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Review

Biorefinery and Stepwise Strategies for Valorizing Coffee By-Products as Bioactive Food Ingredients and Nutraceuticals

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Featured Application: This study presents a comprehensive and stepwise strategy for utilizing coffee by-products as a sustainable source to develop bioactive food ingredients and nutraceuticals. Coffee by-products can be transformed into versatile functional food ingredients and nutraceuticals by implementing green extraction techniques and employing a biorefinery approach. These products offer a wide range of benefits, including antioxidant, anti-inflammatory, and anti-obesity effects, as well as the potential to regulate energy metabolism and blood sugar levels and serve as adjunct therapies for conditions such as cardiovascular disease, diabetes, and neurodegenerative disorders. This research not only contributes to the creation of functional food products and supplements but also promotes sustainability and addresses the prevention and management of chronic diseases.

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Abstract: Coffee production generates significant amounts of by-products, posing challenges for waste management in the industry. Recent research has revealed that coffee by-products are rich in bioactive compounds suitable to produce functional food ingredients and nutraceuticals. In this review, we explore biorefinery strategies for extracting and utilizing bioactive compounds from coffee by-products, including the production of bio-based chemicals and materials, as well as the extraction of phenolic compounds, antioxidants, and dietary fiber for food applications. We propose a stepwise approach for the development of functional food ingredients and nutraceuticals from coffee by-products, covering the identification of needs, comprehensive characterization, in vitro and in vivo research, unraveling the mechanism of action, food and nutraceutical formulation, sensory analysis, shelf-life stability, scale-up, randomized control trials, and biostatistics and bioinformatic integration. Additionally, we discuss the market potential, regulatory issues, and technological innovation surrounding the commercialization of coffee by-product-based products. Emphasizing the importance of regulatory compliance and sustainability in the coffee industry, this review highlights the potential of coffee by-products to be transformed from waste into valuable functional food ingredients and nutraceuticals, offering a promising avenue for waste reduction and promoting sustainability in the coffee industry.

Keywords: bioactive compounds; biorefinery; coffee by-products; functional food ingredients; health benefits; nutraceuticals; sustainability; technological innovation; valorization; waste utilization

1. Introduction

Coffee is one of the world's main commodities representing the second most consumed beverage after water, with annual rates of 42.6 L per capita and a global intake of 3 billion

0.2 L cups of coffee per day [1]. The personal global consumption ranking is led by Scandinavian countries, headed by Finnish people with a yearly consumption of around 9.4 kg of roasted coffee per capita (equivalent to 6–8 cups per day). This superior demand turns coffee beans into one of the globe's top-traded agro-industrial products. According to the International Coffee Organization, about 171.3 million 60 kg bags of coffee beans are estimated to be produced in 2022/2023, following a robust increasing biannual trend in forthcoming years due to the endless rising of consumer demand. Surprisingly, the mentioned production results insufficiently cover the predicted consumption estimations for a second consecutive year, i.e., around 178.5 million bags [2], which could explain the 1.9% volume growth expected for the coffee market in 2024 [2]. This agro-industrial and socioeconomic paradigm rationalizes the worldwide concern relative to the environmental impact of coffee cultivation and manufacturing, owing to the notable amount of by-products delivered by this food sector.

Waste management is one of the most challenging problems we currently handle worldwide. Presently, food systems are highly inefficient since around one-third of the food produced is wasted and not consumed [3]. Food is lost or wasted at every stage of the food supply chain, from farming to consumption. Therefore, to ensure sustainable management of food waste, food by-products should be utilized before they become waste, thus increasing the food system's sustainability which constitutes a milestone of the United Nations' Sustainable Development Goals (SDGs). The SDGs seek to restructure the agriculture and food systems to decrease hunger, achieve food security, and improve nutrition while reducing food waste and losses along supply chains [4]. A sustainable food system delivers food security and nutrition without endangering the economic, social, and environmental foundations for producing safe and nutritious foods for future generations. Consequently, the food system generates economic value-added benefits (economic sustainability), has widespread social benefits including nutritional and health benefits, and is equitable in distributing the economic value-added (social sustainability) plus a favorable or neutral environmental effect (environmental sustainability) [5]. Undoubtedly, the coffee agroindustry must also face this challenge focused on waste management. Indeed, coffee by-products from wet and dry processing—coffee husk, parchment, pulp, mucilage, and silverskin—represent nearly 50% of the coffee cherry on a dry weight basis [2]. Global coffee production delivers over 23 million tons of waste annually, estimating 0.2 and 0.5 tons of coffee pulp and coffee husk by 1 ton of coffee produced by wet and dry processes, respectively, and 8 kg of silverskin by 1 ton of roasted beans [6,7]. Even though the abovementioned coffee by-products have been traditionally used for low-value applications such as animal feed or composting for soil fertilization, coffee waste is liable to end up in landfills where it usually is spontaneously decomposed, producing unpleasant smells and acidic leaches able to damage the neighboring soil by lixiviation. It also releases greenhouse gases with a direct impact on climate change, alongside harming soil and water sources when these by-products are dumped into streams because of their cytotoxic and ecotoxic effects [8]. Moreover, they are known for their remarkable resistance to natural degradation, involving long residence periods, resulting in a severe environmental and even energetic impact. Such circumstances raise awareness and inspire the scientific community to research valorization strategies, which minimize the coffee agroindustry's environmental and energetic impacts and could produce added-value products following circular economy principles [9]. Thereby, novel application outcomes could result in economically gainful opportunities for coffee agro-industry stakeholders through the direct marketing of added-value products. Furthermore, the valorization of coffee waste can contribute to the diversification of income streams for coffee farmers, reducing their dependence on volatile commodity prices [10]. This can help to enhance the stability and resilience of coffee-producing regions, particularly in developing countries where coffee production is a significant source of income. The economic potential of coffee waste is further supported by the growing demand for sustainable and healthy products in the global market [11].

Biorefinery strategies for coffee waste are gaining importance as a means to reduce this environmental impact while generating economic value [12]. Using coffee waste to produce functional food ingredients and nutraceuticals offers a sustainable solution to the waste problem while creating a value-added product with potential health benefits [13]. Over the last few years, scientific research has demonstrated that coffee waste still contains valuable compounds, including carbohydrates, proteins, lipids, and bioactive compounds such as dietary fiber, phenolic compounds, and caffeine. Following the scientometric analysis published by Durán-Aranguren et al. [6], the annual scientific production has experienced a notable rise since 2010, with the highest rate of publications for coffee husk and coffee pulp by-products in recent years. The most renowned biorefinery valorization strategies approached to date are directed at the coffee by-products' microbial transformation; their environmental applications as sources of biosorbents, biopesticides, or fertilizers; their transformation into biofuels from thermochemical processing such as syngas or biodiesel; their contribution to producing sustainable materials such as ceramic aggregates or food packaging substitutes; or their bioactive compounds exploitation [6]. Within the latest news, their use as bioactive ingredients for food and nutraceuticals formulation from both raw materials and their extracts seems one of the most comprehensive applications with greater growth prospects, with a doubtless sustainable benefit for human health because of their evidenced useful properties. In addition, the production of such food-like products from coffee waste offers a unique selling proposition for companies seeking to meet the worldwide demand for sustainable and healthy products. Validation of the new products derived from coffee by-products is essential to ensure their safety, efficacy, and market acceptance [14]. A systematic approach is required to establish a strong scientific foundation for functional food claims and to validate the bioactive compounds and their potential health benefits [15]. This validation process ensures confidence in the economic potential of coffee waste utilization and supports the development of sustainable and healthy products for the market [16].

This comprehensive review aims to provide an in-depth overview of the biorefinery strategies and multistep approaches to producing bioactive food ingredients and nutraceuticals from coffee by-products. We begin by summarizing the relevant aspects of coffee by-products and their potential as food ingredients with health benefits. We explore three key biorefinery strategies: the production of bio-based chemicals and materials, green aqueous extraction of bioactive compounds for food applications, and utilization of coffee by-products in food processing. We cover a wide range of topics, including the characterization of coffee by-products, in vitro and in vivo research studies on the bioactivity and health benefits of coffee by-product-derived compounds, randomized control trials evaluating the efficacy and safety of coffee by-product-derived nutraceuticals in human subjects, and sensory analysis of food products containing coffee by-product-derived ingredients. Furthermore, we address the regulatory considerations and challenges associated with the commercialization of coffee by-product-derived products, along with the technological innovations and optimization strategies for their production. We also explore the economic potential of coffee by-products and their implications for sustainable agriculture and food systems and highlight future directions for research and innovation in this field.

2. Composition, Availability, and Technological and Safety Constraints of Coffee By-Products

Coffea arabica L. (Arabica coffee) and *Coffea canephora* (Robusta coffee), both members of the Rubiaceae family, are the most important plant species in the international coffee trade [17]. During coffee beverage preparation, approximately 90% of the coffee cherry's edible sections are discarded as agricultural waste or by-products. Coffee by-products have aroused considerable interest because of their abundance and excellent chemical composition [18]. The coffee cherry (Figure 1) comprises an outer skin or pericarp, which is green in unripe and red in ripe fruits, covering a soft and sweet pulp or outer mesocarp. Subsequently, a viscous and highly hydrated mucilage layer (pectin layer) and a thin yellowish endocarp (the parchment) are found. Ultimately, the silverskin covers two or three green coffee beans (endosperm) [19].

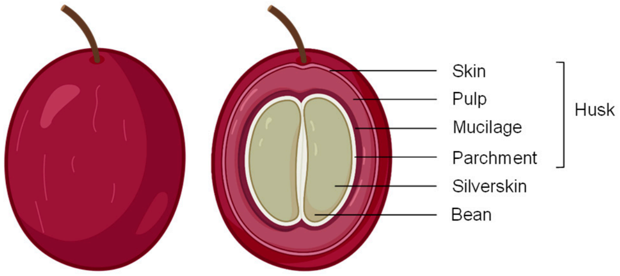

Figure 1. Coffee cherry anatomy from the outside to the inside (skin, pulp, mucilage, parchment—comprising the coffee husk, silverskin, and coffee bean).

