REVIEW

Functional Meat Products as Oxidative Stress Modulators: A Review

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ABSTRACT

High meat consumption has been associated with increased oxidative stress mainly due to the generation of oxidized compounds in the body, such as malondialdehyde, 4-hydroxy-nonenal, oxysterols, or protein carbonyls, which can induce oxidative damage. Meat products are excellent matrices for introducing different bioactive compounds, to obtain functional meat products aimed at minimizing the pro-oxidant effects associated with high meat consumption. Therefore, this review aims to summarize the concept and preparation of healthy and functional meat, which could benefit antioxidant status. Likewise, the key strategies regarding meat production and storage as well as ingredients used (e.g., minerals, polyphenols, fatty acids, walnuts) for developing these functional meats are detailed. Although most effort has been made to reduce the oxidation status of meat, newly emerging approaches also aim to improve the oxidation status of consumers of meat products. Thus, we will delve into the relation between functional meats and their health effects on consumers. In this review, animal trials and intervention studies are discussed, ascertaining the extent of functional meat products' properties (e.g., neutralizing reactive oxygen species formation and increasing the antioxidant response). The effects of functional meat products in the frame of diet–gene interactions are analyzed to *1*) discover target subjects that would benefit from their consumption, and *2*) understand the molecular mechanisms that ensure precision in the prevention and treatment of diseases, where high oxidative stress takes place. Long-term intervention-controlled studies, testing different types and amounts of functional meat, are also necessary to ascertain their positive impact on degenerative diseases. *Adv Nutr* 2021;12:1514–1539.

Keywords: functional meat, bioactive ingredients, metabolism, oxidation status, antioxidant mechanisms, animal trials, intervention studies, precision diet

Introduction

Although meat and meat products are essential foods for most populations worldwide, high meat and meat-product consumption can induce pro-oxidant status in consumers (1). These foods can be a source of oxidized compounds (given their highly perishable nature), which are generated during processing, storage, cooking, digestion, and metabolism (2). Therefore, high meat consumption increases the risk of developing diseases associated with oxidative stress such as obesity, type 2 diabetes mellitus (T2DM), colorectal cancer, and cardiovascular diseases (CVDs) (1–4).

Nonetheless, because the worldwide consumption of meat and meat products is very high, it seems plausible to use them as matrices to ensure adequate consumption of bioactive ingredients (5). Moreover, besides extending the meat product's shelf-life (by minimizing meat oxidation) and improving its composition (by incorporating antioxidant molecules), it might also benefit health by reducing the body's oxidative status (2, 6). There is increasing interest in the search for healthier foods that can provide benefits beyond the merely nutritional (5, 7, 8). In this review, we assess if designing and consuming functional meat products is a suitable strategy to improve meat composition and stability,

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Abbreviations used: AE, arylesterase; CAT, catalase; COX, cyclooxygenase; CVD, cardiovascular disease; CYP7A1, cytochrome P450 7A1; GPx, glutathione peroxidase; GSH, reduced glutathione; GSSG, oxidized glutathione; LPO, lipid peroxidation; LTB4, leukotriene B4; MDA, malondialdehyde; NAFLD, nonalcoholic fatty liver disease; Nrf2, nuclear factor E2-related factor 2; OVN, optimum vitamin nutrition; oxLDL, oxidized LDL; PON1, paraoxonase-1; ROS, reactive oxygen species; SOD, superoxide dismutase; T2DM, type 2 diabetes mellitus; TXB2, thromboxane B2; 4-HNE, 4-hydroxy-nonenal.

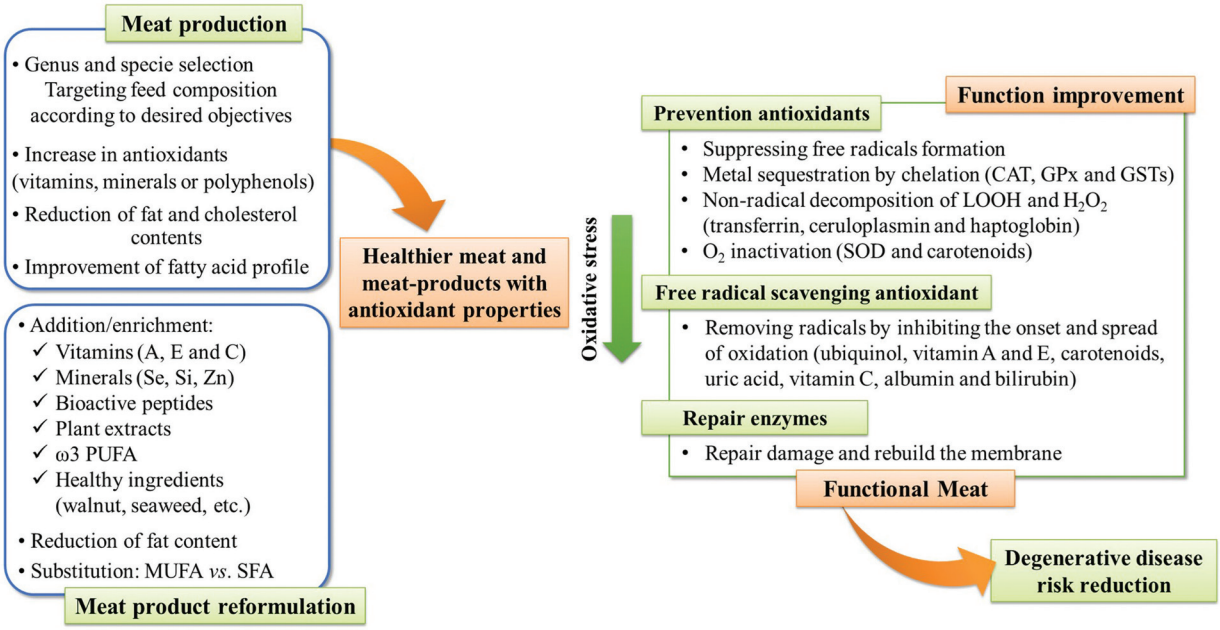

FIGURE 1 Strategies and possibilities for improving antioxidant properties of meat and the effects of its consumption on the antioxidant system. Strategies used for functional-meat development in the production stage (upper left box) and during processing (lower left box). Improvements obtained both in the final product and derived from its consumption in the body (right box). CAT, catalase; GPx, glutathione peroxidase; GST, glutathione *S*-transferase; LOOH, lipoperoxide; SOD, superoxide dismutase.

as well as to palliate the oxidative effects ascribed to the high consumption of different meat types.

Functional Foods

Due to the growing incidence and prevalence of chronic degenerative diseases, a new category of food, known as "functional foods," has arisen (8). According to Ashwell (9), "A food can be regarded as 'functional' if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease." A functional food must also remain a food and demonstrate its effects in quantities consistent with consumption, within the frame of a balanced diet (8, 10, 11). Currently, the term "nutraceutical" is widely used and can be defined as a nutritional complement or supplement of a concentrated bioactive natural substance presented in a nonfood matrix (pills, capsules, powder, etc.) (12).

The main strategies when designing functional foods include: *1*) increasing a component already present in the food, *2*) adding a component not present in the food, *3*) eliminating a harmful component of the food, *4*) substituting a harmful component for a healthier one, *5*) increasing the bioavailability of the ingredient or bioactive substance added, and *6*) mixing some or all of the previous strategies (5) (**Figure 1**).

Although there are several strategies to obtain functional meat, efforts have addressed modifying the lipid and fatty acid content and/or adding functional ingredients such as fiber, vegetable proteins, MUFAs or PUFAs, vitamins, minerals, and phytochemicals; even wholefoods such as walnuts or seaweed can be added (5, 7, 8, 13–16).

Functional Meat and Oxidative Stress

Meat is an excellent source of high biological value proteins, vitamins (thiamine, niacin, vitamins A, B-6, and B-12), and minerals (high bioavailability heme iron and zinc, phosphorus, selenium, sodium, potassium, and cobalt). However, meat can also contain potentially deleterious compounds such as SFAs and cholesterol (14, 17–20). In addition, undesirable compounds can originate during storage and cooking (**Table 1**), as well as during digestion and metabolism (21, 22). As shown, following a meat product–based meal, rich in lipids and proteins, increased susceptibility to bodily oxidative damage has been found (21, 23). Further, there is consensus on the rise in oxidation compounds found in plasma [e.g., malondialdehyde (MDA), advanced glycation end-products, 4-hydroxy-nonenal, oxysterols, or protein carbonyls] after the consumption of oxidized foods in both animals and humans (2). At a low pH in the presence of oxygen, the stomach increases lipid and protein oxidation by acting as a bioreactor. In vitro and in vivo studies have shown that greater MDA and hydroperoxide formation can occur as food passes through the stomach (22, 24, 25), along with the oxidation of other components such as vitamin E and β-carotenes (26). Due to the low pH of the stomach and presence of pepsin, myoglobin is denatured and hydrolyzed, releasing free heme iron, which can act as a pro-oxidant (21). After digestion, the oxidized lipids are absorbed and included in chylomicrons, increasing oxidative stress in different tissues, and activating an inflammatory response (27, 28). Regarding oxidized protein absorption, few studies have established a clear relation between these compounds' formation and meat digestion. It has been hypothesized that reactive oxygen species (ROS) and oxidized lipids

TABLE 1 Antioxidant effects of functional meat components on processing, storage, and cooking[1]

