Hydroxytyrosol in Food Products

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Hydroxytyrosol (HT) is an amphipathic functional phenol found in the olive tree, both in its leaves and fruits, in free or bound forms, as well as in olive oil and by-products of olive oil manufacture. It is recognized as safe by the European Food Safety Authority (EFSA) and Food and Drug Administration (FDA) and has obvious health effect when consumed regularly with the prerequisite to contain at least 5 mg/20 g oil of HT and related compounds. According to the dietary data from the European Union, it is estimated that the mean values of HT consumption in adults is far from the daily recommended intake, which relays the importance of the incorporation of HT in other types of products.

Keywords: phenol ; olive oil ; by-products ; table olives ; antioxidant ; functional ingredient ; novel foods

1. Introduction

The assumption that “diet is the best medicine” embraces the valorization of food ingredients and, in particular, of health-promoting bioactive compounds. Hydroxytyrosol (HT) is a dietary constituent that has received much attention in the last decade due to the many benefits of the ingestion of virgin olive oil, relative to antioxidant capacity and properties against cardiovascular diseases. This phenolic is recognized as safe by the European Food Safety Authority (EFSA) and Food and Drug Administration (FDA). Based on the opinion of the EFSA, in 2017, the European Commission (EC) authorized the placing on the market of HT as a novel food ingredient under Regulation (EC) No 258/97 [1][2], which assumes its use for the general population, excluding children under the age of three years, pregnant women, and lactating women [3]. To promote its widespread consumption, HT has been integrated into the concept of functional foods, i.e., a natural-based food product provider of health benefits beyond the primary nutrition value, which has exponentially increased over the last few years.

According to the EFSA, the average HT content, in mg/kg of product, ranges from 3.5–7.7 in olive oils and it is approximately 556 and 660 in green and black olives, respectively [1]. Thus, considering the dietary data from the European Union, it is estimated that the mean values of HT consumption in adults vary between 0.15–4.0 and 19–185 µg of HT/kg body weight (bw) per day, as a result of olive oil and table olives intake, respectively [1], far from the daily recommended intake. In addition, table olives and olive oil are not consumed by everyone, which relays the importance of the incorporation of HT in other types of products.

2. Applicability of Hydroxytyrosol in Food Products

2.1. Consumption Recommendations

The minimum recommended HT amount (including its derivatives) for manutention of cardiovascular health by the EFSA and FDA panel [1][2] reinforces the necessity to incorporate HT in other food products. As an integrated part of a food product, the EFSA has established HT concentrations for fishery products and vegetable oils, as well as for margarine, of 215 mg/kg and 175 mg/kg, respectively. For other types of food, the amount of HT is suggested to be adjusted, taking into account the HT content in the background diet [1]. Moreover, according to the FDA, final concentrations should comprise between 8 and 21 mg/kg for energy drinks and vegetables/fruits beverages, respectively; 167 to 250 mg/kg for snacks and baked goods; 44 to 333 mg/kg for sauces, condiments, fat and oil products and, finally, about 1.1 g/kg for meat, poultry and fish coating mixes [2].

So far, the HT toxicological data are mainly based on cell and animal studies. Among them, the study of D’Angelo and coworkers [4] represented a hallmark, with no adverse effects (NOAEL) being registered upon the induction of acute toxicity in rats by injection of a single dose of 2 g of HT/kg bw. Afterward, subchronic toxicity studies with oral gavage administration through a daily dose of aqueous olive pulp extract at levels of 500, 1000 or 2000 mg/kg [5], as well as 5, 50 or 500 mg HT/kg bw per day [6], did not cause any adverse effects. Auñon-Calles and his collaborator [6] assumed the lowest observed adverse effect level at 500 mg of HT/kg bw per day and a NOAEL of 250 mg/kg bw per day. The only difference noted was salivation before and after administration in all animals, which the authors attributed to the bitter taste of HT and the oily and dense formulation. Considering these studies, the EFSA panel recommended a maximum daily HT intake of 100 mg/kg body weight per day for children and 200 mg/kg body weight per day for adolescents, adults and elderly [1].

