Review Article

Extraction, benefits and valorization of olive polyphenols

Rosaria Ciriminna¹, Francesco Meneguzzo², Alexandra Fidalgo³, Laura M. Ilharco² and Mario Pagliaro¹

¹ Istituto per lo Studio dei Materiali Nanostrutturati, CNR, Palermo, Italy
² Centro de Química-Física Molecular and IN- Institute of Nanoscience and Nanotechnology, Instituto Superior Técnico, Lisboa, Portugal
³ Istituto di Biometeorologia, CNR, Firenze, Italy

Already used as antioxidants and antimicrobials in functional foods and beverages, as well as in several cosmetic products, olive polyphenols will also play an important role in the treatment and prevention of inflammation, and thus of numerous free-radical mediated chronic diseases. By integrating chemical, health, extraction technology, and market aspects into a unified picture, this study provides arguments supporting the viewpoint that current investments into extraction plants based on green chemistry technologies will shortly translate into widespread utilization of these powerful antioxidants, well beyond the Mediterranean basin countries where the olive tree has been cultivated for >5000 years.

Keywords: Antioxidant / Biophenol / Hydroxytyrosol / Olive polyphenols / Verbascoside

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1 Introduction

A central tenet of the emerging bioeconomy [1] is that by-products from agriculture, so far considered and actually processed as waste, become important sources of high added value compounds [2].

This holds true for d-limonene increasingly obtained from waste orange peel [3], as well as for wastewater from olive mills or olive leaves residual from pruning olive trees, which are abundant sources of polyphenols with powerful antioxidant activity [4], such as hydroxytyrosol and oleuropein (Fig. 1).

Like terpenes, polyphenols are plant secondary metabolites increasingly used in nutraceutical supplements, in new cosmetic formulations as well as in beverages and food due to their antioxidant and anti-inflammatory properties [5]. Their metabolism and nutritional significance [6], and their role in protection from diseases, especially of lifestyle related diseases, is increasingly understood [7].

The olive fruit is rich in phenolic compounds, but only 2% of the total phenolic content of the olive fruit passes in the oil phase. The main fraction is lost in the water phase (approx. 53%) and in the solid pomace residue (approx. 45%; around 2–8 g polyphenols/kg depending on processing) [8].

Olive oil production via the widely adopted three-phase extraction systems involves the addition of large amounts of water (up to 50 L/100 kg olive paste), resulting in the worldwide production of more than 30 million m³ per year of oil mill wastewater (OMWW), a dark and mildly acidic liquid of high conductivity, obtained from mechanical olive processing during olive oil production, containing sugars, tannins, pectins, lipids and a wide range of polyphenols in 1–10 g L⁻¹ concentration [9].

Polyphenols are powerful antioxidants and antimicrobial making difficult to biologically or chemically degrade the oil mill wastewater. As a result, in most oil mills the vegetation water is disposed as waste, or even spread as such either on fertile land, which is readily contaminated with phytotoxic compounds, or in dedicated areas (e.g., in a region of Algeria).

Since the early 2000s, olive polyphenols are extracted from oil mill wastewater (and later on, also from olive leaves) and commercialized for their numerous benefits [10]. Research in the field is flourishing too. For example, the latest academic book [11] on the role of polyphenols in human health comprises 1440 pages and contains >10,000 references to research papers.

In this burgeoning field, we now provide an updated overview summarizing the benefits of olive polyphenols, the techniques used for their industrial extraction, and selected aspects of this nascent large market. The arguments in the conclusions corroborate our viewpoint that olive polyphenols will shortly become the active ingredients of several valued functional,

Correspondence: Dr. M. Pagliaro, Istituto per lo Studio dei Materiali Nanostrutturati, CNR, via U. La Malfa 153, 90146 Palermo, Italy
Fax: +39 091 680 92 47
E-mail: mario.pagliaro@cnr.it

Additional corresponding author: Prof. L. M. Ilharco, E-mail: lilharco@ist.utl.pt
cosmetic and nutraceutical products ubiquitously used, inter alia, to treat and prevent inflammation, ensuring a better quality of life of people in both affluent and economically developing countries.