The coffee cherries are converted into green coffee beans by removing the cherry outer layers using either a wet or dry method (Figure 2) [20]. The dry method (Figure 2A), widely used in Robusta-producing countries, is more technologically simple. To achieve optimal drying, the freshly picked cherries are either uniformly distributed and sun-dried for 2–4 weeks in yards (natural drying) or mechanically dried until the moisture content is reduced to less than 12%. Subsequently, the coffee cherries are mechanically de-husked, and the skin, pulp, mucilage, and parchment are separated from the beans [17,21]. The wet processing (Figure 2B), commonly used for Arabica coffees, is more commercially valued, and needs various tools to extract the green bean. A de-pulper is first utilized to remove the skin and pulp that covers the bean [21]. Once de-pulped, the mucilage still covers the coffee bean; thus, it is removed through a 24–72 h fermentation [17]. Then, the bean covered by the parchment is washed, drained, and dried until the moisture content is about 10% [21]. Finally, a hulling machine is used to remove the parchment [18].

Figure 2. Dry (**A**) and wet (**B**) processing of freshly harvested coffee beans to produce green coffee beans.

2.1. Husk

The coffee husk is the first by-product produced during coffee processing. This by-product is generated in coffee-producing countries at 40 kg per 100 kg of green coffee beans [22]. The definition and composition of the coffee husk depend on the processing method employed. Dry coffee husks obtained through the dry processing method (Figure 3A), consist of skin, pulp, mucilage, and parchment and are rich in insoluble dietary fiber. They contain approximately 30% hemicelluloses, 25% cellulose, and 24% lignin (Table 1) [23–26]. Coffee husks are also sources of phytochemicals, including phenolic compounds, which account for approximately 1.2% and mainly include anthocyanins and proanthocyanidins [27].

Figure 3. Coffee husks obtained by the dry (**A**) and wet (**B**) processing methods.

Table 1. Chemical composition of coffee by-products obtained through coffee processing. Values expressed in dry matter.

	Husk	Pulp	Mucilage	Parchment	Silverskin
Type of processing Processing step	Dry Pulping	Wet Pulping	Wet Hulling	Wet Pulping	Dry/wet Roasting
Macronutrients (%)					
Moisture	13.0–15.0	78.0–81.0	80.0–84.0	8.1–10.0	4.0–7.0
Protein	6.0–16.0	8.7–17.0	8.9–17	3.1–17.4	7.9–20.6
Lipids	1.0–4.1	0.5–2.0	-	0.3–4.1	1.2–3.0
Total sugars	26.0–30.1	10–15	-	-	0.4
Dietary fiber	32–43	21.5–28.0	30	64.3–92.6	52.0–69.8
Ash	1.4–6.2	8–9.5	0.7	0.5–1.0	5.8–9.5
Bioactive compounds (mg/g)					
Total phenolics	10.1–15.0	10.0–13.0	-	2.0–3.0	3.6–20.3
Caffeine	6.8–12.0	2.0–10.1	-	0.1–1.3	0.7–9.5
Tannins	18–93	1.8–8.6	-	-	2.5–7.66
Chlorogenic acids	-	1.8–3.37	-	0.05	1.6–2.5
Caffeoylquinic acid	0.8	1.7–1.8	-	-	0.1–3.1
Hydroxymethylfurfural	-	-	-	-	0.2–3.2
Melanoidins	1.5	-	-	-	1.7–2.3
References	[23–27]	[28–30]	[18,25,31,32]	[14,33–36]	[24,25,37–41]

Coffee husks generated through the wet method (known as wet husk or pulp) (Figure 3B) are composed of skin and pulp and contain significant levels of phenolic compounds (1.5%) and caffeine (1.3%) [28]. The wet husk contains four major groups of phenolic compounds: hydroxycinnamic acids, flavanols, flavonols, and anthocyanidins [28]. The primary phenolic compounds in coffee husks are chlorogenic and protocatechuic acids, which account for more than 80% of the overall phenolic compounds [29]. Other phenolic compounds identified in coffee husks are epicatechin, catechin, rutin, ferulic acid, and cyanidin-3-glucoside and 3-rutinoside [18]. In addition, the coffee pulp presents lower lipid (0.5–2%) and mineral (8–9.5%) content, and higher protein (8–17%), moisture (78%), and carbohydrates content (~58–85%) than the coffee parchment (Table 1). These differences in composition between the dry and the wet husk provide unique opportunities for their utilization in various applications, from dietary fiber enrichment to the extraction of bioactive compounds [42]. Exploring these distinctions and utilizing the specific properties of dry and wet husk can lead to the development of innovative products and contribute to the sustainable utilization of coffee by-products.

The coffee husk is a substantial by-product generated during coffee processing, with a production rate of approximately 40 kg per 100 kg of green coffee beans in coffee-producing countries [22]. Coffee husks obtained from the dry processing method account for nearly 45% of the coffee cherry [19], while coffee husks obtained from the wet processing method represent around 29% of the dry weight of the entire cherry [21]. This indicates a significant quantity of coffee husk being generated annually (around 4 million tons), considering the global coffee production of 171.3 million 60 kg bags [43]. With this global coffee production resulting in millions of tons of coffee husk annually, exploring effective strategies for managing this by-product and maximizing its utilization potential is necessary.

In terms of technological and safety constraints, coffee husk handling and disposal entrain a severe environmental problem due to its high moisture and low bulk density [44]. These characteristics make handling, processing, and utilization of coffee husk more complex. Its fibrous composition and low compactability can hinder efficient extraction and incorporation into value-added products [45]. Additionally, the high moisture content of the coffee husk can contribute to difficulties in storage and transportation, as well as potential mold growth [46]. To overcome the technological constraints and optimize the utilization of the coffee husk, further research and development efforts are necessary. These efforts should focus on developing innovative technologies and processing methods that enable efficient extraction of valuable components, such as dietary fiber, phenolic compounds, and caffeine, while ensuring safety and scalability [47]. Although research seeks value-added applications for the coffee husk, such as in bioprocessing [48], further exploration of alternative uses and applications can contribute to its value as a sustainable resource.

Recently, the European Commission approved the dried coffee husk from *Coffee arabica* L. as a novel food to be used as an ingredient for infusions and non-alcoholic drinks, with its maximum use levels from 2–6 g of husk/100 mL [49]. Considering the history of the use of the coffee husk as food and the proposed uses and use levels, no toxicological studies were required by the European Commission. The precautions and use restrictions are related to caffeine intake, which should not exceed 150 mg/L in the products containing this novel food. No safety concerns are noted regarding the concentration of contaminants (e.g., heavy metals, pesticide residues, organic contaminants) which depends mainly on the production process (cultivation) that has been sufficiently described. Notwithstanding, quality control measures should be implemented throughout the processing of coffee husk to ensure safety and minimize potential contaminants [50]. Regular testing for pesticide residues, heavy metals, mycotoxins, and other contaminants should be conducted to comply with food safety regulations and guarantee the quality and purity of coffee husk-derived ingredients [14]. Addressing the technological and safety constraints associated with the coffee husk will not only contribute to the efficient utilization of this by-product but also promote sustainability and reduce waste within the coffee industry [21]. By implementing appropriate processing techniques and ensuring strict quality control measures, the coffee husk can be transformed into valuable ingredients and contribute to the circular economy.

2.2. Mucilage

The coffee mucilage is a pectin layer found between the pulp and the parchment (Figure 4). After de-pulping, the mucilage remains attached to the coffee bean, and being highly hydrated, is an impediment to further drying the beans. As a result, before the beans can be dried and processed, the mucilage must be degraded by wet fermentation, which is solubilized by yeast, bacteria, and fungi. The mucilage is an extremely hydrated sticky tissue, comprised of 1% pectins with a high degree of esterification with uronic acid being the major constituent, followed by arabinose, galactose, xylose, rhamnose, and glucose as neutral non-cellulosic monosaccharides. In terms of composition, this coffee by-product is mainly constituted of water (84%), protein (7%), soluble sugars (4%), total dietary fiber (1.5%), caffeine (1%), and ash (1%) [18]. The micronutrients found in the coffee mucilage include Ca, Fe, Mg, K, P, and Na [32]. Phenolic compounds, including flavonoids and tannins, have also been reported in the coffee mucilage [25].

Figure 4. Coffee pulp (wet coffee husk) and de-pulped coffee cherry showing the mucilage covering the coffee bean and partially removed.

This by-product is generated in countries that produce coffee using the wet method [12]. The mucilage is produced at 20 kg per 100 kg of fresh coffee cherries [51]. Given its high moisture content, mucilage poses challenges for drying and processing, requiring wet fermentation to facilitate subsequent processing steps [52]. Technological constraints associated with mucilage include the need for specialized equipment and controlled fermentation conditions to ensure the appropriate degradation and removal of the mucilage layer [53]. The sticky nature of the coffee mucilage can complicate handling and processing, requiring specific techniques like washing (a method to rinse off the fermented mucilage) and mechanical de-mucilaging (where a machine is used to physically strip away the mucilage without damaging the coffee bean) for its removal [54]. However, advances in processing technology and optimization of fermentation parameters have been explored to overcome these constraints and enhance the utilization of the coffee mucilage in value-added applications [52].

Nonetheless, it is important to consider potential contaminations in the coffee mucilage due to the fermentation process. Improper fermentation conditions or inadequate hygiene practices during wet fermentation may lead to microbial contamination, including the growth of undesirable microorganisms such as molds, bacteria, or yeasts [53]. These contaminants can affect the quality and safety of the coffee mucilage and its derived products. Proper hygiene practices, strict quality control measures, and adherence to food safety regulations are crucial during wet fermentation and subsequent processing steps to mitigate potential contaminations. Regular monitoring and testing for microbial contaminants should be implemented to ensure the safety of coffee mucilage-derived ingredients and products [52]. By implementing appropriate quality assurance protocols, the risk of contamination can be minimized, allowing for the safe utilization of the coffee mucilage in value-added applications.

2.3. Parchment

The coffee parchment is the yellowish fibrous endocarp covering and dividing the two hemispheres of the coffee seed. The coffee parchment is produced at 39 kg per 100 kg of fresh coffee cherries [51]. In the wet processing, the coffee parchment is separated from other by-products after the beans have been dried and dehulled (Figure 5). This process allows for the collection of the parchment and its use separately from other by-products. In contrast, in the dry process, the coffee parchment is removed from the green bean, along with the skin, pulp, and mucilage, and is part of the coffee husk.

Figure 5. Coffee parchment flakes as obtained by the wet method.

In terms of composition, the coffee parchment primarily consists of a high proportion of carbohydrates (~56%), predominantly in the form of dietary fiber. The main components of the parchment's dietary fiber are cellulose (40–49%), hemicellulose (25–32%), and lignin (33–35%) [26,34,55–57]. It also contains low levels of fat (~0.3%), proteins (~3%), minerals (0.5–1%), and a variable moisture content (~8–10%). Caffeine and total phenolic compounds may account for approximately 1% and 2%, respectively [36,58].