The health-promoting abilities of dietary HT are dependent on metabolism, bioaccessibility and bioavailability issues. Similar to most phenolic compounds, no salivary digestion was reported for HT, possibly due to its inhibitory effect on α-amylase [7]. In the gastric phase, most of HT is released from the food matrix and remains stable [8] while metabolization is triggered in the intestinal phase, due to the basic pH conditions and the presence of enzymes in enterocytes. The compound is absorbed by the enterocytes of the epithelium and reaches the liver through the hepatic portal vein, where metabolism continues. Afterward, HT and its metabolites are further excreted into systemic circulation or can be reabsorbed by the intestine through bile [9]. During this process, it is gradually converted into other metabolites such as 3,4-dihydroxyphenylacetaldehyde, 3,4-dihydroxyphenylacetic acid (DOPAC) and 4-hydroxy-3-methoxyphenylacetic acid (or homovanillic acid), which can be detected in human plasma [10]. Hydroxytyrosol acetate is another metabolite often detected in human plasma, resulting from the alkaline hydrolysis and acetylation of HT in the lumen [11][12]. For the study of the health benefits of HT consumption, it is of utmost relevance to know which metabolites are generated once, similar to HT, some of them exert antioxidant activity, due to the hydroxy group in the 3,4-ortho position [13], such as DOPAC [14] and homovanillic acid [15]. Hydroxytyrosol acetate exhibits less antioxidant activity than HT due to the acetate group of the ester that may hide the scavenging e ect of the hydroxyl groups by intra- or intermolecular hydrogen bonding [16]. Still, it inhibits platelet aggregation in rats [17], an important cardiovascular comorbidity. Otherwise, 3,4-dihydroxyphenylacetaldehyde is a reactive and toxic metabolite [18], which may interfere in the bioactivity of the remaining compounds.

2.2. Application of HT in the Functional Food Market

As for other natural bioactive compounds, obtaining pure HT and its use in food products is hardly considered economically viable. Therefore, a variety of approaches to meet market requirements for a lower cost HT, including its exploitation from natural sources or the use of biocatalysis, have been proposed [19]. Part of this solution involves the use of by-products. In fact, the cheapest sources of HT comprise olive pomace, olive mill wastewaters (OMWW), and olive leaves, from which the obtention of HT-rich extracts or pure HT requires the combination of solvent extraction, membrane filtration technology and stabilization by lyophilization or spray-drying [20]. Thus, it is possible to find many patented adaptations of the olive pressing systems, extraction procedures [21][22][23] and purification methods [24], aiming at the full use of these resources [25], and at the promotion of circular economy processes, through the usage of olive oil by-products for the development of the extracts.

2.3. Supplements and Patented HT-Rich Extracts

HT-rich extracts are widely marketed as food supplements or healthy ingredients. Among them, Hidrox (CreAgri, Hayward, CA, USA) is a formulation of olive polyphenols rich in HT obtained from vegetative waters, certified as Generally Recognized as Safe (GRAS) and patented (patent EP06025262A). It is used to formulate other supplements such as the OLIVACTIV(20–35 weight % of HT), the OLEASELECT (total content of HT of 1.5 weight %), the OLIVE(OLEA)DRY, i.e., a powder containing from 22 to 24 g of HT per kg, and Prolivols (20 mg of HT per g) [26]. Hytolive (Genosa, Spain) is a patented olive extract [27], which was previously shown to be effective in reducing inflammation among early-stage breast cancer patients [28]. Phenolea® (Phenofarm, Scandriglia, Italy) is an active complex also derived from a natural standardized olive pulp extract through a patented mechanical process, in which HT accounts for 30% of all phenols. Evidence has shown that its administration to mice modulates the level of cytokines, having a role in the process of inflammation [29]. Moreover, Aponte et al. [30] used Phenolea® as a source of HT to produce oral granules for co-delivery of L. plantarum and a standardized olive leaf extract (OLE). Through in vivo data, they noticed that co-administration of live L. plantarum bacteria with the olive phenol-containing extract provided higher amounts of bioavailable HT compared to the extract alone. Another example is the Oleaselect® (Indena, Milan, Italy), obtained by a patented process (patent US 6358542B2) from olive-based starting materials, including olives, olive pulps, olive oil, and wastewater from olive oil manufacturing, and claimed to achieve an extract with antioxidant activity four to five times higher than the hydroalcoholic extract of solid olive residue [31]. Mediteanox® (Euromed S.A., Barcelona, Spain) is another registered supplement. Notably, oral administration of three capsules of supplement that contains a combined 3.3 mg of HT from Mediteanox® and 65 mg of punicalagin from Pomanox® (a pomegranate natural extract, Euromed S.A., Barcelona, Spain), per day for eight weeks, significantly improved the endothelial function and blood pressure, and reduced LDL oxidation in middle-aged subjects [32]. In the case of Mediteanox®, the studied dosage gets closer to the minimum daily recommendation (5 mg HT per day).