Bioactive ingredients and doses	Meat product	Storage and cooking conditions[2]	Antioxidant effects[3]	Reference
Vitamins				
α-Tocopherol (250 mg/kg)	Ground pork	Cooked (to an internal temperature of 70°C), storage (20 d) and frozen storage (6 mo)	↓ MDA, polar material, thermal oxidized compounds in both chilling and frozen storage	(16)
α-Tocopherol (200 mg/kg b.w.)	Breast nuggets (chicken)	Storage (45 d)	↓ MDA content	(29)
Vitamin E (200 IU vitamin E/kg feed)	Chicken	Fresh and frozen storage (3 mo); cooked fresh (85°C, 60 min) and frozen storage	↓ MDA content in all cases except in frozen storage; no differences in antioxidant capacity	(30)
α-Tocopherol acetate (100 and 200 mg/kg b.w.)	Chicken breast	Storage (8 d)	↓ MDA content	(31)
Vitamin E (155 IU/kg diet) and plant extracts rich in polyphenols (7 g/kg diet)	Beef steaks	Air packaging (4 d) ; modified atmosphere packaging (7 d) ; vacuum packaging (14 d)	↓ MDA content in all cases except in vacuum packaging when there were no significant differences ; no differences in total antioxidant status	(32)
α-Tocopherol acetate (15, 40, or 200 mg/kg b.w.)	Cooked meat and pork sausages	Heated (180°C, 20 min)	↓ MDA and hydroperoxides content in cooked meat inversely proportional to α-tocopherol acetate dose	(33)
		Boiled (80°C, 90 min)	No MDA and hydroperoxide formation in sausages; ↓ oxysterol formation with higher α-tocopherol acetate concentration in both groups	
α-Tocopherol acetate (75, 150, and 225 mg/kg b.w.)	Raw and cooked chicken	Cooked (80°C) and frozen storage	↓ Lipid hydroperoxides in raw meat; ↓ lipid hydroperoxides and MDA content in cooked chicken	(34)
α-Tocopherol acetate (10 and 400 mg/kg feed)	Cured pork sausages	Storage (8 wk). Vacuum, N_2/CO_2 and air	No differences in MDA content and antioxidant capacity	(35)
α-Tocopherol acetate (200 mg/kg product)	Raw and cooked chicken sausages	Storage (7 d)	No significant difference in MDA content in raw and cooked sausages	(36)
α-Tocopherol acetate (364 ppm feed)	Salami-type sausages (pork)	Storage (8 wk)	↓ MDA content	(37)
α-Tocopherol oil (115 mg/kg product)	Fresh pork sausages	Storage (20 d)	↓ MDA content; no differences in sausage shelf-life	(38)
α-Tocopherol oil (60 mg/kg product)	Beef burgers	Frozen storage (180 d)	↓ Peroxides and MDA content, but ↑ conjugated dienes	(39)
α-Tocopherol acetate (70 and 140 mg/kg b.w.)	Cooked chicken	Cooked (85°C, to an internal temperature of 80°C) and frozen storage (15 d and 5 mo)	No differences in MDA content	(40)
Ascorbic acid (0.05%)	Chicken nuggets	Storage (15 d) of raw and deep fried (190°C, 5 min)	↓ Conjugated dienes, MDA content, and peroxide values	(41)
Ascorbic acid (0.1 g/100 g meat)	Rabbit burgers	Storage (7 d)	↑ MDA content, ABTS, DPPH, and FRAP activities	(42)
Ascorbic acid (500 ppm)	Beef patties	Storage (20 d) in modified atmosphere (70% O_2 + 20% CO_2 + 10% N_2)	↓ Metmyoglobin formation	(43)

(*Continued*)

TABLE 1 (*Continued*)

Bioactive ingredients and doses	Meat product	Storage and cooking conditions[2]	Antioxidant effects[3]	Reference
Ascorbic acid (550 ppm)	Pork patties	Storage (7 d)	↓ MDA content	(44)
Ascorbic acid (100 ppm)	Pork patties	Fresh and frozen storage (8 d)	↑ MDA content in fresh and frozen pork patties; no differences in protein oxidation	(45)
Ascorbic acid (50, 100, 150, and 200 ppm)	Pork patties	Fresh, cooked (70°C, 40 min) and stored	↑ MDA content in both fresh and cooked samples	(45)
Minerals				
Sodium selenite; SeS, selenomethionine; Met-Se or nano-Se (0.3, 0.45, and 0.6 mg Se/kg)	Ross broiler chickens	Frozen storage (4 wk)	↓ MDA content and higher ABTS, DPPH, and FRAP activities with Met-Se and nano-Se (0.45 to 0.6 mg/kg) vs. SeS	(46)
Sodium selenite (50 mg/kg feed) and organic selenium (50 mg/kg feed)	Broiler chickens	Frozen storage (90 d)	↓ Protein carbonyl and MDA content; ↑ total antioxidant capacity (DPPH, ABTS, and FRAP)	(47)
Selenium (0.2 mg/kg feed)	Chicken	Fresh and frozen storage (3 mo); cooked fresh and cooked frozen (85°C for 60 min)	No effects on MDA content ; no differences in antioxidant capacity	(30)
Selenium + vitamin E (0.2 mg Se + 200 IU vitamin E/kg feed)	Chicken	Fresh and frozen storage (3 mo); cooked fresh (85°C for 60 min) and cooked frozen	↓ MDA content in except in frozen storage; no differences in antioxidant capacity	(30)
Zinc (200 mg/kg b.w.)	Cooked chicken	Cooked (85°C, to an internal temperature of 80°C) and frozen storage (15 d and 5 mo)	No differences in MDA content	(40)
Bioactive peptides				
Caseinophosphopeptides (0.5%)	Ground beef	Cooked (75°C) and storage (4 d)	↓ MDA content	(48)
Whey and soy protein hydrolysates (2%)	Pork patties	Cooked (70°C) and storage (7 d)	↓ Conjugated dienes and MDA contents in all samples	(49)
Protein hydrolysates from European eel (0.5 and 1% w/w)	Beef patties	Storage (11 d)	↓ MDA content	(50)
Peptides from raho fish (*Labeo rohita*) (0, 50, 100, 150, 200, and 250 mg/kg feed)	Raw chicken breast	Frozen storage for raw breast (6 mo)	↑ DPPH and FRAP activities (dose-dependent manner); ↓ peroxides and MDA content (dose-dependent manner)	(51)
Plant origin ingredients				
Liposterine (carob fruit extract; 3%)	Ground pork	Cooked (internal temperature of 70°C), storage (20 d) and frozen storage (6 mo)	↓ MDA, polar material, thermal oxidized, but ↑ hydrolytic compounds in chilling storage; ↓ MDA, polar material, thermal oxidized, but ↑ hydrolytic compounds in frozen storage	(16)
Exxenterol (carob fruit extract; 3%)	Ground pork	Cooked (internal temperature of 70°C), storage (20 d), and frozen storage (6 mo)	↓ MDA, polar material, thermal oxidized, but ↑ hydrolytic compounds in chilling storage; ↓ MDA, polar material, thermal oxidized compounds in frozen storage	(16)
Rosemary extract (260 mg/kg of product)	Fresh pork sausages	Storage (20 d)	↓ MDA content; ↑shelf-life	(38)
Rosemary extract (200 mg/kg of product)	Beef burgers	Frozen storage (180 d)	↓ Peroxides, conjugated dienes, and MDA contents	(39)
Artemisia prínceps extract (0.2%)	Raw and cooked chicken nuggets	Raw and deep fried (190°C, 5 min) chicken nuggets storage (15 d)	↓ Conjugated diene formation; ↓ MDA content only in raw chicken nuggets; ↑ peroxide values in raw chicken nuggets but lower in deep-fried chicken nuggets	(41)

(*Continued*)

TABLE 1 (*Continued*)

Bioactive ingredients and doses	Meat product	Storage and cooking conditions[2]	Antioxidant effects[3]	Reference
Turmeric powder (3.5 g/100 g meat)	Rabbit burgers	Storage (7 d)	↑ MDA content, ABTS, DPPH, and FRAP activities	(42)
Rosemary powder (1000 ppm)	Beef patties	Storage (20 d) in modified atmosphere (70% O_2 + 20% CO_2 + 10% N_2)	↓ MDA content	(43)
Se yeast (2 g/kg), linseed:algae (3:2) emulsion (62.5 g/kg), and lyophilized water extract of *Melissa officinalis* (686 mg/kg)	Dry fermented sausages (pork)	Storage (30 d)	No differences in MDA and volatile aldehydes	(52)
Green banana flour (*Musa paradisiaca*; 3, 4, and 5%) and soybean hulls flour (*Glycine max*; 3, 4, and5%)	Chicken meat nuggets	Storage (25 d)	↓ MDA content	(53)
Oat flour (8%), casein (2.5%), and refined wheat flour (7%)	Chicken kofta	Cooked (80°C, 30 min) and storage (15 d)	↓ MDA content	(54)
Guava powder (*Psidium guajava*; 0.5 and 1%)	Sheep meat nuggets	Cooked (90°C, 35 min) and storage (15 d)	↓ MDA content	(55)
Citrus fiber (0.5, 1, 1.5, and 2%)	Bologna sausage (beef)	Storage (28 d)	↓ MDA content in a dose-dependent manner under lighting conditions; only doses 1.5% and 2% revealed a decrease in MDA content in darkness conditions	(56)
Rosemary extract (200 ppm)	Precooked pork patties	Storage (10 d)	↓ MDA and hexanal contents	(57)
Green tea extract (200 ppm)	Precooked pork patties	Storage (10 d)	↓ MDA and hexanal contents	(57)
Coffee extract (50 ppm)	Precooked pork patties	Storage (10 d)	No differences in MDA and hexanal content	(57)
Grape skin extract (200 ppm)	Precooked pork patties	Storage (10 d)	↓ MDA and hexanal content	(57)
Rosemary extract (100 ppm)	Pork patties	Fresh and frozen storage (8 d)	↓ MDA content in fresh and frozen patties; ↓ protein oxidation in frozen samples	(45)
Rosemary extract (50, 100, 150, and 200 ppm)	Pork patties	Cooked (70°C, 40 min) and storage (4 d)	↓ MDA content in both fresh and cooked samples	(45)
Green tea extract (100 ppm)	Pork patties	Fresh and frozen storage (8 d)	↓ MDA content in fresh and frozen patties; ↓ protein oxidation in frozen samples	(45)
Green tea extract (50, 100, 150, and 200 ppm)	Pork patties	Cooked (70°C, 40 min) and storage (4 d)	↓ MDA content in both fresh and cooked samples	(45)
Phenolic-rich avocado extract (*Persea americana*; ~600 GAE/kg patty)	Emulsified porcine patties	Raw (frozen storage, 4 wk), cooked (170°C for 18 min), and cooked and chilled (170°C, 18 min; and storage 15 d)	No differences in cholesterol oxidation products in raw samples, but ↓ hexanal content	(58)
			↓ cholesterol oxidation products and MDA content in cooked and cooked/chilled samples, but no differences in hexanal and protein carbonyls	
Ginkgo extract (*Ginkgo biloba*; 500 ppm)—different solvents	Meatballs	Cooked (72°C, 20 min) and storage (21 d)	↓ Peroxides, aldehydes, and MDA content; trend to decrease cholesterol oxidation products	(59)
Arbutus berries (*Arbutus unedo*, 3%)	Pork burger patties	Cooked (170°C, 18 min) and storage (12 d)	↓ Protein carbonyls	(60)
Common hawthorn (*Crataegus monogyna*, 3%)	Pork burger patties	Cooked (170°C, 18 min) and storage (12 d)	↓ Protein carbonyls	(60)

(*Continued*)

TABLE 1 (*Continued*)

