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Extraction of phenolic compounds from agro-industrial by-products by fungal fermentation with potential use as additives for meat and meat products. A review

Extracción de compuestos fenólicos de subproductos agroindustriales por fermentación fúngica con uso potencial como aditivos para carne y productos cárnicos. Revisión

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ABSTRACT

The present manuscript reviews the findings of different research studies that evaluate the use of fungal fermentation-assisted extraction, in solid-state fermentation (SSF) and submerged culture fermentation (SCF) with agro-industrial residues as substrates, to obtain phenolic compounds with possible applications as food additives. Some agro-industrial by-products (peels, pulps and seeds) are an important source of phenolic acids such as *p*-coumaric, *p*-hydroxybenzoic, chlorogenic, cinnamic, ferulic, gallic, protocatechuic, rosmarinic, syringic, and vanillic acids and flavonoids (apigenin, chrysin, (+)-catechin, kaempferol, myricetin, quercetin, rutin, hesperetin, and naringin). In addition, the utilization of these by-products as substrates in SSF and SCF allowed obtaining phenolic compounds with antioxidant and antimicrobial activities. Thus, fungal fermentation-assisted extraction provides a potential alternative to obtain natural additives for meat and meat products industry.

Keywords: Mushroom, Fermentation, Compound extraction, Food additives

RESUMEN

El presente manuscrito revisa los hallazgos de diferentes estudios de investigación que evalúan el uso de la extracción-asistida por fermentación fúngica, en medio sólido (SSF) y cultivo sumergido (SCF) con subproductos agroindustriales como sustratos, para obtener compuestos fenólicos con posible uso como aditivos alimentarios. Algunos subproductos agroindustriales (pulpas, cáscaras y semillas) son una fuente importante de ácidos fenólicos como *p*-cumárico, *p*-hidroxibenzoico, clorogénico, cinámico, ferúlico, gálico, protocatecuico, rosmarínico, siríngico, y vanílico, y de flavonoides (apigenina, crisina, (+)-catequina, kaempferol, miricetina, quercetina, rutina, hesperetina y naringina). Además, la utilización de estos subproductos como sustratos en SSF y SCF permitió obtener compuestos fenólicos con actividad antioxidante y antimicrobiana. Por lo que, la extracción-asistida por fermentación fúngica proporciona una alternativa potencial para obtener aditivos naturales para la industria de la carne y productos cárnicos.

Palabras clave: Hongos, Fermentación, Extracción de compuestos, Aditivos alimentarios.

INTRODUCTION

Meat and meat products are considered an important source of many essential nutrients in the human diet, including lipids such as fatty acids (mono- or polyunsaturated) and proteins rich in essential amino acids such as isoleucine, leucine, lysine, methionine, phenylalanine, threonine, and valine, which are highly susceptible to oxidation processes (Hammad *et al*., 2020). Oxidative deterioration of lipids and proteins, and microbial growth are considered the main causes of quality loss in any type of meat or meat products leading to organoleptic and technological changes such as color, odor, flavor, appearance, and texture, as well as water holding capacity and water loss by cooking. In addition, both factors promote nutrient losses and toxic compound formation (Jiang and Xiong, 2016; Aziz and Karboune, 2018). However, the uncontrolled uses of antioxidant and antimicrobial additives to preserve meat and meat products is a practice that generate negative effects on consumer health; thus, strict regulations for their controlled used in foods has been promoted (Poljsak *et al*., 2013; Aziz and Karboune, 2018).

In previous investigations to reduce lipid and protein oxidation and microbial growth in meat and meat products, extracts rich in phytochemicals have been obtained from plants, herbs, and species, and used instead of synthetic preservatives (Jiang and Xiong, 2016). In addition, the reuse of agro-industrial by-products such as peel pomace and seeds offers an alternative source of additives with antioxidant and antimicrobial properties (Hernández-Carlos *et al*., 2019).

Moreover, several extraction methods have been developed to obtain bioactive compounds from agro-industrial by-products, such as conventional (maceration and

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hydrodistillation extraction) and unconventional (ultrasonic, microwave, supercritical fluid, and enzyme extraction) methods. These extraction methods in combination with a solvent system of different polarities, including water, acetone, ethanol, methanol, hexane, and petroleum ether, improve the types of compounds that can be extracted (Azmir *et al*., 2013; Hernández-Carlos *et al*., 2019). However, biotechnological methods such as fungal fermentation-assisted extraction (SSF and SCF) has been suggested as an additional alternative to obtain bioactive compounds from agro-industrial by-products (Papaspyridi *et al*., 2012; Santana-Méridas *et al*., 2012). In this review, a general description of the uses of fungal fermentation-assisted extraction (SSF and SCF) to obtain phenolic compounds from agro-industrial by-products, and their possible applications as food additives are discussed.