2.4. HT as a Food Ingredient

2.4.1. Edible oils

Edible oils, particularly refined ones, are prone to oxidation [33], but fortification with HT can delay this phenomenon [34][35][36][37][38][39]. The fortification of edible oils has been obtained by the addition of the pure compound or through extracts. OMWW extract (containing 1225.6 mg/L of HT, among other phenols), added to **refined olive oils** at a concentration of 200 mg/kg, reduced the peroxide values and delayed the oxidation rate, even better than 2,6-di-t-butyl-4-methylphenol (BHT) [36]. In addition to HT, this OMWW extract also contained DOPAC, an HT derivative, which could contribute to these effects [36]. Additionally, with OMWW extract, the supplementation of **oils for French fries** significantly hampered the oxidation of α-tocopherol and the formation of unwanted compounds (e.g. acrolein and hexanal) during the frying process. Curiously, this supplementation increased the number of available sugars and, consequently, the extension of Maillard reactions, resulting in French fries with a more positive taste and better color [38]. In **echium oil**, which is more susceptible to oxidation than other vegetable oils, 200 mg of HT/kg substantially protected the oil from the oxidation process [34]; however, this was only verified under non-thermal conditions [40]. In addition to HT, other compounds that exist in HT-rich extracts may exhibit a synergic effect. This observation was made by Lama-Muñoz and coworkers [37], who reported that a mixture of HT with 3,4-dihydroxyphenylglycol (DHPG) (proportion 2:1) was more efficient in delaying the oxidation of the vegetable oil than the commercial Olivefen®. This reinforces the idea that natural antioxidants' activity is affected by multicomponent foods and varies according to the extract composition.

Nevertheless, regarding the health effects of HT in oils, the main studies focus on **olive oil**, which is the best natural source of HT through diet. For example, Valls et al. [39] tested a single dose of 30 mL of olive oil supplemented with a phenolic-rich extract from olive cake (with 6.64 mg HT/kg olive oil cake) in hypertensive patients (in pre- and stage 1). They found that the olive oil supplement caused more positive effects on the patient's endothelial function than the ingestion of a standard virgin olive oil, especially in terms of the decrease in oxidized low-density lipoproteins (LDL) and blood stimulation flow (reactive hyperemia). Similarly, Farràs et al. [35] evaluated the regular intake of 25 mL per day of distinct olive oil that provided 0.01, 0.12 and 0.21 mg of HT, for three weeks in hypercholesterolemic patients, and they noticed benefits, namely in the improvement of HDL levels and blood plasma antioxidant activity, without increasing the individual's fat intake. Thus, in addition to the ability of HT to stabilize oily matrices, edible oils fortified with HT may also be suitable to act as a functional food to prevent cardiovascular comorbidities.