Bioactive ingredients and doses	Meat product	Storage and cooking conditions[2]	Antioxidant effects[3]	Reference
Dog rose (*Rosa canina*, 3%)	Pork burger patties	Cooked (170°C, 18 min) and storage (12 d)	↓ Protein carbonyls	(60)
Elm-leaf blackberries (*Rubus ulmifolius*, 3%)	Pork burger patties	Cooked (170°C, 18 min) and storage (12 d)	↓ Protein carbonyls	(60)
Quercetin (230 mg/kg)	Pork burger patties	Cooked (170°C, 18 min) and storage (12 d)	↓ Protein carbonyls	(60)
Haematoccocus pluvialis extract (0.15, 0.3, or 0.45 g/kg meat)	Raw ground pork meat	Storage (7 d)	↓ MDA content in a dose-dependent manner	(61)
Hypericum perforatum. extract (5 and 10 mg/kg)	Enriched ω-3 PUFA pork meat	Storage (19 d)	↓ Polar compounds, oxidized TG, and MDA content, and higher antioxidant activity in both concentrations	(62)
Flaxseed meal (100 g/kg feed)	Broiler chicken meat	Storage (30 d)	↓ Antioxidant activity; ↑ peroxide and MDA content	(63)
Flaxseed meal (100 g/kg feed) + turmeric rhizome powder (5.0, 7.5, 10.0, and 12.5 g/kg)	Broiler chicken meat	Storage (30 d)	↑ Antioxidant activity only in the highest doses (10 and 12.5 g/kg); ↑ peroxides and MDA contents in low doses (5 and 7.5 g/kg), but ↓ in high doses (10 and 12.5 g/kg)	(63)
Guar-xanthan gum mix (0.5, 1, and 1.5%)	Low-fat meat emulsions	Boiled (85°C, 30 min)	↓ Metmyoglobin, MDA, carbonyl, and sulfhydryl contents in a dose-dependent manner	(64)
Konjac (*Amorphophallus konjac*) gel (5.2, 10.5, and 13.5%)	Modified pork patties	Storage (9 d)	↓ MDA content dose-dependent manner	(65)
Konjac (*Amorphophallus konjac*) gel (20%)	PUFA-enriched pork frankfurters	Storage (40 d)	No differences in MDA content	(66)
Walnuts				
Walnut (20%)	Restructured beef steaks	Cooked. Conventional oven (170°C, 15 min); microwave oven (700 W, 2.5 min, followed by 2.5 min at 300 W); electric grill (210°C, 3 min); pan-frying (170°C, 5 min)	↑ MDA content in all cooking procedures	(67)
Seaweed				
Sea spaghetti (*Himanthalia elongata*; 5.6%)	Meat emulsion	Meat emulsion process (70°C, 30 min)	↑ FRAP antioxidant capacity	(68)
Wakame (*Undaria pinnatifida*; 5.6%)	Meat emulsion	Meat emulsion process (70°C, 30 min)	↑ FRAP antioxidant capacity	(68)
Nori (*Porphyra umbilicalis*; 5.6%)	Meat emulsion	Meat emulsion process (70°C, 30 min)	↑ FRAP antioxidant capacity	(68)
Fats				
Ethyl cellulose oleogel (660 mg)	Pork burgers	Cooked (180°C, 4 min) and storage (6 d)	↑ MDA content in cooked samples and also after stored	(69)
Ethyl cellulose (660 mg) oleogel with curcumin (12 mg)	Pork burgers	Cooked (180°C, 4 min) and storage (6 d)	↓ MDA content in cooked samples but ↑ in stored samples	(69)
Beeswax oleogel (660 mg)	Pork burgers	Cooked (180°C, 4 min) and storage (6 d)	↑ MDA content in cooked samples and also after stored	(69)

(*Continued*)

TABLE 1 (*Continued*)

Bioactive ingredients and doses	Meat product	Storage and cooking conditions[2]	Antioxidant effects[3]	Reference
Beeswax oleogel (660 mg) with curcumin (12.8 mg)	Pork burgers	Cooked (180°C, 4 min) and storage (6 d)	↓ MDA content in cooked samples; no differences in MDA values in stored samples	(69)
Hydroxytyrosol in a gelled double emulsion	Pork patties	Storage (14 d)	↑ Hydroperoxides and MDA content	(70)
Ethyl cellulose (11 g/100 g oleogel) as a substitute partial/total for animal fat	Pork pâté	Storage (60 d)	No differences in MDA content	(71)
Beeswax (11 g/100 g oleogel) as a substitute partial/total for animal fat	Pork pâté	Storage (60 d)	No differences in partial substitution samples, but ↑ MDA content in samples with total animal fat substitution	(71)
Olive and chia oils (80:20) as pork fat replacers	Dry fermented sausages (pork)	Storage (30 d)	↑ MDA content and volatile compounds (hexanal, heptanal, octanal, and nonanal)	(72)
Low fat (2.0% fat) and medium fat (13.0% fat)	Restructured beef steaks	Cooked. Conventional oven (170°C, 15 min); microwave oven (700 W, 2.5 min, followed by 2.5 min at 300 W); electric grill (210°C, 3 min); pan-frying (170°C, 5 min)	↑ MDA content in low fat after cooking with microwave oven and electric grill, but ↓ in a conventional oven vs. medium fat; no differences in MDA content between low fat and medium fat in raw and pan-fried samples	(67)
Perilla oil as a substitute for animal fat (8.4%)	Pork frankfurter-type sausages	Frankfurters formulation process	↑ MDA content	(73)

[1] ↑ or ↓ indicates significantly more or less than control meat, respectively. ABTS, 2,2′-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid; b.w., body weight; DPPH, 2,2-diphenyl-1-picrylhydrazyl; FRAP, ferric reducing antioxidant power; GAE, gallic acid equivalents; MDA, malondialdehyde; Met-se, selenomethionine; TG, triglycerides.
[2] Storage refers to temperatures from 2 to 4°C whereas frozen storage is from −18 to −20°C.
[3] Functional meat vs. control comparison.

generated during digestion might also contribute to meat protein oxidation (21). Therefore, it seems plausible to design functional meat that minimizes oxidative processes at all possible stages (Figure 1).

Meat from animals fed optimum vitamin nutrition (OVN) has been proposed as a functional meat type (74). Besides guaranteeing the vitamin quantity required by livestock to have an adequate state of health and optimal development (74), OVN meat would also guarantee an increased amount of vitamins and bioavailability within the consumer, resulting in improved health status. However, evidence concerning OVN meat is rather limited. In these sections, meat and meat products, modified with additional functional ingredients aimed at reducing oxidative processes during production and storage, will be reviewed and discussed.

Vitamins

Although meat is a naturally excellent source of A- and B-group vitamins, some meat products have been enriched with supplemental vitamins to produce more stable and healthier formulations (5). The most common strategies when fortifying meat have been based on fortifying animal feed with vitamins to produce meat with higher concentrations of these vitamins (5, 75).

Retinol equivalents and other carotenoids.

The antioxidant activity of retinol and carotenoids is due to the long hydrophobic chain in their structure, which can interact with peroxyl radicals and stop lipid peroxidation (LPO), eliminating singlet oxygen and glutathione radicals (76). Vitamin A has been shown to play an important role in meat oxidative stability by protecting PUFAs from oxidation (7), thus the meat industry frequently fortifies animal feed with β-carotenes (77–79). However, this strategy is not employed to enrich meat with vitamin A, because meat already contains "optimal" concentrations of this micronutrient. Moreover, the European Food Safety Authority takes no antioxidant-vitamin A health claims into consideration (80).

Tocols.

Vitamin E includes a group of 4 tocopherols (α, β, δ, γ) and 4 tocotrienols (α, β, δ, γ) with vitamin E activity, among which α-tocopherol stands out. The α-tocopherol blocks LPO by donating a hydrogen from the hydroxyl group of its chromanol head to the peroxy lipid radical, and by eliminating ROS (**Figure 2**). Vitamin E accumulates in cell membranes protecting against free radicals in vivo. Therefore, the food industry has developed functional meat products enriched in vitamin E, supplementing animal feed with α-tocopherol acetate (81). Adding the acetate group protects the α-tocopherol from oxidation; a linear increase of vitamin E concentration can be shown in muscle after adding 5–95 mg/kg to the feed (81). In recent years, dietary supplementation with α-tocopherol has transformed meat and meat products into a major source of vitamin E (7).

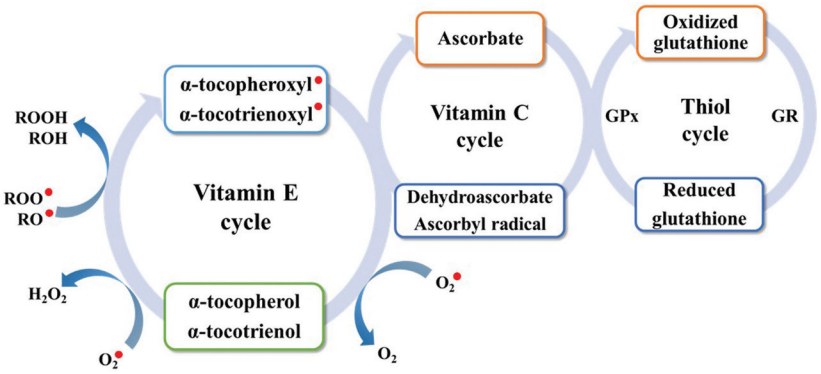

FIGURE 2 Mechanisms of ROS elimination and oxidized vitamin regeneration. Vitamin E, vitamin C, and the thiol cycle form a complex antioxidant network to maintain an adequate redox balance. α-Tocopherol is a powerful antioxidant capable of donating a hydroxyl and reducing potentially toxic oxidation compounds, resulting in its oxidized forms (α-tocopheroxyl and α-tocotrienoxyl). Vitamin C can be oxidized to ascorbate and help regenerate α-tocopherol. Likewise, ascorbate can be reduced by GPx action, giving rise to the antioxidant form of vitamin C and oxidized glutathione, which is eliminated by other systems. GPx, glutathione peroxidase; GR, glutathione reductase; RO•, alkoxy radical; ROH, alcohol; ROO•, peroxyl radical; ROOH, hydroperoxide; ROS, reactive oxygen species.

Some authors, after supplementing chicken feed with α-tocopherol, found a higher muscle vitamin E concentration compared with the controls, giving rise to lower oxysterol, MDA, and TBARS production during storage and cooking (29, 30, 31–34, 82, 83). Likewise, vitamin E supplementation combined with polyphenols also appears to be effective (84, 85). This last study (85) revealed an increase in antioxidant activity in meat, and drip loss reduction, and improvement of the meat's water retention capacity, suggesting better meat quality. These results suggest that cell membranes containing high tocopherol concentrations are more resistant to lipid oxidation. This would also contribute to maintaining meat quality by reducing myoglobin oxidation and inhibiting PUFA oxidation (86).