Phenolic Compounds from Agro-Industrial By-Products

The definition of food losses and waste could be associated with a reduction in the availability of food, a decrease in nutritional value and a deterioration in food safety, involving many players in food supply chains, such as farmers and processors. Furthermore, food losses could occur by accidental causes (intrinsic or extrinsic factors), and food waste occurs for reasons of negligence (FAO, 2017). The Mexican normative (NOM-251-SSA1-2009) defines food residue/by-product as 'waste from processed raw material'. In this regard, the food processing industry generates large amounts of by-products, including pomace, husks, seeds, leaves, stems, and wood (Peanparkdee and Iwamoto, 2019; Rico *et al*., 2020). In some cases, these by-products are treated to decrease negative environmental impact, making them a useful product with the added benefits of solving a problem and generating additional income (Rico *et al*., 2020).

Agro-industrial by-products are commonly disposed of, used on-site or used off-site or after pre-treatment. These can be pre-treated by physicochemical (combustion, pyrolysis, and gasification) or biochemical (anaerobic digestion and fermentation) processes, to generate biodiesel and electricity or bio-alcohol and biogas, respectively. In addition, agro-industrial by-products can be pre-treated by bio-reduction to produce animal feed, and by chemical modifications, and by SSF and SCF to obtain bioactive compounds (Santana-Méridas *et al*., 2012). Thus, agro-industrial by-products are considered a rich source of bioactive compounds, including alkaloids, terpenoids, saponins, essential amino acids and fatty acids, minerals, carotenoids, vitamins, polysaccharides, and phenolic compounds like phenolic acids, and flavonoids (Wijngaard *et al*., 2012; Azmir *et al*., 2013; Peanparkdee and Iwamoto, 2019; Rico *et al*., 2020).

The major by-products of fruit processing are peel and seed, and in a minor proportion, pulp (Santana-Méridas *et al*., 2012). However, the extraction, identification and uses of phenolic compounds are widely investigated in commercial sectors such as the pharmaceutical, chemical, and food industries (Azmir *et al*., 2013; Santana-Méridas *et al*., 2012). In this context, table 1 compiled literature reports of these residues as an important source of phenolic acids, including peel (apple, potato, and tomato), pulp (avocado) and seeds (avocado, citrus, and tomato). In addition, table 2 demonstrate that by-products also are a significant source of flavones, flavonols, and flavanones compounds. It has been reported that phenolic compounds are present ubiquitously in all parts of plants such as wood, leaves, roots, and fruits (Vermerris and Nicholson, 2008; Rico *et al*., 2020). In this regard, these compounds are commonly trapped or bound to the dietary fiber of plant material, through hydrogen bonds between the phenol hydroxyl group ($HO^{\cdot}$) of the phenolic component, hydrophobic interactions, and covalent bonds like ester bond between phenolic acids and polysaccharides (Quirós-Sauceda *et al*., 2011).

Chemical structure plays a key role in the bioactivity of phenolic compounds, which have been associated with several key factors such as OH-group location in the benzene ring, the substitution patterns by the OH-group (*ortho*-, *meta*-, *para*-, *meta-tri*-, *vic-tri*-), the presence of glycosylation, and double bounds in the benzene structure (Vermerris and Nicholson, 2008; Rico *et al*., 2020). However, the types of phenolic compounds obtained, and their bioactivity are closely associated with the extraction method employed (Azmir *et al*., 2013).

Extraction Methods

Phenolic compounds are widely found as a mixture of different components in a solid, and for extraction that are dispersed in a liquid phase, which allows their separation from the solid phase. This process is known as liquid-solid extraction, and to increase the diffusion rate of the solvent in the solute and yields, it is necessary to dry and reduce the particle size of the solid or plant material (fruits, leaves, stem, roots, wood, flowers or seeds) (Pinelo *et al*., 2007; Pronyk and Mazza, 2009; Orphanides *et al*., 2013).

Furthermore, several methods are frequently employed to obtained phenolic compounds, including rustic methods (extraction by cooking, percolation, and infusion), conventional methods (extraction by maceration, Soxhlet, and hydrodistillation) and unconventional methods, including enzymes-assisted extraction, microwave-assisted extraction, pressurized liquid-assisted extraction, supercritical fluids-assisted extraction, and ultrasound-assisted extraction (Wijngaard *et al*., 2012; Azmir *et al*., 2013). However, the solvent type, solvent-solid ratio, number of extractions, pH, temperature, time, vacuum and fermentation process, among other conditions used, influences phenolic yields (Spigno *et al*., 2007; Ramírez-Rojo *et al*., 2018).

