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Olive Biophenols as New Antioxidant Additives in Food and Beverage

Rosaria Ciriminna,[a] Francesco Meneguzzo,[b] Riccardo Delisi,[c] and Mario Pagliaro*[a]

Replacing synthetic phenols, sulfites and other synthetic antioxidants and antimicrobials, olive biophenols can be successfully used as multipurpose additives in foodstuffs and beverages. Are these natural phenolics suitable for large-scale replacement of synthetic additives? This study aims to provide an answer to this and related questions of significant health and environmental significance.

Introduction

Antioxidant food and beverage additives are widely used by industry to prolong shelf-life by inhibiting the oxidation of fat (oxidative rancidity), vitamins and various amino acids molecules, ensuring also retention of taste and colour.[1] In the food industry, the purpose of adding one ore more antioxidants is twofold,[2] namely *i*) to suppress lipid oxidation and free radicals in foodstuff under conditions of long storage or of cooking, and *ii*) to reduce the concentration of free radicals in vivo after food ingestion.

For over 70 years, the most commonly used antioxidant food additives have included BHA (butylated hydroxyanisole), BHT (butylated hydroxytoluene), PG (propyl gallate) and TBHQ (tert-butyl hydroquinone), namely phenolic compounds, often used in combination, to stabilize fat in baked and fried products, vegetable oils and margarine.

It has been at least two decades since consumer safety concerns are driving a major trend in the food industry,[1] namely the shift from the use of synthetic to natural ingredients in food products. A range of natural antioxidants are nowadays increasingly used in industry as food and beverage antioxidant additives, including ascorbic acid (vitamin C, contained in many citrus fruits) to protect soft drinks, jams, condensed milk and meat, and tocopherols (vitamin E family) for preserving vegetable oils, margarine and cocoa products.[3] Arguing that natural antioxidants are preferred over synthetic antioxidants by most consumers "for emotional reasons",[2] Pokorny and Parkányiová emphasized the poor stability and carry through properties of natural antioxidants, suggesting that their optimal utilization consists in direct addition as food ingredients without any fractionation,[4] such as in the case of rosemary resins (see below).

Other major changes driven by consumer changing lifestyles are the increasing demand of precooked meals, the progressive elimination of hydrogenated fats, and the incorporation of oxidatively unstable nutritional ingredients such as polyunsaturated fatty acids (omega-3) and vitamins in today's complex foods. All this will require better ways for controlling oxidation. involving "blends of antioxidants that operate on different components of the oxidation mechanism and act synergistically".[5]

One suitable replacement for synthetic antioxidants for preventing rancidity in meat, fish, baked and dairy products, might be olive biophenols due to their antioxidant, antimicrobial and anti-inflammatory properties.[6] Obtained from olive fruits and also from its by-products (olive tree leaves, olive pomace and olive mill waste water) these phenolics have exceptionally high antioxidant activity,[7] and generally show no adverse health effects.

Besides extended shelf life, they would impart new health benefits to foodstuffs. In other words, olive biophenols may act as antioxidant food additives and as food supplements endowing new and relevant properties to foodstuffs and also to beverages.[8]

The most interesting biophenols are found in the olive mill waste water (OMWW, containing $>50\%$ of the total olive biophenols),[9] in the pomace and in the leaves from which they are increasingly extracted. The aim of this study is not to provide a complete overview on food applications of olive biophenols, but rather to provide a critical answer to the question: Are olive biophenols suitable for large-scale replacement of synthetic antioxidants and preservatives?