As it represents 6% of the cherries' dry weight, it is produced at a rate of approximately 39 kg per 100 kg of fresh coffee cherries [51]. Therefore, it is an abundant by-product of coffee processing. Technological constraints associated with the coffee parchment include its fibrous nature, which can make it challenging to process and incorporate into various applications [59,60]. Further research and development efforts are needed to explore efficient and cost-effective methods for the extraction, purification, and utilization of the valuable components present in the coffee parchment [61]. This will help maximize its potential as a sustainable resource and enhance its value as a functional food ingredient [35].

The coffee parchment is generally considered safe for consumption, with studies confirming the absence of pesticides and mycotoxins, except for a minimal content of ochratoxin A (OTA) below the European Commission limit [14,62]. A toxicity analysis was performed to complete the safety assessment, showing no adverse effects or mortality following the administration of 2 g/kg body weight of parchment to rats [14]. However, it is important to note that the coffee parchment, like other coffee by-products, should undergo rigorous quality control measures to ensure safety and minimize potential contaminants. Regular testing for pesticide residues, mycotoxins, and other contaminants should be conducted to ensure compliance with food safety regulations [63]. This is especially important as the coffee parchment is often used as a raw material to produce functional food ingredients and nutraceuticals, where the safety and purity of the starting material are crucial for the final product quality.

2.4. Silverskin

Green coffee beans are shipped to coffee-consuming countries, where their quality is evaluated based on odor and taste tests, as well as by size, form, color, hardness, and existence of defects [20]. Once received, beans are checked to confirm their quality and stored until being roasted. The roasting process consists of three steps: drying, roasting, and cooling. During the drying process, water and volatile compounds are slowly released, and the color of the coffee beans changes from green to yellow. Roasting reactions alter both the beans' physical and chemical properties, resulting in a complex mixture of Maillard reaction products [21].

The silverskin, the thin tegument covering the bean, is detached at this point (Figure 6). The coffee silverskin is the only by-product of the coffee roasting process [17,64]. This by-product contains low moisture (4–7%), lipids (1.2–3%), and mineral content (5–9%). Proteins (8–20%) and carbohydrates (62–67%), mainly forming dietary fiber (52–70%), are the main component of the coffee silverskin [14,38,39,65]. The dietary fiber fraction comprises celluloses (~18–24%), hemicelluloses (~13–17%), and lignin (~29%) [39]. Caffeine is the main phytochemical in the coffee silverskin, followed by the chlorogenic acids (caffeoylquinic acids, dicaffeoylquinic acids, lactones of caffeoylquinic acids, coumaroylquinic acids, feruloylquinic acids, lactones of feruloylquinic acids, and feruloyl-caffeoylquinic acids) [38,40]. Other phenolic compounds found in coffee silverskin include caffeic, protocatechuic, and vanillic acids [41].

The coffee silverskin represents about 4% of the green coffee beans [17,64]. The roasting of 4 tons of coffee yields approximately 30 kg of coffee silverskin [66]. Considering the world coffee annual production (171.3 million 60 kg bags of coffee beans) [43], 76 thousand tons of the coffee silverskin are produced each year worldwide in coffee-transforming countries. Its fibrous and thin nature poses unique technological constraints for its processing and utilization in various applications [67]. Challenges arise due to its low density and high inflammability, requiring careful handling and storage to ensure safety and prevent potential fire hazards [68]. Moreover, the physical characteristics of the coffee silverskin, including low compactability and poor flowability, may require specialized equipment and processing techniques to achieve effective extraction, purification, and incorporation into value-added products [69]. To overcome these challenges and maximize the commercial viability of the coffee silverskin as a sustainable resource, further research and development efforts are needed to explore innovative solutions and optimize processing methods [70]. This includes the development of efficient and cost-effective technologies that enable the extraction and recovery of valuable components from the coffee silverskin while ensuring safety and scalability [71]. Exploring alternative uses and applications that potentiate the unique properties of the coffee silverskin, such as its antioxidant and antimicrobial potential, can further enhance its value as a functional food ingredient and nutraceutical resource [72].

Figure 6. Obtention of coffee silverskin during the roasting of green coffee beans.

The occurrence of chemical, biological, and processing contaminants has also been examined to guarantee the nutritional quality and safety of the ingredients derived from the coffee silverskin [14]. The absence of pesticides and mycotoxins was confirmed in the coffee silverskin, although it was close to the limit set by the European Commission for roasted coffee (400 µg/kg) but less than the amount established for instant coffee (900 µg/kg) [73]. Nevertheless, no genotoxicity and cytotoxicity were observed in human liver cells treated with various concentrations of coffee silverskin [74]. Acute and sub-acute oral administration studies in animals have also demonstrated the safety of the coffee silverskin extract at the tested doses [55]. Nevertheless, it remains essential to maintain strict quality control measures during processing and conduct regular testing for contaminants to ensure the safety of coffee silverskin-derived ingredients [75]. Addressing the technological and safety constraints associated with the coffee silverskin not only maximizes its utilization potential but also contributes to the circular economy by reducing waste and creating value from this by-product of the coffee roasting process [76].

3. Biorefinery Strategies for Upcycling Coffee By-Products

3.1. Biorefinery as a Sustainable Approach for Circular Bioeconomy

Biorefinery is a sustainable approach that generates a variety of products from multiple biomass materials, utilizing relevant conversion technologies to carry out this transformation [77]. The biorefinery concept emerges as a possible solution to the present waste disposal challenges facilitating high value-added compounds production [78]. This approach complements conventional waste use practices (animal feed, composting, incineration, and landfill). Biorefinery has been identified as the second generation of waste valorization and reuse strategies for higher-value marketable production products [79]. Furthermore, this innovative valorization strategy has also been regarded as one of the most promising approaches to achieving a resource-efficient circular bioeconomy because it reduces human-induced environmental risks, creates new business possibilities, and uses energy more efficiently [80].

Likewise, the circular bioeconomy seeks to increase human well-being and social justice while substantially reducing environmental risks and resource scarcity [81]. The bioeconomy concept has long been associated with converting biological resources into goods and materials. The circular bioeconomy is a bioeconomy in which products and materials are recycled and reduced to a high degree [82]. Recycling and other circular waste management strategies are critical components of the circular bioeconomy model, as shown by the sustainable, resource-efficient valorizing of biomass using biorefineries and repurposing residues and wastes [83].

This biorefinery approach could result in active biomolecules for medicinal, cosmetic, food, and non-food applications. Proteins, polysaccharides, fibers, and flavor compounds are examples of high-value materials that can be processed and reused as food ingredients [84,85]. They are commonly used as texturizing, preserving, or coloring ingredients in the food industry, as well as active compounds in cosmetic or pharmaceutical products. These components must be obtained using extraction methods to isolate the targeted components from the matrix. In this regard, plenty of green chemical and biochemical procedures are pursuing that goal through process optimization to obtain higher extraction efficiency while reducing extraction time, energy use, the amount of solvent consumed in the process, environmental impact, economic costs, and waste generation [86,87]. Within them, the solute to solvent dissolution and its further diffusion abroad the matrix (solid-liquid extraction's phenomenon) could be considered the most widely used strategy for compound recovery, using both organic solvents and water (or their combinations). On this matter, the usefulness of water as a solvent for bioactive compound extraction has been deeply explored since one of the associated advantages is compliance with the safety requirements for food-like applications. Indeed, water is the most eco-friendly traditional solvent to consider for green processes. At room temperature, ionic and polar compounds dissolve easily in water, while less polar compounds dissolve more easily at higher temperatures. Moreover, water is non-toxic, non-flammable, inexpensive, and readily available [88]. This conventional extraction method is well-established and relatively easy to operate [89]. Water-based extraction techniques play a crucial role within the biorefinery framework. They are extensively used to extract and recover active biomolecules from the biomass matrix, such as phenolic compounds from coffee by-products. However, for some purposes, water-based extractions could result in nonselective procedures involving high economic, energy, and resource expenses [2]. Thus, advanced chemical and physicochemical techniques based on mass transfer enhancement through the water's solvation power tuning and/or cell wall weakening (i.e., high pressurized hot water, microwave-assisted or ultrasound-assisted extraction), are gaining interest within the scientific community because of their improved efficiency and selectivity rates, while being more environmentally sustainable compared to other alternatives [90,91].

Therefore, water-based green extractions from coffee agroindustry by-products following a biorefinery approach (Figure 7) involve obtaining the targeted compounds (i.e., phenolic compounds) from the food matrices and valorizing the possible co-products generated (i.e., enriched dietary fiber material) to safely create value-added products that are free of toxic compounds.

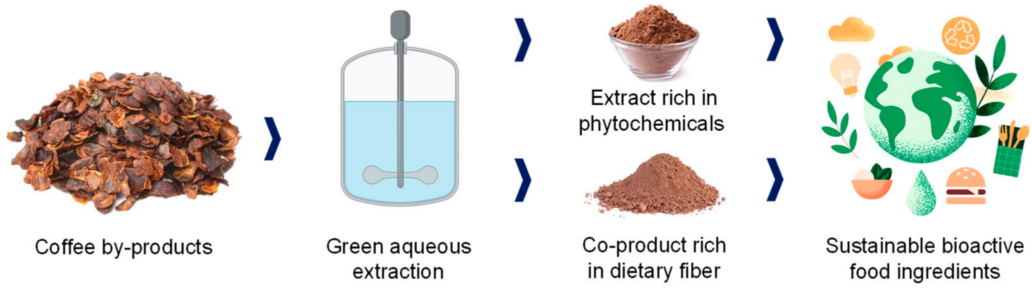

Figure 7. Biorefinery approach in the revalorization of coffee by-products through green extraction.

3.2. Biorefinery and Coffee By-Products for Bioactive Food Ingredients Production

3.2.1. Husk

The conventional use of the coffee husk is to prepare the "Cascara Beverage" traditionally consumed in Yemen and Ethiopia [29], and for composting in coffee-producing countries [92,93]. Current uses for the coffee husk include mushroom cultivation [94], lignin extraction [95], recovery of biomolecules from the lignin alkali hydrolysate [96], bioethanol production [45,97], biosorbents preparation [98,99], and animal feed [46]. Other biotechnological applications proposed for this by-product are the production of enzymes: amylase [100], xylanase [101], endoglucanase [102], protease [103], peptidase [104], and tannase [105], among others [106]; and biomolecules such as carotenoids [107], gallic [108], citric [109], succinic [110], lactic [111], and gibberellic acids [112], and fruity flavor compounds [113].

