writing - review & editing. **Anastasios Koidis:** Conceptualization, Writing – original draft, Writing – review & editing.

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.

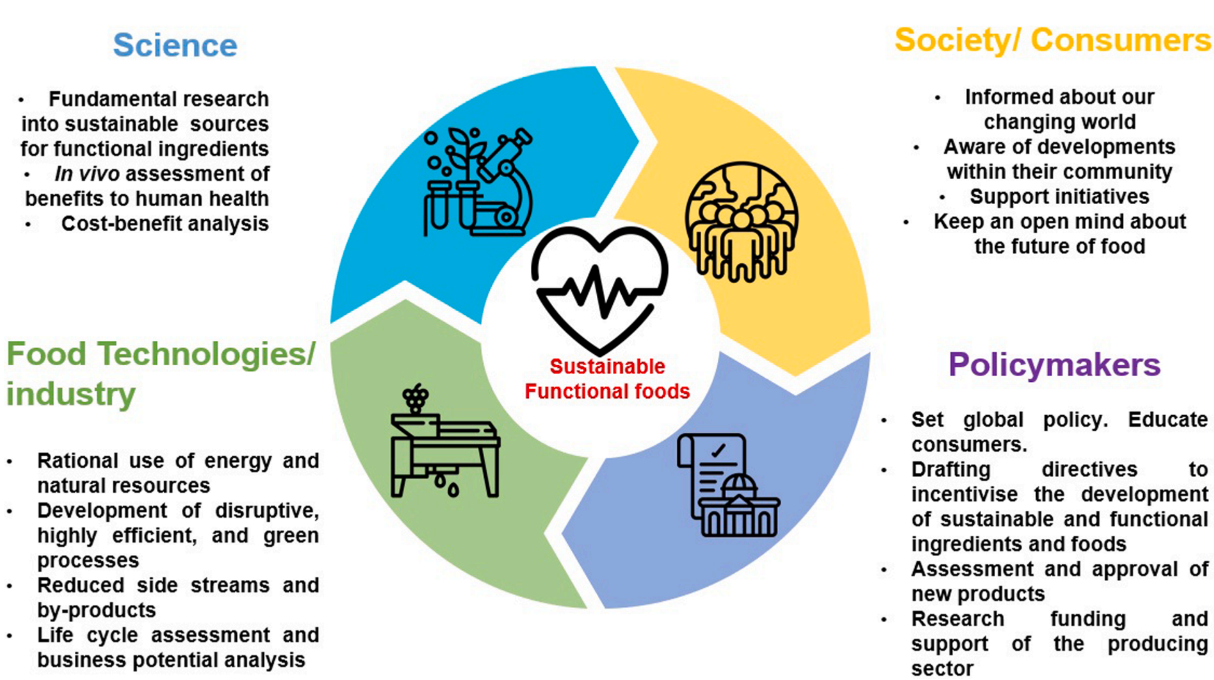

Fig. 3. Integrative representation of the main stakeholders for developing sustainable functional foods.

Data availability

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

References

Abdul-Hamid, A., & Luan, Y. S. (2000). Functional properties of dietary fibre prepared from defatted rice bran. *Food Chemistry, 68*(1), 15–19.

Agboola, S. O., Mofolasayo, O. A., Watts, B. M., & Aluko, R. E. (2010). Functional properties of yellow field pea (Pisum sativum L.) seed flours and the in vitro bioactive properties of their polyphenols. *Food Research International, 43*(2), 582–588.

Agyemang, P., Kwofie, E. M., & A, F. (2022). Integrating framework analysis, scenario design, and decision support system for sustainable healthy food system analysis. *Journal of Cleaner Production*, *372*, 133661. https://doi.org/https://doi.org/10.1016/j.jclepro.2022.133661.

Ahmed, S. R., El-sherei, M. M., Michel, C. G., Musa, A., Al-Sanea, M. M., & Qasim, S. (2022). Botanical description, bioactivity guided isolation and in silico mode of action of anti-diabetic constituents of Pterocarpus dalbergioides flowers. *South African Journal of Botany, 147*, 163–175.

