Plant Antioxidants from Agricultural Waste: Synergistic Potential with Other Biological Properties and Possible Applications

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Abstract

The increasing world population entails a great necessity to produce large amounts of food, leading to an increase in organic waste. Unlike traditional agriculture, based on the circular sustainability, modern agriculture produces tons of residues, which are accumulated in landfills or, in some cases, burnt. Numerous studies have demonstrated that agricultural residues are rich in bioactive compounds, particularly phenolic compounds, with antioxidant properties. Antioxidant activity has been widely related with protective effects and prevention potential for different diseases. Also, the scavenging and protective effects of antioxidant compounds have shown a connection and synergistic effect with other biological properties, such as anti-inflammatory, anti-tumor, anti-aging, neuroprotective, cardioprotective, or antidiabetic. These compounds can be applied in several fields, including food, cosmetic, and pharmaceutical industry. This chapter will be focused on the interconnected bioactive properties and possible applications of plant-origin compounds with antioxidant potential to valorize different agricultural waste.

Keywords

Agriculture waste · Antioxidant · Application · Biological properties · Synergy

1 Introduction

The term antioxidant is used for those molecules capable of significantly delaying or inhibiting the oxidation of other molecules, *i.e.*, lipids, proteins, carbohydrates, and DNA. Oxidation reactions produce free radicals harmful to cells that are responsible for common diseases, such as cancer and neurological or cardiovascular diseases (CVD). The physiological role of antioxidants is to neutralize the effect of these free radicals [1, 2]. Antioxidants may be synthetic or natural. However, recent studies have revealed that some of the most widely used synthetic antioxidants by the food, cosmetic, and pharmaceutical industry, such as hydroxytoluene butylated (BHT) or hydroxynisole butylated (BHA), may entail some potential health risks [3, 4]. Therefore, the search for alternative antioxidants of natural origin has increased, since they are considered safer than synthetics [5]. Moreover, the use of natural antioxidants can be a suitable alternative due to their low cost, compatibility with dietary intake, and safety for the human body [6].

Most natural antioxidants are extracted from plants and thus, they are referred as phytochemicals [7]. Among those phytochemicals with antioxidant activity some compounds can be mentioned: cinnamic acids; carotenoids; coumarins; mono-, di-, and tri-terpenes; flavonoids; lignans; sulforaphane; phenylpropanoids; and tannins [8–10]. Natural antioxidants can be found in all parts of the higher plants, from wood, bark, and roots, to stems, pods, leaves, fruits, flowers, pollen, and seeds [9]. Berries, cherries [11], citrus fruits [12], plums, olives, pomegranates [13], and onions have shown elevated antioxidant capacity [14]. Green and black teas are also associated with high-antioxidant activity, with phenolic compounds constituting up to 30% of their dry weight [15]. The antioxidant content of tubers and roots varies according to species, with ginger and red beet showing higher concentrations up to 3.85 and 1.98 mmol/100 g, respectively, and carrot lower values of 0.04 mmol/100 g. Within the genus *Solanum*, there are also important differences, blue potatoes (*Solanum andigenum*) show higher concentrations (0.80 mmol/100 g) than white potatoes (*Solanum tuberosum*) with 0.09 mmol/100 g [16]. Higher levels of antioxidants have been reported in plants that show greater resistance to different types of environmental stress [6].

Antioxidants have been widely studied, especially in the field of pharmacology, due to their multiple beneficial effects on human health and disease prevention (Fig. 1) [6]. Vegetables and fruits generally contain phenolic acids, flavonoids, and carotenoids with high antioxidant activity. Therefore, by including these foods into the diet, cells are protected from oxidative damage, and the risk of suffering certain diseases is reduced [8]. Oxidative stress contributes to defective spermatogenesis leading to male factor infertility. Several antioxidants have been shown to positively influence fertility and pregnancy rates [17]. Also, antioxidants are considered potential treatments for neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Various pathological conditions including rheumatoid arthritis, ulcerogenesis, CVD, and acquired immunodeficiency diseases can also be the result of excessive oxidative damage to cells [6]. There are many reports and evidences about how oxidative stress is involved in the pathogenesis of diabetes and its complications, and how the use of antioxidants reduce oxidative stress and relieves diabetic complications [9]. Also, supplementing infants with enzymatic and/or non-enzymatic antioxidants may be helpful in reducing damage caused by excessive production of reactive oxygen species (ROS) and preventing diseases such as necrotizing enterocolitis, premature retinopathy, periventricular leukomalacia, and

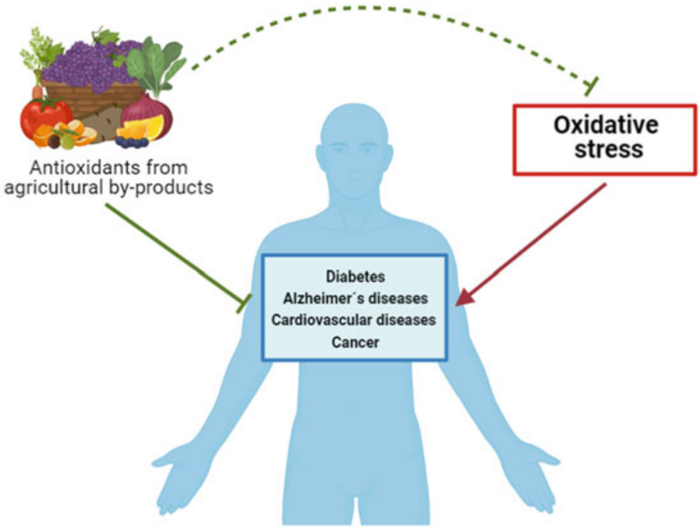

Fig. 1 Protective effect of antioxidants in disease prevention

bronchopulmonary dysplasia [18, 19]. Some antioxidant compounds, such as lanthanides, flavonoids, lycopenes, and glutathiones, have been reported to act as anticancer agents in medical chemistry [20]. Other clinical assessments have confirmed the efficacy of treating hepatocellular carcinoma patients with antioxidants (vitamin C, E...) [21]. Antioxidants also prevent oxidative damage to cerebellar development and play an important role in maintaining overall well-being [22]. In addition, antioxidant enzymes are found in red blood cells to prevent them from damage caused by intracellular ROS [6, 23]. Furthermore, the potent antioxidant activities in fruits and vegetables are the result of the additive or synergistic effects of phytochemicals [10, 24].

Both in plants and food, antioxidants are present in the form of mixtures, showing synergistic or antagonistic interactions between them and mediated by interaction mechanisms. Synergism occurs when a series of compounds, which are present together in the same system, has a more pronounced effect than would be derived from a concept of simple additivity [25]. It is complex to predict interactions between various antioxidants. The same pair of antioxidants can show different effects, depending on the reaction environment, their mutual quantitative relationships, and the presence of other ingredients in the mixture [26]. Therefore, the measurement of components isolated from natural sources does not allow knowing the total antioxidant capacity of a product, due to the combined and synergistic effect of a large number of compounds [27, 28]. Previous studies have found that concentration and proportion were the main factors affecting the interaction between antioxidants [29]. For example, when the proportion of α-tocopherol and β-carotene in liposomes is similar, the synergistic effect disappears and the antagonistic effect occurs [30].