Fungal Culture Fermentation

SSF involves the fermentation of solids or semi-solids in the absence of water, where the substrate used to be the source of moisture to support microbial growth (Pandey, 2003; Castañeda-Casasola *et al*., 2018), while in SCF, microorganisms grow submerged with an excess of water and limited oxygen (Castañeda-Casasola *et al*., 2018). In this context,

Table 1. Basic structure of phenolic acids identified in some agro-industrial by-products.
Tabla 1. Estructura básica de ácidos fenólicos identificados en algunos subproductos agroindustriales.

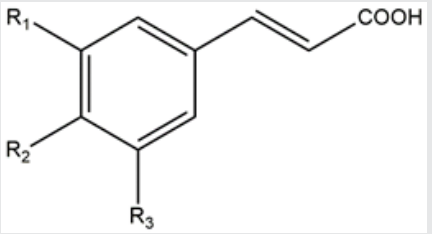
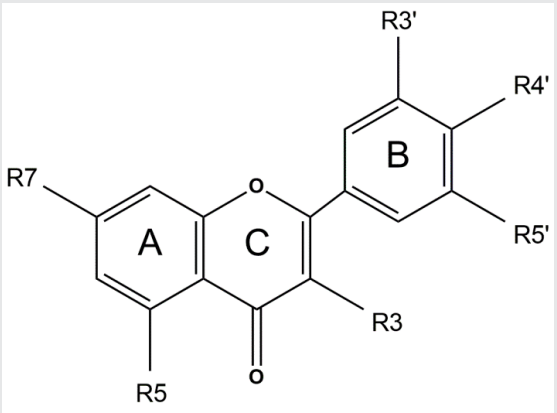
Basic structure						
						
Phenolic acids identified						
Compound	**R1**	**R2**	**R3**	**-COOH**	**Source**	**Reference**
p-coumaric acid	H	OH	H	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Apple peel	Łata et al. (2009)
					Tomato peel and seed	Valdez-Morales et al. (2014)
p-hydroxybenzoic acid	OH	H	H	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Avocado peel, pulp and seed	Rodríguez-Carpena et al. (2011)
					Citrus seed	Moulehi et al. (2012)
Caffeic acid	OH	OH	H	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Apple peel	Łata et al. (2009)
					Citrus seed	Moulehi et al. (2012)
					Tomato peel and seed	Valdez-Morales et al. (2014)
Chlorogenic acid	OH	OH	H	Esterified	Potato peel	Onyeneho and Hettiarachchy (1993)
					Apple peel	Łata et al. (2009)
					Citrus seed	Moulehi et al. (2012)
					Tomato peel and seed	Valdez-Morales et al. (2014)
Cinnamic acid	H	H	H	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Tomato peel and seed	Valdez-Morales et al. (2014)
Ferulic acid	OCH3	OH	H	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Citrus seed	Moulehi et al. (2012)
					Tomato peel and seed	Valdez-Morales et al. (2014)
Gallic acid	OH	OH	OH	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Citrus seed	Moulehi et al. (2012)
					Tomato peel and seed	Valdez-Morales et al. (2014)
Protocatechuic acid	H	OH	OH	*	Potato peel	Onyeneho and Hettiarachchy (1993)
Rosmarinic acid	OH	OH	H	Esterified	Citrus seed	Moulehi et al. (2012)
Syringic acid	OCH3	OH	OCH3	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Citrus seed	Moulehi et al. (2012)
Vanillic acid	H	OH	OCH3	*	Potato peel	Onyeneho and Hettiarachchy (1993)
					Citrus seed	Moulehi et al. (2012)
					Tomato peel and seed	Valdez-Morales et al. (2014)

Table 2. Basic structure of flavonoids identified in some agro-industrial by-products.
Tabla 2. Estructura básica de algunos flavonoides identificados en subproductos agroindustriales.

Basic structure of flavonoids



Flavonoids identified										
Compound	R3	R5	R7	R2′	R3′	R4′	R5′	C2-C3	Source	Reference
Flavones										
Apigenin	H	OH	OH	H	H	OH	H	+	Citrus seed	Moulehi *et al*. (2012)
									Tomato peel and seed	Valdez-Morales *et al*. (2014)
Chrysin	H	OH	OH	H	H	H	H	+	Apple peel	Balasuriya and Rupasinghe (2012)
Flavanols										
(+) catechin	OH	OH	OH	H	H	OH	OH	-	Apple peel	Łata *et al*. (2009)
									Avocado peel, pulp and seed	Rodríguez-Carpena *et al*. (2011)
									Citrus seed	Moulehi *et al*. (2012)
Kaempferol	OH	OH	OH	H	H	OH	H	+	Citrus seed	Moulehi *et al*. (2012)
									Tomato peel and seed	Valdez-Morales *et al*. (2014)
Myricetin	OH	OH	OH	H	OH	OH	OH	+	Tomato peel and seed	Valdez-Morales *et al*. (2014)
Quercetin	OH	OH	OH	H	OH	OH	H	+	Apple peel	Łata *et al*. (2009)
									Citrus seed	Moulehi *et al*. (2012)
									Tomato peel and seed	Valdez-Morales *et al*. (2014)
Rutin	Gly	OH	OH	H	OH	OH	H	+	Apple peel	Łata *et al*. (2009)
									Citrus seed	Moulehi *et al*. (2012)
									Tomato peel and seed	Valdez-Morales *et al*. (2014)
Flavanones										
Hesperetin	H	OH	OH	H	OH	OCH_3	H	-	Citrus seed	Moulehi *et al*. (2012)
Naringin	H	OH	OH	H	H	OH	H	-	Apple peel	Balasuriya and Rupasinghe (2012)
									Citrus seed	Moulehi *et al*. (2012)
									Tomato peel and seed	Valdez-Morales *et al*. (2014)