Table 1 summarizes the effects of vitamin addition in meat. Greater stability in vitamin E–enriched sausages, with a slight decrease of α-tocopherol, during storage and cooking has been reported (35, 36, 87, 88). However, vitamin E losses were greater after 6 wk of storage when sausages were formulated with a lower nitrite concentration (37). In contrast, the results regarding the LPO of vitamin E–enriched meat products are contradictory (35–40), because tocopherol addition to processed meats did not effectively delay lipid oxidation due to the difficulty of distributing the antioxidants in the food homogeneously, especially in nonground meat (79). Unfortunately, to the best of our knowledge, the antioxidant impact of vitamin E–enriched meat on consumer antioxidant status has scarcely been tested (**Table 2**).

Vitamin C.

Another vitamin that protects biological systems against oxidative damage is vitamin C because it can donate a hydrogen atom and form a relatively stable ascorbyl free radical, thus protecting biological systems against oxidative damage (76). Given its solubility, it can act both inside and outside cells by removing hydroxyl and superoxide radicals, while minimizing lipid peroxide formation. Vitamin C also plays an important role in α-tocopherol regeneration by reducing the tocopheroxyl radicals produced (Figure 2) (89). Interestingly, in the presence of redox-active ions such as iron or copper, vitamin C in large amounts can act as a pro-oxidant, contributing to hydroxyl radical formation and lipid, DNA, or protein oxidation (86, 90).

Unlike vitamins A and E, vitamin C is frequently added to a greater extent to meat products (81). This strategy prevents and reduces oxidation and discoloration (metmyoglobin formation) during storage and cooking, especially in ground meat, which increases consumer acceptance of the meat (Table 1) (41–44, 91). Intravenous vitamin C infusion, immediately before slaughter, has been proposed as an effective means of increasing skeletal muscle ascorbic acid concentrations (92). Meat with higher vitamin C concentrations has greater oxymyoglobin and lipid stability, which results in less discoloration and rancidity. However, no information is available on the functional effects of vitamin C–enriched meat products.

Minerals

Minerals are essential micronutrients that participate and regulate several bodily functions (93). Some minerals such as copper, magnesium, selenium, silicon, and zinc have antioxidant properties and can be a good nutritional alternative to develop functional meat (94).

Selenium.

Selenium is a trace mineral that acts in neutralizing and eliminating a body's reactive species (95). It is a component of certain enzymes such as selenoproteins, among which glutathione peroxidase (GPx) stands out.

TABLE 2 Selected in vivo studies of effects of functional-meat consumption on oxidative stress[1]

Meat product	Bioactive ingredient	Amount of meat in the diet	Study design	Subjects	Biomarkers	Results	Reference(s)
Animal studies							
Restructured pork	Nori (5.6%)	15% of RM in NC diet	Longitudinal, parallel, 5 wk	Wistar rats (10 FM vs. 10 CM)	AE activity	↑ AE activity	(96)
					Liver SOD, CAT, GR, GPx activities and expression	↑SOD and ↑GPx activities	(97)
					Liver redox index	↑ SOD, ↑CAT and ↑ GPx expression	
					Liver TBARS	Non-significant differences	
Restructured pork	Nori (5.6%)	15% of RM in HC diet	Longitudinal, parallel, 5 wk	Wistar rats (10 FM vs. 10 CM)	AE activity	↓ AE activity	(96)
					Liver SOD, CAT, GR, GPx activities and expression	↑ GR activity	(97)
					Liver redox index	↑ SOD, ↑ GR, ↓ CAT, ↓ GPx expression	
					Liver TBARS	Non-significant differences	
Restructured pork	Wakame (5.6%)	15% of RM in NC diet	Longitudinal, parallel, 5 wk	Wistar rats (10 FM vs. 10 CM)	AE activity	↑ AE activity	(96)
					Liver SOD, CAT, GR, GPx activities and expression	↑ GR activity	(97)
					Liver redox index	↑ GPx, ↑ GR, ↓ GPx expression	
					Liver TBARS	↑ GSH concentration and ↓ redox index	
Restructured pork	Wakame (5.6%)	15% of RM in HC diet	Longitudinal, parallel, 5 wk	Wistar rats (10 FM vs. 10 CM)	AE activity	Non-significant differences	(96)
					Liver SOD, CAT, GR, GPx activities and expression	↑ GR, ↓ SOD activities	(97)
					Liver redox index	↑ SOD, ↑ GR and ↓GPx expression	
					Liver TBARS	↑ GSH concentration and ↓ redox index	
Restructured pork	Sea spaghetti (5.6%)	15% of RM in NC diet	Longitudinal, parallel, 5 wk	Wistar rats (10 FM vs. 10 CM)	Liver SOD, CAT, GR, GPx activities and expression	↑ GR activity	(98)
					Liver redox index	↓ GSSG concentration and ↓ redox index	
					Liver TBARS	↑ SOD, ↑ GPx and ↓ GR expression	
					AE activity	↑ AE activity	(99)

(*Continued*)

TABLE 2 (*Continued*)

Meat product	Bioactive ingredient	Amount of meat in the diet	Study design	Subjects	Biomarkers	Results	Reference(s)
Restructured pork	Sea spaghetti (5.6%)	15% of RM in HC diet	Longitudinal, parallel, 5 wk	Wistar rats (10 FM vs. 10 CM)	Liver SOD, CAT, GR, GPx activities and expression	↓ CAT, SOD and ↑ GR expression	(98)
					Liver redox index	Non-significant differences	
					Liver TBARS	Non-significant differences	
					AE activity	↓ AE activity	(99)
Restructured pork	Glucomannan (2.25%)	15% of RM in NC diet	Longitudinal, parallel, 7 wk	12 Zucker fa/fa rats (6 FM vs. 6 CM)	Liver SOD, CAT, GR, GPx levels, expression and activities	↓ SOD and ↓ CAT expression	(100)
					Liver redox index	↓ SOD, ↓ CAT and ↓ GR levels	
Restructured pork	Glucomannan (2.25%)	15% of RM in HC diet	Longitudinal, parallel, 7 wk	12 Zucker fa/fa rats (6 FM vs. 6 CM)	Liver SOD, CAT, GR, GPx levels, expression, and activities	↓ SOD expression	(100)
					Liver redox index	↑ CAT levels	
Restructured pork	Glucomannan + spirulina (2.25% + 0.3%, respectively)	15% of RM in NC diet	Longitudinal, parallel, 7 wk	12 Zucker fa/fa rats (6 FM vs. 6 CM)	Liver SOD, CAT, GR, GPx levels, expression, and activities	↓ SOD and ↓ CAT expression	(100)
					Liver redox index	↓ SOD, ↓GPx and ↓ GR levels	
Restructured pork	Glucomannan + spirulina (2.25% + 0.3%, respectively)	15% of RM in HC diet	Longitudinal, parallel, 7 wk	12 Zucker fa/fa rats (6 FM vs. 6 CM)	Liver SOD, CAT, GR, GPx levels, expression, and activities	↓ SOD, ↓ GR and ↓ GPx expression	(100)
					Liver redox index	Non-significant differences	
Restructured pork	Chia oil (1.52%)	21.7% of RM in HC diet	Longitudinal, parallel	16 Wistar rats (1 y old) (8 FM vs. 8 CM)	Liver SOD, CAT, GR, GPx activities, levels, and expression	↑ CAT and GR and Nrf2 expression	(101)
					Liver eNOS and iNOS levels and expression	↑ CAT and ↓SOD and GPx levels	
					Liver Nrf2 expression	↑ Nrf2 expression	
					Liver GSH/GSSG ratio and TBARS	↓ GSSG, GSH/GSSG ratio, and TBARS levels	
Restructured pork	Hydroxytyrosol (0.36%)	21.7% of RM in HC diet	Longitudinal, parallel	16 Wistar rats (1 y old) (8 FM vs. 8 CM)	Liver SOD, CAT, GR, GPx activities, levels, and expression	↑ CAT and GR and ↓ SOD and GPx	(102)
					Liver GSH/GSSG ratio and TBARS	↓ GSSG, GSH/GSSG ratio, and TBARS levels	
					Liver eNOS and iNOS levels and expression	↑ SOD and ↓ eNOS activities	(101)
					Liver Nrf2 expression	Non-significant differences	

(*Continued*)

TABLE 2 (*Continued*)

Meat product	Bioactive ingredient	Amount of meat in the diet	Study design	Subjects	Biomarkers	Results	Reference(s)
Restructured beef/pork (1:1)	Carob fruit extract (0.4%)	30% of RM in NC diet	Longitudinal, parallel, 8 wk	16 Wistar rats (early stage T2DM) (8 FM vs. 8 CM)	Plasma and liver AE activity	↓ Plasma AE activity	(103)
					oxVLDL and liver TBARS	↑ Liver AE activity	
Restructured beef/pork (1:1)	Carob fruit extract (0.4%)	30% of RM in HC diet	Longitudinal, parallel, 8 wk	24 Wistar rats (late-stage T2DM) (16 FM vs. 8 CM)	Plasma and liver AE activity	↑ AE activity	(104)
					oxVLDL and liver TBARS	↓ oxVLDL and liver-ox	
Sausages	Anthocyanins (0.11%)	66.6% of sausages	Longitudinal, parallel, 20 wk	30 Fischer-344 rats (10 FM vs. 10 CM)	Plasma FRAP	↑ Plasma FRAP	(105)
Cured pork	Pomegranate extract (0.6% w/w)	50% of meat product	Longitudinal, parallel, 100 d	36 Fischer-344 rats (10 FM vs. 26 CM)	Fecal water TBARS	↓ TBARS	(106)
					Urinary DHN-MA	↓ Urinary DHN-MA	
Cured pork	Red wine extract (2% w/w)	50% of meat product	Longitudinal, parallel, 100 d	36 Fischer-344 rats (10 FM vs. 26 CM)	Fecal water TBARS	↓ TBARS	(106)
					Urinary DHN-MA	↓ Urinary DHN-MA	
Cured pork	White grape extracts (0.055% w/w)	50% of meat product	Longitudinal, parallel, 100 d	36 Fischer-344 rats (10 FM vs. 26 CM)	Fecal water TBARS	↓ TBARS	(106)
					Urinary DHN-MA	Non-significant differences	
Cured pork	Rosemary extract (0.66% w/w)	50% of meat product	Longitudinal, parallel, 100 d	36 Fischer-344 rats (10 FM vs. 26 CM)	Fecal water TBARS	↓ TBARS	(106)
					Urinary DHN-MA	Non-significant differences	
Cured pork	Carnosic acid (1% w/w)	50% of meat product	Longitudinal, parallel, 100 d	36 Fischer-344 rats (10 FM vs. 26 CM)	Fecal water TBARS	↓ Urinary DHN-MA	(106)
					Urinary DHN-MA	Non-significant differences	
Cured pork	Green tea extract (0.08% w/w)	50% of meat product	Longitudinal, parallel, 100 d	36 Fischer-344 rats (10 FM vs. 26 CM)	Fecal water TBARS	↓ TBARS	(106)
					Urinary DHN-MA	↓ Urinary DHN-MA	
Restructured pork	Silicon (0.13%)	21.7% of RM in HC diet	Longitudinal, parallel	16 Wistar rats (1 y old) (8 FM vs. 8 CM)	Plasma and liver AE activity, oxVLDL levels (TBARS and conjugated dienes)	↑ Liver AE and ↓ oxVLDL	(107)
					Liver SOD, CAT and GR, GPx activities, levels, and expression	↑ CAT and GR and ↓ SOD and GPx levels	(102)
					Liver GSH/GSSG ratio	↓ GSSG and GSH/GSSG ratio ↑ SOD and Nrf2 expression	
Human studies							
Beef burger	Wine grape pomace flour (7%)	1 burger per day	Crossover trial (vs. CM), 12 wk	27 males with components of MS	Plasma vitamin C, tocopherol, and uric acid	↑ Vitamin C and ↓ uric acid	(108)
					Plasma AOPPs and oxLDL	↓ AOPPs and ↓ oxLDL	
					Plasma DPPH, TRAP, and MDA	↓ DPPH	