Alongi, M., & Anese, M. (2021). Re-thinking functional food development through a holistic approach. *Journal of Functional Foods, 81*, Article 104466.

Alshehri, M. A. (2022). Cardioprotective properties of Artemisia herba alba nanoparticles against heart attack in rats: A study of the antioxidant and hypolipidemic activities. *Saudi Journal of Biological Sciences, 29*(4), 2336–2347.

Alves, E., Simoes, A., & Domingues, M. R. (2021). Fruit seeds and their oils as promising sources of value-added lipids from agro-industrial byproducts: Oil content, lipid composition, lipid analysis, biological activity and potential biotechnological applications. *Critical reviews in food science and nutrition, 61*(8), 1305–1339. https://doi.org/10.1080/10408398.2020.1757617

Araújo, R. G., Chavez-Santoscoy, R. A., Parra-Saldívar, R., Melchor-Martínez, E. M., & Iqbal, H. M. N. (2023). Agro-food systems and environment: Sustaining the unsustainable. *Current Opinion in Environmental Science & Health, 31*, Article 100413. https://doi.org/10.1016/j.coesh.2022.100413

Arayess, S., & de Boer, A. (2022). How to Navigate the Tricky Landscape of Sustainability Claims in the Food Sector. *European Journal of Risk Regulation, 13*(4), 643–664.

Azevedo, L., Serafim, M. S. M., Maltarollo, V. G., Grabrucker, A. M., & Granato, D. (2022). Atherosclerosis fate in the era of tailored functional foods: Evidence-based guidelines elicited from structure-and ligand-based approaches. *Trends in Food Science & Technology*.

Bhatt, S., & Gupta, M. (2023). Dietary fiber from fruit waste as a potential source of metabolites in maintenance of gut milieu during ulcerative colitis: A comprehensive review. *Food Research International, 164*, Article 112329. https://doi.org/10.1016/j.foodres.2022.112329

Boyacı-Gündüz, C. P., Ibrahim, S. A., Wei, O. C., & Galanakis, C. M. (2021). Transformation of the food sector: Security and resilience during the COVID-19 pandemic. *Foods, 10*(3), 497.

Brown, L., Caligiuri, S. P., Brown, D., & Pierce, G. N. (2018). Clinical trials using functional foods provide unique challenges. *Journal of Functional Foods, 45*, 233–238.

Calcio Gaudino, E., Colletti, A., Grillo, G., Tabasso, S., & Cravotto, G. (2020). Emerging Processing Technologies for the Recovery of Valuable Bioactive Compounds from Potato Peels. *Foods, 9*(11), 1598.

Carvalho, A. M. d., Verly Jr, E., Marchioni, D. M., & Jones, A. D. (2021). Measuring sustainable food systems in Brazil: A framework and multidimensional index to evaluate socioeconomic, nutritional, and environmental aspects. *World Development*, *143*, 105470. https://doi.org/https://doi.org/10.1016/j.worlddev.2021.105470.

Clément, C.-W.-Y. (2022). Copping Out on Food Systems: How COP26 Failed to Address Food and Climate and How COP27 Can Solve It. *Journal of Agricultural and Environmental Ethics, 35*(4), 20.

Coelho, C. R., Peters, G., Zhang, J., Hong, B., Abdollahi, M., & Undeland, I. (2022). A comparative life cycle assessment of cross-processing herring side streams with fruit pomace or seaweed into a stable food protein ingredient. *Future Foods, 6*, Article 100194.

Cole, M. B., Augustin, M. A., Robertson, M. J., & Manners, J. M. (2018). The science of food security. *npj Science of Food, 2*(1), 14.

Costa, J. R., Monteiro, M. J., Tonon, R. V., Cabral, L. M., Pastrana, L., & Pintado, M. E. (2021). Fortification of coconut water with microencapsulated grape pomace extract towards a novel electrolyte beverage: Biological, sensorial and quality aspects. *Future Foods, 4*, Article 100079.