Scope of Application

Without an antioxidant added, unsaturated fats (polyenoic acid esters) abundant in food products in contact with air's oxygen rapidly oxidise with formation of peroxides.[1] Lipid oxidation is initiated by reactive oxygen species such as hydroxyl radical, singlet oxygen, and anion peroxide radical which attack the

[a] *Dr. R. Ciriminna, Dr. M. Pagliaro*
Istituto per lo Studio dei Materiali Nanostrutturati
CNR
via U. La Malfa 153, 90146 Palermo, Italy
E-mail: mario.pagliaro@cnr.it
[b] *Dr. F. Meneguzzo*
Istituto di Biometeorologia
CNR
via Caproni 8, 50145 Firenze, Italy
[c] *Dr. R. Delisi*
Renovo Bioindustry
via Pietro Verri 1, Centro direzionale Boma, 46100 Mantova, Italy

double bonds in the unsaturated lipid molecule, forming (lipid) peroxyl radical ROO which, in its turn, rapidly evolves into secondary oxidation products.[3] Antioxidant phenols (ArOH) stop the propagation reaction by the following mechanism (Eq.s 1 and 2):

$$ROO\bullet + ArOH \rightarrow ROOH + ArO\bullet \quad (1)$$

$$ROO\bullet + ArO \rightarrow \text{Harmless, non radical product} \quad (2)$$

As expected, lipid oxidation is greatly accelerated by increasing temperature. For example, the peroxide value indicating the quality depletion of biscuits during shelf life rapidly increases with storage temperature, with acceptability (linearly correlated to peroxide value) going from 69 days for the product stored at 20 °C, to 26 days when stored at 37 °C.[10]

Olive phenols are excellent free radicals scavengers. Hydroxytyrosol, for example, is a free radical scavenger[11] with an ORAC value (oxygen radical absorbance capacity) exceeding 42,000 μmol TE/g (micromoles Trolox Equivalents per g dry matter), and even freeze-dried OMWW has an high ORAC (2011 μmol TE/g).[12] Yet, biophenols protect lipid from oxidation synergistically, also by chelating metal ions (phenolic acids and flavonoids), and by decomposing peroxides.[13]

In 2011 Russo and co-workers published the outcomes of a quantum chemistry study of the molecular mechanism of biophenols antioxidant activity.[14] Theory suggests that activity increases with the number of hydroxyl groups and the extent of double bonds conjugation, which is in full agreement with results concerning the antioxidant activity of typical olive biophenols in preserving meat lipid from oxidation, whose activity is strongly dependent on the number and position of free hydroxyl groups attached to the aromatic ring (Figure 1).[15]

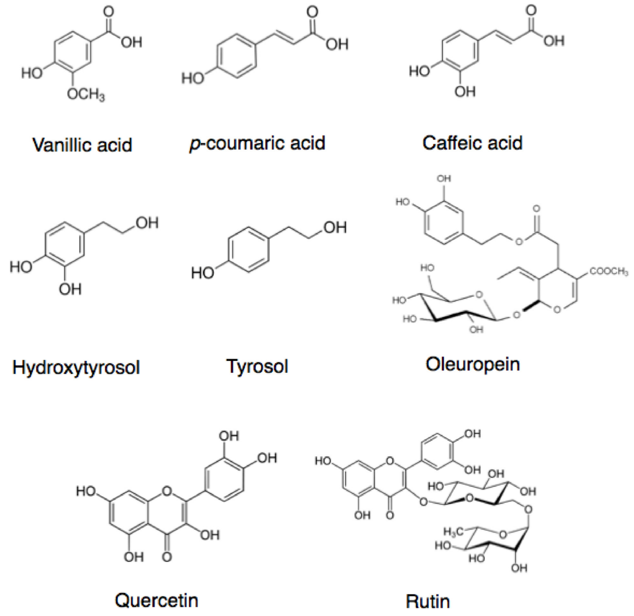

Figure 1. Chemical structures of the olive biophenols teste das antioxidants in meat. [Adapted from Ref.15, with kind permission].