Concurrently, the demand for fruit and vegetables has increased significantly in recent years due to the growth of the world population and dietary changes. However, these large-scale productions are accompanied by great loss and waste of fruit, vegetable, and cereal by-products during all phases of the supply chain [31]. Therefore, the recovery and transformation of by-products from the agro-food industry is considered a suitable strategy not only because it is a low-cost source of antioxidant compounds, but also it can contribute to the creation of new employment opportunities and reduce environmental pollution. Certainly, with the increasing demand for fruits and vegetables, the agricultural industry generates more and more waste every year, loosing phytochemicals with high antioxidant activity. The aim of this review is to highlight the high antioxidant potential of plant waste products, as well as to show the industrial and human health applications of antioxidant compounds.

2 Agricultural Waste and Green Technologies: A New Approach

2.1 Agro-Industrial by-Products as a Source of Antioxidant Compounds

Agro-industrial by-products of plant origin have been treated such as wastes in recent decades, since they do not originate a cost or a benefit [32]. Generally, agro-industrial by-products are treated as waste and are eliminated by burning, or used as animal feed or fertilizer without previous treatments, in the best-case scenario [33]. However, these processes can cause serious environmental problems, namely, an increase in the emission of greenhouse gases and, consequently, a greater risk of global warming. Hence, higher waste amounts can produce pollution and economic losses, and so, landfills are no longer sustainable. In addition, an increase in world population is expected (about 9 millions of people in 2050), so more waste will be generated. Nowadays, 800,000 tons/year of vegetal residues from several industries are produced, therefore new strategies to deal with these by-products are needed [34].

Recently, agro-food industries have begun to seek proper waste management strategies due to the existence of strict regulations, their possible impact on human health, costs of elimination, increasing public concern for environmental sustainability, and also increasing awareness about the benefits of bioactive compounds present in waste products and their possible valorization [33]. Residues from agriculture are rich in bioactive compounds which are beneficial to human health and have many applications in food, nutraceutical, or pharmaceutical industries. Therefore, research is focused on how to develop feasible procedures to recovery these bioactive compounds from agro-industrial wastes and transform them into value-added products for other industries.

On the other hand, by-products obtained from the agro-food industry are considered an inexpensive source of bioactive compounds, including dietary fibers, phenolic compounds, fatty acids, amino acids, prebiotics, minerals, vitamins, carotenoids, and other phytochemicals, which can be used in the pharmaceutical industry or to produce functional foods, among others [35]. Peels, pomace, and seed fractions are the main industrial by-products of fruits and vegetables [33, 36]. Inedible portions of fruits are considered to have the same or even higher amount of antioxidants components and nutritional content than their edible portion. In addition to containing bioactive compounds with antioxidant activity, non-edible portions have shown phytochemical profiles different from other parts of the fruit [5]. These agro-industrial by-products of plant origin contain important quantities of antioxidant compounds with protective and preventing potential against different diseases, and which also present a connection with other biological properties. These compounds generally have dual important role in health promotion and food preservation by eliminating or preventing harmful effects of oxidation mechanisms [37].

2.2 Green Extraction

Along the history of humankind, extraction processes have been necessary for obtaining target natural compounds from plant biomass and used for medicine, food, and perfumes. Since that moment, extraction techniques have evolved from those conventional procedures (*e.g.*, maceration) to more innovative extraction processes. The first evolution of these techniques started at the 20th century, when extraction processes were performed by using large solvent quantities derived from petroleum (*e.g.*, methanol or hexane). However, nowadays, petroleum era is nearing its end due to its overutilization. Also, these extraction procedures present an important environmental pollution and can be harmful to human health due to the use of hazardous substances. So, by the end of 20th century, a new alternative of extraction processes appeared, characterized by the reduction, elimination, or use of a new type of solvents (Fig. 2). Briefly, this new approach, usually referred as Green Chemistry, seeks to minimize the use of solvents and reagents, the intensification of the processes, and the cost-effective production of high-quality extracts while being more respectful with the environment and human health [38, 39].

From this last definition, green extraction techniques of natural products can be defined as the discovery and design of extraction processes which can reduce energy consumption, allow the use of alternative solvents and renewable natural products, and ensure a safer and higher quality extract or product. The main characteristics of a green extract (or eco-extract) are: (i) naturalness (not chemically modified), (ii) quality (high content of active compounds and absence of denatured molecules), (iii) functionality (determinate aim in final products), (iv) safety (lesser contaminants occurrence); (v) legislation (regulated by law); (vi) Life Cycle Analysis (low environmental footprint) (Fig. 3) [40].

Nowadays, the principal challenge of natural product extraction processes is their intensification, that is, to obtain the highest quality extraction process while reducing the time of extraction, unit operation number, global energy consumption, solvent used, environmental impact, economic cost, and waste quantity generated. The list of "Six principles of green extraction of natural products" reflect the aim to innovate not only in process, but in all aspects of conventional extraction, to improve human safety, and to protect the environment [38]. Materials for extraction should be plant biomass, but always preserving biodiversity, *i.e.*, without overusing those resources. In conventional extraction, large quantities of solvents are used, and consequently, huge energy consumption and environmental pollution are generated. Therefore, using alternative solvents, such as green solvents (water) or eco-solvents (glycerol), among others, is the best way to reduce those economic and environmental problems. In fact, the last objective for the future would be not to use solvents (free solvents) (Fig. 2). As a consequence ofthe application of these new techniques, different extracts have been obtained from agro-industrial by-products and have been tested for their antioxidant capacity. Still, solid-liquid extraction is the most used by industries (Table 1) [41].

3 Molecules with Antioxidant Potential

During the last decades, ROS have attracted researchers' attention. In normal conditions, ROS are produced by the body in low concentrations and have beneficial functions in cells. However, oxidative stress occurs when there are imbalances between ROS and antioxidant defense systems, thus levels of ROS are higher than the reducing potential of defense mechanisms and can inhibit many cell functions by damaging nucleus acids, oxidizing proteins, and causing lipid peroxidation. Antioxidants can neutralize these free radicals and inhibit their oxidation reactions by exchanging one of their own electrons with the free radical molecules to stabilize