Crippa, M., Solazzo, E., Guizzardi, D., Monforti-Ferrario, F., Tubiello, F. N., & Leip, A. (2021). Food systems are responsible for a third of global anthropogenic GHG emissions. *Nature Food, 2*(3), 198–209.

da Silva, A., Silveira, B. K. S., de Freitas, B. V. M., Hermsdorff, H. H. M., & Bressan, J. (2022). Effects of Regular Brazil Nut (Bertholletia excelsa H.B.K.) Consumption on Health: A Systematic Review of Clinical Trials. *Foods, 11*(18). https://doi.org/10.3390/foods11182925

Davis, D. W., Tallent, R., Navalta, J. W., Salazar, A., Lyons, T. J., & Basu, A. (2020). Effects of acute cocoa supplementation on postprandial apolipoproteins, lipoprotein subclasses, and inflammatory biomarkers in adults with type 2 diabetes after a high-fat meal. *Nutrients, 12*(7), 1902.

de Vries, H. (2023). The role of food science and technology in the future partnership sustainable food systems. *Trends in Food Science & Technology, 131*, 28–30. https://doi.org/10.1016/j.tifs.2022.11.019

Deng, Q., Li, X. X., Fang, Y., Chen, X., & Xue, J. (2020). Therapeutic potential of quercetin as an antiatherosclerotic agent in atherosclerotic cardiovascular disease: a review. *Evidence-Based Complementary and Alternative Medicine, 2020*.

EU Fusion Projects. (2016). https://www.eu-fusions.org.

European Commission. (2021). *The European Green Deal: Striving to be the first climate-neutral continent*. Retrieved from https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/european-green-deal_en.

European Commission Directorate-General for Research Innovation. (2021). *Horizon Europe, the EU research and innovation programme (2021-27): for a green, healthy, digital and inclusive Europe*. Publications Office of the European Union. https://doi.org/doi/10.2777/052084.

Farré, A. L., & Macaya, C. (2006). Efectos antitrombóticos y antiinflamatorios de los ácidos grasos omega-3. *Revista Española de Cardiología Suplementos, 6*(4), 31D-37D.

Ferraboschi, C., Monroy-Gomez, J., Gavin-Smith, B., Beesabathuni, K., Tshering, P., Lingala, S., … van Zutphen, K. G. (2022). Principles for Evidence-Based and Sustainable Food System Innovations for Healthier Diets. *Nutrients, 14*(10), 2003.

Ferreira, B. L., Junior, T. K., Block, J. M., Granato, D., & Nunes, I. L. (2021). Innovative approach for obtaining phenolic compounds from guava (Psidium guajava L.) coproduct using ionic liquid ultrasound-assisted extraction (IL-UAE). Biocatalysis and Agricultural. *Biotechnology, 38*, Article 102196.

Flint, H. J., Scott, K. P., Duncan, S. H., Louis, P., & Forano, E. (2012). Microbial degradation of complex carbohydrates in the gut. *Gut microbes, 3*(4), 289–306.

Fossi, B. T., Ekabe, D. E., Toukam, L. L., Pambou, H. O. T., Gagneux-Brunon, A., Nguefeu, C. N., & Bongue, B. (2022). Probiotic lactic acid bacteria isolated from traditional cameroonian palm wine and corn beer exhibiting cholesterol lowering activity. *Heliyon, 8*(11), e11708.

Frum, A., Dobrea, C. M., Rus, L. L., Virchea, L.-I., Morgovan, C., Chis, A. A., … Georgescu, C. (2022). Valorization of Grape Pomace and Berries as a New and Sustainable Dietary Supplement: Development, Characterization, and Antioxidant Activity Testing. *Nutrients, 14*(15), 3065.

Galanakis, C. M., Brunori, G., Chiaramonti, D., Matthews, R., Panoutsou, C., & Fritsche, U. R. (2022). Bioeconomy and green recovery in a post-COVID-19 era. *Science of The Total Environment, 808*, Article 152180. https://doi.org/10.1016/j.scitotenv.2021.152180

Gao, L., Gou, N., Amakye, W. K., Wu, J., & Ren, J. (2022). Bioactivity guided isolation and identification of phenolic compounds from Citrus aurantium L. with anti-colorectal cancer cells activity by UHPLC-Q-TOF/MS. *Current Research in Food Science, 5*, 2251–2260.