2 Health benefits

The health benefits of olive polyphenols have been widely demonstrated [12]. In brief, it is today generally recognized that consumption of these olive phytonutrients has certain health benefits, and no known adverse effects. Today claims such as those in Table 1 can be easily retrieved from online advertising of nutraceutical companies commercializing olive polyphenols.

In 2011, the European Food Safety Authority has endorsed the health claim that “olive oil polyphenols contribute to the protection of blood lipids from oxidative stress,” [13] (and the European Commission authorized a health claim to olive oil polyphenols) [14], but it rejected many other health claims concerning blood pressure and anti-inflammation.

In 2005, Hercberg, an eminent nutritionist, was wisely recommending “more patience”

“We need to collect enough information from experimental, clinical, and epidemiologic research before we can support any specific recommendations regarding polyphenols (in particular, which polyphenols, at which doses, to achieve which benefits for which populations). To do this, we need more research, more funds, more patience, and more exchanges within the scientific community and among all research disciplines (basic and applied research).” [15]

According to a research team recently led by Cutfield, a physician based in New Zealand, clinical studies examining the effects of olive polyphenols supplementation on cardiovascular disease risk are “scarce, flawed, or contradictory” [16]. The same researchers, along with co-workers from Australia, thus recently conducted a randomized, double-blinded, placebo-controlled, crossover trial to assess whether supplementation with olive leaf polyphenols would affect cardiovascular risk factors in overweight males.

In a trial involving 46 overweight middle-aged men at risk of developing metabolic syndrome, participants were randomized to receive four commercial capsules with olive leaf extract (OLE, from Comvita, a total of 51.1 mg of oleuropein and 9.7 mg of hydroxytyrosol) or placebo once a day for 12 weeks, which is the minimum study period that can reliably detect a sustained effect of dietary intervention.

Independently of lifestyle factors (such as dietary intakes and physical activity levels), supplementation with

<table>
<thead>
<tr>
<th>Table 1. Claimed health benefits of olive polyphenols</th>
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<tbody>
<tr>
<td>Helps reduce swelling &amp; maintains joint health</td>
</tr>
<tr>
<td>Helps in skin conditions due to auto immune disorder</td>
</tr>
<tr>
<td>Supports cardiovascular wellness</td>
</tr>
<tr>
<td>Helps counter premature aging skin</td>
</tr>
<tr>
<td>Improves skin moisture retention</td>
</tr>
<tr>
<td>Reduces joint inflammation and pain</td>
</tr>
<tr>
<td>Helps in production and repair of cartilage</td>
</tr>
<tr>
<td>Increases joint flexibility and improves mobility</td>
</tr>
<tr>
<td>Supports healthy and supple radiant skin</td>
</tr>
<tr>
<td>Reduces damage from sun exposure</td>
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<tr>
<td>Supports peak mental and physical performance</td>
</tr>
<tr>
<td>Reduces fatigue due to excess free radicals</td>
</tr>
<tr>
<td>Converts fatty acids into energy</td>
</tr>
<tr>
<td>Helps reduce swelling &amp; maintains joint health</td>
</tr>
<tr>
<td>Helps in skin conditions due to auto immune disorder</td>
</tr>
<tr>
<td>Supports healthy and supple radiant skin</td>
</tr>
<tr>
<td>Reduces damage from sun exposure</td>
</tr>
<tr>
<td>Supports cardiovascular wellness</td>
</tr>
</tbody>
</table>

Figure 1. Chemical structures of selected olive biophenols. Olive leaves, fruit, and juice present a broad bouquet of phenolic compounds.
olive leaf polyphenols for 12 weeks was clearly found to improve two aspects of glucose regulation (both insulin action and secretion). The use of olive polyphenols in improving the management of type 2 diabetes was readily patented [17].

The major anti-inflammatory compound in aqueous olive extracts is hydroxytyrosol (HT). The molecule is an exceptional free radical scavenger [18], with an ORAC value (oxygen radical absorbance capacity) exceeding 42,000 μmol TE/g (micromoles Trolox Equivalents/g dry matter). Table 2 shows the ORAC values of pure HT, olive oil, leaf and vegetation water (both as such and freeze-dried) [19]; which also shows that olive oil itself has ultralow levels of HT and oleuropein (the phenolics measured and reported in Table 2).