However, recent studies have provided new evidence to support the use of the coffee husk as a food ingredient for human consumption [114–116]. Simple, low-cost, and eco-friendly aqueous extraction methods were used to produce extracts enriched in bioactive compounds with antioxidant, anti-inflammatory, antimicrobial, and anti-adipogenic properties [117–120], demonstrating the feasibility of using water as the only extractant of the coffee husk's phenolic compounds. Aqueous extracts yielded around 7–29%, being composed of caffeine (1%), chlorogenic acids (0.3%), and protocatechuic acid (0.1%), among other phenolic compounds [115,117,118]. Soluble sugars (glucose, fructose, and sucrose) were also present (~12%), as well as soluble proteins (5–7%). Most aqueous extracts are composed of soluble dietary fiber (~68%), which is solubilized together with phenolic compounds and other non-identified phytochemicals [114,115,117].

Therefore, the existing evidence concerning coffee husk aqueous extracts supports the potential use of these extracts to modulate metabolic syndrome biomarkers and, consequently, prevent cardiometabolic diseases. Likewise, the valorization of the whole coffee husk flour and the water-insoluble residue obtained after the aqueous extractions, which are rich in antioxidant dietary fiber [114,115], provide a more sustainable approach for the complete revalorization of coffee husks. All ingredients from the coffee husk revealed health-promoting properties associated with the prevention of metabolic syndrome. In conclusion, the coffee husk has shown a high concentration of dietary fiber and phenolic compounds. Considering its chemical composition and its biological activities demonstrated in multiple investigations, the coffee husk could be converted into two ingredients: an aqueous extract that could be used as a health-promoting food ingredient and another fraction that could be implemented as a source of antioxidant dietary fiber. This mixed high-fiber and phenolic compound content makes the coffee husk very appealing as a nutraceutical and ingredient in functional foods since combined antioxidant and fiber contents are likely to positively impact health, from the gastrointestinal tract to peripheral tissues.

3.2.2. Mucilage

The coffee mucilage, a by-product of coffee processing, holds promise for various applications in the food industry. It contains valuable nutrients, including protein, carbohydrates, fiber, fat, and potassium, which can be utilized in flour, baking mixes, nutritional supplements, and nutraceuticals [121]. The fermentation of the coffee mucilage involves microorganisms such as yeasts and lactic acid bacteria, which contribute to the breakdown of mucilage and the creation of flavor-active components. These components find use in food additives, flavorings, and extracts [53]. Additionally, the extraction of simple sugars from the coffee mucilage can serve as a substrate for anaerobic digestion, enabling the production of methane and bioethanol [122,123]. Fermentation of coffee mucilage can also yield ethanol, which finds application as a biofuel or in beverage production [123,124]. The microbial community involved in coffee mucilage fermentation significantly influences the process and impacts the final product quality [125]. The introduction of yeasts in the fermentation process has been found to enhance coffee quality [54]. Furthermore, coffee mucilage fermentation involves microorganisms that play a crucial role in mucilage degradation and the generation of flavor-active components [52]. Research has investigated the fate of mucilage cell wall polysaccharides during coffee fermentation, revealing high levels of uronic acids in crude pectic substances [126]. The microbial utilization of the mucilage as a growth substrate results in the production of secondary metabolites, including organic acids, alcohols, esters, ketones, and aldehydes, which can affect the fermentation's impact on the final product quality [31]. Moreover, the coffee mucilage exhibits functional and technological properties suitable for producing bioplastics in the food industry [127]. However, it is important to note that the substantial waste generated by the coffee industry can pose environmental risks [123].

In addition to its potential environmental impact, the coffee mucilage presents an opportunity for extracting bioactive compounds for use in food applications. The mucilage extract and flour derived from coffee fruits contain phenolic compounds, antioxidants, caffeine, lipidic compounds, dietary fiber, proteins, and peptides, as well as aromatic and volatile compounds [24]. By utilizing waste products like the coffee mucilage, bioactive molecules can be produced for pharmaceutical, cosmetic, food, and non-food applications [24]. Furthermore, coffee mucilage exhibits industrial potential, with studies highlighting its value as a source of raw pectins, antioxidants, and flavonoids [24]. Recent findings have demonstrated the inhibitory effect of coffee mucilage extracts on certain Gram-positive bacteria, although the specific compounds responsible for this activity remain unknown. The chemical composition of the mucilage and its potential as a prebiotic that impacts gut microbiota are areas that require further exploration [25]. Additionally, the potential of the total mucilage, including cellulose, as a thickener or in other applications warrants further investigation [128].

3.2.3. Parchment

Studies exploring coffee parchment's use as a food ingredient are recent. However, the product's significant health-promoting and technologically appealing features are opening its potential use as an ingredient in the food industry. The optimal conditions yielded high phytochemicals as reported by Iriondo-deHond et al. [14], who found a 2.3% yield and an extract containing high caffeine levels (1.3 mg/g) and a lower concentration of chlorogenic acid (0.14 mg/g). The main phenolic compounds in the coffee parchment are hydroxybenzoic and hydroxycinnamic acids (chlorogenic, vanillic, protocatechuic, and *p*-coumaric acids) [58]. These compounds are associated with the coffee parchment's in vitro antioxidant and antifungal properties [36,58].

In addition, the coffee parchment is also a potential source of dietary fiber. The coffee parchment is rich in insoluble dietary fiber (89%), mostly lignin (~30%), xylans (~28%), and cellulose (~10%). In previous studies, the presence of xylans [129], cellulose, and lignin [14] was similarly confirmed. The antioxidant capacity of the dietary fiber compared to the antioxidant potential associated with phenolic compounds was also studied, showing higher dietary fiber antioxidant potential than that of associated phenolic compounds, indicating that cell wall components (mainly lignin and xylans) may also be contributing to the antioxidant properties [19].

The coffee parchment's technological features (water holding capacity, water absorption, swelling capacities, oil holding capacity, and gelation capacities) open the potential for food applications both as physiological and technological ingredients. The main factors influencing hydration properties are the polysaccharide composition and their organization within the cell walls. In general, coffee parchment showed good hydration properties, suggesting that this by-product could be used as a functional ingredient to reduce calories or modify the viscosity and texture of formulated foods. Moreover, hydration properties are also related to some physiological effects such as hypoglycemic and hypolipidemic, exhibiting a potential for glucose adsorption, retarded diffusion, and inhibited α-amylase, which led to lower starch digestibility. Similarly, the coffee parchment exhibited in vitro hypolipidemic properties, including pancreatic lipase inhibition and cholesterol and bile salts binding [34].

Recent investigations also explored the synthesis of xylo-oligosaccharides from coffee parchment [129]. Xylo-oligosaccharides could be a valuable product since they possess prebiotic features as functional food ingredients with tremendous potential [130]. The aqueous extracts could also be produced if the extracted phytochemicals are economically profitable (nutraceutical or pharmaceutical purposes). Following a biorefinery approach, the water-insoluble residue could also be revalorized as a dietary fiber source exhibiting properties similar to the non-extracted coffee parchment [34].

The main use of the parchment is addressed as a source of antioxidant dietary fiber. Coffee parchment has been added to gluten-free bread (2–4%) [35]. The addition led to increases in dietary fiber, phenolic compounds, and antioxidant capacity without modifying the appearance of the bread and its texture properties. Consumer acceptance studies found that a 4% replacement gave the final product a distinct bitter taste due to the presence of caffeine [35]. The work suggested that a debittering step should be considered to increase the coffee parchment quantity in gluten-free bread in order to enhance its sensory and nutritional properties [35]. Therefore, using the water-insoluble residue from the coffee parchment would allow for producing bread with higher dietary fiber content and maintain its health-promoting properties. Similarly, cookies with 1–5% coffee parchment flour were developed by Cubero-Castillo et al. as a strategy to increase the dietary fiber content and enhance cookies' antioxidant capacity [56]. In this research, adding the coffee parchment flour to the cookie dough did not generate consumer rejection.

Furthermore, coffee parchment could be transformed into other renewable products. It may be a source of cellulose to produce cellulose-based goods [131]. Lignocellulosic fibers and lignin are two of the world's most valuable natural resources and have great potential to increase bioplastics biodegradability by replacing synthetic fibers. Lignin has proven to function as a bioplastic plasticizer, stabilizer, or bio-compatibilizer, making coffee parchment an outstanding candidate for sustainable packaging [132]. Coffee parchment can also be a source of caffeine and phenolic compounds for edible film production with antifungal properties [36]. Additionally, coffee parchment has also been utilized for various purposes, including the production of non-food-related products such as particleboard [26,133], composite reinforcement [134], and, ultimately, as a source of renewable energy via combustion [135].

Until now, coffee parchment applications as a food ingredient remain largely unexplored. Notwithstanding the favorable chemical composition of the coffee parchment aqueous extract and in vitro antioxidant capacity, this coffee by-product should preferably be used as a source of antioxidant dietary fiber since extraction yields are relatively low. Nonetheless, research pinpoints the need to fractionate the coffee parchment, generating a soluble extract and an insoluble residue. Both fractions can be revalorized into differentiated products through a biorefinery approach, avoiding more waste production. New coffee parchment applications in the food industry as a natural source of antioxidant dietary fiber should be strongly considered to revalue this by-product.

3.2.4. Silverskin

Studies have explored the aqueous extraction of the coffee silverskin to develop food ingredients with healthy properties. Sustainable aqueous extraction of phytochemicals from coffee silverskin has been proposed according to del Castillo et al. (patent number WO 2013/004873) [136]. This extract is a sustainable source of bioactive compounds such as chlorogenic acid (2.8 mg/g) and caffeine (19.2 mg/g), but the major component in coffee silverskin extract is soluble dietary fiber (22%) [137].

Based on its chemical composition and observed biological activity, the green aqueous extract could be used as a healthy food ingredient. Coffee silverskin extract could be consumed as a nutraceutical or added to the most appropriate food matrix based on sensory customer acceptance. The food applications of coffee silverskin extract in beverages [137], biscuits [138], and bread [114] have been described. Coffee silverskin extracts can also be applied to produce functional yogurts [67]. Other sustainable potential uses for this extract include cosmeceuticals production since compounds from coffee silverskin protect skin cells from UV damage and prevent skin aging. Moreover, the extract presents adequate properties to be included in a cosmetic formulation [139,140].