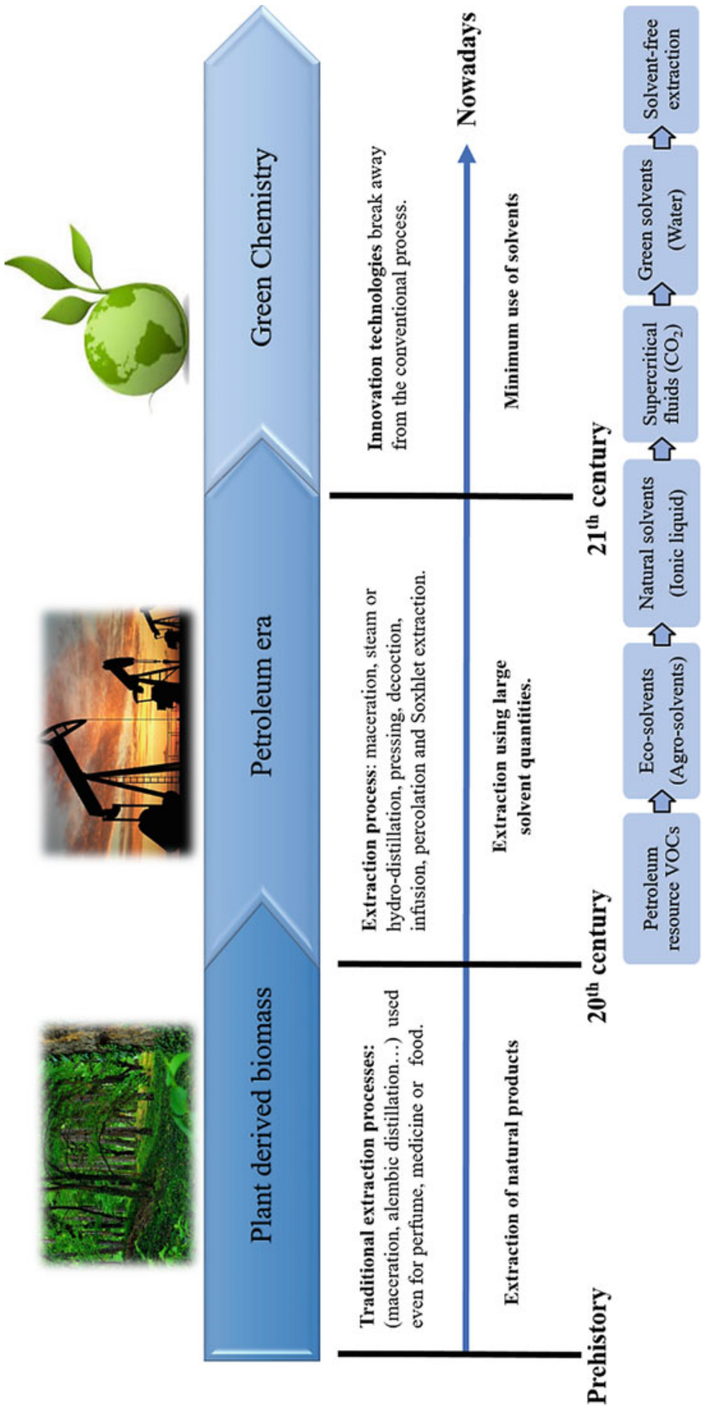

Fig. 2 Different extraction types and solvents along the history of humankind

Fig. 3 Total system of green extraction process related to six principles

it. They can also interact with transcription factors involved in the gene expression of antioxidant enzymes, which are the first-line defense against ROS. Therefore, antioxidant agents are needed for cell protection against oxidative stress [65, 66].

Antioxidants can be divided in two groups, namely, [67]: (i) endogenous antioxidants, and (ii) dietary antioxidants. Proteins (metal-binding proteins and enzymes) and low molecular weight antioxidants (glutathione, vitamin C) can be found within the endogenous antioxidants group. Vitamin A, E, flavonoids, polyphenols, polysaccharides, and β-glucan correspond to the dietary antioxidant group (Fig. 4). Also, a division can be made according to the mechanisms of action of the molecule, allowing to build two large groups: enzymatic and non-enzymatic antioxidants (Table 2).

In plants, the most abundant will be phenolic compounds (non-enzymatic compounds), which have been proved to have antioxidant capacity [68] and are present in all parts of the plant, including fruits, vegetables, nuts, seeds, leaves, roots, and barks [69]. Therefore, the occurrence of these compounds in differing kingdoms is mainly as a result of the consumption of plants which produce them as secondary metabolites [70]. Epidemiologic studies and related meta-analyses forcefully suggest that long-term plant-based diets can contribute with phenolics that act as defense mechanism against tumors development, CVD, diabetes, osteoporosis, and several neurodegenerative diseases due to their antioxidant properties [71]. However, antioxidant capacity will depend on the chemical structure of each phenolic compound, highlighting the action of flavonoids, tannins, chalcones, coumarins, and phenolic acids [72]. This diversity of compounds and matrices makes their analysis complex, being necessary to carry out different analysis depending on the type of phenolic compound, and requiring in all cases high-resolution chromatographic methods. Also, determinations of the total content of phenolic compounds can be carried out by spectrophotometric analysis [73].

Table 1 Examples of bioactive compounds with antioxidant capacity from several by-products of agricultural origin and by different extraction techniques

Matrix	Waste	Bioactive compounds	Essay	Extraction	Solvent	Ref.
Apple	Peel	TPC, flavonoids, anthocyanins	TOSC	S/L	A	[42]
	Seed	TCP, phlozidzin, ellagic acid	ABTS	S/L	M	[43]
		Epicatechin, caffeic acid, catechin, ferrulic acid, protocatechuic acid, gallic acid	DPPH			
	RJP	TCP	FTC	Soxhlet	W, M, E, A, H	[44]
	ABP	TCP	FTC			
Avocado	Peel	Hydroxybenzoic acids	DPPH	S/L	E/W (80/20 v/v)	[45]
		Hydroxycinnamic acids derivatives	TEAC	HAE	A/W (80/20 v/v) or M/W (80/20 v/v)	[46]
		Flavonoids	DPPH	S/L	M	[47]
		Dietary fiber	DPPH	S/L	M	[48]
	Seed	Quinic, citric, 1-caffeoyl quinic, 4-caffeoylquinic acids	DPPH	UAE	E/W (80/20 v/v)	[45]
		Procyanidin B1				
		Quinic, citric, 1-caffeoylquinic, 4-caffeoylquinic acids	TEAC	HAE	A/W or M/W (80/20 v/v)	[46]
		Procyanidin A1 and A2				
Mango	Peel	PP, flavonoids, carotenoids, dietary fiber, vitamins	DPPH, ABTS	MAE	A/W	[49]
		PP	FRAP	N.D.	N.D.	[50]
		PP, IF	ABTS, FRAP	EAE	*Enzymes: Pepsin, Pancreatin, α-amylase	[51]
	Seed	PP	DPPH	MAE	A/W	[49]
			ABTS	MAE	A/W (1/1 v/v)	[52]
	MSK	PP	DPPH	HAE	A/W (95/5 v/v)	[53]
	MDF	PP, dietary fiber	DPPH	S/L	M/W (50/50 v/v)	[54]
Beetroot	Pomace	PP, betalain, flavonoids, dietary fiber, vitamins	DPPH, RP	UAE	E/W (50/50); 0.5% AA	[55]
			DPPH, OH, O_2^-			[56]

(continued)

Table 1 (continued)

Matrix	Waste	Bioactive compounds	Essay	Extraction	Solvent	Ref.
	BWF	Dietary fiber, betalain	DPPH, RP	S/L	E/W (70/30 v/v)	[57]
Carrot	Peel	PP, flavonoids, carotenoids, dietary fiber, vitamins	DPPH, FRAP	S/L	M, W, E, H	[58]
	Pomace	Dietary fiber, carbohydrates	N.D	HAE	PE	[59]
Garlic	Husk	Phenolic acids	DPPH	CXE	E	[60]
				PEE	E	
				Soxhlet	M, E	
		Trans-coumaric, GCAE, *Trans*-ferulic, TCOA, GFAE, TFOA		S/L	E/W (80/20 v/v)	[61]
		Flavonoids (quercetin), dietary fiber	DPPH	S/L	W, M, E, M/W (50/50), E/W (50/50)	[62]
Onion	Skin	PP, flavonoids, dietary fiber	FRAP	HAE	M/W/HCl (70/29.5/0.5)	[63]
	OSW	PP, flavonoids	DPPH	S/L	M/W or E/W (80/20 v/v)	[64]