At present, there are also several patented applications of HT in edible oils, Más et al. [41] patented fortified edible oils, fortified edible oil-containing products and dietary supplements in the form of soft gel capsules containing fortified edible oils, with increased antioxidant capacity to be used as a source of HT for prevention or treatment of cardiovascular diseases, plaque build-up in the arteries, arterial hypertension and metabolic syndrome [41]. In the same line, Bulbarello and collaborators [42] patented capsules for oral consumption of an edible oil fortified with HT (more than 250 mg HT/kg fortified oil). Moreover, the addition of an extract of bisphenol with more than 60% of HT and a terpene extract with more than 80% of maslinic acid to an extra virgin olive oil (VOO) or olive oil was also patented [43].

2.4.2. Beverages

In beverages, **wine** is valorized as a functional food towards cardiovascular diseases due to its polyphenol content, especially resveratrol and HT, the latter resulting from tyrosol through alcoholic fermentation [44]. However, the use of sulfur additives, such as a sulfur oxide (SO2), to prevent the degradation of wine, including oxidation, may induce a range of adverse health effects in sensitive individuals [45]. Thus, e orts have been made to reduce or replace its usage, betting on the use of HT as a promising natural antioxidant alternative [46][47], although the characteristic aroma of HT-rich extracts may hinder its application [48]. In fact, Raposo et al. [46] demonstrated that the use of 80 mg of HT/L in white wine (Sauvignon Blanc) intensified its color when compared to control samples, even after six months of storage in a bottle, but its score was injured with regard to the olfactometric.

The application of HT was also demonstrated in **fruit juices** [49][50] to improve their nutritional properties. In fruit smoothies, the addition of OLE (HT-rich extract) increased their bitterness, but this could be masked if lower concentrations were used (below 20 mg/100 g), or by adding ingredients with known bitterness-masking properties [49]. However, the lower concentrations proposed had lower phenolic content compared to coffee or tea [49]. In an attempt to formulate a functional juice, Larrosa et al. [50] added enzymatically-synthesized HT at a concentration of 1mg/mL to **tomato juice** and claimed that 200 mL of this juice would provide 4 mg of HT, which is close to the minimum recommended by the ESFA. In this matrix, the HT was more efficient than a commercial antioxidant (3-t-butyl-4-hydroxyanisole, BHA) in improving antioxidant activity and deaccelerating lipid oxidation (over eight- and three-fold, respectively). Additionally, HT remained stable in the tomato juice matrix at room temperature and light exposure storage conditions for 48 days without affecting the sensory properties (flavor and color) in great extension [50].

More recently, Guglielmotti and coworkers [51] incorporated HT as part of brewing to fortify a **beer**. They used olive leaves as an ingredient of beer, in the form of dry crumbled leaves (1.27 mg of HT/g), infusion (3.43 mg of HT/g), and an atomized extract (5.58 mg of HT/g), that were added near to the boiling phase of brewing, thus promoting the hydrolysis of oleuropein of the leaves to HT. The addition of 10 g/L of olive leaves conferred to the beers a sour/astringent taste and herbal aroma, whereas 5 g/L olive left a more soft and pleasant sensory profile. Both results could be interesting to formulate distinct beers, especially with increased antioxidant capacity and polyphenol content. Regarding HT's sensorial impact, efforts have been made to overcome HT's bitter taste in the products. An example of this is a patented beverage with HT (in the amount of 0.5–50 mg/100 mL) that claims to be easily drinkable due to the presence of ethanol, propylene glycol, and caffeine at a specific rate that disguises the characteristics of the flavor of HT [52].

2.4.3. Vegetable-based products

Although **table olives** are a source of HT, their fermentation process often changes and/or reduces their phenolic fraction. Some authors proposed the supplementation with HT or HT-rich extracts to balance this loss (Table 1). In fact, even supplemented with OLE, there was a decrease in the concentration of total phenolics during the fermentation of table olives, but, in the case of HT, it increased upon 120 days in brine and olive flesh samples, achieving in the final of fermentation the levels of 2489 mg/L of HT and 187 mg HT/kg, respectively, with no or only slight changes in their sensory acceptability [53]. These observations were consistent with the work of Schaide et al. [54], who reported that the addition of OLE to table olives increased the levels of HT (1700 mg/kg in olive flesh and 3500 mg/L in brined olive flesh) as compared to control conditions (900 and 2500 mg/L respectively), and provided olives without bitterness after 121 days of fermentation. In line with the previous studies, the sensory acceptability was unchanged in Lalas et al.'s study [55], after the addition of OLE (200 mg HT/kg extract) to table olives fermented for a week, while the HT content increased from 408 to 855 mg/kg in flesh table olives.