The coffee silverskin flour and water-insoluble residue (from the phytochemicals green extraction) can also be used as a fiber-rich food ingredient, with the ultimate goal of recycling the whole by-product. The coffee silverskin water-insoluble residue contains 70% dietary fiber, with the majority being insoluble. This fraction also comprises 10–20% proteins and about 3% fat, depending on the species. This fraction also reported in vitro antioxidant and prebiotic properties [65]. Likewise, dietary fiber fermentation releases short-chain fatty acids, which modulate anti-inflammatory gene and protein expression [141]. OTA was detected in the coffee silverskin water-insoluble residue at lower levels (2.9 μg/kg) than those permitted by the European Commission. However, no other mycotoxins or pesticides were found [62]. Furthermore, coffee silverskin dietary fiber has been used to enhance the nutritional quality of biscuits by improving the moisture, texture, thickness, and color of the novel biscuits [138]. The coffee silverskin has been used as a dietary fiber ingredient to formulate bread, reducing its caloric density. Moreover, cakes with up to 30% coffee silverskin water-insoluble residue as a flour substitute have been developed, improving moisture content, textural, and sensory attributes [142,143]. Cakes with coffee silverskin water-insoluble residue exhibited physical and sensory properties similar to the control cake [142].

Alternative sustainable uses of coffee silverskin are polylactic acid production as a replacement for synthetic polymers [144], cellulose isolation and purification for the development of sustainable packaging [145] and biofilms [146], the production of butanol [147], succinic acid [148], bio-oil [149], composites [69], and adsorbent [150], as well as an energy source through pyrolysis [151]. Antioxidants and value-added bioactive compounds are produced from the coffee silverskin via pyrolysis [152]. More research is being conducted demonstrating the presence of a plethora of bioactive compounds and coffee bean roasting-derived phytochemicals that provide health benefits in biological systems [153].

According to circular economy strategies, the coffee should be fully revalorized either as flour or fractionated into two different ingredients (extract and water-insoluble residue), generating zero residues. Research has corroborated the coffee silverskin components' nutritional properties and biological activity. Thus, the different applications of coffee silverskin as a food ingredient and its safety validation have confirmed its viability as a sustainable food ingredient or nutraceutical for human consumption.

4. Stepwise Strategy for Valorizing and Validating Coffee By-Products as Bioactive Food Ingredients and Nutraceuticals

Based on the knowledge generated around the chemical composition of coffee by-products and the growing interest in their valorization as healthy food ingredients, specific research strategies need to be gradually addressed to gather all the information required to use coffee by-products as bioactive food ingredients and nutraceuticals for the prevention of chronic diseases [154]. A stepwise approach is essential to ensure the revalorization of coffee by-products and enhance the food system's sustainability (Figure 8). Harmoniously, the green production of healthy food ingredients from these by-products can result in a strategy to prevent chronic diseases [155].

4.1. Identification of the Needs

The first step is to identify the specific needs that the products should meet. This involves considering the desired bioactive compounds and functional properties, as well as the market demand and feasibility of the food products [156]. Through this process, a clear set of goals and priorities is established, effectively guiding the development of these products.

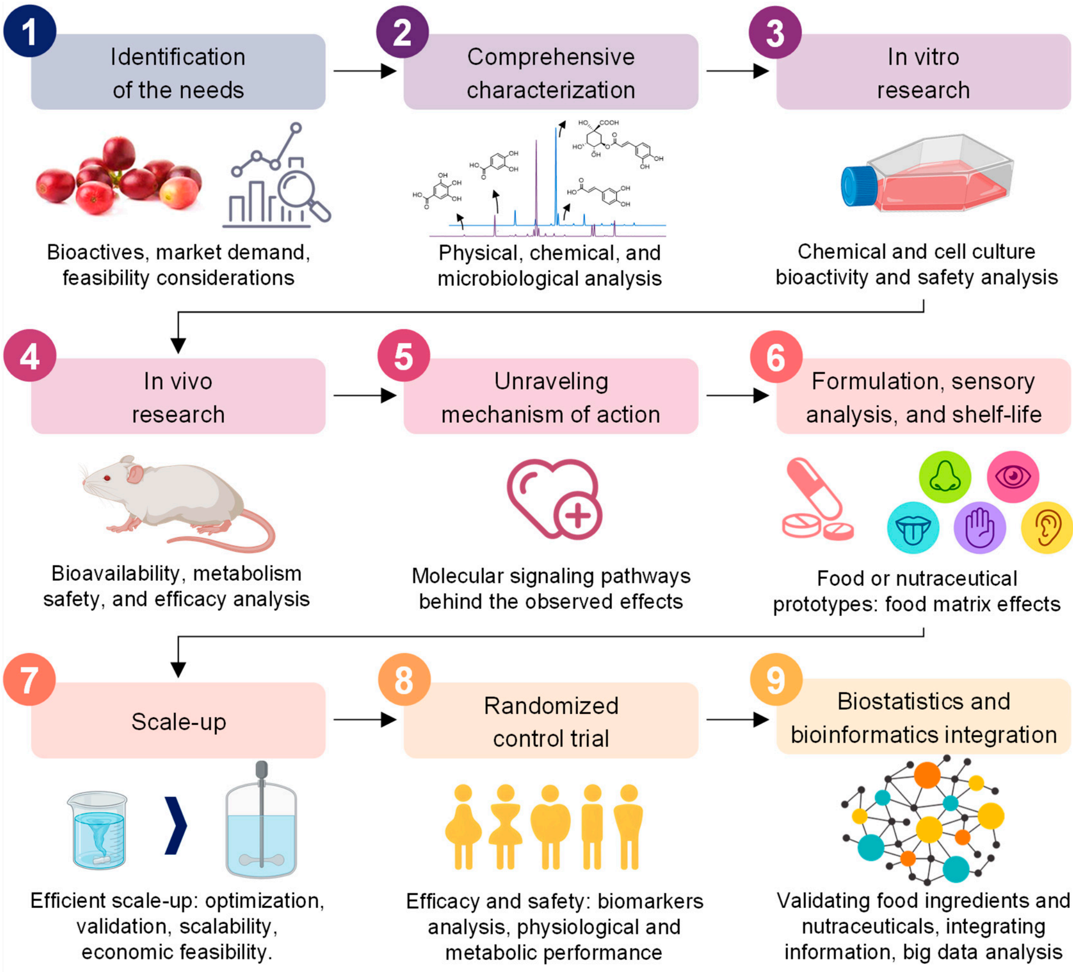

Figure 8. The different steps followed to valorize and validate coffee by-products into bioactive food ingredients or nutraceuticals.

One important issue in identifying the needs is the bioactivity of the compounds present in coffee by-products. They are known to contain various bioactive compounds, such as phenolic compounds and caffeine, which have been linked to various health benefits [89]. Therefore, it is essential to determine which compounds are of interest and how they can be extracted and utilized in the development of functional food ingredients and nutraceuticals [157]. Another consideration is the functional properties of the products. For example, if the goal is to develop a nutritional supplement, the product should have a high concentration of the desired bioactive compounds and be formulated to ensure maximum absorption and bioavailability in the body [158]. Similarly, if the target is to develop a food ingredient, the product should have desirable functional properties such as flavor, texture, and stability [159].

In addition to considering the technical aspects of the products, it is important to contemplate market demand and feasibility. This involves assessing consumer preferences and trends, as well as the availability and cost of raw materials and the processing methods [160]. By taking these factors into account, the development of functional food ingredients and nutraceuticals from coffee by-products can be guided by market demand and feasibility, leading to more successful and sustainable products [161].

4.2. Comprehensive Characterization

After identifying the needs, the next step is to characterize the coffee by-products-derived food ingredients or nutraceuticals comprehensively. This involves analyzing the composition and properties of the product to ensure it meets the identified needs and is safe for consumption, including a range of analyses such as chemical, physical, and microbiological analyses. These analyses provide information on the product's nutritional content, functional properties, and safety [162]. For example, proximate analysis can be used to determine the product's moisture, protein, fat, and carbohydrate content, while rheological testing can be used to evaluate the texture and viscosity [163]. The microbiological examination is also important to ensure that the product is free from harmful microorganisms [164].

In addition to the traditional analyses, newer techniques such as metabolomics and proteomics can provide a more detailed understanding of the product's composition [165]. Metabolomics can be used to identify and quantify small molecule metabolites in the product, while proteomics can be used to analyze the protein content and identify potential bioactive peptides [166]. Comprehensive characterization is essential to ensure that the food ingredient or nutraceutical meets the identified needs and is safe for consumption [167]. By analyzing the product's composition, properties, and safety aspects, any potential issues can be identified and addressed, leading to a more successful and safer product. These techniques allow for the characterization of extracts obtained using the biorefinery strategy and ingredients rich in bioactive compounds [168]. It is essential to employ a range of analytical tools to gain a comprehensive understanding of the constituents from coffee and its by-products. Spectrophotometric analysis methods such as UV-VIS and fluorimetry are complemented by the use of advanced techniques like LC-MS/MS, GC-MS/MS, and NMR to characterize the diverse array of bioactive compounds present [169].

4.3. In Vitro Research

In vitro studies play a crucial role in the initial evaluation of the bioactivity and safety of coffee by-product-derived ingredients, as they provide a controlled laboratory environment to examine their effects on biological systems [170]. Given the abundance of bioactive compounds found in coffee by-products and their diverse biological effects, employing multiple experimental approaches is necessary to gain a comprehensive understanding of their activity [171]. These in vitro studies allow for the assessment of various properties, including antioxidant, anti-inflammatory, and antimicrobial activities of coffee by-product-derived compounds. Of particular interest is evaluating the antioxidant activity, as coffee by-products are known to contain phenolic compounds which exhibit potent antioxidant properties [15]. Phenolic compounds from coffee by-products have been recognized as bioactive components with antioxidant properties [58,115,172]. In vitro studies have also been conducted to compare the phytochemicals from coffee by-products and their potential to reduce markers of inflammation, oxidative stress, adipogenesis, and insulin resistance [41,119,173]. Coffee silverskin melanoidins, formed via the Maillard reaction, have been assessed for their bioactivity [174]. The coffee husk has been evaluated as an innovative antioxidant dietary fiber ingredient [42]. Additionally, in vitro assays can determine the potential of coffee by-product-derived ingredients to inhibit the growth of pathogenic bacteria [175]. Moreover, in vitro studies serve as a valuable tool to optimize the processing conditions and formulation of food ingredients or nutraceuticals [176]. For example, researchers can investigate the effects of different processing parameters, such as temperature and pH, on the bioactivity and stability of the final product. In vitro studies also aid in determining the optimal concentration of coffee by-product-derived compounds to maximize their bioactivity in the formulation [89].