TCP total phenolic contents, *PP* polyphenols, *TOSC* total oxyradical scavenging assay, *FTC* ferric thiocyanate, *ABTS* 2,2′-azino-bis-(3-ethylbenzothiazoline)-6-sulfonic acid, *DPPH* 2,2′-diphenil-1-picrylhydrazil, *FRAP* ferric reducing ability assay, *HRA* hydroxyl radical assay, *OH* reactive hydroxyl, O_2 superoxide anion, *RP* reducing power, *RJP* residues from juice production, *ABP* apple by-product, *MSK* mango seed kernel, *MDF* mango dietary fiber concentrate, *BWF* beetroot waste flour, *OSW* onion solid waste, *GCAE* guaiacylglycerol-β-caffeic acid ether, *TCOA N-trans*-coumaroyloctopamine, *GFAE* guaiacylglycerol-β-ferulic acid ether, *TFOA N-trans*-feruloyloctopamine, *S/L* Solid-Liquid extraction, *HAE* heat assisted extraction, *MAE* microwave assisted extraction, *UAE* ultrasound assisted extraction, *CXE* carbon dioxide expanded ethanol extraction, *PEE* pressurized ethanol extraction, *IF* indigestible fraction, *N.D* no determinate, *A* acetone, *M* methanol, *E* ethanol, *H* hexane, *W* water, *AA* acetic acid, *PE* petroleum ether

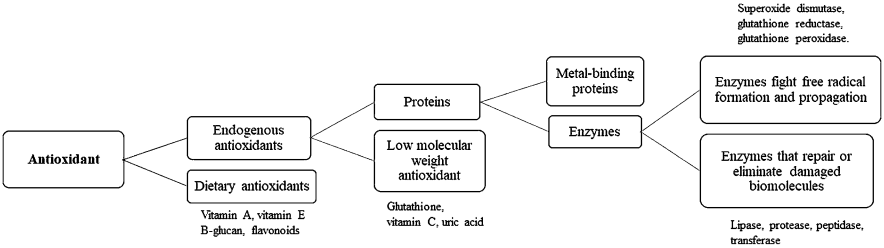

Fig. 4 Schematic representation of antioxidants

Table 2 Classification of natural non enzymatic antioxidants [70, 74, 75]

Type	Compounds	Sub-class	Sources	Solubility	Concentration	Ref.
Phenols	Flavonoids	Flavones, falvonols, flavanones, isoflavonones, anthocyanins	Potatoes, wheat, tomatoes, berries, peaches	H	Vary among sources	[76]
	Non-flavonoids	Lignans, stilbenes, tannins	Pumpkin, potato, grape fruits, legumes	H	Lignans (linseed): secoisolariciresinol up to 3.7 g/kg dry wt; Resveratrol (red wine) (0.3–7 mg aglycones/L and 15 mg glycosides/L)	[76]
	Phenolic acids	Hydroxycinnamic, hydrobenzoic acids	Strawberries, apple, mango, blueberries, kiwis, plums, cherries	H	Hydroxycinnamic acids (0.5–2 g hydroxycinnamic acids/kg fresh wt)	[76]
Terpenoids	Terpenes	Monoterpenes, sesquiterpenes, dipertenes	Tea, thyme, cannabis, Spanish sage, and citrus fruits	H,F	19.82 mg quercetin equivalents per gram in *S. oblonga*	[77]
	Carotenoids	β-carotene, lycopene, lutein, and zeaxanthin	All colorful edible plants, especially dark green and yellow-orange leafy	F	Lycopene (tomatoes) (79–91%)	[76]
Minerals	Enzymes cofactors	Iodine, zinc, copper, manganese, selenium	Nuts, beans and lentils	H	Vegetarian diets 13 mg/day Fe, 12 mg/day Zn, 1 mg/day Cu	[78]
Vitamins	A		Mangos, papaya, squashes, carrots, sweet potatoes, maize	F	Red palm oil 500–700 ppm/100 g	[79, 80]
	E		Legumes, cereals	F	23.7 g nuts, 168.7μg/mL *C. officinalis*	[81]
	C		Citrus fruits	H	0.23 mg/g in potatoes and tomatoes	[82]

H Hydrosoluble, *F* Fat-soluble

Other interesting group of compounds with antioxidant properties are terpenoids and carotenoids. In fact, tetraterpenes and carotenoids have shown potent antioxidant activity in *in vivo* and *in vitro* studies [83]. They have shown synergistic interactions with other antioxidants, mixtures of carotenoids are more effective than single compounds [84]. These compounds are highly efficient in inactivating singlet oxygen, capturing ROS, and acting as chemical inhibitors subjected to irreversible oxygenation. However, their mechanisms of action have not been fully understood yet, especially in the context of the antioxidant and pro-oxidant activity of carotenoids [85]. This is the case of β-carotene, which at high concentration and oxygen pressure acts as pro-oxidant [86].

Minerals, a group of essential nutrients, also have antioxidant capacity. In particular, plants are an essential source of large amount of minerals, precisely electrolytes [75]. Among the antioxidant minerals are iron, zinc, selenium, copper, and manganese. Their mechanism of action is based on its capacity to act as cofactor of several antioxidant enzymes. Therefore, its nonappearance will alter the activity of their enzymatic scavenging activity [87]. The mechanism of action differs from one compound to another. For instance, Zn^{2+} can regulate Nrf2 activity and down-regulate the generation of ROS [88, 89]. Therefore, it has been proved that diets supplemented with Zn^{2+} reduce oxidative stress biomarkers as well as lower the production of inflammatory cytokines in the older population [90]. Selenium is also of great interest since low levels in humans are related to a bigger risk of ailments. The study of selenoproteins (predominant form selenomethionine) has shown great efficacy in the defense against oxidative stress originated by ROS and reactive nitrogen species (NOS) [91, 92]. Furthermore, a deficient or excessive manganese exposure in the diet could increase ROS generation and result in further oxidative stress [93].

Vitamins are considered micronutrients as they are only required in minor amounts. Besides, vitamins cannot be synthetized by the human body so they have to be incorporated through the diet [70]. Among them, only vitamins A, E, C and β-carotene (pro-vitamin A) possess antioxidant activity. Their mechanism of action consists in their capacity of donating electrons and hydrogen atoms, thereby producing an effective neutralization of free radicals. However, their action is limited due to their lipophilic properties which restricts their pass through membranes [94]. For instance, in the case of vitamin E, only α-tocopherol can be absorbed by the human body [95]. Vitamin C (ascorbic acid), apart from its own antioxidant capacity, is also capable of regenerating pigments as well as vitamin E. Regarding its mechanism of action, the molecule is produced during aerobic metabolism and then, it reacts with O_2^{-}, singlet oxygen, ozone, and H_2O_2 through ascorbate peroxidase to counteract their toxic properties [83]. Regarding vitamin A, both retinal and retinoic acid are considered biologically active forms. However, the supplementation with vitamin A is controversial since an excessive consumption can have toxic effects [96].