(*Continued*)

TABLE 2 (*Continued*)

Meat product	Bioactive ingredient	Amount of meat in the diet	Study design	Subjects	Biomarkers	Results	Reference(s)
Beef meat and restructured sausages	Walnuts and walnut paste (20%)	4 × 150 g walnut-enriched steaks and 150 g walnut-enriched sausages per week	Nonblinded, crossover trial (vs. CM), 14 wk	22 males and females with ≥3 CVD risk factors	Antioxidant enzymes (SOD, CAT, GR, GPx, AE, PON1, GSH, and GSH/GSSG ratio)	↑ Antioxidant pathway and ↑ PON1 activity	(109, 110)
					Plasma tocopherol, LPO, and oxLDL	↑ γ-Tocopherol and ↓ lipoperoxides	(111, 112)
Cooked ham and cooked turkey	Rosemary extract, salmon oil (ω-3 PUFA) and vitamin E (0.02%, 0.6%, and 0.001% w/w, respectively)	450 g/wk	Randomized, double-blind, crossover trial (vs. CM), 12 wk	43 males and females with CVD risk factors	Plasma FRAP and TBARS	↑ Plasma FRAP	(113)
					Plasma 8-iso-$PGF_{2\alpha}$	↓ Plasma 8-iso-$PGF_{2\alpha}$	
Chicken breast	Selenium (25.5 μg/100 g)	800 g/wk	Randomized, double-blind, parallel (vs. CM), 10 wk	24 healthy males and females	Plasma selenium and GPx activity	Non-significant differences	(114)
Pork	Selenium (1.29 mg/kg)	450 g/wk	Longitudinal, 4 wk	25 healthy males and females	Plasma selenium	↑ Selenium	(115)
					Plasma antioxidant status	↑ Antioxidant status	
Meat	Microencapsulated polyphenol-rich water extract of olives	30 g/d	Parallel (vs. CM), 4 wk	35 healthy males and females	Plasma oxLDL and FRAP	↓ oxLDL	(116)
Frankfurters and pâtés	Reduced-fat (−15%) vs. control	200 g frankfurters + 250 g pâtés per week	Blind, nonrandomized, sequential, 5 mo	18 males at increased CVD risk	AE activity	↑ AE activity	(117)
					AE/oxLDL ratio Plasma oxLDL	↑ AE/oxLDL ratio Non-significant differences	
Frankfurters and pâtés	Reduced-fat (−15%) + PUFA ω-3 vs. control (2g ω-3/d)	200 g frankfurters + 250 g pâtés per week	Blind, nonrandomized, sequential, 5 mo	18 males at increased CVD risk	AE activity	↑ AE activity	(117)
					AE/oxLDL ratio Plasma oxLDL	↑ AE/oxLDL ratio Non-significant differences	

[1] ↑ Indicates an increase or higher levels; ↓ indicates a decrease or lower levels. AE, arylesterase activity; AOPPs, advanced oxidation protein products; CAT, catalase; CM, control meat; CVD, cardiovascular disease; DHN-MA, dihydroxynonene mercapturic acid; DPPH, 2,2-diphenyl-1-picrylhydrazyl; eNOS, endothelial nitric oxide synthase; FM, functional meat; FRAP, ferric reducing antioxidant power; GPx, glutathione peroxidase; GR, glutathione reductase; GSH, reduced glutathione; GSSG, oxidized glutathione; HC, hypercholesterolemic; iNOS, inducible nitric oxide synthase; LPO, lipid peroxidation; MDA, malondialdehyde; MS, metabolic syndrome; NC, normocholesterolemic; Nrf2, nuclear factor E2-related factor 2; oxLDL, oxidized low-density lipoproteins; oxVLDL, oxidized very-low-density lipoproteins; PON1, paraoxonase-1; RM, restructured meat; SOD, superoxide dismutase; TRAP, total radical trapping potential; T2DM, type 2 diabetes mellitus.

Although meat and meat products are excellent sources of selenium, its concentration differs depending on the geographical area of production (118). Most studies have focused on increasing the selenium contribution via animal feed (86, 46, 119). This practice increases selenium concentrations in different muscle types destined for consumption, while also protecting meat products from oxidation during storage (Table 1). Thus, ABTS (2,2′-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid), DPPH (2,2-diphenyl-1-picrylhydrazyl), FRAP (ferric reducing antioxidant power), and TBARS are reduced in relation to their controls (7). In addition, selenium increases the expression of key antioxidant enzymes [GPx, superoxide dismutase (SOD), and catalase (CAT)], reduces microbial growth, and improves the rheological properties of the final meat product (46, 47, 52, 119, 120). Limited and contradictory evidence is available on the effectiveness of selenium-enriched meat on animal or human antioxidant status. Some researchers revealed an increase in GPx expression and activity (52, 115, 121), whereas others reported no significant difference in antioxidant status after the consumption of selenium-enriched meat (114). This suggests the need to conduct more studies aimed at evaluating the antioxidant effectiveness of selenium-enriched meats.

Silicon.

Silicon is an essential trace element for the growth and biological function of various microorganisms, plants, and animals (122). Although health benefits from silicon have been reported (122–124), to date no dietary reference intakes have been defined. In vitro studies have shown a higher level of antioxidant activity of silicon in different cell types (125, 126).

Silicon inclusion in restructured meat would ensure the intake of this essential micronutrient and would confer meat-functional properties (127). However, no data have been reported on the oxidative stability of silicon-enriched meat during storage, cooking, and digestion. Unpublished data from our research group suggest that silicon-enriched pork suffers less oxidation than its nonsilicon counterpart in an in vitro digestive system model. Moreover, animal studies have revealed significant improvements in antioxidant status after silicon-enriched meat consumption. For example, a reduction in VLDL oxidation, along with less LPO and conjugated diene formation, were reported in old Wistar rats fed silicon-enriched meat as part of an atherogenic diet (107). Likewise, a hepatic antioxidant response pathway improvement, especially for SOD concentrations, via nuclear factor E2-related factor 2 (Nrf2) activation, was observed in rats suffering from nonalcoholic fatty liver disease (NAFLD) fed silicon-enriched meat (102). The improvement in antioxidant status could be partially responsible for the reduction in liver apoptosis found in these animals, suggesting a hepatoprotective role for consumption of silicon-enriched meat in an NAFLD animal model (128).

Zinc.

Zinc is an essential mineral for human health and growth because it is a cofactor for many enzymes and transcription factors, as well as a mediator of cell signaling and immune response (129). Zinc inhibits NADPH oxidase, acts as an ROS scavenger, and affects many enzyme cofactors that contribute to proper antioxidant pathway functioning. Specifically, it plays a key role in GPx regulation and is a SOD cofactor (94, 130). In vitro studies with zinc- and selenium-formulated meat have revealed a greater bioavailability of these minerals compared with their controls (131).

Several studies have evaluated the convenience of including zinc to improve meat production (131–134) and storage (40, 132), but no studies have been performed testing the functional effects of zinc-enriched meat on the antioxidant status of animals or humans (Tables 1 and 2). The vast majority of studies were based on supplementing a diet with different zinc concentrations, depending on the mineral source (132–134). Moreover, subcutaneous injections with a mineral mix were also performed (135). A rise in the zinc concentrations in the production stage resulted in an increase in Nrf2, a major transcriptional switch for the antioxidant response element and pathways. This increased antioxidant enzyme activities (SOD, CAT, GPx, and glutathione reductase) and the content of reduced glutathione (GSH), diminishing meat ROS and lipid peroxide concentrations during production and storage. These outcomes indicate better meat stability (132–134, 136).

Bioactive peptides

Proteins contain short amino acid sequences (2–30 amino acids), called bioactive peptides, which are released by enzymatic hydrolysis in the gastrointestinal tract or during food processing, including drying, curing, and fermentation (137, 138). These peptide sequences are characterized by their high bioavailability and their ability to modulate several physiological functions by acting as antioxidants, antihypertensives, antimicrobials, antidiabetics, and immunomodulators (120, 139).

Bioactive peptides can be included in meat products using 2 key strategies: *1*) adding proteins that contain active peptide sequences, which are released after intestinal hydrolysis; and *2*) hydrolyzing proteins using enzymatic technology, concentrating the fractions of the resulting bioactive peptides, and incorporating them into the meat (140). The drawback of strategy 1 is that large protein amounts are necessary to achieve a sufficient and effective dose of bioactive peptide to exert a physiological effect. Strategy 2 reduces consumer acceptability of the meat product because a high level of bioactive peptide incorporation produces a certain bitter taste (7). Notably, bioactive peptide effectiveness can be modified when the peptides are incorporated into different matrices, making it necessary to check their stability during the formulated foods' digestion (141, 142). Further information on bioactive peptide production is available in other reviews (137, 140, 143).

Many studies have shown that bioactive peptides exert antioxidant effects at different levels. In meat products, they help to protect cells from damage caused by electrophilic and oxidative stress by sequestering metal ions, eliminating ROS,

minimizing LPO, or enhancing the antioxidant pathway activity (138–141). The bioactive peptides most widely used by the meat industry are those originating from casein, egg white, whey protein, soy protein, or fish protein (144). Their use in pork, beef, or poultry, both original and minced structures, has shown a significant reduction in LPO of ≤70% during processing and storage, preventing oxidation and providing greater stability to the meat product (48–51, 145) (Table 1). However, there are no studies testing the bioavailability of these peptides after cooking, or the in vivo antioxidant effectiveness of functional meat formulated with bioactive peptides (146). As demonstrated by in silico predictive analysis (137), meat already contains large amounts of protein that can release bioactive peptides. These findings, coupled with high production costs, taste modifications, limited data on bioavailability and metabolic fate, and the lack of standardized analytical methods, predispose the commercialization of these bioactive peptides as nutraceuticals rather than functional ingredients (147).