(+) double; (-) single.

fungal mycelia is widely produced in SSF using substrates such as grains, sawdust or wood from different plant species (Yang and Liau, 1998). Nevertheless, it has been reported that SCF improves potential advantage than SSF, because inoculums can be uniformly dispersed in the substrate, and the time and/or harvest speed are reduced (Yang and Liau, 1998; Xu and Zhu, 2011; Xu *et al*., 2015).

Moreover, fungal mycelia production during the fermentation process varies extensively, depending on the species of fungus and environmental or culture conditions used (temperature, initial pH, surface-aeration, aeration rate, rotating speed, and stimulatory agents, among others), which consequently affect phytochemical extraction from the substrate (Yang and Liau, 1998; Xu and Zhu, 2011; Xu *et al*., 2015).

Phenolic Compounds Extraction by Fungal Fermentation

In relation to the aforementioned, the use of agro-in-

dustrial by-products as substrates in combination with fungal fermentation-assisted extraction (SSF and SCF), are considered an alternative method for the extraction of phytochemicals, including triterpenoids, polysaccharides, and phenolic compounds, which could be obtained through agro-industrial by-products (Xu and Zhu, 2011; Xu *et al*., 2014; Xu *et al*., 2015; Dey *et al*., 2016).

In this context, the extraction of phenolic compounds and triterpenoids from citrus peel like pomelo, lemon, orange, and tangerine, through SCF (25 °C at 100 rpm, 28 d) with *Antrodia cinnamomea* has been reported (Ma *et al*., 2014). Also, polysaccharide and triterpenoid extraction from citrus peels, including pomelo, lemon, orange, and grapefruit, using SCF (25 °C at 100 rpm, 28 d) with *A. cinnamomea* was also demonstrated (Yang *et al*., 2012). Xu and Zhu (2011), reported the extraction of phenolic compounds with antioxidant properties (DPPH$^{\cdot}$ and hydroxyl scavenging activity) from ground corn stover by SCF (28 °C at 150 rpm, 12 d) using *Inonotus obliquus*. In addition, Vattem and Shetty (2002) demonstrated the extraction of phenolic compounds such as ellagic acid, resveratrol and rosmarinic acid with antioxidant properties (antiradical DPPH$^{\cdot}$ and β-carotene antioxidant protection factor) from cranberry pomace by SSF (28 °C, 16 d) using *Rhizopus oligosporus*.

Additionally, table 3 compile literature reports focused on the extraction of phenolic compounds with antioxidant and antibacterial properties, from agro-industrial by-products using fungal fermentation-assisted extraction

Table 3. Obtaining phenolic compounds from agro-industrial by-products through fungal fermentation-assisted extraction.
Tabla 3. Obtención de compuestos fenólicos de subproductos agroindustriales mediante extracción-asistida por fermentación fúngica.