4 Interconnected Activities of Antioxidant Compounds

The food industry generates large amounts of waste that can be considered as a source of bioactive compounds with biological properties [97]. Phenolic compounds, terpenes, peptides, or phytosterols, among others, have demonstrated to have antioxidant, anti-inflammatory, antidiabetic, anti-obesity, antihypertensive, anticancer, and antibacterial properties [35, 98, 99] (Table 3). This section will address the biological properties connected to the antixidant capacity of compounds extracted from plant materials from food industry waste.

4.1 Antioxidant

Oxidative process occurs when there is an imbalance between the production of ROS and the antioxidant systems, causing damage to other molecules such as lipids, proteins, and DNA. These molecules can act as second messengers in cell signaling targeting regulatory pathways and give rise to the activation of other signals related to inflammatory or proliferative processes, among others [100–103]. Therefore, oxidative stress has been associated with the incidence and progression of various chronic and degenerative diseases, including diabetes, cancer, cardiovascular, neurological diseases, etc. [104].

Plant residues have been highlighted as a source for obtaining compounds with antioxidant activity [142]. For instance, wine production by-products have demonstrated its antioxidant potential: *i.e.*, catechins present in the skin, seed, and stems from grapes were tested, by means of the ABTS method obtaining 80.6, 206.3, and 97.9μmol Trolox equivalent/g of residue, respectively. The higher antioxidant activity was related to a higher content of phenolic compounds [116]. Additionally, grape stalks from Duero region presented an important antioxidant capacity related to their high content of polyphenols [143]. Furthermore, a wide variety of plant residues have shown antioxidant potential. Phenolic compounds from avocado peels and seeds showed antioxidant properties against ROS [45]. Lycopene from tomato skin could significantly protect cells from oxidative damage induced by H_2O_2, showing its potential to counteract the redox imbalance in cells induced by oxidative stress conditions [130]. In addition, lutein, a carotenoid present in lettuce or cabbage residues, showed depurative activity against peroxy radicals (ROO) in human erythrocytes, reducing lipid peroxidation [131, 144]. Also, pepper *(Capsicum annuum)* seed extracts enriched in sterols reduced the superoxide radical formation [145]. These studies point out the potential for valorization of plant residues as an important source of molecules with antioxidant capacity. However, this property has been related to other biological properties.

Table 3 Biological properties of chemical compounds extracted from agricultural waste

Matrix	Waste	Chemical compound	Activity	Ref.
Pomegranate	P	Punicalagin, cyanidin-3,5-*O*-diglucoside, delphinidin-3-*O*-glucoside, cyanidin-3-*O*-glucoside, pelargonidin-3-*O*-glucoside	AX, AD	[105, 106]
Passion fruit	P	Caffeic acid and isoorientin	P, AX	[107, 108]
	S	(+) – Catechin, −(−) Epicatechin, Veratric acid	AD, AX	[109]
Solanum quitoense	Sk	Chlorogenic acid and rutin hydrate.	AX	[109]
	Pu, S	Chlorogenic acid	AD, AX	[109]
Tree tomato	P	Chlorogenic acid, sinapic acid, and rutin hydrate	AD, AX	[109]
	Pu	Chlorogenic acid, trans-cinnamic acid	AD, AX	
Pistachio	Sk	Gallic acid, protocatechuic acid, (+)-catechin, *p*-hydroxybenzoic acid, caffeic acid, (−)-epicatechin, syringic acid, *p*-coumaric acid, hesperidin, quercetin, apigenin	AX	[110]
Red grape	Sk	Gallic acid, (+)-catechin, caffeic acid, (−)-epicatechin, rutin, *trans*-resveratrol, quercetin	AX	[111]
	S	Epicatechin, catechin, tannins, gallocatechin, epigallocatechin and epicatechin 3-*O*-gallate	AX, AC, AP	[112–115]
	St	Polyphenols, (+)-Catechin, quercetin-3-glucoside, *trans*-ε-viniferin	AX, AM, AA	[116–118]
	L	Anthocyanins, cyanidin-3-*O*-glucoside and peonidin-3-*O*- glucoside, flavonoids, quercetin-3-*O*- glucuronide, quercetin-3-*O*-galactoside	ACh	[119]
White grape	S	Linoleic acid	AX	[120]
Pineapple	H, Sh	Phenolic compounds	AX	[121]
Peanut	Sh	Phenolic compounds	AX, AM	[122]
Potato	n.d.	Chlorogenic acid and caffeic acid	AX	[123]
Broccoli	L, St	β-carotene, phenolic compounds, chlorophylls and phytosterols	AX, CY	[124]
Mango	P	Phenolic compounds (mangiferin)	AX	[125]
Kiwi	Sk	Syringic, chrysin, and quercetin	AX	[126]
	S	*P*-hydroxybenzoic acid, protocatechuic acid	AX	[127]
Walnut	Sh	Gallic acid, ellagic acid pentose, ellagic acid, dimethyl ellagic acid	AX	[128]
Avocado	Sk, S	Procyanidin B2 and B1, catequina, epicatechin, trans-5-*O*-cafeoil-*D*-quinic acid	AX, AI, CY	[45, 129]
Tomato	P	Lycopene	AX	[130]

(continued)

Table 3 (continued)

Matrix	Waste	Chemical compound	Activity	Ref.
Lettuce and cabbage	L	Lutein	AX	[131]
Sweet orange	P	Hesperidin vanillic acids, *p*-hydroxybenzoic acid, rutin	AX	[132, 133]
Mandarin orange	P	Hesperidin, naringin, tangeritin, rutin	AX, APr	[134]
Cashew	Sk	Epicatechin	AX	[135]
Pear	Sk	Arbutin, oleanolic acid, ursolic acid, chlorogenic acid, epicatechin, rutin	AI, AX, AD	[136, 137]
Pinus koraiensis	C, EO	*a*-pinene, *b*-myrcene, 3-carene, *d*-limonene	AT	[138]
Carrot	Sk	Phenolic compounds, tannins	AT	[139]
Watermelon	Sk	Phenolic compounds, tannins	AT	[139]
Blueberry	P	Anthocyanins	AT	[140]
Apple, blueberry	P	(+) catechin and quercetin	AA	[141]

AX Antioxidant, *AD* Antidiabetic, *AA* Antiaging, *AT* Antitumor, *AI* Anti-inflammatory, *P* Prebiotic, *AC* Anticoagulation, *AP* Antiplatelet, *AM* Antimicrobial, *ACh* Antichemotactic, *CY* Cytoprotective, *APr* Anti-proliferative, *P* Peel, *Pu* Pulp, *S* Seeds, *Sk* Skin, *St* Stem, *L* Leaves, *Sh* Shell, *Po* Pomace, *EO* Essential oil, *C* Cones, *H* Heart, *n.d.* not determined

4.2 Anti-Inflammatory

Inflammation is a pathological condition characterized by the infiltration of immune cells into the vascular wall and the release of ROS by these cells, causing tissue damage [146]. So, oxidative stress is considered the initiator and the consequence of inflammatory responses, and, in turn, inflammation is involved in the genesis of many other diseases [147, 148]. On the other hand, inflammation is regulated by nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) [147]. In general, the use of antioxidants is sought in the prevention of inflammation and the reinforcement of cell repairing processes, either by eliminating or inhibiting their precursors [149]. Currently, research is directed towards finding new drugs with fewer side effects than traditional anti-inflammatory drugs [149]. Many phytochemicals have demonstrated to have anti-inflammatory and antioxidant effects on inflammatory disease model systems, both *in vitro* and *in vivo* [149]. Flavonoids and their derivatives are known to be widely used in inflammatory drug design research, as well as other compounds such as triterpenoids, alkaloids, saponins, and tannins [150].