In addition to table olives, the fortification of **bean purée, potato purée, and tomato juice** with an OMWW extract (0.44, 1.00, 2.25, or 5.06 g extract/kg food product) increased bitterness and intensified the sourness and astringency. Pungency was suppressed in bean purée and perceived at a weak-moderate intensity in potato purée and tomato juice samples at the highest phenol concentration [56]. As table olives are already a natural source of HT, their application should be more explored in other vegetable-based products.

2.4.4. Bakery products

Bakery products are attractive food products for HT supplementation since they are largely consumed by different populational groups of all ages. Among bakery products, a major part of the studies investigated **biscuits**. For instance, Mateos et al. [57] reported that the human intake of HT-fortified biscuits (30 g biscuits that provide 5.25 mg of HT, after an overnight fast) was able to reduce the levels of oxidized LDL in blood, even though there was no increase in the antioxidant activity in blood serum. In the same line but with a different source of HT, Conterno et al. [58] found that the 90 g daily doses of biscuits supplemented with an olive pomace extract (8.11 g of HT/g biscuit, provides 729.9 g of HT), consumed daily for eight weeks, increased homovanillic acid and DOPAC levels, which were suggested by the authors to be involved in the reduction in oxidative LDL cholesterol. Note, however, that sensory changes may occur, as noticed by Navarro and Morales [59] in HT and OLE-fortified **biscuits** (at different concentrations of HT, 2.55, 5.11 and 10.22 mg of HT/g dough, and OLE, 0.127 and 0.537 mg of OLE/g dough), which became darker than the plain products. Yet, in some conditions, a synergy between components of the extract can contribute to the antiglycative effect; hence, suppressing these changes. A similar pattern of results was obtained in the work of Cedola et al. [60]. In the **Italian biscuit "taralli"**, the replacement of the ingredient white wine by OLE (17% weight/weight, 24.08 mg gallic acid equivalent/g dry weight) turned the biscuit color darker without changing the overall quality score. Moreover, the addition of OLE improved the nutritional quality of "taralli", increasing antioxidant activity, total phenols and, especially, flavonoid content from 0.09 mg quercetin/g dry weight in plain samples to 0.39 and 0.36 mg quercetin/g dry weight of uncooked and cooked, respectively [60].

Apart from this, one must also remark the promising application of HT as a functional ingredient in bakery products, aiming to improve their quality. In this regard, the fortification of **bread and rusk** with olive polyphenols by emulsion was reported to extend their shelf-life from 10 to 15 days. Among the tested concentrations (50–3000 mg olive phenols/kg bread, 100–400 mg olive phenols/kg rusk), that of 200 mg of polyphenols/kg was the most efficient in terms of antimicrobial activity, particularly in rusk [61]. Furthermore, related to this topic, a bread containing Hytolive 2 developed from Genosa (Spain), and the Puratos' Nostrum brand **bread** is possible to find on the market [62]. However, in vivo tests are needed to support the potential of these breads as a functional food.

2.4.5. Meat products

Meat products with high-fat content, such as lard or sausages, are prone to lipid oxidation either during manufacturing, storage or cooking, and this may lead to a decline in nutritional quality, color changes, texture deterioration, off-odors and off-flavors, and generation of toxic compounds [63]. Concerns about the negative health impacts of the industrial use of nitrites and synthetic antioxidants, such as BHT or BHA [64][65][66], have increased over the last few years and they have clearly prompted the search for natural antioxidant alternatives, such as HT. The fortification of HT in meat-based products has been reported by several authors (Table 2), most of them already considered in the review of Martínez et al. [67]. In this context, Cofrades et al. [68] studied the antioxidant activity of HT-fortified **sausage frankfurters** with 100 mg of HT/kg meat batter, highlighting that HT effectively inhibited oxidation to the same extent of BHA and BHT. A smaller amount was applied by Nieto et al. [69], 50 mg of HT/kg **sausages**, which still prevented the lipid oxidation and the loss of thiol groups, in comparison with control samples. The authors suggested that the replacement of animal fat by olive oil and walnuts could be an alternative to produce healthier meat products. Similar antioxidant potential was noticed with the application of 150 mg OMWW extract/kg of lard (HT representing 66.8%) [70], as well through the use of a purified phenolic-rich extract obtained from olive vegetation water in **fresh pork sausages** [71].