Genovese, A., Balivo, A., Salvati, A., & Sacchi, R. (2022). Functional ice cream health benefits and sensory implications. *Food Research International, 111858*.

Goff, Z. D., & Nissen, S. E. (2022). N-3 polyunsaturated fatty acids for cardiovascular risk. *Current Opinion in Cardiology, 37*(4), 356–363.

Gohara-Beirigo, A. K., Matsudo, M. C., Cezare-Gomes, E. A., Carvalho, J. C. M. d., & Danesi, E. D. G. (2022). Microalgae trends toward functional staple food incorporation: Sustainable alternative for human health improvement. *Trends in Food Science & Technology*, *125*, 185-199. https://doi.org/https://doi.org/10.1016/j.tifs.2022.04.030.

Gómez-García, R., Campos, D. A., Oliveira, A., Aguilar, C. N., Madureira, A. R., & Pintado, M. (2021). A chemical valorisation of melon peels towards functional food ingredients: Bioactives profile and antioxidant properties. *Food Chemistry, 335*, Article 127579.

Granato, D. (2022). Functional foods to counterbalance low-grade inflammation and oxidative stress in cardiovascular diseases: A multilayered strategy combining food and health sciences. *Current Opinion in Food Science, 47*, Article 100894. https://doi.org/10.1016/j.cofs.2022.100894

Granato, D., Barba, F. J., Bursać Kovačević, D., Lorenzo, J. M., Cruz, A. G., & Putnik, P. (2020). Functional foods: Product development, technological trends, efficacy testing, and safety. *Annual review of food science and technology, 11*, 93–118.

Granato, D., Carocho, M., Barros, L., Zabetakis, I., Mocan, A., Tsoupras, A., Cruz, A. G., & Pimentel, T. C. (2022). Implementation of Sustainable Development Goals in the dairy sector: Perspectives on the use of agro-industrial side-streams to design functional foods. *Trends in Food Science & Technology*.

Granato, D., Nunes, D. S., & Barba, F. J. (2017). An integrated strategy between food chemistry, biology, nutrition, pharmacology, and statistics in the development of functional foods: A proposal. *Trends in Food Science & Technology, 62*, 13–22.

Granato, D., Reshamwala, D., Korpinen, R., Azevedo, L., Vieira do Carmo, M. A., Cruz, T. M., Marques, M. B., Wen, M., Zhang, L., Marjomäki, V., & Kilpeläinen, P. (2022). From the forest to the plate – Hemicelluloses, galactoglucomannan, glucuronoxylan, and phenolic-rich extracts from unconventional sources as functional food ingredients. *Food Chemistry*, *381*, 132284. https://doi.org/https://doi.org/10.1016/j.foodchem.2022.132284.

Grau, L., Soucek, R., & Pujol, M. D. (2023). Resveratrol derivatives: Synthesis and their biological activities. *European Journal of Medicinal Chemistry, 246*, Article 114962.

Harishkumar, R., Hans, S., Stanton, J. E., Grabrucker, A. M., Lordan, R., & Zabetakis, I. (2022). Targeting the Platelet-Activating Factor Receptor (PAF-R): Antithrombotic and Anti-Atherosclerotic Nutrients. *Nutrients, 14*(20), 4414.

Hossain, A. M., Brennan, M. A., Guo, X., Zeng, X.-A., & Brennan, C. S. (2020). Cellular biological activity and regulation of gene expression of antioxidant dietary fibre fraction isolated from blackcurrant incorporated in the wholemeal cereals cookies. *Food Chemistry, 312*, Article 125829.

Innovation, U. R. a. (2022). ***Eligibility of technology readiness levels (TRL)***. https://www.ukri.org/councils/stfc/guidance-for-applicants/check-if-youre-eligible-for-funding/eligibility-of-technology-readiness-levels-trl/.