Plant origin ingredients

Plant foods or their extracts contain nutrients and bioactive compounds rarely present in meat products (5, 17, 148). Their incorporation to meat matrices should preserve both the composition and quality of functional meat and meat products (149) as well as the antioxidant status of consumers (150). Throughout this section, we will discuss the main plant ingredients with antioxidant properties used in functional-meat product formulation.

Fiber, polyphenols, and plant extracts.

Meat is high in fat and proteins but lacking in dietary fiber (151, 152). Incorporation of dietary fiber in functional-meat development has been extensively studied because, depending on the ingredient incorporated, it can have noticeable technological properties (water retention, lubrication, ability to decrease cooking losses, product stabilization, texture modification, and neutral flavor) and nutritional properties (high fiber source, intestinal microbiota diversification, and hypocholesterolemic, antioxidant, and/or satiating effects) (13, 153). In addition, many antioxidant compounds, such as polyphenols and carotenoids, have been associated or linked to dietary fiber (154, 155). Although there are several types of polyphenols, their phenolic structure makes them effective electron or hydrogen donors to neutralize ROS and reactive nitrogen species (156). Polyphenols have been reported: *1*) to interrupt the propagation stage of lipid autoxidation chain reactions as effective radical scavengers; *2*) to act as metal chelators to convert hydroperoxides or metal pro-oxidants into stable compounds with the consequent decrease in reactive •OH caused by the Fenton reaction (157) (**Figure 3**); and *3*) to activate, as a free or glycosylated form, the antioxidant pathway by promoting Nrf2 translocation to the nucleus, activating the antioxidant response element (158, 159). These properties suggest the convenience of designing meat products enriched with fiber-associated antioxidant compounds.

Maintaining optimal conditions and meat stability during storage and cooking is an important technological and nutritional challenge (160). Some researchers have designed meat products enriched with green banana flour, soybean hulls, or oats, which improved the antioxidant rheological properties and antioxidant characteristics (53, 54). Likewise, adding guava or orange powders rich in vitamin C and polyphenols to nuggets or sausages, improved meat product stability by delaying LPO (as TBARS values) during storage and cooking (55, 56).

Ascorbic acid, rosemary extract, grape skin, and tea extract added to beef patties can reduce MDA formation in storage conditions (43, 45, 57). Other authors have shown that adding avocado (*Persea americana* Mill.) or *Ginkgo biloba* L. extracts prevents oxysterol formation in meat products during storage and cooking (58, 59). Enriching meat products with different fruit extracts reduces their oxidative alteration during cooking and subsequent refrigeration. Thus, the decrease of carbonyl production in meat has been linked to a high flavonoid concentration, which blocks the oxidation of lysine, proline, arginine, and histidine residue side chains (60). Furthermore, 2 carob fruit (*Ceratonia siliqua* L.) extracts, rich in proanthocyanidins, reduced LPO and thermo-oxidized compound formation during meat storage and cooking (16) (Figure 3). More information on plant- or extract-derived natural antioxidants used in meat preparation can be found elsewhere (161).

Several in vivo studies have evaluated the functional antioxidant effects of plant extract–enriched meat products, considering both their technological properties and oxidative stability (Table 2). In one study using a colorectal cancer animal model, the consumption of cured pork meat enriched with red wine (2%), pomegranate (0.6%), and α-tocopherol (0.045%), reduced both fecal LPO and the formation of urine 1,4-dihydroxynonane mercapturic acid (the main urinary metabolite of 4-HNE and an LPO indicator) (106). Likewise, sausages enriched with anthocyanins (0.11%) were developed to study the protective effect of anthocyanins on colorectal cancer. Results showed an increase in total plasma antioxidant activity and a reduction of proinflammatory bacteria (105) (Table 2).

Our research group has tested the effect of a carob fruit extract–enriched meat (0.4 g/100 g meat) during 8 wk on 2 animal models of T2DM (Table 2). In the early stage of T2DM, functional-meat consumption increased arylesterase (AE) activity and 1 of the 3 activities of the paraoxonase-1 (PON1) enzyme in the liver, but reduced AE in plasma (103). In the T2DM late stage, the intake of carob fruit extract–enriched meat increased both the plasma and liver AE and reduced liver and VLDL oxidation (104). PON1 is defined as a suicide enzyme, exerting pleiotropic antioxidant effects and protecting many macromolecules (such as lipoproteins) from oxidation in high oxidative stress conditions with the absence of antioxidants (162). Proanthocyanidins are metabolized by the microbiota, releasing large amounts of antioxidant

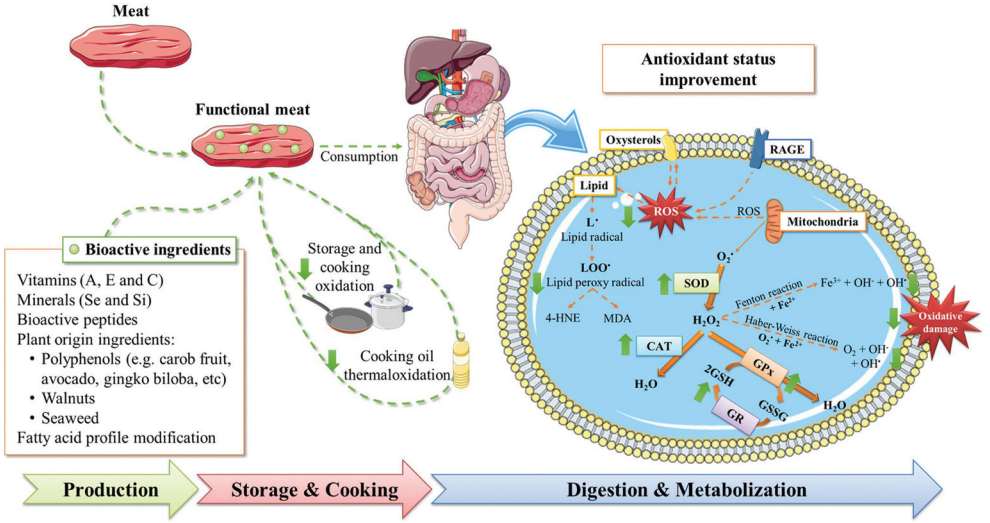

FIGURE 3 Illustrative scheme of functional-meat antioxidant effect in the different steps from production to metabolization. Development of functional meat with bioactive ingredients with antioxidant potential reduces the intrinsic formation of oxidized compounds during storage and cooking, as well as the thermo-oxidation of cooking oil. Once consumed, the functional ingredient can reduce ROS and lipoperoxide formation and minimize the heme-iron pro-oxidant effect of meat, while increasing the endogenous antioxidant machinery (CAT, GR, GPx and SOD). CAT, catalase; GPx, glutathione peroxidase; GR, glutathione reductase; GSH, reduced glutathione; GSSG, oxidized glutathione; L●, lipid radical; LOO●, lipid peroxyl radical; MDA, malondialdehyde; RAGE, receptor for AGEs (advanced glycation end-products); ROS, reactive oxygen species; SOD, superoxide dismutase; 4-HNE, 4-hydroxy-nonenal.

metabolites into the plasma. This suggests that meat enriched in proanthocyanidin extract can reduce the oxidative stress in the early stage of T2DM, because no extra plasma AE activity is required (103, 104).

Although numerous studies have examined the effects of plant extract–enriched meat products on animals, few studies have been performed in humans. In a crossover trial, the daily consumption of 1 burger enriched with 7% wine grape pomace flour for 1 mo improved the antioxidant status of participants with various metabolic syndrome markers (108). Flour derived from polyphenol-rich grape pomace, when added to meat, reduced postprandial oxidative stress, advanced oxidation protein product formation, uric acid, and oxidized-LDL (oxLDL) plasma concentrations. In addition, vitamin C concentrations increased along with antioxidant activity in the plasma. This suggests a clear improvement in antioxidant defense (24). The most reliable and accepted marker for evaluating LPO in vivo is 8-iso-$PGF_{2\alpha}$ (163). The same marker was used in a randomized and double-blind crossover trial in volunteers at increased CVD risk, who consumed cooked ham and turkey (450 g/wk) enriched with 0.03% rosemary extract and 0.9% salmon oil; this showed an increase in plasma antioxidant capacity with a decrease in 8-iso-$PGF_{2\alpha}$ (113). In a parallel study, healthy individuals who consumed meat enriched with microencapsulated olive aqueous extract (30 g/d) showed a decrease in oxLDL, but no change in plasma antioxidant activity (116).

Walnuts.

Walnuts are rich in arginin (14, 164), an amino acid precursor of NO, an endogenous anti-inflammatory vasodilator and a platelet aggregation inhibitor, which partially explains why walnuts exert CVD protection (164). Walnuts contain antioxidant minerals such as magnesium, selenium, copper, and zinc (14, 165). They also contain noticeable amounts of antioxidant vitamins (e.g., γ-tocopherol), polyphenols (e.g., quercetin), and plant sterols (14). In addition, walnuts are the nuts richest in ω-3 PUFAs, which induce lower cyclo-oxygenase (COX) production than their ω-6 PUFA counterparts (166).

Thus, to promote their consumption, walnuts could be an ingredient in regularly consumed foods (e.g., meat/meat products), which would make meat products healthier (5, 14). Due to their specific compositional differences from other nuts (165, 167), walnuts were selected by our group as a functional ingredient to be included in meat. This approach did not substantially reduce other important nutritional components of walnuts, such as iron and zinc (5, 14). Furthermore, like any functional food, meat products containing walnut paste must maintain the original health properties of the walnuts after cooking. At least 80% of α-linolenic acid and total PUFAs remain in walnut paste–enriched meat after surface frying (15, 67) (Table 1).

As summarized in Table 2, a 5-wk randomized placebo-controlled crossover study was conducted in men and women at high risk of CVD, to assess the functional effects of the weekly consumption of restructured steaks (4 × 150 g) and frankfurters (150 g) containing 20% walnut paste. Besides the lipoprotein results obtained, interesting outcomes were observed for antioxidant and inflammatory markers, notably thromboxane and prostacyclin production (110). The

improvement in thromboxane and prostacyclin concentrations suggests a reduction in COX, an enzyme that may activate ROS production (109). The intake of these meat products 5 times a week increased the concentrations of CAT, SOD, total glutathione, and GSH/oxidized glutathione (GSSG) redox index, but reduced concentration of lipid peroxides compared with the volunteers consuming the low-fat control products (110). These findings follow previous studies that showed walnuts can reduce systemic oxidation (168, 169) and brain oxidative stress (170). A dietary intervention of walnut-enriched meat increased PON1 activity without changing HDL cholesterol concentrations. Thus, the increase of PON1 activity, despite HDL cholesterol changes, denotes increased antioxidant activity for pleiotropic uses, corroborating the results of other studies (171). Furthermore, the reduction of thromboxane B2 (TXB2) and the $TXB2/PGI_2$ thrombogenic ratio suggests that consumption of walnut-enriched meat diminishes the activity of enzymes such as COX, and thus, ROS production, which explains the difference in PON1 and AE in different meat treatments and periods (110). These results suggest the improvement in antioxidant status in the participants was due to the consumption of meat enriched with walnuts.