In detail, hydroxytyrosol, caffeic acid and oleuropein, three *o*-diphenols, are more effective antioxidants than tyrosol, vanillic and *p*-coumaric acids with only one OH available. The introduction of a second *o*-hydroxyl group in the tyrosol or the *p*-coumaric acid molecules to form, respectively, hydroxytyrosol or caffeic acid increases the antioxidant activity in meat by 85 % and 420 %, respectively.[15]

Rosaria Ciriminna *is a research chemist based at Italy's Research Council. Developed at Palermo's Institute of Nanostructured Materials in cooperation with numerous research groups in Italy and abroad, her research focuses in green and nanochemistry. Rosaria has published over 160 research papers, four books and numerous book chapters. Currently, she coordinates her Institute's activities in the BIOPIC sustainable biopesticides research project.*

Francesco Meneguzzo *is a physicist based at the Institute of Biometeorology of Italy's CNR in Florence, where he coordinates a research group focusing on agri-food processes and bioeconomy, meteorology and solar energy. Co-author of over 100 research papers on these and related topics, his achievements include the development of a new clean production and sanification process for beer making based on hydrodynamic cavitation. Since 2016, chair of the SuNEC solar energy conference held annually in Sicily.*

Riccardo Delisi *holds a PhD in pharmaceutical chemistry from Palermo's University. After an intensive post-doc in Dr Pagliaro's research Group in 2015–2016 working on the extraction of bioactive molecules from natural matrices, heterogeneous catalysis and photocatalysis for organic synthesis, he was hired by Renovo Bioindustry where he coordinates research in the field of bioproducts.*

Mario Pagliaro *is a chemistry and energy scholar at Italy's Research Council based in Palermo. His research Group co-operates with scholars based in numerous countries. Co-author of more than 180 research articles, 20 books and several book chapters, he is one of Italy's most cited scientists in nanotechnology and materials science.*

In further detail, the antioxidant activity of biophenol extracts towards lipid protection is directly correlated to the amount of hydroxytyrosol (HT) present in the OMWW extract. This may not be surprising given the exceptional ORAC value of HT mentioned above, and was clearly demonstrated by De Leonardis and co-workers in 2009 (Figure 2).[16] In a previous

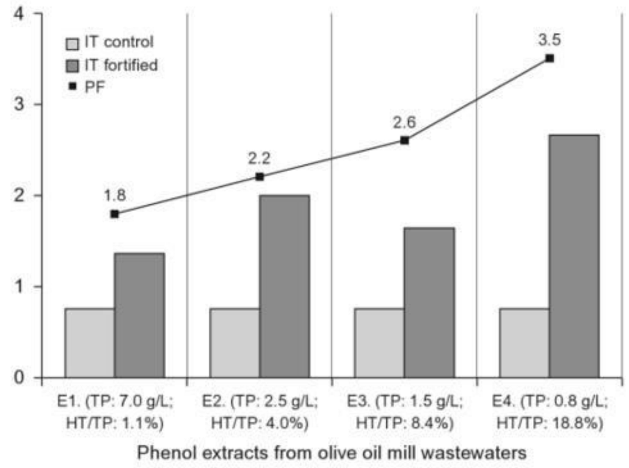

Figure 2. Antioxidant activity of different OMWW extracts on lard (Rancimat test, 120 °C, air flow = 20 L h-1). IT = induction time, PF = protection factor, TP = total phenols, HT/TP = free hydroxytyrosol/total phenols [Reproduced from Ref.16, with kind permission].

cytotoxicity assay the team had found that OMWW extract obtained via liquid-liquid extraction, added (in 100–200 ppm doses) to lard significantly increased its oxidative stability, giving lard added with olive phenols the nature of "novel food" with health benefit.[17]

Olive biophenols such as HT suppress the mechanism through which bacteria in a colony interact with each other,[18] adding value to the use of olive juice extract in foods not only for preventing oxidation but also bacterial contamination. In detail, HT alters cell-to-cell communication mechanism, by blocking the key steps of quorum sensing, such as signal generation, signal accumulation or signal reception. Remarkably, the amount of HT needed to behave as a quorum-quencher is much lower (between 0.005 and 0.04 wt%) compared to the amount needed to behave as antimicrobial agent. As usual with phenolics, the OMWW extract comprising several phenols shows higher antimicrobial activity against five microbial species (*Escherichia coli, Salmonella poona, Bacillus cereus, Saccharomyces cerevisiae and Candida albicans*) when compared to HT or oleuropein alone.[19]