Jenkins, D. J. A., Kendall, C. W. C., Nguyen, T. H., Marchie, A., Faulkner, D. A., Ireland, C., … Singer, W. (2008). Effect of plant sterols in combination with other

cholesterol-lowering foods. *Metabolism, 57*(1), 130–139. https://doi.org/10.1016/j.metabol.2007.08.016
Jiang, R., Wang, H., Su, S., Li, R., Hu, Y., Zhu, M., … Gao, Y. (2022). Effects of the tea polyphenol content on the properties and structural characteristics of simulated meat. *Future Foods, 5*, Article 100150.
Jing, X., Chen, Z., Tang, Z., Tao, Y., Huang, Q., Wu, Y., … Liu, Z. (2022). Preparation of camellia oil oleogel and its application in an ice cream system. *Lwt, 169*, Article 113985.
Kaczmarek, J. L., Liu, X., Charron, C. S., Novotny, J. A., Jeffery, E. H., Seifried, H. E., … Holscher, H. D. (2019). Broccoli consumption affects the human gastrointestinal microbiota. *The Journal of nutritional biochemistry, 63*, 27–34.
Kuc-Czarnecka, M., Markowicz, I., & Sompolska-Rzechuła, A. (2023). SDGs implementation, their synergies, and trade-offs in EU countries–Sensitivity analysis-based approach. *Ecological Indicators, 146*, Article 109888.
Kurniawan, T. A., Othman, M. H. D., Liang, X., Goh, H. H., & Chew, K. W. (2022). From liquid waste to mineral fertilizer: Recovery of high-value macro-nutrients from landfill leachate to contribute to circular economy, food security, and carbon neutrality. *Process Safety and Environmental Protection*.
Lacirignola, C., Capone, R., Debs, P., El Bilali, H., & Bottalico, F. (2014). Natural resources - food nexus: Food-related environmental footprints in the mediterranean countries. *Front Nutr, 1*, 23. https://doi.org/10.3389/fnut.2014.00023
Lang, T. (2007). Functional foods. In (Vol. 334, pp. 1015-1016): British Medical Journal Publishing Group.
Leite, A. K. F., Fonteles, T. V., Alves Filho, E. G., da Silva Oliveira, F. A., & Rodrigues, S. (2023). Impact of orange juice containing potentially prebiotic ingredients on human gut microbiota composition and its metabolites. *Food Chemistry, 405*, Article 134706.
Lie-Piang, A., Möller, A. C., Köllmann, N., Garre, A., Boom, R., & van der Padt, A. (2022). Functionality-driven food product formulation – An illustration on selecting sustainable ingredients building viscosity. *Food Research International, 152*, Article 110889. https://doi.org/10.1016/j.foodres.2021.110889
Lordan, R., Tsoupras, A., & Zabetakis, I. (2017). Phospholipids of Animal and Marine Origin: Structure, Function, and Anti-Inflammatory Properties. *Molecules, 22*(11), 1964.
Lugo, S. D. R., Kimita, K., & Nishino, N. (2022). Circular Food Economy framework: Challenges and initiatives. *Procedia CIRP, 112*, 28–33.
Lyu, Q., Chen, L., Lin, S., Cao, H., & Teng, H. (2022). A designed self-microemulsion delivery system for dihydromyricetin and its dietary intervention effect on high-fat-diet fed mice. *Food Chemistry, 390*, Article 132954. https://doi.org/10.1016/j.foodchem.2022.132954
Ma, H., Zhang, B., Hu, Y., Li, X., Wang, J., Yang, F., … Wang, S. (2020). The novel intervention effect of cold green tea beverage on high-fat diet induced obesity in mice. *Journal of Functional Foods, 75*, Article 104279.
Mazloomi, S. M., Samadi, M., Davarpanah, H., Babajafari, S., Clark, C. C. T., Ghaemfar, Z., … Rostami, H. (2022). The effect of Spirulina sauce, as a functional food, on cardiometabolic risk factors, oxidative stress biomarkers, glycemic profile, and liver enzymes in nonalcoholic fatty liver disease patients: A randomized double-blinded clinical trial. *Food Sci Nutr, 10*(2), 317–328. https://doi.org/10.1002/fsn3.2368
Moslemi, E., Dehghan, P., & Khani, M. (2022). The effect of date seed (Phoenix dactylifera) supplementation on inflammation, oxidative stress biomarkers, and performance in active people: A blinded randomized controlled trial protocol. *Contemporary Clinical Trials Communications, 28*, Article 100951. https://doi.org/10.1016/j.conctc.2022.100951
Moughan, P. J. (2008). Chapter 17 - Milk proteins: A cornucopia for developing functional foods. In A. Thompson, M. Boland, & H. Singh (Eds.), *Milk Proteins* (pp. 483–499). Academic Press.