To illustrate some examples, the olive oil industry generates by-products rich in lignans, secoiridoids, and especially hydroxytyrosol, with important anti-inflammatory effects [151]. In addition, oleocanthal has anti-inflammatory functions similar to ibuprofen, both inhibiting the same cyclooxygenase enzymes in the prostaglandin biosynthesis pathway [152, 153]. It is known that phenolic compounds from extra virgin olive oil (EVOO) decrease edema, cell migration, cartilage degradation, and bone erosion, significantly reducing the levels of pro-inflammatory cytokines and prostaglandin E2 in the joint [154]. On the other hand, it is known that hydroxytyrosol manages to inhibit the activation of granulocytes and monocytes, and the modulation of miR-146a expression and Nrf2 activation [155]. Furthermore, hydroxytyrosyl stearate (HtySte) and hydroxytyrosyl oleate (HtyOle), both compounds formed during EVOO processing, decrease nitric oxide (NO) production by RAW264.7 macrophages in a concentration-dependent manner [156].

Similarly, orange and mango by-product extracts have shown an anti-inflammatory potential by reducing the levels of NO produced by RAW 264.7 macrophages stimulated by lipopolysaccharides (LPS) [157]. Also, extracts from the skin of 10 varieties of pears have demonstrated anti-inflammatory properties, corresponding to higher proportions of phenolic compounds [137]. Anti-inflammatory effect of lemon and hot pepper by-products (especially, peels and leafs) was evaluated in induced arthritis mice and showed a reduction of cytokines IL-6 and tumor necrosis factor alpha (TNF-α) [158]. Furthermore, other authors explored the effect of lemon peel flavonoids on UVB-simulated skin damage in irradiated mice, observing an increase in catalase (CAT) and superoxide dismutase (SOD) oxidase activity and decreased levels of interleukins -1β (IL-1β), IL-6, IL-10, and TNF-α thus evidencing an excellent protective effect of the skin with a satisfactory application value [159]. On the other hand, the effect of apple peels in an experimental model of arthritis in mice was studied and a decrease in the levels of the mediators of synovial inflammation KC/CXCL-1 and TNF-α levels was observed [160].

4.3 Anti-Tumor

Current research indicates that phytochemicals present in fruits, vegetables, and plants have antitumor activity through several mechanisms, including antioxidant activity, regulation of gene expression, induction of apoptosis, and arrest of the cell cycle, in addition to modulation of enzymatic activities, strengthening of the immune system, regulation of hormonal metabolism, and antibacterial and antiviral effects [161, 162]. Furthermore, it has been described that the potentially carcinogenic oxidative damage may be limited by the dietary antioxidants found in fruits, vegetables, and therefore, in their residues [163]. In fact, in many cases, these agro-food by-products have a greater amount of bioactive compounds than the pulp of the fruit or vegetable [164]. These natural compounds can interrupt or reverse carcinogenesis by modulating the intracellular signaling molecules involved in the initiation and/or promotion of cancer [161, 165]. On the other hand, in the progression stage, they can inhibit proangiogenic factors, regulate proteins related to metastasis, and induce apoptosis [166].

Considering the olive oil example, oleocanthal have inhibited the growth of three breast cancer cell lines, BT-474, MCF-7, and T-47D. Furthermore, when combined with tamoxifen, it inhibited cell proliferation [167]. Additionally, hydroxytyrosol causes apoptosis in papillary (TPC-1 and FB-2) and follicular (WRO) thyroid cancer cell lines through mitochondrial apoptosis and up-regulating p53 [168]. Regarding the different type of residues, skin or peels have been highlighted as sources of bioactive compounds. Gallic acid and kaempferol 3-*O*-glucoside, obtained from the pomegranate skin extract, achieved DNA cleavage induced by peroxyl and hydroxyl radicals in addition to inhibiting the oxidation of LDL cholesterol [106]. Hesperetin, obtained from the skin of citrus fruits, induced apoptosis in human cervical cancer SiHa cells [169]. Carrot and watermelon skin (rich in phenolic compounds and tannins) possessed antitumor activity against the breast cell line (MCF-7) and a high antioxidant action [139]. Blueberry skin extracts showed anti-proliferative activity in human tumor cells (HeLa) and human skin cells (HaCaT) by inducing apoptotic processes on tumor cells [140]. Avocado peel, rich in procyanidins, showed preferential cytotoxicity in B16F10 melanoma cells [129].

On the other hand, grape stem extracts was evaluated in three cancer lines (Caco-2, MCF-7 and MDA-MB-231), demonstrating anti-proliferative effect through cell death by apoptosis associated with a modification of the mitochondrial potential and the levels of ROS [117]. Another work pointed out that grape seed extract could inhibit the proliferation of MCF-7 cells in a concentration-time dependent manner. It stated that this extract caused the arrest of the cell cycle in the G2/M phase, followed by cell apoptosis [115].

4.4 Anti-Aging

Oxidative stress and free radicals are considered important factors in aging and in many degenerative diseases associated with age, since antioxidant systems deteriorate during aging [170]. Natural compounds are known to exhibit anti-aging effects through different mechanisms [171]. For example, proanthocyanidins, curcumin, and resveratrol are effective in protecting against age-related cognitive decline and depression-related damage through hypothalamic-pituitary-adrenal, serotonergic transmission and hippocampal neurogenesis [172]. In this sense, epigallocatechin gallate (EGCG) extended the life of healthy rats by reducing liver and kidney damage and improving age-related inflammation and oxidative stress by inhibiting NF-κB signaling [173]. On the other hand, allicin significantly improved cognitive dysfunction in elderly mice by enhancing the signaling pathways of two antioxidants similar to nuclear factor [174].

On the other hand, the anti-aging effect of grape stem extracts by means of anti-tyrosinase and anti-elastase effects has been reported, showing potential for the cosmetic, pharmaceutical, and food industries [118]. Also, the mixture of apple peel and blueberry extracts increased the life of *Caenorhabditis elegans* by 31.4%, besides improving resistance to heat stress and UV-B radiation [141]. In agreement with these works, other authors reported that the orange extract lengthens *C. elegans* life in a dose-dependent manner by decreasing the accumulation of age pigment and the levels of intracellular ROS without damaging fertility [133].

4.5 Antidiabetic and Anti-Obesity

The origin of obesity involves genetic and environmental factors that result in an excessive increase in body fat and a decrease in energy expenditure. Obesity is associated with a whole host of metabolic diseases known as metabolic syndrome [175]. At present, there is a growing interest about the potential of phenolic compounds as inhibitors of the carbohydrate enzymes, α-glucosidase, and α-amylase (targets of drugs to treat diabetes) to prevent increased plasma glucose levels after dietary intake [176, 177].