In the same line, in **lamb meat patties** enriched with omega-3 (n-3) fatty acids, the addition of the olive waste extract Hytolive® (containing 10.5% of HT), at concentrations of 100, 200 or 400 mg gallic acid equivalent/kg muscle, was demonstrated to delay meat discoloration, lipid oxidation, and protein carbonylation, and increased the loss of thiol groups relative to controls, during six days of storage [72]. Nevertheless, Nieto et al. [69] reported changes in the general acceptability of the **sausages** supplemented with olive oil and HT-rich extract (50 mg/kg), mostly in flavor and odor, especially when supplemented with olive oil, which lowered the sensorial acceptability score. Yet, the opposite trend was observed by Aquilani et al. [73] and Chaves-López et al. [74] in HT-fortified **fermented sausages** under different concentrations (higher, around 11.65 mg HT/kg) or even using a distinct supplementation method (submersion in 2.5% of OMWW extract), for which the authors only noticed a color change. Additionally, it was also pointed out that the HT supplementation resulted in a more compact meat emulsion, less porous structure, and more reddish color as a consequence of the possible interaction of HT with fat and protein particles with myoglobin [69]. In the context of in vivo experiments supporting the health-promoting effects caused by HT-fortified meat products, Santos-López et al. [75] studied the impact on **pork meat** supplemented with 3.6 g HT/kg of fresh batter on the lipoprotein profile of aged rats fed high cholesterol/high saturated fat diets. The results show a decrease in adverse effects associated with the diet, mainly by reducing the amount of total cholesterol.

In addition to preventing lipid oxidation, HT-rich extracts have also been claimed to be able to inhibit the growth of major foodborne pathogens, such as *Escherichia coli*, *Listeria monocytogenes*, *Staphylococcus spp*., *Clostridium spp*. and *Salmonella spp*. This effect was comparable to sodium nitrite, i.e., a commercial preservative usually used in meat products [73]. In the study of Chaves-López et al. [74], **fermented sausages** dipped in 2.5% of OMWW extract (100.23 mg HT/g of extract) resisted the development of fungal species and volatile compound characteristics of fatty acid oxidation. In the work of Rounds and colleagues [76], the authors demonstrated that the addition of an olive oil extract to **ground beef** (1 and 3%) reduced the *E. coli* population to levels below detectable limits, as well as the amine formation (i.e., carcinogenic compounds that resulted from the heating process) to about half of their initial values. Moreover, the application of olive leaf extracts from *Olea europaea* var. sylvestris (rich in oleuropein and HT) to raw **halal minced beef** at 1 and 5% was shown to improve the levels of antioxidants in the food products, and simultaneously reduce psychrotrophic counts and pathogens, without any influence on the overall acceptability [77]. More recently, the effect of a HT-rich extract from vegetative waters on the shelf-life of **lamb meat burger patties** was tested [78], allowing the conclusion that the fortification of this product in 200 mg/kg patties prevented lipid oxidation and microbiological growth, although with less effeciency when compared to pure HT.