Substrate	Fungi	Fermentation	Relevant results	Reference
Black rice bran	*Aspergillus awamori* and *Aspergillus oryzae*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▼ Total phenolic and anthocyanin content, in the order *A. awamori* > *A. oryzae* ▲ Total phenolic content obtained by decomposing anthocyanin content ▲ Protocatechuic, OH-benzoic, vanillic, caffeic, *p*-coumaric and ferulic acids ***'Fungal fermentation effect on bioactivity'*** ▲ DPPH$^{\cdot}$ radical-scavenging activity	Shin *et al*. (2019)
Peanut press cake	*Aspergillus awamori*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Total phenolic, flavonoid and tannin content ***'Fungal fermentation effect on bioactivity'*** ▲ ABTS$^{\cdot+}$ and DPPH$^{\cdot}$ radical-scavenging activity ▲ Metal chelating activity	Sadh *et al*. (2018)
Rice bran extract	*Aspergillus oryzae* and *Rhizopus oryzae*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Ferulic, caffeic, and protocatechuic acids, by *A. oryzae* ▲ Sinapic, vanillic, caffeic, syringic, protocatechuic, and 4-hydroxybenzoic acids, by *R. oryzae* ***'Fungal fermentation effect on bioactivity'*** ▲ FRAP, by both fungi ● DPPH$^{\cdot}$ radical-scavenging activity	Razak *et al*. (2017)
Corncob, pea pod, rice straw, sugarcane bagasse, and wheat straw	*Aspergillus terreus* and *Penicillium citrinum*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Total phenolic content, by both fungi ***'Fungal fermentation effect on bioactivity'*** ▲DPPH$^{\cdot}$ and NO$^{\cdot}$ radical-scavenging activity, by both fungi ▲ Fe^{2+} scavenging activity, by both fungi ▲ FRAP, by both fungi	Chandra and Arora (2016)
Plum fruit	*Aspergillus niger* and *Rhizopus oligosporus*	SSF	Plum pomace ***'Fungal fermentation effect on phenolic compounds'*** ▲ Total phenolic and flavonoid content, in a similar manner for both fungi ▲ Chlorogenic acid, isoquercetin, and rutin ▼ neochlorogenic acid, isorhamnetin-3-galactoside, Isorha-3-gluc, isorhamnetin-3-glucoside, cyaniding-3-glucoside, and cyaniding-3-rutinoside ● Quercetin-3-galactoside ***'Fungal fermentation effect on bioactivity'*** ▲ DPPH$^{\cdot}$ radical-scavenging activity, in a similar manner for both fungi Waste from plum brandy production ***'Fungal fermentation effect on phenolic compounds'*** ▲ Total phenolic and flavonoid content, in a similar manner for both fungi ▲ Neochlorogenic acid, chlorogenic acid, isoquercitrin, quercetin-3-galactoside, and rutin ▼ Isorhamnetin-3-galactoside ● Isorhamnetin-3-glucoside, and cyaniding-3-glucoside and cyaniding-3-rutinoside ***'Fungal fermentation effect on bioactivity'*** ▲ DPPH$^{\cdot}$ radical-scavenging activity, in a similar manner for both fungi	Dulf *et al*. (2016)

Substrate	Fungi	Fermentation	Relevant results	Reference
Apple pomace	*Rhizopus oryzae*	SSF and SCF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Fumaric acid production, by both culture methods	Das *et al*. (2015)
Orchid	*Fusarium avenaceum* and *Fusarium oxysporum*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Total phenolic content ***'Fungal fermentation effect on bioactivity'*** ▲ DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ radical-scavenging activity, as well as reducing power ▲ Inhibition of *Staphylococcus aureus* and *Bacillus subtilis* growth	Dong *et al*. (2015)
Peanut shell	*Inonotus obliquus*	SCF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Phenolic compounds such as epigallocatechin-3-gallate, epicatechin-3-gallate, phelligridin G, davallialactone, and inoscavin B ▼ Phenolic acid, including gallic and ferulic acids ***'Fungal fermentation effect on bioactivity'*** ▲ DPPH$^{\bullet}$ and $^{\bullet}$OH radical-scavenging activity	Xu *et al*. (2014)
Algae	*Candida utilis*	SCF	***'Fungal fermentation effect on bioactivity'*** ▲ Inhibition of methicillin-resistant *Staphylococcus aureus*	Eom *et al*. (2013)
Herbal residues	*Aspergillus oryzae*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Gallic acid formation ***'Fungal fermentation effect on bioactivity'*** ▲ DPPH$^{\bullet}$ radical-scavenging activity and reducing power ▲ Inhibition of *Bacillus cereus*, *Listeria monocytogenes*, *Staphylococcus aureus*, and *Escherichia coli*	Wen *et al*. (2013)
Sugarcane bagasse	*Inonotus obliquus*	SCF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Phenolic compounds such as epicatechin-3-gallate, epigallocatechin-3-gallate, and phelligridin G ***'Fungal fermentation effect on bioactivity'*** ▲ DPPH$^{\bullet}$ and $^{\bullet}$OH radical-scavenging activity	Zhu and Xu (2013)
Coffee silverskin and coffee grounds	*Aspergillus ustus*, *Aspergillus niger*, *Neurospora crassa*, and *Penicillium purpurogenum*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Total phenolic content	Machado *et al*. (2012)
Pineapple and guava	*Rhizopus oligosporus*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Total phenolic content ***'Fungal fermentation effect on bioactivity'*** ▼ DPPH$^{\bullet}$ radical-scavenging activity	Sousa and Correia (2012)
Corn cob	*Yarrowia lipolytica*	SCF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Ferulic acid production	Huang *et al*. (2011)
Cashew husk	*Aspergillus oryzae*	SSF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Gallic acid production	Lokeshwari and Reddy (2010)
Citrus peel	*Cordyceps sinensis*	SCF	▲ Total phenolic and flavonoids content ▲ ABTS$^{\bullet+}$ radical-scavenging activity	Choi *et al*. (2010)
Wheat bran	*Agrocybe chaxingu*, *Auricularia auricula-judae*, *Cordyceps militaris*, *Hericium erinaceus*, and *Pleurotus ostreatus*	SCF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Ferulic acid production, in the order *H. erinaceus* > *P. ostreatus* > *C. militaris*	Xie *et al*. 2010
Valonia acorns extract	*Aspergillus oryzae* and *Trichoderma reesei*	SCF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Ellagic acid production, in the order *A. oryzae* > *T. reesei*	Huang *et al*. (2007)
Shrimp and crab shell powder	*Monascus purpureus*	SCF	***'Fungal fermentation effect on bioactivity'*** ▲ Antimicrobial effect against *Bacillus subtilis*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Escherichia coli*	Wang *et al*. (2002)
Tannic acid	*Aspergillus awamori*	SCF	***'Fungal fermentation effect on phenolic compounds'*** ▲ Gallic acid production	Seth and Chand (2000)