Furthermore, it is essential to conduct in vitro bioaccessibility, bioavailability, and toxicological studies to evaluate bioactive compounds' release, absorption, and safety [177]. Bioaccessibility studies have been conducted to evaluate the release and absorption of bioactive compounds from coffee by-products and the changes in antioxidant activity during in vitro gastrointestinal digestion [33,120,153]. Safety studies allow for a comprehensive assessment of potential allergenicity, genotoxicity, and other safety aspects associated with coffee by-product-derived ingredients [37]. While in vitro research provides valuable insights into the bioactivity and safety of coffee by-product-derived compounds, it is important to acknowledge its limitations in predicting their effects in vivo [178]. Hence, conducting subsequent in vivo studies using animal and human models is necessary to confirm the bioactivity and safety of these ingredients.

4.4. In Vivo Research

Animal studies provide valuable information on the bioactivity, safety, and efficacy of coffee by-product-derived compounds [179]. In vivo animal models can be used to evaluate the effect of the coffee by-product-derived ingredients on specific health conditions, such as obesity, diabetes, cardiovascular diseases, or neurodegenerative diseases [180]. In a study by Benyelles et al., an aqueous extract from the coffee parchment was investigated for its anti-obesity effects in a rat model of fructose-induced obesity. The study found that the coffee parchment extract reduced adipose fat accumulation and improved glucose metabolism. It also alleviated metabolic disorders associated with obesity, such as hyperglycemia, hyperinsulinemia, hyperlipidemia, and oxidative stress [181]. Similarly, Bhandarkar et al. conducted a study on the effects of dietary supplementation with freeze-dried coffee pulp in rats with metabolic syndrome induced by a high-carbohydrate, high-fat diet. The results demonstrated that the coffee pulp supplementation improved various metabolic parameters, including body weight, abdominal fat, blood pressure, lipid profiles, glucose tolerance, and gut microbiota composition [182]. Animal studies can also provide valuable information on the bioavailability and metabolism of the compounds [183]. For example, animal models can be used to evaluate the absorption and distribution of the compounds in the body, as well as their metabolism and excretion [183]. Fernandez-Gomez et al. investigated the bioaccessibility, bioavailability, and bioactivity of a coffee silverskin extract, demonstrating that chlorogenic acids and caffeine were metabolized in the gastrointestinal tract and their metabolites exhibited chemo-protective effects on pancreatic cells under diabetic conditions [184]. Animal models can also be employed to assess the potential for adverse effects associated with coffee by-product-derived compounds. Conducting thorough safety evaluations and toxicological studies in animal models is essential to ensure the absence of harmful contaminants or adverse effects associated with the coffee by-product-derived bioactive ingredients [185]. Assessing potential allergenicity, genotoxicity, and long-term safety profiles is crucial [186]. Iriondo-DeHond et al. conducted a study on a coffee silverskin extract to assess its nutritional value, safety, and effects on key biological functions, evidencing no adverse effects on hormone secretion, antioxidant, or anti-inflammatory biomarkers. The results indicate that coffee silverskin is a safe and beneficial food ingredient with potential health benefits that might improve gut health by leading to the production of short-chain fatty acids (SCFAs) [55]. Regulating gut health is of utmost importance as it reinforces the intestinal function as the primary defense against various disorders, including those affecting cardiometabolic health [187].

4.5. Unraveling Mechanism of Action

Unraveling the mechanism of action of coffee by-products and understanding how these compounds exert their beneficial effects is crucial for optimizing the final bioactive ingredients or nutraceuticals and exploring new applications [180]. Mechanistic studies typically employ in vitro and in vivo models to identify the cellular and molecular pathways targeted by coffee by-product-derived compounds. In vitro studies allow for the evaluation of the compounds' effects on specific enzymes or signaling pathways, while in vivo studies may provide insights into the compounds' impact on biomarkers of oxidative stress, inflammation, and other relevant biological processes [188].

Numerous mechanisms of action have been proposed for the beneficial effects of bioactive compounds found in coffee by-products. These mechanisms include antioxidant and anti-inflammatory activities, as well as the regulation of signal transduction and gene expression [189]. Phytochemicals present in coffee by-products can exhibit biological activity through various mechanisms, such as direct free radical scavenging, down-regulation of radical production, inhibition of enzymes involved in the production of reactive oxygen species (ROS), and up-regulation of antioxidant enzymes [190]. Extract from the coffee husk (dry and wet) and the coffee silverskin have proven to stimulate the activity of catalase and superoxide dismutase upon a pro-oxidant elicitation [191,192]. These protective effects of coffee by-product-derived compounds may be attributed to their ability to modulate the nuclear factor erythroid 2-related factor 2 (Nrf2)/antioxidant response element (ARE) signaling pathway [191,193]. Additionally, coffee by-product-derived bioactive compounds may contribute to the regulation of energy metabolism, making them potential candidates for combating obesity and metabolic disorders. These compounds can affect lipid metabolism (AMPK and CPT-1), adipogenesis (FASN and SREBP-1c), and thermogenesis (PGC1-α and UCP-1) pathways, thereby influencing body weight and energy balance [119]. Coffee by-product-derived compounds have been found to exhibit the ability to inhibit SREBP-2 and HMGCR, thus modulating cholesterol homeostasis [194,195]. Furthermore, some coffee by-product-derived compounds, such as chlorogenic acids, have been associated with antidiabetic effects through their ability to enhance insulin sensitivity and regulate glucose metabolism. Coffee by-products can modulate INSR, AKT-PI3K, and IRS-1 related pathways and can modulate the expression of glucose transporters (GLUT-2 and GLUT-4) [192]. Therefore, a molecular nutrition approach is needed to assess the effect of coffee by-products' bioactive compounds on whole-body physiology and health status at the molecular and cellular levels. The precise identification of the molecular pathways underlying human metabolism is essential for promoting health and preventing disease [196]. Mechanistic studies also provide valuable insights into the potential adverse effects associated with coffee by-product-derived compounds. Evaluating their interactions with specific receptors or signaling pathways can help identify possible side effects and guide the development of safe and effective products [37].

4.6. Food and Nutraceutical Formulation, Sensory Analysis, and Shelf-Life Stability

After identifying bioactive compounds and evaluating their efficacy and safety through in vitro and in vivo studies, the next step for upcycling coffee by-products into bioactive food ingredients and nutraceuticals is food production and sensory analysis [156]. Food production involves the formulation and development of food prototypes that incorporate coffee by-product-derived ingredients. This process requires careful consideration of various factors, such as the selection of suitable extraction, concentration, and purification methods to optimize the bioactive compound content and functionality [197]. When formulating nutraceuticals, specific considerations need to be addressed. These include ensuring that appropriate dosages of the bioactive compounds are incorporated, maximizing their bioavailability and bioactivity in the body, and complying with regulatory guidelines for health claims and safety [198]. Nutraceutical formulations may require additional processing steps, such as encapsulation or microencapsulation, to protect the bioactive compounds and enhance their stability and delivery [199]. One crucial aspect to consider during food and nutraceutical formulation is the effect of the food matrix on the bioactivity and bioavailability of the incorporated bioactive compounds [200]. The interaction between the bioactive compounds and other components in the food matrix can influence their release, absorption, and subsequent physiological effects in the body. Understanding these interactions is crucial for optimizing the formulation to maximize the desired health benefits [201].

Sensory analysis plays a critical role in food production, as it assesses the acceptability and palatability of the final product. This evaluation encompasses various sensory attributes, including appearance, aroma, taste, texture, and overall acceptability [202]. By conducting sensory analysis, either through trained sensory panelists or consumer panels, valuable insights can be gained into the product's sensory characteristics and potential areas for improvement [202].

Furthermore, thoroughly studying the final product's stability and shelf-life is crucial. Assessing the potential degradation or loss of bioactivity in coffee by-product-derived ingredients during storage and transportation is of great importance. Stability testing is typically performed under various storage conditions to monitor changes in bioactivity, sensory attributes, and microbiological quality, ensuring that the product maintains its efficacy and safety throughout its intended shelf-life [203].

4.7. Scale-Up

Scale-up involves transitioning from laboratory-scale production to larger-scale production to meet the demands of commercial production. The production process is optimized during the scale-up process to ensure efficiency and accommodate increased volume. This may involve adjusting the production equipment, modifying the processing methods, and sourcing raw materials in larger quantities [204]. Validation studies play a crucial role in the scale-up process, as they are conducted to ensure that the final product meets rigorous safety and quality standards. These studies verify the consistency and reliability of the product, addressing factors such as composition, stability, and microbiological safety [32]. Additionally, it is essential to assess the scalability of the production process, considering factors such as the scalability of the extraction methods, the availability of raw materials at a larger scale, and the environmental impact of the scale-up process [205]. Furthermore, during scale-up, it is essential to evaluate the economic feasibility of the production process. This involves assessing the cost-effectiveness of larger-scale production, including considerations such as raw material costs, equipment investments, labor requirements, and market demand [206]. Economic feasibility studies help determine the viability of scaling up the production of bioactive food ingredients and nutraceuticals derived from coffee by-products, ensuring that the final product can be produced and marketed sustainably and economically.

4.8. Randomized Control Trial

Conducting randomized control trials (RCTs) is essential to evaluate the efficacy and safety of the final product in human subjects [207]. RCTs employ a study design and methodology that includes randomization, blinding, and control groups to minimize bias and confounding variables. The study population should be carefully selected to ensure they meet the inclusion and exclusion criteria, and the sample size should be large enough to provide sufficient statistical power [208]. In addition to assessing the efficacy of coffee by-product-derived nutraceuticals, it is important to consider their nutrikinetics, which involves studying their absorption, distribution, metabolism, and excretion in the human body [209]. Furthermore, the gut microbiota plays a crucial role in the metabolism and bioactivity of bioactive compounds. Therefore, evaluating the impact of coffee by-product-derived nutraceuticals on gut microbiota composition and function is essential [210]. Advancements in personalized and precision nutrition have highlighted the importance of considering individual variations in response to dietary interventions. Integrating personalized and precision nutrition approaches into RCTs can enhance the understanding of how coffee by-product-derived nutraceuticals interact with individual characteristics, leading to more effective and personalized nutritional interventions [211]. Evaluation of safety is also a critical component of RCTs. Adverse events and side effects should be carefully monitored and reported [208].