Seaweed.

Different algal bioactive compounds, such as dietary fiber, proteins, minerals (sodium, calcium, potassium, iron, magnesium, selenium, and manganese), trace elements, vitamins (C and B-group), unsaturated fatty acids, polyphenols, carotenoids, and tocopherols, have been reported to exert functional properties (17, 172–175). However, any generalization about algal functionality has to be avoided, because seaweed composition depends on the species, habitat, and state of maturity, among other factors (172, 174). Additionally, seaweed can have high amounts of poisonous trace elements (e.g., arsenic) that would partially block antioxidant properties (176). It is also important to differentiate between whole seaweed and extracts, because the extraction process determines the subsequent antioxidant activity. However, there is a lack of efficacy and reproducibility between studies (177).

Our group produced different types of meat enriched with sea spaghetti (*Himanthalia elongata*), wakame (*Undaria pinnatifida*), or nori (*Porphyra umbilicalis*) through a gel/emulsion system (17, 96–99). The resulting products (frankfurters, patties, and restructured steaks) showed increased amounts of minerals and soluble polyphenols, which are responsible for the high antioxidant activity and stability during processing and storage (68, 178–180). These results align with other studies that included fucoxanthin or astaxanthin in meat, which are the main carotenes of wakame and *Haematococcus pluvialis*, respectively (61). Adding algal extracts improves color stability, and decreases production of lipid peroxides following storage and cooking (181). In addition, algal inclusion reduced the oxidation induced by high copper and iron concentrations in meat (172).

In relation to functionality, animal studies have been performed to assess the effect of algae-enriched meat consumption on the antioxidant pathway (Table 2) (96–99). Thus, for 5 wk, growing Wistar rats were fed diets (with or without added plasma cholesterol-raising factors) of restructured meats containing 5% w/w nori, wakame, or sea spaghetti. Interestingly, hypocholesterolemic effects resulted in lower antioxidant concentrations. Thus, wakame might act as an antioxidant because it showed little hypocholesterolemic effect. Sea spaghetti could partially block the prooxidant effects induced by the cholesterol elimination via cholic acid thanks to the cytochrome P450 7A1 (CYP7A1) enzyme action. The CYP7A1 hemoenzyme produces high ROS concentrations in the presence of iron, requiring large amounts of antioxidants, which explains the relatively low antioxidant properties of nori in our experimental conditions (98). Nonetheless, seaweed-enriched meat seems to exert buffering effects, because it induced moderate antioxidant enzyme expression (CAT, Mn-SOD, Zn-SOD, and GPx) in rats fed the seaweed-enriched meat (96, 97, 99). All tested algae contained sizeable amounts of xanthophils and polyphenolic compounds, whose antioxidant activity could help to eliminate ROS, making it unnecessary to increase antioxidant pathway expression in the body (182, 183). Likewise, some algal bioactive peptides called phycobiliproteins (protein and pigment complexes) have antioxidant activities that could be beneficial in reducing the negative effects of diseases associated with oxidative stress and inflammation (184). Our group has tested the antioxidant and hypocholesterolemic effects of functional meat formulated with a mix of glucomannan plus spirulina (*Spirulina platensis* or *Arthrospira maxima*) regarding those of a glucomannan-enriched meat in fa/fa rats fed an atherogenic diet (100) (Table 2). The joint action of glucomannan and spirulina halted the ROS production linked to the active elimination of cholesterol in the rats (100). Despite the positive effects of *Spirulina* on antioxidant activity and the stability provided by its incorporation into meat, more studies are needed to evaluate its functional properties both in animal and human models (17, 173, 177).

Fatty acid profile modification

Fatty acid profile modification is one of the most used technological strategies to obtain functional meat. It is based on the meat-fat substitution, rich in SFAs, by PUFAs and/or ω-3 PUFAs to obtain meat products whose ω-6/ω-3 PUFA and PUFA/SFA ratios would be adjusted to nutritional guidelines (5). Therefore, by taking the health benefits of ω-3 PUFAs into account (166), the food industry has developed strategies to increase their concentration in meat products (65, 66, 69, 70, 117, 185, 186).

Because meat lipid composition largely depends on an animal's diet, mainly in monogastric animals, one of the most used strategies is incorporating ω-3 PUFA-rich sources (e.g., fish, rapeseed, or flax oils) into animal feed. This method is effective in the production of pork or poultry (187, 188); however, there are conflicting results for beef or lamb,

mainly because dietary unsaturated fatty acids are subject to rumen biohydrogenation (189, 190). Still, increasing PUFA concentration in meat could be a somewhat risky strategy because PUFAs are the main substrates for LPO (2). A related study reported that the increased oxidation with PUFA enrichment can be reduced if the animals are fed grass because it increases their vitamin E concentrations (191).

Furthermore, PUFA addition is especially problematic for meat products because processing conditions such as milling, cooking, and drying involve exposure to relatively high temperatures, decomposition of antioxidants, or increased oxygenation of the substrate (62, 69–72). Therefore, many studies include antioxidant compounds, besides ω-3 PUFAs, to guarantee the stability of ω-3 PUFA-enriched meat until consumption (Table 1) (63, 67, 113, 192). However, a fat reduction of 10–20% in the final product diminishes meat oxidation whereas partially replacing fat with guar gum decreases the formation of protein carbonyls in meat (64).

In a 5-mo nonrandomized, sequentially controlled study, our research group has tested the effect of consuming reduced-fat meat products in volunteers at increased CVD risk. ω-3 PUFA-enriched/fat-reduced frankfurters and pâtés with 15% total fat (200 g/wk and 250 g/wk, respectively) were tested compared with control meat products for several CVD biomarkers (117). The results revealed an increase in the AE activity, and a lower AE/oxLDL ratio, suggesting enhancement in the antioxidant status of lipoproteins after the consumption of the fat-modified functional meat products.

Although the positive effects of ω-3 PUFAs seem irrefutable, there is growing evidence that these fatty acids exert a pro-oxidant effect initially to stimulate the antioxidant pathway, which can have a high therapeutic value in pathologies associated with oxidative stress and inflammation (193). The mechanism by which this response is induced is not clear, but 4-hydroxy-2E-hexenal, a final product of LPO, has been suggested to upregulate heme oxygenase-1 expression through Nrf2 activation (194, 195).

Despite the promising results associated with ω-3 PUFA consumption, as far as we know, few industrial meat products enriched with ω-3 PUFAs are available. The technological difficulty in guaranteeing their stability could be one cause, which represents an interesting line of research and product development to improve consumers' health.

Functional Meat and Mitotic and Nonmitotic Tissues: Potential Role for Preventing Chronic Diseases

From a practical viewpoint, diseases are normally classified according to their location or the presence of specific altered physiological mechanisms. Thus, functional foods or their ingredients can also be classified according to their specific and/or systemic effects and action mechanisms available from clinical or preclinical studies (110, 196). Most prevalent chronic, noncommunicable diseases have a similar origin based in pro-oxidant/inflammatory factors (2, 196), and are related or caused by aging (4, 197, 198) (**Figure 4**), a phenomenon linked, among several factors, to mitochondrial oxidative disturbances and dysfunction (199, 200). Thus, as reviewed in the section entitled functional-meat and oxidative stress, several ingredients and their functional meat products exert their health benefits through downregulating oxidative pathways (86, 96, 98, 99, 101, 104, 108, 145). Moreover, hypercholesterolemic animals have lower activities of antioxidant enzymes, which can be largely improved by functional meat consumption (96, 98–101,104). This antioxidant effect would help prevent CVD and have hepatoprotective effects, because adding polyphenols, tocols, silicon, and fiber to meat positively affects atherosclerosis and protects liver cells under oxidative stress by activating Nrf2 and promoting glutathione synthesis (100–102, 128) (Figure 4). However, the scientific evidence for the antioxidant effects of functional meat products is limited to the liver and plasma of normocholesterolemic and hypercholesterolemic Wistar, fa/fa, and Fischer rats (affected or not by T2DM), with almost no data being available for the pancreas, brain, kidneys, spleen, and heart (Table 2). Therefore, unfortunately, we cannot clearly link functional meat consumption with improvement in antioxidant function in specific organs besides the liver. Likewise, in humans information on the effects of functional meat products is restricted to plasma, urine, and feces, in which routine markers were tested (redox index, plasma antioxidant enzyme activities, AE, and oxLDL) (108, 110–115, 117, 151).

Moreover, the effects of aging and/or diet differ in distinct body organs (199, 200). Therefore, the antioxidant effects of functional meat products have to be differentially tested in mitotic (e.g., liver, intestine) and nonmitotic organs (muscle, heart, brain, and retina), because mitochondrial alterations differ considerably among tissues depending on the tissue's capability to repair or replace altered cells and to recover a given function. Further, liver has been found to partially buffer the damage as suggested by the non-effect found on cytochrome c activity (a marker of mitochondrial integrity) and therefore, is more effective in repairing mitochondrial DNA damage (199). Cytochrome c oxidase activity is a marker for mitochondrial function. A decrease of this enzyme activity leads to the uncoupling of the mitochondrial electron transport with subsequent increases in ROS production (201). However, mitochondria from nonmitotic tissue partially buffer unfavorable situations by increasing cytochrome b, cytochrome c oxidase, and/or the lipoprotein membrane unsaturation (e.g., increasing PUFA-enriched cardiolipin), which makes those tissues more prone to oxidation (199). Thus, dietary intervention based on functional meat containing antioxidants could attenuate the ROS process, but their effects should be tested in different body organs, because a PUFA/antioxidant imbalance would be highly deleterious for nonmitotic organs but less so for mitotic ones.