The synergy (cooperative interaction) among the polyphenol constituents of olive extracts is indeed a well known feature of biophenols. For example, a mixture of HT and caffeic acid is considerably more effective than single components in protecting DNA from oxidative damage and inhibiting the growth of cancer cells.[20] According to the excellent activity against bacterial proliferation mentioned above, added in small amount (50-60 ppm) to wine right after fermentation, the *Hidrox* biophenol OMWW extract not only did not alter the red wine (from Cabernet-Sauvignon grapes grown in Italy) antioxidant profile after nine years, but also prevented the bacterial conversion of alcohol into vinegar,[21] thereby safely replacing toxic SO_2 conventionally used to extend the shelf life of bottled wines. SO_2 used in wines is an effective antioxidant and antimicrobial agent that inhibits the development of yeast, and lactic acid bacteria but, as known to many consumers, inducing headache and abdominal pain, forcing wine makers to declare its presence in the label of each bottle.

Pointing to important differences among different commercial extracts (OMWW, leaf or solid olive oil by-product), researchers in Spain recently tested another commercial olive biophenols extract (HT80) obtained by solvent extraction of the pomace.[22] The scavenging effect (antioxidant activity, in %) of the extract (17 % and 40 % at 50 mg/L and 80 mg/L concentration) was lower when compared with olive mill wastewater (90–100 %), in agreement with the higher biophenol concentration in OMWW when compared to pomace. The extract was not found sufficiently effective to replace SO2 leading the researchers to suggest a combination SO2 + pomace extract in wines to enlarge the antimicrobial activity and reduce the odor extract contribution.

As mentioned above, olive polyphenols can also successfully preserve meat products from lipid oxidation and microbial spoilage. This was first shown in 2009 using an OMWW extract obtained from freeze-drying olive oil pomace to isolate an olive extract containing hydroxytyrosol (70.6 %), tyrosol (17.5 %), caffeic acid (9.5 %), *p*-coumaric acid (1.9 %) and vanillic acid (0.3 %).[15]

Added to pre-cooked beef and pork meat at either 50 or 100 ppm levels, the team in Argentina found that the degree of lipid oxidation in the meat was reduced between 47 % and 66 % in pork, and 63 % to 83 % in beef. In comparison with commercial biophenol-based antioxidants obtained from tea and grape, the ranking of efficacy was green tea > olive > grape skin.

Finally, pointing to their broad scope of application, olive-derived biophenols can be used as antioxidant, antimicrobial, and antibrowning agents, to maintain or improve the quality of fish and seafood products.[15] In mince mackerel muscle, for example, a concentration of 50 ppm of HT optimally maintains a longer initial level of vitamin E (R-tocopherol), and completely preserves from oxidation valued omega-3 polyunsaturated fatty acids.[24]

From Health Threat to Health Benefits

Synthetic antioxidants such as BHA and BHT, suspect carcinogens, are included as food additives in the stabilization of vegetable and animal fats into products consumed every year by billions of consumers across the world (meat, burgers, hot dogs, cereal, chewing gum, dry breakfast cereals, etc.). Regulation governing the use of food and beverage additives varies from country to country. In the European Union, food additives (all identified by an E number) are reviewed by the European

Table 1. Examples of widely used antioxidants in the EU		
E-Number	Substance	Foodstuffs in which they are used
E 300	Ascorbic acid	Soft drinks, jams, condensed milk, sausage
E 301	Sodium ascorbate	
E 302	Calcium ascorbate	
E 304	Ascorbyl palmitate	Sausage, chicken broth
E 306–309	Tocopherols	Vegetable oils
E 310	Propyl gallate	Fats and oils for professional manufacture, frying oils and fats, seasoning, dehydrated soups, chewing-gum
E 311	Octyl gallate	
E 320	Butyl hydroxyanisol (BHA)	Sweets, raisins, processed cheese, peanut butter, instant soups
E 321	Butyl hydroxytoluene (BHT)	
E 392	Antioxidant rosemary extract	Fish and algal oils, butter, bakery products, meats, dehydrated soups and potatoes

Food Safety Agency (EFSA) and eventually approved by the European Commission.