Among the waste derived from the food industry, skin and pomace are the main matrices that have been used for their antidiabetic and anti-obesity properties [178]. In a recent study, they managed to reduce the glycemic index in cookies by adding apple pomace extract [179]. Also, pomegranate peel extracts exerted inhibitory properties against α-glucosidase and pancreatic lipase [106]. Accordingly, a study indicated the positive effect of pomegranate skin on induced diabetic rats to which 200 mg/kg of pomegranate skin extract was administered for 56 days, achieving a decrease in blood glucose levels, total lipid cholesterol, LDL-C, and glycated hemoglobin [180]. On the other hand, the inhibitory potential of α-glucosidase of the extracts of mango, jackfruit, pineapple, papaya, and banana peels obtained by green extraction methods has been also reported [181]. Finally, through an observational study with PREDIMED patients it was concluded that a high intake of flavanones, dihydroflavonols, and stilbenes was associated with a reduced risk of diabetes in older people at high risk of CVD [182].

4.6 Neuroprotective

Neuronal damage is mainly due to oxidative stress and chronic inflammation, defective mitochondria, decreased energy homeostasis, discrepancies in neurotrophic factors, altered protein aggregation, and neuroinflammation [183, 184]. Another crucial event is the relation between the oxidative stress and the increased production of free radicals, ROS, and RNS in mitochondria, which leads to a decrease in the antioxidant/pro-oxidant effect in cells [184, 185]. In normal physiological conditions, the central nervous system (CNS) consumes a high amount of oxygen, causing a high generation of free radicals [186]. Therefore, CNS is susceptible to ROS attack due to the lack of antioxidant mechanisms and the limited passage of some antioxidants, such as vitamin E, because of the selectivity of the blood-brain barrier [183]. Additionally, other factors such as inflammation, the toxic action of NO, and mitochondrial dysfunction contribute to the progression of neurological diseases [187].

It has been suggested that several individual natural antioxidants or combinations may be neuroprotective and decrease the risk of neurological diseases or delay their progression [188]. In this way, the effects produced by various phytochemicals are associated with the counteracting of ROS alterations, mitochondrial damage, as well as the intracellular accumulation and release of potentially harmful substrates [189, 190]. In animal studies and *in vitro* experiments, the antioxidant and anti-inflammatory functions of compounds extracted from plants have been widely confirmed since they manage to restrict the activities of ROS and RNS, as well as NF-κB and cytokines such as TNF-α, IL-6, IL-1β, and interferon (IFN)-γ [191, 192]. Among the wide variety of phytochemicals that can exert neuroprotection, polyphenols are the most studied natural compounds with neuroprotective properties [10, 193]. Quercetin, kaempferol, and myricetin are the most highlighted [194–196]. Also, resveratrol has shown remarkable neuroprotective properties through antioxidant mechanisms [194, 197].

4.7 Cardio-Protective

Oxidative stress and other behavioral factors such as smoking, alcohol abuse, sedentary lifestyle, and high-fat diets are the origin of CVD [198]. Also, an imbalance in the redox system can lead to the development of CVD (atherosclerosis, arrhythmia, heart failure, ischemia-reperfusion injury) [100]. On the other hand, lipids, especially PUFA and cholesterol, are considered target substrates of oxidative stress [102]. These are susceptible to lipid peroxidation and generate highly reactive carbonyl species (RCS), which can covalently bind to molecules such as phospholipids, proteins, and nucleic acids, forming reversible and/or irreversible modifications that generate lipid oxidation [101, 199].

Traditional treatment for CVD include the use of different bioactive compounds. Phenolic compounds can prevent LDL oxidation, increase HDL levels, and induce vasodilation, lowering the risk of coronary problems and cardiomyopathies. They also promote antiplatelet aggregation, improve endothelial function, and decrease the expression of cell adhesion molecules [146, 200]. In clinical and animal studies, it has been shown that different types of polyphenols can have significant effects on CVD [201]. On the other hand, it has been described that the flavanones naringenin, hesperetin, and eridicitol, obtained from grapefruits, oranges, and lemons, respectively, possess protective properties, such as antioxidant effects in cardiometabolic disorders [202]. Furthermore, nobiletine, an *O*-methylated flavone derived from citrus peel, has been described in both *in vitro* and *in vivo* studies to inhibit platelet coagulation and the phosphorylation of the PKC protein kinase, PLCγ2 phospholipase [203].

Other compounds of interest in cardiovascular protection are quercetin and tangeretin. Quercetin exerts favorable effects on hypertension and their potential sources include apples, onions, black tea, and red grapes [204]. Tangeretin, an *O*-polymethoxylated flavone found in citrus peels, is known to exert antiplatelet activity by inactivating platelet-forming growth factor, which induces the multiplication and alteration of smooth muscles [205, 206]. Citrus peels have been found to contain more amounts of these compounds than the corresponding edible parts of fruits [207]. Furthermore, anthocyanins reduce the risk of coronary heart disease and CVD mortality [8]. Astaxanthin, a carotenoid belonging to the phytochemical series of terpenes, has beneficial effects on cardiovascular health due to its antioxidant and anti-inflammatory properties and its ability to modulate the metabolism of lipids and glucose [208]. On the other hand, the content of phenols present in EVOO improves oxidative damage and lipid profile, in the particular case of HDL cholesterol [209]. Also, the high concentration of antioxidant molecules such as hydroxytyrosol, tyrosol, and oleuropein aglycone typically found in greater quantities in EVOO by-products are related with these effects [210, 211]. Therefore, phytochemicals could be suitable candidates to prevent and treat CVD through direct antioxidant activity, as well as their other bioactivities such as anti-inflammatory and prevention of platelet aggregation and adhesion.

5 Applications of Antioxidant Compounds

5.1 Food Industry

Natural antioxidants have been studied in a wide range of applications; they are used as preservatives in various food products, in edible coatings, and in films intended for its application in food packaging [212]. Concerning fruit and vegetables, industries are trying to reduce by-products due to the environmental issues and the socioeconomic losses. For example, the production of juices or canned fruits generates specific by-products in the form of peels, hearts, or seeds, among others [213]. Recently, the human diet has been gaining attention since it has been demonstrated that an appropriate nutritional diet can prevent different noncontagious diseases, such as obesity, cancer, or diabetes mellitus, among others [214]. Therefore, it has been suggested that diet could be complemented with target compounds with beneficial properties, this is, dietary antioxidants (*i.e.*, tocopherols, carotenoids, ascorbate, phenolic compounds) [215].

The evolution of new functional products represents a challenge for the scientific community, health authorities, and the food industry. Diet may adjust various body functions, meet nutritional needs, and it is expected to have beneficial effects against some diseases. According to European experts "a food can be explored as functional if it is adequately shown to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way which is relevant to either the state of well-being and health or the reduction of the risk of a disease" [216]. Different studies have been performed to study the formulation of functional ingredients from agricultural waste and their incorporation into food products. A recent study demonstrated that substituting wheat flour by10–20% with apple pomace was able to reduce the glycemic index when incorporated to biscuits [179]. Passion fruit peel extract was evaluated as a potential preservative for frozen meat products due to its antioxidant and antimicrobial properties [217]. Also, autolyzed biomass derived from wine fermentation process was used to formulate cereal bars with higher protein content [218].