Potential Negative Effects of Functional Meat Formulation and Consumption

Although legislation urges further testing, marketing, and redacting claims for functional foods (80, 202), several

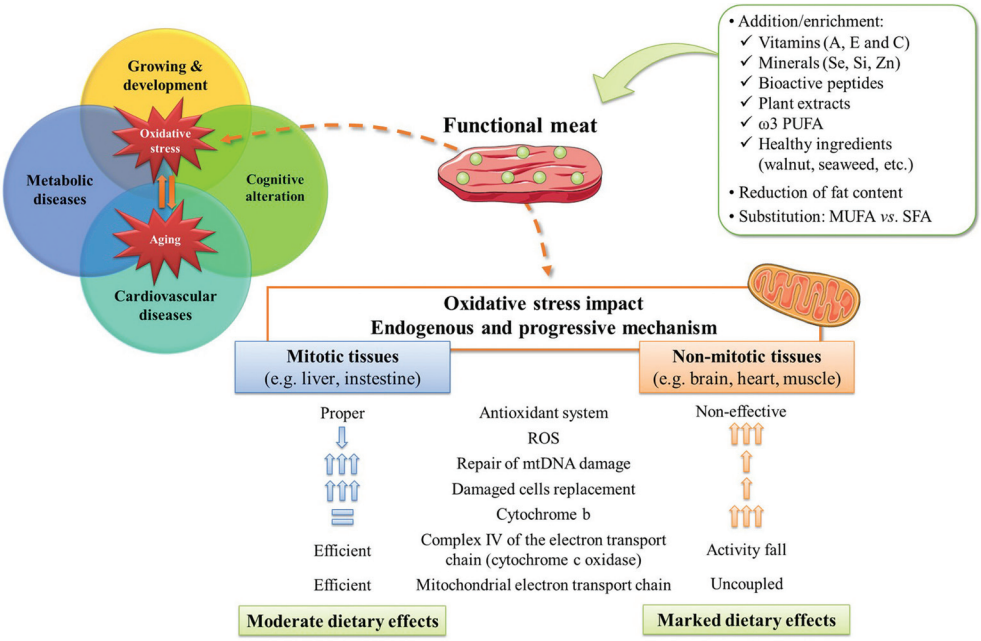

FIGURE 4 Functional meat products as modulators of oxidative stress and chronic degenerative diseases. Tentative differential effects on mitotic and nonmitotic organs. Most chronic, noncommunicable diseases have a similar origin based in pro-oxidant factors and aging, a phenomenon linked, among several factors, to mitochondrial oxidative disturbances and dysfunction. Functional meat products because of the functional ingredients added in formulation exert their health benefits through diminishing oxidative pathways (for more details see text). Differences in the antioxidant effects of functional meat products in mitotic (e.g., liver and intestine) and nonmitotic organs (muscle, heart, brain, and retina) appear important because mitochondrial alterations differ considerably between tissues depending on their ability to repair damage, to induce mitochondriogenesis, or to replace altered cells and functions. Mitochondrial dysfunction leads to the uncoupling of mitochondrial electron transport and increased ROS production. Mitotic organs partially buffer the damage, because little effect on mitochondrial integrity according to cytochrome c activity suggests they are more effective at repairing mtDNA damage. Mitochondria from nonmitotic tissue partially buffer unfavorable situations by increasing cytochrome b, cytochrome c oxidase, and/or the lipoprotein membrane unsaturation that makes this tissue more prone to oxidation. A diet rich in PUFAs and poor in antioxidants will be highly deleterious for nonmitotic organs, but not for mitotic organs. mtDNA, mitochondrial DNA; ROS, reactive oxygen species. Adapted from reference 200 with permission.

other aspects (e.g., doses, frequency, incompatibilities, and interactions) must be considered. The general notion that improving food composition and stability always implies health benefits should be avoided because, sometimes, bioactive compounds added to meat in specific amounts can be adequate in food for oxidation, but inadequate for specific consumers. Our group reported that adding hypericum (*Hypericum perforates* L.) reduces the oxidation in ω-3 PUFA-enriched meat products (62) and assures a pharmacological and nontoxic dose of hypericum extracts with a maximum of 0.3% hypericin. However, the interactions of hypericum with selective serotonin reuptake inhibitors have to be considered. Thus, hypericum extract–enriched meat consumption should be avoided by people treated with certain pharmaceutical drugs (203). Similar considerations should be given for bioactive compounds (e.g., oligopeptides from meat, eggs, milk, and fish) added to meat undergoing liver metabolization by the cytochrome P450 isoenzymes (204, 205). Changes in cytochrome P450 isoenzyme activity would modify the therapeutic action of several medicines.

Because algae contain antioxidant compounds (e.g., polyphenols and xanthophylls), they can have positive effects on the consumer's antioxidant status (17, 172). However, trace elements (e.g., arsenic) in seaweeds can induce a poor endogenous antioxidant status in consumers (176). Therefore, special care should be taken to ensure low concentrations of such trace elements in algae-enriched meat. The benefits of adding iodine to food, especially in countries with a low iodine intake, are appealing (206, 207). Nonetheless, the consumption of iodine-rich algae has been found to increase thyrotoxicosis risk, mostly in people adapted to a low iodine intake (208), requiring caution when consuming algae-enriched meat. β-Sitosterol and other plant sterols can be added to meat and other foods. Some plant sterols (e.g., Δ^5-avenasterol) (209) reduce food oxidation. However, plant sterols should not be consumed during pregnancy or childhood, because negative effects in early child development have been reported (209). Dietary fiber, ω-3 PUFAs, and some bioactive compounds (such as polyphenols or related compounds) appear to interact with statins, reducing their presystemic metabolism and

decreasing their half-life. Consequently, the therapeutic efficacy of such pharmaceuticals is modified (210).

Lastly, some meat and its functional ingredients (e.g., algae) can contain substantial concentrations of sodium (172, 211), which increases water retention and thus blood pressure, decreasing the effectiveness of hypotensive drugs (211). Therefore, strict analysis for detecting and removing any potential negative compounds present in functional meat should be performed.

Functional-Meat Consumption and Precision Nutrition

The effect of any functional food should be considered according to the phenotypic characteristics of a person, in whom the genome and the environment are in continuous dialog (212–214). Thus, precision nutrition seems necessary to precisely ascertain the effect of dietary nutrients and bioactive compounds on gene expression by using new omics approaches (215, 216).

Nutrigenomics was initially defined as the study of the effects of nutrients/foods on an individual's gene expression. Subsequently, it has been expanded to cover the nutritional factors that protect the genome from damage (217). In addition, food and its components can cause epigenetic modifications in DNA transcription and mRNA translation, contributing to the improvement or worsening of the pathophysiology of a disease, which reinforces the importance of conducting adequate nutritional intervention studies (212, 214, 215). However, diet–gene interactions are complex and difficult to predict, prompting a high number of studies based on genome-wide association studies, genetic risk score applications, and next generation sequencing techniques (212, 213, 215). Likewise, mRNA sequencing analyses, transcriptomics, proteomics, metabolomics, lipidomics, and epigenomic-wide association studies will also improve precision nutrition (212–216).

Our group has reported that the antioxidant responses in volunteers at high CVD risk consuming walnut paste–enriched meat varied in 2 major polymorphic forms of the *PON1* Q192R (rs662) and L55M (rs854560) gene variants, and the *APOA4* gene Q360H (rs5110) (109, 111, 112). Although the samples tested were limited in size, the results obtained suggest that changes in antioxidant status markers in walnut-enriched meat after a 5-wk period were greater in *PON1* QQ carriers than in *PON1* QR+RR (109, 112). Furthermore, the *PON1* Q192R polymorphism was more closely related to antioxidant status than the *PON1* L55M (111). Interestingly, AE activity isolated from *PON1* QQ volunteers was more resistant to inactivation than the AE from *PON1* RR counterparts, suggesting higher antioxidant activity and antiatherogenic properties, because the remaining active enzyme hydrolyzed greater amounts of lipid peroxides in the atherosclerotic lesions (218).

Nutrients and bioactive compounds exert their health effects through nutrigenomic and epigenomic mechanisms (214). Previous sections have discussed how the consumption of plant extracts, seaweeds, silicon, and so forth affects antioxidant enzyme gene expression, thus modifying consumers' antioxidant status.

The importance of transcriptomics, and other "omics" technologies in precision nutrition seems evident, because several gene polymorphisms engaged in metabolic pathways have been linked to degenerative diseases (216). The negative effects of high meat consumption on colon cellularity appear closely related to the nature and presence of the proteolytic microbiome. A diet rich in carbohydrates made colonic saccharolytic bacteria predominant. Thus, the conjoint consumption of meat and indigestible carbohydrates allows buffering of such negative effects (219), highlighting the importance of consuming a plural diet or including some fermentable plant compounds in foods consumed every day, such as meat. Despite these challenges, functional meat products formulated with antioxidant ingredients should not only reduce the formation of ROS and other oxidation compounds, but also enhance antioxidant pathways by modulating the levels of several transcription factors (e.g., Nfr2, NF-κB, retinoid X receptor, and vitamin D receptor). These effects appear mediated by epigenetic changes associated with consumption of these ingredients, which indicates that they are a potential nutritional weapon to help improve chronic pathologies. In addition, vitamins A and D have been getting more attention due to their antioxidant activity and their antitumor properties (220). Thus, if cancer has been epidemiologically associated with meat consumption (19, 221, 222), the inclusion of vitamin A and/or D as functional ingredients in meat products would diminish this negative relation. Nonetheless, cancer is a complex topic and some antitumor properties of functional ingredients (such as vitamin D) can be dysregulated (220). Therefore, studies evaluating the effects of functional-meat consumption on the genome are required to advance this complex topic.

Conclusions and Future Works

- Numerous potential meat-based functional foods have been designed and developed to cover 2 main objectives: improving composition and shelf-life of meat products, and enhancing the health status of consumers by ameliorating $\geq$1 bodily functions and/or reducing the risk of degenerative disease development.
- Modified meat products ensure acceptable quality attributes in terms of physicochemical and sensory properties, as well as stability and health benefits.
- Animal feeding and food formulation are the 2 most usual ways to obtain functional foods with antioxidant properties.
- Meat and meat products have become ideal food matrices for delivering bioactive compounds, (e.g., fiber, ω-3 PUFAs, and bioactive peptides) or whole foods (e.g., walnuts, and seaweeds) without changing dietary habits, which helps to improve the dietary nutritional quality and adequacy.
- Information on meat oxidation protection with functional ingredients is broad, but few studies have

evaluated the in vivo antioxidant effects of functional meat after consumption.

- Little evidence is available on the functional ingredients remaining in functional meat after cooking, and its effects on functionality.
- Regular consumption of adequately formulated meat products ensures an improvement in antioxidant status, because it reduces the levels of some specific oxidation markers (TBARS, MDA, and the glutathione system) and their metabolic consequences (DNA modification, IL production, cell apoptosis, etc.).
- Future work is needed not only to assess health effects mediated by functional-meat products but also to target people who might benefit by their consumption.
- The antioxidant effects of functional-meat products must be tested in mitotic and postmitotic organs of males and females and in the frame of several diets and physiopathological situations.
- Long-term, controlled studies should be designed to understand how the effects of functional meats are affected by "omics" measurements.

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