(▲), significant increase with respect to the control group; (▼), significant reduction with respect to the control group; (●), without significant differences with respect to the control group.

(SSF and SCF). Mycelial growth during fungal fermentation depends on the nutrient supply (nitrogen, phosphorus and carbon) and any type of energy source or substrate, as well as substrate digestibility, which are essential for extraction of bioactive secondary metabolites (Hölker *et al*., 2004).

Likewise, an increase in enzyme production (lipases, xylanase, pectinase, proteases, cellulolytic, and ligninolytic enzymes) during fungal fermentation has been demonstrated (Hölker *et al*., 2004; Sadh *et al*., 2018). The enzymatic hydrolysis produced during fungal fermentation increase the extraction of phenolic compounds, such as *p*-coumaric, caffeic, chlorogenic, ferulic, protocatechuic, sinapic, syringic, and vanillic acids, quercetin, and rutin. Also, improve antioxidant activity like antiradical (DPPH$^{\bullet}$ and ABTS$^{\bullet+}$ activity), chelating metal properties, ferric reducing antioxidant power, and nitric oxide chelating properties. As well as antimicrobial activity by microbial growth and foodborne pathogens reduction (Hölker *et al*., 2004; Das *et al*., 2015; Dong *et al*., 2015; Dulf *et al*., 2016; Razak *et al*., 2017; Sadh *et al*., 2018; Shin *et al*., 2019). Thus, the enzymatic hydrolysis produced during fungal fermentation appears to be an attractive strategy to extract phenolic compounds with potential uses as food additives (Papaspyridi *et al*., 2012).

Phenolic Compounds as Possible Meat and Meat Product Additives

The NOM-213-SSA1-2002 define a 'food additive' as 'those substances, which added directly to food and beverages during their elaboration, provide or intensify aroma, color, and flavor, to improve stability and conservation'. Also, the FDA (2008) indicate that a 'Food Additive' is 'any substance that when use directly or indirectly, become a component or otherwise affect the characteristics of any food, including any substance intended for use in packaging, production, manufacturing, processing, preparation, treatment, transportation or storage of food; and including any source of radiation intended for such use'. The *Codex Alimentarius* (2017) defined it as 'any substance that, regardless of its nutritional value, is intentionally added to a food in controlled quantities for technological purposes'.

Moreover, in the meat and meat products industry, additives are widely employed for preservative purposes (i.e., as antioxidants and antimicrobials). An antioxidant additive, is defined as a 'substance added to foods to prevent the oxygen present in the air from causing undesirable changes in flavor and color' (USDA, 2015). In another context, an antimicrobial additive, is defined as 'a substance that meets the definition of food additive and is used to control microorganisms such as bacteria, viruses, fungi, among others, in food or food contact items' (FDA, 2008).

The following is a list of additives commonly used in meat and meat products as preservatives are: α-tocopherol (E307), acetic acid (E260), ascorbic acid (E300), citric acid (E330), erythorbic acid (E315), fumaric acid (E297), lactic acid (E270), sorbic acid (E200), tartaric acid (E334), sodium ascorbate (E301), calcium ascorbate (E302), sodium benzoate (E211), butylhydroxyanisole (E320), and butylhydroxytoluene (E321). Also, calcium carbonate (E170i), sodium citrate (E330), potassium citrate (E332), tricalcium citrate (E333iii), trisodium citrate (E331iii), isopropyl citrate (E384), sodium diacetate (E262ii), sodium erythorbate (E316), ethyl lauroyl arginate (E243), propyl gallate (E310), nitrite/sodium nitrate (E250 and E252), tert-butylhydroquinone (E319), potassium sorbate (E202), among others (NOM-122-SSA1-1994; FDA, 2004; European Commission, 2014; FAO, 2018). The preservative compounds mentioned above have phenolic groups in their structure, which in phenolic compounds (phenolic acid and flavonoids) are widely associated with their antioxidant and antimicrobial activity (Sova, 2012).