Actually, given all the benefits that functional ingredients can incorporate to food products, research efforts are directed towards the perfection and standardization of incorporation processes using different techniques. For instance, techno-functional characteristics of fiber can make the process of incorporation difficult. Hence, coffee co-products have been studied to obtain functional ingredients by means of dynamic high pressure (DHP), acetylation, and hydrolysis by cellulose, showing that DHP was the least harmful for the integrity of chlorogenic acid [219]. However, most of the research is aimed at developing new techniques for encapsulation and new systems of food active packaging [220].

5.2 Cosmetic Industry

The global cosmetic market accounted for 507.75 billion USD in 2018 and is estimated to reach 758.45 billion USD by 2025, growing at a rate of 5.9%. Among the cosmetic products, skincare formulations currently possess the highest market share while oral cosmetics would be the fastest increasing during the estimated period. In the cosmetic industry, there is a continuous demand for new and innovative ingredients for product development and both, cosmetic companies and customers, are particularly interested in compounds derived from natural sources due to their several benefits [221]. For instance, some studies have shown the importance of catechins as antioxidants due to their ability to prevent and reduce skin damage. The major sources of catechins are *Camellia sinensis* and *C. assumica* (tea leaves) [222]. Moreover, green tea contains 75–80% water and polyphenol compounds, among which catechins account for more than 75% of them in tea waste. Extensive research on the protective properties of catechins against UV radiation have shown that they can enhance the photo stability and protection of skin from UV rays. Their use in the prevention of skin aging has increased due to their efficacy and stability and other properties, such as antimicrobial effects [223].

Nutricosmetics are a recent trend in skin care that joins food, cosmetics, and pharmaceuticals in one area and involves the use of supplements to improve and preserve skin health. These supplements include different micronutrients such as vitamins, minerals, and amino acids, and especially point to skin, hair, and nail care. Nowadays, cosmetic industries are also focused on producing these supplements with a high content in due errant ingredients, such as collagen, hyaluronic acid, vitamins C and E, elastin, and other molecules [224]. In this context, even though not considered agricultural waste derived from plants, invasive macroalgae species could be considered as potential residues to be eliminated from coastal systems without a specific usage [225]. Seaweeds have been subject of interest due to their structural biomolecules (proteins, carbohydrates, and lipids) but also for their bioactive compounds with different activities, that allow them to be used as an active ingredient during the formulation of cosmetics products [226].

5.3 Pharmaceutical Industry

Recently, development of medicinal chemistry has become crucial for improving the design of drugs, reducing toxic side effects, and understanding their mechanism of action. In the last decades, multiple epidemiological researches have demonstrated that dietary intake of nutrients rich in natural antioxidants is related to reduced risk of heart attack, among others [227]. Furthermore, the main reason, to add antioxidants in pharmaceutical products, is to enhance the stability of therapeutic agents that are susceptible to chemical degradation by oxidation. Recently, bioactive compounds from rice by-products have been used as an alternative treatment that suggested that could reduce the toxicity of chemotherapy by lowering the drug concentration, although maintaining potency the effects against cancer cells [228]. However, expectations about using natural compounds facing cancer must be cautious since even though some molecules have proven their potential, further studies are needed for the majority of the candidates' compounds [229]. Currently, the application of by-products extracts continues to be studied for their biological properties to be applied in the pharmaceutical industry [118] and other less common approaches, such as the use of cellulose to formulate nanofibrillated cellulose and cellulose nanocrystals or the use of oils extracted from seeds to formulate new functional pharmaceutical ingredients [230, 231].

6 Future Perspectives: Valorization Expectations

In the recent decades, the number of studies recovering antioxidants and other bioactive compounds from agricultural waste has increased significantly, due to the variety of biological properties attributed to the compounds but also to give added value to these matrices [232]. Most of these studies are focused on the evaluation of biological properties of extracts and compounds obtained from diverse agricultural waste; the use of nonconventional techniques, the improvement of extraction yields, and the reduction of cost and environmental impact, comparing with the conventional techniques; and also optimize the extraction conditions of certain compounds [233–235]. However, although the scientific community has widely described the benefits of waste re-valorization strategies to obtain extracts rich in bioactive compounds to develop new industrial products, its application at industrial-scale is still limited by several aspects, some of them will be mentioned below.

Firstly, from a technological point of view, extraction techniques have experienced a great development and the most advanced such as supercritical, subcritical fluid, microwave, or ultrasound-assisted extraction have been proposed for scaling up processes. Similarly, new solvents have been developed, such as the deep eutectic solvents, with desired characteristics like easy preparation, low toxicity, or biodegradability [236, 237]. However, not as much progress has been performed in the isolation and purification steps. In some cases, these phases are expensive, complex, and time consuming, which limits the industrial application of the extracts and compounds from agricultural waste [238].

Secondly, despite the numerous biological properties that have been attributed to agricultural waste compounds, in some cases, it exists a lack of information regarding the action mechanisms and their absorption, distribution, metabolism, excretion, bioavailability, and toxicological dynamics, which are key parameters that should be evaluated for developing safe and quality products. Thus, to enhance the industrial possibilities of agricultural waste antioxidants, it is necessary to carry out more in vivo and clinical studies [233].

Thirdly, there are several aspects that should be considered before the scale up from laboratory to pilot and industrial scale. For example, factors related to the matrices (perishability, variable composition of the matrices depending on the season, wastes generated only in a certain season, etc.) and related to the technical, economic, environmental, and social viability of the industrial process. The selection, transport, and conservation of the materials to obtaining the final product represents a challenge that hinders the application of re-valorization strategies [236, 239, 240]. In recent years, several studies have evaluated the technical and economic viability of re-valorizing strategies [241, 242]. For example, Cristobal et al. [242] carried out a techno-economic and profitability analysis of four food waste bio-refineries, based on tomato, potato, orange, and olive waste. The authors pointed out that not all the matrices had the same potential and several factors influenced the profitability of the process. In particular, value-added product market price was the most influencing factor, but the availability and transport of the residue were also important variables. Thus, these factors should be analyzed to evaluate the feasibility of a re-valorization strategy [242]. The environmental impact of the different re-valorization strategies should be also considered, but few studies have evaluated this aspect [241].

Fourthly, it has been also considered that consumer response to the products containing extracts derived from agricultural residues is still limited. Nevertheless, recent studies have shown that consumer concern about the sustainability of the food chain has increased. A positive evaluation of products with labels indicating sustainable products and even those with terms related to food waste has been observed [243, 244]. Finally, regulatory frameworks regarding valorization strategies should be stablished, to ensure that companies comply with the environmental and consumers sustainability concerns [243, 245] and also implement public subsidies and local public-private cooperation [244].

7 Conclusions

Agricultural waste can be considered a potential source of bioactive molecules with antioxidant potential. However, antioxidant effects are related with many other properties that can act synergistically for the prevention of certain diseases, health improvement, and formulation of new products for the food, cosmetic, and pharmaceutic industries. For this purpose, deep knowledge about antioxidant molecules, action mechanisms, extraction techniques, and the connections with other properties is still needed. Moreover, the application of re-valorization strategies still has to face many technical, economic, environmental, and social challenges. However, although it seems difficult to implement re-valorization strategies, meet industrial goals, and reduce the environmental impact of waste, the expectations are positive and successful examples could be found along the literature.

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