In detail, the Directive 95/2/EC of 20 February 1995 ("Directive on Food Additives other than Colours and Sweeteners Antioxidants") governs authorization, use and labelling. All added additives need to be declared on food packaging by their category (antioxidant, preservative, colour, etc) with either their E-number or name (Table 1).

The EFSA re-evaluated the safety of BHA in 2011,[25] and that of BHT in 2012,[26] concluding in the former case that at the current levels of use intake estimates are generally below the acceptable daily intake (ADI) dose, whereas in the case of BHT the EFSA established a new ADI (0.25 mg/kg/day), half of the previous one. On the other hand, the EFSA concluded in 2008 that dietary exposure and use levels of rosemary extracts, whose antioxidant activity is largely ascribed to phenolic diterpenes carnosol and carnosic acid, are of no safety concern.[27]

Contrary to synthetic antioxidants, furthermore, which are partly stored in adipose tissue, olive biophenols are completely metabolized with numerous health benefits. Significant health beneficial properties (antioxidant, anti-inflammatory, anti-microbial, antifungal, cardioprotective, hypoglycemic and anticarcinogenic) are reported for all major components of olive biophenols, including hydroxytyrosol, tyrosol, caffeic acid, oleuropein, oleocanthal and verbascoside.[28] Their bioavailability greatly differs,[29] but the most important (hydroxytyrosol and tyrosol)[30] are readily bioavailable supporting dietary supplementation, as lately shown for instance by biscuits incorporated with hydroxytyrosol in which HT is extensively metabolised and rapidly eliminated, contributing to a decrease of plasma oxidized-LDL (low density lipoprotein);[31] and by clinical trials on tyrosol bioavailability in volunteers after ingestion of virgin olive oil showing extensive hepatic metabolism (only 6–11% of total tyrosol excreted in free form).[32] Accordingly, the use of olive biophenols in place of synthetic antioxidants in food and beverage might boost the body's antioxidant activities to combat oxidative stress, transforming an industry's issue (the use of toxic synthetic oxidants in low dosage) into an opportunity by which the antioxidant activity of synthetic antioxidants is retained (and even improved), while the consumer enjoys the health benefits of these valued substances.[3]

Barriers to Overcome

Food antioxidants should be low cost substances, effective in very small quantities and with a carry-through property. Concerning cost, and thus the large scale possible replacement of synthetic antioxidant with biophenol extracts, the raw material (OMWW and other byproducts) is available at no or moderate cost in all olive growing countries. The natural antioxidant cost will therefore mostly depend on the applied extraction process, and on the dose values to obtain good replacement of synthetic antioxidants, which in its turn are related to the amount of active biophenols available in each extract.

We have discussed elsewhere the main recovery and extraction methodologies,[34] showing that commercial extracts are generally obtained under standardized extraction, cultivation and harvesting conditions. Extracts from OMWW are chemically different from those obtained from olive tree leaves. The chemical composition of available extracts further varies depending on the cultivar, zone of cultivation and ripening (harvesting time).

Like synthetic antioxidants, and contrary to vitamin E and ascorbic acid, olive biophenols remain stable at high temperatures, and at the dosage typically required (50-100 ppm) they do not interfere with taste or color of foodstuffs.