Munialo, C. D., Stewart, D., Campbell, L., & Euston, S. R. (2022). Extraction, characterisation and functional applications of sustainable alternative protein sources for future foods: A review. *Future Foods, 6*, Article 100152. https://doi.org/10.1016/j.fufo.2022.100152
Muscio, A., & Sisto, R. (2020). Are Agri-Food Systems Really Switching to a Circular Economy Model? Implications for European Research and Innovation Policy. *Sustainability, 12*(14), 5554.
Nasopoulou, C., Lytoudi, K., & Zabetakis, I. (2018). Evaluation of olive pomace in the production of novel broilers with enhanced in vitro antithrombotic properties. *European Journal of Lipid Science and Technology, 120*(4), 1700290.
Nystrand, B. T., & Olsen, S. O. (2020). Consumers' attitudes and intentions toward consuming functional foods in Norway. *Food Quality and Preference, 80*, Article 103827.
Oliveira, A. S., Pereira, J. O., Ferreira, C., Faustino, M., Durão, J., Pintado, M. E., & Carvalho, A. P. (2022). Peptide-rich extracts from spent yeast waste streams as a source of bioactive compounds for the nutraceutical market. *Innovative Food Science & Emerging Technologies, 81*, Article 103148.
Othman, S., Añibarro-Ortega, M., Dias, M. I., Ćirić, A., Mandim, F., Soković, M., … Barros, L. (2022). Valorization of quince peel into functional food ingredients: A path towards "zero waste" and sustainable food systems. *Heliyon, 8*(10), e11042. https://doi.org/10.1016/j.heliyon.2022.e11042
Pap, N., Reshamwala, D., Korpinen, R., Kilpeläinen, P., Fidelis, M., Furtado, M. M., Sant'Ana, A. S., Wen, M., Zhang, L., & Hellström, J. (2021). Toxicological and bioactivity evaluation of blackcurrant press cake, sea buckthorn leaves and bark from Scots pine and Norway spruce extracts under a green integrated approach. *Food and Chemical Toxicology, 153*, 112284.
Papadaki, A., Manikas, A. C., Papazoglou, E., Kachrimanidou, V., Lappa, I., Galiotis, C., … Kopsahelis, N. (2022). Whey protein films reinforced with bacterial cellulose nanowhiskers: Improving edible film properties via a circular economy approach. *Food Chemistry, 385*, Article 132604.
Pattnaik, M., Pandey, P., Martin, G. J. O., Mishra, H. N., & Ashokkumar, M. (2021). Innovative Technologies for Extraction and Microencapsulation of Bioactives from Plant-Based Food Waste and Their Applications in Functional Food Development. *Foods, 10*(2), 279.
Peled, S., & Livney, Y. D. (2021). The role of dietary proteins and carbohydrates in gut microbiome composition and activity: A review. *Food Hydrocolloids, 120*, Article 106911.
Peredo-Lovillo, A., Hernández-Mendoza, A., Vallejo-Cordoba, B., & Romero-Luna, H. E. (2021). Conventional and in silico approaches to select promising food-derived bioactive peptides: A review. *Food Chemistry, X*, Article 100183.
Pérez-Ramírez, I. F., de Diego, E. H., Riomoros-Arranz, M., Reynoso-Camacho, R., Saura-Calixto, F., & Pérez-Jiménez, J. (2020). Effects of acute intake of grape/pomegranate pomace dietary supplement on glucose metabolism and oxidative stress in adults with abdominal obesity. *International Journal of Food Sciences and Nutrition, 71*(1), 94–105. https://doi.org/10.1080/09637486.2019.1607831
Pérez-Ramírez, I. F., Reynoso-Camacho, R., Saura-Calixto, F., & Pérez-Jiménez, J. (2018). Comprehensive Characterization of Extractable and Nonextractable Phenolic Compounds by High-Performance Liquid Chromatography-Electrospray Ionization–Quadrupole Time-of-Flight of a Grape/Pomegranate Pomace Dietary Supplement. *Journal of Agricultural and Food Chemistry, 66*(3), 661–673. https://doi.org/10.1021/acs.jafc.7b05901
Rakić, S., Povrenović, D., Tešević, V., Simić, M., & Maletić, R. (2006). Oak acorn, polyphenols and antioxidant activity in functional food. *Journal of Food Engineering, 74*(3), 416–423.
Redfern, S., Dermiki, M., Fox, S., Lordan, R., Shiels, K., Saha, S. K., … Zabetakis, I. (2021). The effects of cooking salmon sous-vide on its antithrombotic properties, lipid profile and sensory characteristics. *Food Research International, 139*, Article 109976.