4.9. Biostatistics and Bioinformatics Integration

Building a solid and reliable scientific foundation for functional food claims requires demonstrating the bio-efficacy of functional food components in vivo, extending beyond in vitro experiments [212]. Therefore, comprehensive evaluations are necessary to validate the functionality of coffee by-product-derived food ingredients, utilizing a range of experimental models, including in vitro models, cell culture models, animal studies, and, ultimately, human preclinical and clinical trials [207]. These diverse approaches allow for a thorough understanding of the effects of coffee by-product-derived compounds on human health. Biostatistical and bioinformatic techniques play an indispensable role in effectively integrating and interpreting the wealth of information generated throughout the various steps, from extraction to characterization, in vitro and in vivo analyses, and human clinical trials [213,214]. These techniques enable the synthesis and analysis of large and complex datasets, facilitating a more comprehensive understanding of the effects of coffee by-product-derived compounds on human health. Moreover, the advent of big data science and analysis has further enriched the capabilities of researchers. Through the application of advanced data analytics, researchers can extract valuable insights from vast amounts of information, uncovering patterns and associations that were previously inaccessible [215]. Recent advancements in artificial intelligence have drawn attention to its capacity to learn and model both linear and non-linear relationships between variables, unveiling hidden and valuable information for decision-making [216]. Artificial intelligence algorithms, such as machine learning and deep learning, can significantly enhance the analysis and interpretation of complex datasets related to coffee by-products. These approaches provide deeper insights into coffee by-product-derived compounds' chemical composition, biological activity, and toxicity, supporting informed decision-making in developing functional food ingredients and nutraceuticals [217]. Integrating biostatistical and bioinformatic tools, coupled with emerging technologies like artificial intelligence and big data analysis, empowers researchers to unlock the full potential of coffee by-products and contribute to developing innovative and evidence-based functional food ingredients and nutraceuticals [218]. Consequently, after following a holistic approach for gathering the information needed to valorize coffee by-products as food ingredients, all the new knowledge generated about their chemistry, biological activity, and toxicity could be adequately managed, integrated, and interpreted.

5. Commercialization, Regulation, and Technological Innovation

5.1. Market Potential and Commercialization

The development of functional food ingredients and nutraceuticals from coffee by-products presents an opportunity for the coffee industry to expand its product portfolio and enter new markets [197,219]. The market potential for these products is significant, with increasing consumer demand for sustainable and health-promoting food options [220]. In addition, using coffee by-products in these products can contribute to a circular economy and promote waste reduction, further enhancing the appeal of these products to environmentally conscious consumers [221]. To fully realize the market potential of these products, however, it is important to consider the commercialization process. This includes identifying target markets, developing effective marketing strategies, and establishing distribution channels [222]. Collaboration between coffee producers, processors, and food companies may be necessary to ensure the success of these products in the market [223].

In this context, coffee's primary by-products are traditionally consumed in several coffee-producing countries, although few commercial products are currently available in the market. In countries such as Yemen (where it is called Qishr), Ethiopia (where it is referred to as Hashara), and Bolivia (known as Sultana), coffee husk drinks are quite common, with each having a unique method of consumption [224]. These coffee by-products are typically prepared as infusions with hot water and various spices and can be enjoyed either hot or cold. Baba Seed, a leading coffee company, is recognized for creating Qishr Sparkling Iced Tea, a beverage that is helping to alleviate the environmental impact of coffee production [225]. This beverage is prepared by brewing husks with spices (cinnamon and ginger) and is characterized by high phenolic compounds and a low caffeine content (a quarter of the caffeine of a cup of black coffee). In contrast, Nestlé has developed a product called Nescafé Nativ Cascara, which is made from upcycled coffee berry husks after farmers separate and sun-dry the coffee berry [226]. The result is a refreshing, lightly sparkling, caffeinated beverage with floral and fruity notes. An American multinational chain of coffeehouses, like Starbucks Coffee Company, launched the Cascara Latte in 2017 [227]. In this case, cascara is not consumed as tea but as a syrup, made by boiling coffee cherry skin with sugar and water. It is important to note that the primary coffee by-products are being marketed globally as tea bags. This innovative approach maximizes resources and encourages the production of more sustainable products. For instance, Tabifruit from the Spanish roaster Supracafé Ltd. commercialized coffee husk tea bags with different aromas (such as orange, passion fruit, and berries) to enhance the sweet and fruity flavors of the coffee husk [228]. Overall, the commercialization of coffee by-product-derived products requires a multifaceted approach that considers market potential, regulatory considerations, and technological innovation. Collaboration and continuous research and development will be essential to ensure the success of these products in the market.

5.2. Regulatory Issues and Standards

Regulatory considerations are an important aspect to consider in the development and commercialization of functional food ingredients and nutraceuticals derived from coffee by-products [229]. The regulatory landscape for these products varies by region, and it is vital to comply with the relevant regulations in order to ensure market success and consumer safety [230,231]. In Europe, functional food ingredients and nutraceuticals are regulated under the European Union's novel food regulation. This regulation requires a safety assessment and authorization for any novel food or food ingredient that has not been consumed significantly in the EU prior to 1997. The authorization process can be lengthy and expensive, but it is necessary to ensure the safety and efficacy of these products [232]. In Asia, regulations for functional food ingredients and nutraceuticals vary by country. In Japan, for example, functional food ingredients are regulated under the Foods for Specified Health Uses (FOSHU) system, which requires a scientific review of the health claims made by these products [233]. In China, they are regulated under the Food Safety Law, which requires safety assessments and labeling requirements [234]. In Canada, functional food ingredients and nutraceuticals are classified as either foods or natural health products (NHPs) based on their intended use and claims. Functional food ingredients that make health claims are categorized as NHPs and require authorization from Health Canada before they can be legally marketed. The authorization process for NHPs involves a comprehensive review of safety, efficacy, and quality evidence submitted by manufacturers [235]. In the United States, these ingredients are regulated by the Food and Drug Administration (FDA) and are subject to safety and efficacy requirements. The FDA requires that these products be safe, effective, and labeled appropriately [236].

Including coffee by-products in the European food sector and ensuring human health protection is essential to know if these are considered novel foods. The European specific legislation about novel food is contained in regulation (EU) No. 2015/2283 and (EU) No. 2017/2468 and No. 2017/2469 [232,237,238]. Dried coffee berries (husk or cascara) are considered novel. The term novel food included in this regulation is referred as "a food is considered to be novel if it has not been regularly consumed by humans in the EU before 15 May 1997, when the first novel food Regulation came into force" [239]. Moreover, there is another pathway for the approval of novel foods: a notification for a traditional food from a third country. The implementation of the dried cherry pulp and its infusion, specified in the regulation from the European Commission as traditional foods, has been recently published [240]. For the silverskin, a consultation request is currently determining its novel food status. The food products must be evaluated for safety and toxicological aspects during the approval procedure. Limitations on the utilization of coffee by-products are associated with their caffeine and acrylamide content (obtained after the roasting process). The caffeine content in foods formulated with coffee by-products should be below the European Food Safety Authority (EFSA) safety level for daily caffeine consumption of 400 mg for the general population and 200 mg for lactating women. The acrylamide limit established by the EFSA for coffee and instant coffee is 450 and 900 μg/kg, respectively [241]. The absence of pesticides and mycotoxins is a required determination that must also be carried out.

In conclusion, navigating the regulatory landscape for functional food ingredients and nutraceuticals derived from coffee by-products can be complex, but it is essential to ensure compliance and safety. Companies need to work closely with regulatory agencies in their respective regions to ensure compliance and to stay up to date with evolving regulations.

5.3. Technological Innovation

Technological innovation is a crucial factor for successfully developing and commercializing functional food ingredients and nutraceuticals derived from coffee by-products. Patents play a pivotal role in protecting the intellectual property of these innovations and providing a competitive advantage in the market. Numerous patents have been developed to enhance the utilization value of coffee processing by-products for various applications (Table 2). Coffee by-products have been explored for waste utilization in the industrial sector. For instance, coffee by-products can be mixed with steel-making slag as an organic adsorbent to recover or remove phosphorus [242]. Additionally, they can be used in conjunction with acid mine drainage sludge to remove formaldehyde from the air [243]. Coffee husk, through composting processes, can also serve as a fertilizer [244].

Table 2. Summary of the main patents developed from different coffee by-products.

Patent Number	Title	Key Knowledge/Advantages/Benefits	Country	Ref.
KR20220129225A	A method for preparing organic adsorbent based on coffee wastes and steel-making slag for selective recovery or removal of phosphorus an organic adsorbent therefrom and use of the same	Efficient coffee waste recovery	Korea	[242]
KR102348305B1	Formaldehyde removal adsorption comprising coffee waste and acid mine drainage sludge and method for manufacturing the same	Absorbent capable of absorbing and removing formaldehyde in the air	Korea	[243]
CN114075093A	Composting method for improving the utilization rate of the coffee pericarp	Effective utilization of the coffee husk as a fertilizer	China	[244]
CN114601000A	Method for producing high-aroma instant coffee powder from cold extraction coffee processing byproducts	By-products generated in the production of cold extraction coffee are reused, and the resource utilization rate is increased	China	[245]
US2022071249A1	Extracted and fermented composition of coffee cherry pulp and skin and method for producing	Coffee cherry pulp and skin have an increased β-damascenone content	Japan	[246]
CN114568571A	Production method of coffee fresh fruit extract	The fragrance of the coffee fresh fruit is prominent, and effective ingredients can be more sufficiently extracted	China	[247]
KR102364057B1	Method for microorganism cryoprotectant using coffee residue	Economical lactic acid bacteria cryopreservation material by recycling existing resources	Korea	[248]
WO2022113120A1	A method for extracting phytochemicals from coffee waste	A phenol powder rich in coumaric acid with antioxidant, anti-inflammatory, anti-carcinogenic, anti-diabetic, anti-melanogenic, and oxidative stress-reducing properties	India	[249]
US2022125067A1	Coffee pulp extract and production method	Eco-sustainable physical methods to get active extracts	Colombia	[250]
CN114651850A	Coffee pericarp superfine powder crisp biscuit and preparation method thereof	Biscuits rich in dietary fiber, high in antioxidant activity, and rich in flavor, improving the development and utilization value of the coffee husk	China	[251]
KR102358649B1	Pellet manufacturing method	Pellets with excellent properties (calorific value, moisture content, density, and durability)	Korea	[252]