Before being widely used as food additives, olive biophenol extracts need to be chemically and toxicologically scrutinized according, for example, to rules and guidelines by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the Food and Drug Administration (FDA) or the EFSA. In the US, for example, prior to commercialization food additives must be approved by the FDA, unless the substance is generally recognized as safe under the conditions of its intended use (GRAS status). When a substance has the GRAS status, it can be freely used under the conditions of its intended use reported in the GRAS certification. In 2004, the first toxicity study on Hidrox administered to mice up to 2000 mg/kg/day resulted in no adverse clinical, haematological, biochemical, or reproductive effects.[35]

To the best of our knowledge, in Europe so far olive biophenol extracts did not yet receive approval and consequently an E-number. This will be very important as shown for example by the approval of rosemary extracts as antioxidant food additive by the EFSA in 2008 which transformed the "legal status" of rosemary extract from flavor to antioxidant,[36] and contributed to dramatic increase in rosemary oil market volume and value.

The safety of olive phenolics compared to synthetic antioxidant BHT was shown as early as of 2003 by Farag and co-workers, who administered rats with olive and olive leaf extracts, and butylated hydroxytoluene for 7 weeks.[37] Administration of BHT at 200 ppm dosage was enough to induce severe damage to the tissues of the rat kidney, while kidney and liver tissues of rats administered with olive phenolic compounds even at 1200 ppm showed no histological changes (at 1600 ppm total phenolic dosage, the mice tissues were affected as in the case of BHT at 200 ppm).

A most recent toxicological study on a commercial extract of olive tree leafs (Bonolive) excluded mutagenicity and genotoxic activity on mice;[38] whereas oral administration of another commercial leaf extract (Benolea EFLA 943) containing 20% oleuropein (500 mg twice daily) for 8 weeks to 162 patients suffering from hypertension did not induce any relevant changes in liver and renal function, while significantly reducing pressure, triglycerides, and low-density lipoprotein cholesterol levels.[39]

Outlook and Conclusions

Natural food additives are the future of food preservation due to the health benefits and synergies.[40] Two main limitations were found to hamper widespread adoption of natural antioxidants, namely missing legislation and approval, and limited supply of standardized extracts. Once approved olive phenolic extracts of high and standardized quality will be available in the large amount required (thousand tonnes), this will affect the food and beverage industries' utilization of antioxidants and preservatives. These substances, indeed, have the potential to transform their products into functional foodstuffs and beverage[41] with improved nutritional properties that will be claimed on the label, as it happens with olive oil rich in phenols, following the large "Eurolive" clinical study[42] that in 2006 showed evidence that olive polyphenols decrease lipid oxidative damage.

Eventually, numerous food and beverage companies will switch from conventional, synthetic antioxidants to olive biophenol extracts to reap the additional health benefits. The advantages are simply too many, whereas the legislative and availability barriers to their widespread adoption will be overcome as it happened with the use of health claims based on health effects of olive oil biophenols.[43] For instance, fast food restaurants using hydrogenated canola oil protected from oxidation by low doses of TBHQ to fry, might consider to replace TBHQ with olive biophenols for which recent evidence suggests not only that they can cope with the fast rates of oxidation and oxidative polymerization that take place at frying temperatures, but also effective migration in the fried food.[44]

A recent antioxidants market study[45] points out, indeed, that rising demand for functional food and beverages is expected to be the primary driver for rising polyphenol demand as antioxidants, owing to a growing trend towards healthy lifestyles. Eventually, olive phenols will compete with both natural and synthetic antioxidants.[46]

The natural antioxidants segment mainly comprises vitamin C, vitamin E and carotenoids, with polyphenols (including rosemary extracts) being mainly applied in functional beverages (44% of the 14,000 tonnes polyphenols > market), followed by functional foods (33%).[47] Said natural biophenols in 2013 were mainly derived from grape seed (50% of the total market consumption) followed by the green tea and apple (32%), with olive phenolics being a minor fraction. Following the first successful large-scale applications, we forecast in conclusion, the utilization of olive-derived phenolics as multipurpose food additives, showing beneficial properties even for brain health,[48] will become ubiquitous in the 21st century nutritional industry.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: olive · biophenols · antioxidant · natural · preservatives

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