Repar, L., & Bogue, J. (2023). Market-oriented methodologies that integrate the consumer into the functional foods new product development process: Part 2 advanced approaches. In *Case Studies on the Business of Nutraceuticals, Functional and Super Foods* (pp. 57-84). Elsevier.
Rinninella, E., Tohumcu, E., Raoul, P., Fiorani, M., Cintoni, M., Mele, M. C., … Ianiro, G. (2023). The role of diet in shaping human gut microbiota. *Best Practice & Research Clinical Gastroenterology, 101828*. https://doi.org/10.1016/j.bpg.2023.101828
Rivero-Pino, F. (2022). Bioactive food-derived peptides for functional nutrition: Effect of fortification, processing and storage on peptide stability and bioactivity within food matrices. *Food Chemistry, 135046*.
Ruscica, M., Pavanello, C., Gandini, S., Gomaraschi, M., Vitali, C., Macchi, C., … Calabresi, L. (2018). Effect of soy on metabolic syndrome and cardiovascular risk factors: A randomized controlled trial. *European Journal of Nutrition, 57*, 499–511.
Sabater, C., Calvete-Torre, I., Villamiel, M., Moreno, F. J., Margolles, A., & Ruiz, L. (2021). Vegetable waste and by-products to feed a healthy gut microbiota: Current evidence, machine learning and computational tools to design novel microbiome-targeted foods. *Trends in Food Science & Technology, 118*, 399–417. https://doi.org/10.1016/j.tifs.2021.10.002
Siegrist, M., & Hartmann, C. (2020). Consumer acceptance of novel food technologies. *Nature Food, 1*(6), 343–350.
Tabassum, S., Ahmad, S., Rehman, K.-U., Khurshid, U., Rao, H., Alamri, A., … Saleem, H. (2022). Phytochemical, biological, and in-silico characterization of Portulacaria afra Jacq.: A possible source of natural products for functional food and medicine. *South African Journal of Botany, 150*, 139–145.
Temple, N. J. (2022). A rational definition for functional foods: A perspective [Perspective]. *Frontiers in Nutrition, 9*. https://doi.org/10.3389/fnut.2022.957516
Topal, M., & Gulcin, İ. (2022). Evaluation of the in vitro antioxidant, antidiabetic and anticholinergic properties of rosmarinic acid from rosemary (Rosmarinus officinalis L.). Biocatalysis and Agricultural. *Biotechnology, 43*, Article 102417.
Tsoupras, A., Lordan, R., Shiels, K., Saha, S. K., Nasopoulou, C., & Zabetakis, I. (2019). In vitro antithrombotic properties of salmon (Salmo salar) phospholipids in a novel food-grade extract. *Marine drugs, 17*(1), 62.
Tsoupras, A., Lordan, R., & Zabetakis, I. (2018). Inflammation, not Cholesterol, Is a Cause of Chronic Disease. *Nutrients, 10*(5), 604.
Tweeten, L. (1999). The economics of global food security. *Applied Economic Perspectives and Policy, 21*(2), 473–488.
United Nations. (2022). *The Sustainable Development Goals Report 2022*. Retrieved from https://unstats.un.org/sdgs/report/2022/The-Sustainable-Development-Goals-Report-2022.pdf.
Veldkamp, T., Meijer, N., Alleweldt, F., Deruytter, D., Van Campenhout, L., Gasco, L., … van der Fels-Klerx, H. J. (2022). Overcoming Technical and Market Barriers to Enable Sustainable Large-Scale Production and Consumption of Insect Proteins in Europe: A SUSINCHAIN Perspective. *Insects, 13*(3), 281.
Viñas-Ospino, A., Panić, M., Radojčić- Redovniković, I., Blesa, J., & Esteve, M. J. (2023). Using novel hydrophobic deep eutectic solvents to improve a sustainable carotenoid extraction from orange peels. *Food Bioscience, 53*, Article 102570. https://doi.org/10.1016/j.fbio.2023.102570
Wang, Y., Liu, T., Xie, Y., Li, N., Liu, Y., Wen, J., … Guo, Y. (2022). Clitoria ternatea blue petal extract protects against obesity, oxidative stress, and inflammation induced by a high-fat, high-fructose diet in C57BL/6 mice. *Food Research International, 162*, Article 112008.
WHO (2021). Cardiovascular diseases (CVDs). Retrieved from https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)#:~:text=An%20estimated%2017.9%20million%20people,%2D%20and%20middle%2Dincome%20countries.