Moreover, extensive research has demonstrated that lipid oxidation and microbial growth, are the main factors involved in the quality loss of raw and cooked meat products. These factors lead to the formation of some compounds that affect sensory attributes, including changes in texture, odor, flavor, and color, which consequently have an adverse effect on meat acceptability and meat purchase intention (Faustmant *et al*., 2010; Aziz and Karboune, 2018). Therefore, there have been efforts to obtain antioxidant and antimicrobial compounds from natural sources, including agro-industrial by-products (Faustmant *et al*., 2010; Jiang and Xiong, 2016).

Table 4 shows the possible uses of phenolic compounds, obtained by SSF and SCF using agro-industrial residues as substrate, including as meat and meat product additives. In this context, it has been demonstrated that phenolic compounds and flavonoids can preserve raw and cooked meat and meat products from different species (beef, camel, chicken, and pork), against undesirable changes caused by lipid oxidation and microbial growth during refrigerated

Table 4. Uses of phenolic compounds as additives for meat and meat products.
Tabla 4. Usos de compuestos fenólicos como aditivos para carne y productos cárnicos.

As an antioxidant additive			
Phenolic compounds	**Conditions**	**Relevant results**	**References**
Flavonoids: catechin ***Phenolic acids***: tannic, caffeic, and gallic	***Product***: Minced camel meat ***Storage***: 4 °C for 9 days ***Addition level***: 200 ppm	▲ Inhibition of lipid oxidation (catechin 72.7%, as well as tannic 95.5%, caffeic 80%, and gallic acids 70% approximately) ▲ Red color, 1 point in sensory score for all phenolic compounds	Maqsoo *et al*. (2015)
Phenolic acids: caffeic, *t*-cinnamic, *p*-coumaric, ferulic, gallic, *p*-hydroxybenzoic, gentisic, sinapic, and syringic	***Product***: Beef ***Storage***: 4 °C for 6 days ***Addition level***: 0.05 mmol/kg	▲ Inhibition of lipid oxidation precooked beef in the order sinapic acid > caffeic acid > ferulic acid > gentisic acid > syringic acid > *t*-cinnamic acid > *p*-coumaric acid > *p*-hydroxybenzoic acid	Brettonnet *et al*. (2010)