Table 2. *Cont.*

Patent Number	Title	Key Knowledge/Advantages/Benefits	Country	Ref.
CN107568408A	Processing technology for ice cream containing coffee pulp pigment powder	Coffee pulp pigment ice cream has more healthcare functions due to its high anthocyanin content	China	[253]
CN115379990A	Container made of composite material with affinity between substances	Economic utilization of coffee by-product, resulting in a packaging with a high degree of biodegradation	Spain	[254]
KR101344471B1	Bioplastic using coffee residual products and methods making the same	Degradable bioplastic that contributes to resource saving by recycling waste	Korea	[255]
CN115515866A	Composite material having components obtained from the solver sheet of coffee	Biodegradable coffee capsule providing an optimal use of silverskin byproduct	Germany	[256]
CN115583435A	Beverage capsule and method for sealing coffee beverage capsule	Coffee parchment layer with a high wet and dry rupture (ratio 50–70%)	Finland	[257]
KR20220062702A	Pellet using coffee waste	Pellet using coffee waste capable of controlling water content	Korea	[258]
WO2022158885A1	Composition comprising coffee, coffee extract, and byproduct as an active ingredient for the prevention of cancer metastasis or for alleviation or treatment of cancer	Active ingredient with inhibitory activity against cancer metastasis, cancer growth, and VCAM1 protein expression	Korea	[259]
KR20220108263A	Composition for preventing, improving, or treating metastasis of cancer comprising coffee extract and byproduct as effective components	Material with the ability to inhibit cancer metastasis, inhibit cancer growth, and inhibit VCAM1 protein expression	Korea	[260]
WO2013004873A1	Application of products of coffee silverskin in anti-aging cosmetics and functional food	Coffee silverskin products obtained through water extraction, with uses in cosmetics and functional food.	Spain	[136]

Extraction efficacy and selectivity of bioactive compounds from coffee wastes have been the focus of many studies, which heavily rely on the extraction method and conditions employed. Cold extraction methods have been used to produce high-aroma instant coffee powder [245], while lactic fermentation of coffee pulp and skin can yield β-damascenone, a potent fruity floral flavor compound [246]. Freeze concentration, a low-temperature processing technology, has been utilized to obtain an extract with a high coffee fresh fruit fragrance from coffee pulp [247]. Conversely, hot water extraction of coffee residues has been explored as an economical cryoprotectant for lactic acid bacteria due to the presence of chlorogenic acid, caffeic acid, and caffeine as active ingredients [248]. Conventional solvent extraction methods involving centrifugation, separation, and distillation steps have also been developed to obtain a phenolic compound-rich powder with beneficial effects [249]. Nowadays, eco-friendly physical methods based on mechanical extraction, filtering, and concentration of fresh pulp under pressure and temperature conditions are used to achieve active extracts from coffee pulp [250].

In the food industry, coffee by-products have found applications in the bakery sector, where enriched dietary fiber products with high antioxidant capacity and rich flavor have been developed. For instance, crisp biscuits have been prepared by mixing coffee pericarp powder (outer skin) with other ingredients, resulting in a product that combines bioactive properties with desirable sensory characteristics [251]. Grinding coffee by-products, mixed with rice husk, have been utilized to create pellets with bioactive properties [252]. Coffee pulp as a pigment powder has been employed in ice cream formulations, conveying health-enhancing properties due to its anthocyanin content [253]. Moreover, coffee by-products have recently gained interest as bioactive ingredients for preventing cancer metastasis or alleviating and treating cancer [259,260].

Another area of interest is the development of new materials with a high degree of biodegradability for packaging purposes. For example, roasted coffee by-products have been used as composite materials for containers or mixed with other agri-food by-products, such as coconut and grains, to enhance packaging and manufacturing processes [254]. Bioplastics incorporating coffee residual products have emerged as an alternative to sustainable packaging solutions [255]. Composite materials comprising components made from coffee silverskin or parchment have been utilized for the production of dispensing capsules [256,257]. Recent innovations include the utilization of coffee beans as solid fuels; however, challenges related to incomplete combustion and the generation of harmful gases, such as carbon monoxide, have been observed. To address this, a patent was developed to produce pellets containing coffee by-products that burn more efficiently and can be smoothly used as a solid fuel [258].

Overall, technological innovation, as demonstrated by patents, is a critical driver for the development and commercialization of functional food ingredients and nutraceuticals derived from coffee by-products. Continued investment in research and development in these areas is essential for companies and researchers to stay competitive and meet the evolving needs and demands of the market.

6. Challenges, Opportunities, and Directions for Research in Coffee By-Products Valorization

The stepwise strategy and biorefinery approach have shown promising results in upcycling coffee by-products into functional food ingredients and nutraceuticals. However, several technical challenges need to be addressed in the production of functional food ingredients and nutraceuticals from coffee by-products. These include optimizing extraction and processing methods, stabilizing bioactive compounds, and obtaining and maintaining safe coffee by-products. The extraction and processing methods used to obtain coffee by-products greatly affect the yield and quality of the final product. Current methods, such as solvent extraction and enzymatic hydrolysis, have limitations in terms of efficiency, sustainability, and cost-effectiveness [261]. Novel methods such as microwave-assisted extraction, supercritical fluid extraction, and pulsed electric field extraction show potential for improving the production of bioactive compounds from coffee by-products [262–264]. Other potential research areas include the use of enzymatic hydrolysis and fermentation to produce novel functional food ingredients and nutraceuticals [265,266]. Optimization of these methods can help maximize the recovery of bioactive compounds such as phenolic compounds and caffeine to allow their use in industry [89]. The stabilization processes of these compounds are crucial for maintaining the functional properties of the final product. Therefore, the development of appropriate methods is necessary to ensure the stability and bioactivity of coffee by-product-derived ingredients and nutraceuticals [36,267]. To further enhance our understanding of coffee by-products and their potential as a source of bioactive compounds, future research should not only investigate innovative extraction and processing techniques but also emphasize the identification and isolation of novel bioactive compounds. Advanced foodomic and multi-omic strategies coupled with big data analysis can be employed to unravel the intricate mechanisms of action underlying the bioactivity of these compounds [165]. While in vitro and in vivo studies have yielded valuable insights into the bioactivity of coffee by-product-derived compounds, expanding our knowledge regarding their safety and toxicity profiles is crucial, especially concerning higher doses or long-term exposure. Further research is warranted to comprehensively assess the potential risks associated with these compounds and ensure their safe utilization.

Additionally, coffee by-product-derived products face several economic challenges that must be addressed to ensure their successful integration into the market. One of the main challenges is the cost-effectiveness of producing and marketing coffee by-product-derived products [268]. The production costs associated with these products' extraction, processing, and formulation can be high, making them less competitive in the market. The functional food ingredients market can be complex and competitive, requiring effective marketing strategies to ensure successful commercialization. In this regard, regulations related to food additives, dietary supplements, and functional foods are constantly evolving and can be subjected to interpretation by regulatory agencies [269,270]. Another challenge associated with commercializing coffee by-product-derived functional food ingredients and nutraceuticals is compliance with labeling and health claim regulations [271].

On the other hand, coffee production can negatively impact the environment and social welfare, including deforestation, soil degradation, and labor issues. Nevertheless, coffee by-products present opportunities for promoting a circular economy and reducing waste generation [272]. Biorefinery strategies can be implemented to extract valuable components from these by-products and generate new products. The production of functional food ingredients and nutraceuticals from coffee by-products can present an opportunity for a circular economy, offer consumers health benefits, and further contribute to social sustainability [273]. Integrating biorefinery strategies into coffee production can then help mitigate these impacts by reducing waste generation, promoting sustainable agricultural practices, and creating economic opportunities for small-scale farmers [274]. In fact, developing integrated biorefinery systems that use coffee by-products and other agro-industrial residues can maximize the value and impact of these materials, potentially transforming the industry into a more sustainable and circular model [275]. By embracing a holistic approach that considers the entire value chain of coffee production, we can create a more sustainable and resilient coffee industry for the future.

Overall, future research and innovation in coffee by-product valorization should aim to increase the efficiency, sustainability, and diversity of functional food ingredients and nutraceuticals that can be produced. This approach will further reduce food waste, improve public health, and promote sustainable agriculture. Further research and innovation in this field can lead to the development of new products with enhanced bioactivity, safety, and sustainability, ultimately benefiting both consumers and the environment. While the valorization of coffee by-products presents both challenges and opportunities in pursuing sustainable and innovative solutions, there are promising research directions and opportunities for improvement. With continued research, innovation, and collaboration, we can pave the way for a more efficient, sustainable, and resilient coffee industry that delivers health benefits to consumers while protecting the environment. The journey towards maximizing the value of coffee by-products is ongoing, and by building on existing knowledge and exploring new frontiers, we can create a brighter future for coffee by-product valorization.

7. Conclusions

In conclusion, this review underscores the significant potential of coffee by-products as bioactive food ingredients and nutraceuticals. The comprehensive characterization, utilization of a stepwise strategy, and biorefinery approaches have demonstrated their effectiveness in valorizing coffee by-products. The major conclusions of this study are as follows: (i) coffee by-products possess substantial potential as a source of bioactive compounds with diverse health benefits; (ii) the stepwise strategy and biorefinery approach offer efficient and sustainable pathways for transforming coffee by-products into value-added food ingredients and nutraceuticals; (iii) commercialization of coffee by-product-derived products will require overcoming technological and regulatory barriers. However, several gaps and limitations in the current knowledge have been identified to advance our understanding. These include the need for in-depth investigations to elucidate the precise mechanisms of action and identify specific bioactive compounds responsible for the observed effects of coffee by-products. Additionally, comprehensive studies are necessary to evaluate the long-term safety and potential adverse effects of consuming coffee by-product-derived products. Future research directions have been proposed to address these gaps and drive innovation in this field. Conducting comprehensive studies to identify and characterize the bioactive compounds present in coffee by-products and unravel their mechanisms of action will provide valuable insights. Investigating the safety profiles and potential interactions of coffee by-product-derived products for long-term consumption is crucial for ensuring their suitability as functional food ingredients and nutraceuticals. Exploring innovative extraction techniques and biorefinery processes will optimize the production efficiency, yield, and quality of bioactive compounds from coffee by-products. Furthermore, assessing food products' sensory and functional properties incorporating coffee by-product-derived ingredients will enhance their acceptability, market potential, and consumer satisfaction. Addressing these gaps and pursuing these research directions will foster the development of bioactive, safe, and sustainable new food products. This will benefit consumers by offering functional and nutritious options and contribute to the coffee industry's environmental and economic sustainability. Overall, this review has provided comprehensive insights into the potential of coffee by-products, identified key research gaps, and outlined future research directions, thus advancing our understanding of their applications in functional food ingredients and nutraceuticals.

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