World Health Organisation (2020). *Information note on COVID-19 and NCDs*. Retrieved from https://www.who.int/publications/m/item/covid-19-and-ncds.

Xia, M., Ahn, D. U., Liu, C., & Cai, Z. (2022). A basis for IgY-themed functional foods: Digestion profile of oral yolk immunoglobulin (IgY) by INFOGEST static digestion model. *Food Research International, 162*, Article 112167.

Yan, Y. L., Hu, Y., & Gänzle, M. G. (2018). Prebiotics, FODMAPs and dietary fiber—conflicting concepts in development of functional food products? *Current Opinion in Food Science, 20*, 30–37.

Yi, C., Sun, W., Ding, L., Yan, M., Sun, C., Qiu, C., … Wu, L. (2022). Short-Chain Fatty Acids Weaken Ox-LDL-Induced Cell Inflammatory Injury by Inhibiting the NLRP3/Caspase-1 Pathway and Affecting Cellular Metabolism in THP-1 Cells. *Molecules, 27*(24), 8801.

Zabetakis, I. (2013). Food security and cardioprotection: The polar lipid link. R1101-1104 *J Food Sci, 78*(8). https://doi.org/10.1111/1750-3841.12194.

Zabetakis, I., Lordan, R., Norton, C., & Tsoupras, A. (2020). COVID-19: The Inflammation Link and the Role of Nutrition in Potential Mitigation. *Nutrients, 12*(5), 1466.

Zabetakis, I., Lordan, R., Tsoupras, A., & Ramji, D. (2022). *Functional Foods and Their Implications for Health Promotion*. Elsevier.

Zhang, F., Fan, D., Huang, J.-L., & Zuo, T. (2022). The gut microbiome: Linking dietary fiber to inflammatory diseases. *Medicine in Microecology, 14*, Article 100070. https://doi.org/10.1016/j.medmic.2022.100070

Zhong, H., Huang, Y., Deng, X., Liu, M., & Luo, W. (2020). Cucurbitacin B supplementation reduces inflammatory responses and alveolar bone loss via regulating MPO, COX-2 and RANK/RANKL/OPG signals in a rodent model of ligature-induced periodontitis. *Journal of King Saud University-Science, 32*(3), 1889–1895.

Zurek, M., Hebinck, A., & Selomane, O. (2022). Climate change and the urgency to transform food systems. *Science, 376*(6600), 1416–1421.