Phenolic compounds	Conditions	Relevant results	References
Flavonoids: quercetin and rutin	***Product***: beef patties ***Storage***: 2 °C for 11 days ***Addition level***: 1 and 5 mM	▼ L* values in concentration dependence (quercetin 1.9%; rutin 3.0%) ▼ C values in concentration dependence (quercetin 12.3%; rutin 16.6%) ▲ h values in concentration dependence (quercetin 8.9%; rutin 16.4%) ▲ Inhibition of metmyoglobin formation in concentration dependence (quercetin 47.0% approximately; rutin 66.0% approximately) ▲ Inhibition of lipid oxidation in concentration dependence (quercetin 14.3%) ▼ Inhibition of lipid oxidation (rutin -23.8%)	Bekhit *et al*. (2004)
Flavonoids: quercetin	***Product***: cook-chill chicken ***Storage***: 5 °C for 5 days ***Addition level***: 1.6% and 3.0%	▲ Inhibition of lipid oxidation (83.9% and 97.3% in concentration dependence)	Karastogiannidou (1999)
Flavonoids: (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG), and (-)-epigallocatechin gallate (EGCG)	***Product***: ground white muscle of mackerel ***Storage***: cooked at 75 °C, 4 °C for 7 days ***Addition level***: EC and EGC (200 mg/kg). ECG and EGCG (300 mg/kg)	▲ Inhibition of lipid oxidation (EC 40.5%; EGC, ECG, and EGCG 65.5%)	He and Shahidi (1997)
Flavonoids: kaempferol, morin, myricetin, naringenin, naringin, quercetin, and rutin ***Phenolic acids***: gallic, caffeic, coumaric, ferulic, syringic, vanillic, sinapic, chlorogenic, and tannic	***Product***: cooked ground pork ***Storage***: 4 °C for 4 weeks ***Addition level***: 30 and 200 ppm	▲ Inhibition of lipid oxidation in concentration dependence Kaempferol (95.3%), morin (96.4%), myricetin (98.7%), naringenin (3.3%), naringin (2.3%), quercetin (98.9%), rutin (33.0%), as well as gallic (73.5%), caffeic (69.3%), coumaric (54.3%), ferulic (56.6%), syringic (55.3%), vanillic (23.6%), sinapic (38.5%), chlorogenic (35.0%), and tannic (98.9%) acids	Shahidi *et al*. (1993)
Flavonoids: kaempferol, morin, myricetin, naringenin, naringin, quercetin, and rutin ***Phenolic acids***: ellagic, gallic, vanillic, syringic, and tannic	***Product***: pork model system, cooked at 75 °C ***Storage***: 4 °C for 3 weeks ***Addition level***: 200 ppm	▲ Inhibition of lipid oxidation Kaempferol (41%), morin (30%), myricetin (1.0%), naringenin (4.7%), naringin (4.7%), quercetin (97%), and rutin (28.4%), as well as ellagic (99.0%), gallic (44.7%), vanillic (21.3%), syringic (39.6%), and tannic (57.0%) acids	Shahidi *et al*. (1992)
As an antimicrobial additive			
Phenolic compounds	**Conditions**	**Relevant results**	**References**
Flavonoids: catechin ***Phenolic acids***: tannic, caffeic, and gallic	***Product***: Minced camel meat ***Storage***: 4 °C for 9 days ***Addition level***: 200 ppm	▲ Inhibition of mesophilic bacteria count, 1 log approximately (catechin and tannic acids) ▲ Inhibition of psychrotrophic bacteria count, 1 log approximately (catechin, tannic, and gallic acids)	Maqsoo *et al*. (2015)
Flavonoids: rutin ***Phenolic acids:*** caffeic acid and *p*-coumaric	***Product***: chicken soup ***Storage***: 4 and 25 °C for 48 h ***Addition level***: 0.2 mg/mL	▲ Inhibition of *Staphylococcus aureus* growth (100% by all phenolic compounds)	Stojković *et al*. (2013)
Phenolic acids: benzoic	***Product***: Raw and cooked chicken meat ***Storage***: 4 and 20 °C for 14 days ***Addition level***: 5000 ppm	▲ Inhibition of *Listeria monocytogenes* and growth in raw and cooked meat (1.2 and 3.5 log, respectively) ▲ Inhibition of *Salmonella typhimurium* and growth in raw and cooked meat (1.2 log by both)	Ravichandran *et al*. (2011)
Flavonoids: Mixture of quercetin and rutin ***Phenolic acids***: Mixture of gallic and caffeic Mixture of gallic and protocatechuic	***Product***: meat model system ***Storage***: 4 °C for 24 h days ***Addition level***: 100 and 200 mg	▲ Inhibition of *Listeria monocytogenes* growth in concentration dependence (mixture quercetin and rutin 6.7 log; mixture gallic and caffeic acids 6.3 log; mixture gallic and protocatechuic acids 3.7 log)	Rodríguez-Vaquero *et al*. (2011)
Phenolic acids: carvacrol and thymol	***Product***: bovine meat stake ***Storage***: 7 °C for 96 h ***Addition level***: <1 µL/mL	▲ Inhibition of *Staphylococcus aureus* growth of carvacrol and thymol in combination with organic acids (lactic and acetic)	De Oliviera *et al*. (2010)
Flavonoids: Mixture of quercetin and rutin ***Phenolic acids***: Mixture of gallic and caffeic Mixture of gallic and protocatechuic	***Product***: meat model system ***Storage***: 20 °C for 14 days ***Addition level***: 100 and 200 mg	▲ Concentration- and temperature-dependent inhibition of *Escherichia coli* growth (mixture of quercetin and rutin 100%; mixture of gallic and caffeic acids 100%; mixture of gallic and protocatechuic acids 50% approximately)	Rodríguez-Vaquero *et al*. (2010)

(▲), significant increase with respect to the control group; (▼), significant reduction with respect to the control group.

storage (Stojković *et al*., 2013; Maqsoo *et al*., 2015). Furthermore, phenolic compounds can act through two pathways: (1) by breaking chain reactions triggered by free radicals, which implies hydrogen atom transfer (HAT), then electron transfer followed by a proton transfer mechanism (SET-PT) and sequential proton-loss electron-transfer (SPLET), and (2) by reducing metals such as copper (Cu^{2+}) and iron (Fe^{3+}) (Marković *et al*., 2012). Additionally, phenolic compounds can act against nucleic acid and protein synthesis and alter the components of cellular membranes (Cushnie and Lamb, 2005).

CONCLUSION

The agro-industrial by-products are an important source of phenolic compounds, including phenolic acids and flavonoids. The uses of agro-industrial residues as substrates (seeds, pulps, and peels) during fungal fermentation-assisted extraction (SSF and SCF), can be used as an alternative or complementary strategy to obtain phenolic compounds like rustic, conventional and unconventional extraction methods. These compounds could be use as antioxidant and antimicrobial additives to extend the shelf life of raw and cooked meat and meat products from different species (beef, camel, chicken, and pork) during refrigerated storage.

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