2.4.6. Fishery products

Fishery products are a great source of lipids, particularly of long-chain polyunsaturated fatty acids ω-3 (PUFAs), which makes them well recommended by the World Health Organization for preventing cardiovascular diseases. Within this scope, their preservation becomes essential and many antioxidant compounds have been tested to prevent oxidative deterioration of PUFAs during processing and storage. Curiously, the fortification of **horse mackerel**, **bulk cod liver oil** and **cod liver oil-in-water emulsions** with HT (50 mg of HT/kg) showed comparable results with the propyl gallate (a synthetic phenol) (Table 2) regarding the prevention of lipid oxidation, while in cod liver bulk oil and cod liver oil-in-water emulsions, the best oxidative stability was obtained at 100 mg of HT/kg. In horse mackerel muscle, the peroxide values stayed below 20 milliequivalent (meq) oxygen/kg fat even after four weeks of frozen storage (control showed 100 meq oxygen/kg fat). Furthermore, HT allowed good preservation of the original content of docosahexaenoic acid (DHA), as well as of α-tocopherol (decrements are often used as a reflection of oxidative stress of fish) [79]. Moreover, the application of an OLE was effective to hinder the microbial growth of psychrophilic bacteria in **anchovy fillets** [80], as well to preserve fish patties against *Staphilococcus aureus*, *E. coli*, and *L. monocytogenes* [81], simultaneously contributing favorable sensory and preventive oxidation properties.

2.4.7. Dairy products

Consumers of a wide range of ages consume dairy products, which make them promising functional foods. A functional **milk beverage (yogurt-like)** was developed by mixing an OMWW extract in pasteurized cow's milk concentrated to a final concentration of 100–200 mg/L (expressed in HT equivalent) (Table 2). The added phenols did not interfere either with the fermentation nor with functional lactic acid bacteria, and the HT content increased during the storage. In fact, the authors claimed that, in terms of phenolic content, the consumption of 100 mL of this beverage is almost equivalent to 20 g of VOO (containing 500 mg/kg phenols), and hence extends the health benefits of olive phenols to a milk beverage [82]. Curiously, a HT-rich product obtained from olive fruits (Medoliva©, 0.5 g HT/g powder) added to **yogurt** was shown to improve the growth of lactic acid bacteria and to contribute to preventing spoilage during fermentation, as well as to promote benefits towards the lipid metabolism of consumers. In non-declared pathology individuals, the daily consumption of two yogurts (200 g each) for two weeks did not change blood redox status but reduced LDL cholesterol [83]. Thus, this yogurt may be integrated into the concept of functional food. In fact, another HT-fortified **yogurt** (HT concentration ranges of 0.1 and 0.01%) was developed and patented by Villanova and her collaborators [84], which suggests some competition regarding this type of food. In addition to yogurt, the application of HT in **regular milk** has also been reported before. In this regard, Fei et al. [85] described that the addition of an olive oil extract (at concentrations of 0.625 mg/mL, containing 6% HT) exhibited antimicrobial activity, decreasing the vegetative cells to undetectable levels. In **milk or egg-based mayonnaise**, the addition of VOO also showed bactericidal activity for *Salmonella enteritidis* and *L. monocytogenes* [86], which may be relevant considering mayonnaise's application in raw products, such as salads.

3. Conclusion

The vastness of information regarding bioactivity, metabolism, and absorption of HT makes it an exciting compound to be considered as a potential functional ingredient. The valorization of HT towards diet improvement is an excellent opportunity to use it as a source of natural antioxidants to replace (or reduce) synthetic additives. Among bioactive properties, HT has been claimed to activate endogenous defense systems, such as the antioxidant enzymes that control and regulate the detoxifying mechanism of mitochondrial biogenesis. So far, clinical studies have been focused on HT ingestion together with olive oil, hindering possible conclusions on the real potential of HT. Additionally, information related to the metabolization process and absorption of the compound is still scarce. Although the bioactivity of some HT metabolites is known, further studies are required to investigate their potential applications. A great diversity of food products supplemented with HT have been reported. However, the impact of the food matrix on the delivery of HT requires further studies. As HT may provide a bitter taste to food, a sensorial analysis should be considered more often to predict the acceptability of consumers to HT supplementation. The costs of the process of HT recovery, pure or in extracts, and the overall impact of HT-fortification on the price of new HT-enriched food products are also important factors to be considered, in order to obtain a fair balance between the valorization of the product and the acquisition price.

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