Hydroxytyrosol scavenges free radicals during the oxidation process, inhibits human LDL oxidation [20], platelet aggregation [21], and the production of leukotriene for human neutrophils [22]. The biophenol impairs inflammatory mediators cytokines with a significant impact in the treatment of chronic inflammatory processes such as arthritis [23]. Additionally, HT induces mitochondrial biogenesis leading to enhanced mitochondrial function in tissues [24], and influences the melanin pigments, inducing the skin to become lighter and dark patches to disappear.

Easily absorbed by the gastrointestinal tract and readily transferred into the blood stream, polyphenol HT helps fight the toxic effects of free radicals accumulated in the human tissues, helping also in the prevention of bone loss. A proprietary polyphenol extract from olive leave (Bonolive), e.g., was recently found to clearly support the bone remodelling process in a double-blind, placebo-controlled 12 months intervention study in a population of postmenopausal women (n = 32 per group) with identified osteopenia [25]. In detail, daily intake of the extract over 12 months resulted in a consistent and continuous increase in plasma levels of the established bone formation biomarker osteocalcin, as compared to the placebo.

Previously, in 2007, a clinical trial on 100 patients (aged from 55 to 75 years) suffering from osteoarthritis and rheumatoid arthritis showed the efficacy of freeze-dried olive vegetation water, with significant improvements in pain, inflammation and movement [26].

Hydroxytyrosol has also therapeutic benefits towards psoriasis, a serendipitous finding of a study carried out in Japan to examine the effects of olive polyphenols on blood fats and inflammatory markers linked to heart health. Subjects affected by psoriasis, after taking the olive extract for a couple of months, saw the skin unexpectedly improved. In detail, out of 35 patients with skin conditions, including psoriasis, allergic dermatitis and seborrheic dermatitis treated with the same product improved following 6 months of treatment, with the majority of patients showing considerable improvement within 60–90 days, with no adverse effects [27].

An even more powerful anti-oxidant, actually the most powerful antioxidant among natural products known thus far [28], is the glycoside verbascoside (Fig. 2). Its unique antioxidant activity is due to the cooperative activity of the two polyphenol constituents, namely caffeic acid and hydroxytyrosol.

More concentrated in the olive fruit (and present also in the leaves) [29], verbascoside exerts a free radical scavenging

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Table 2. ORAC and total phenolic concentrations for olive oil, OMWW, and freeze-dried OMWW

<table>
<thead>
<tr>
<th>Sample</th>
<th>ORAC† (μmol TE/g)</th>
<th>Phenolics mg/g</th>
<th>HT μmol TE/g</th>
<th>ORAC (μmol TE/g phenolics)</th>
<th>ORAC (μmol TE/g HT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OMWW</td>
<td>140</td>
<td>5.0</td>
<td>2.5</td>
<td>28,000</td>
<td>56,000</td>
</tr>
<tr>
<td>Freeze-dried OMWW</td>
<td>2011</td>
<td>69</td>
<td>35</td>
<td>29,145</td>
<td>57,460</td>
</tr>
<tr>
<td>Olive oil</td>
<td>0</td>
<td>&lt;1</td>
<td>&lt;0.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Olive leaf</td>
<td>1079</td>
<td>51</td>
<td>0</td>
<td>21,157</td>
<td>–</td>
</tr>
<tr>
<td>HT (pure)</td>
<td>42,560</td>
<td>1000</td>
<td>1000</td>
<td>42,560</td>
<td>42,560</td>
</tr>
</tbody>
</table>

†ORAC, oxygen radical absorbance capacity; TE, trolox equivalents.

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Figure 2. Chemical structure of verbascoside.
activity which has a direct impact on skin health, preventing oxidative damage associated with wrinkle formation, skin thinning and dehydration. The first cosmetic product (Opextan) showing activity against UV damage, wrinkle formation and hair tonic was commercialized in 2006 in Europe and in Japan [30].

As mentioned above, the co-operative antioxidant interaction among the polyphenol constituents of olive extracts is known since 2006, when Aldini and co-workers reported [28] that the commercial extract (total polyphenol content 35%; verbascoside content 5%) extracted from solid olive residue (Oleoselect) showed a greater antioxidant activity for the purified extract compared to either that of verbascoside (the main Oleoselect component) or caffeic acid (the basic constituent of verbascoside) alone.

Besides good radical quenching activity, the Oleoselect extract exhibits a significant cytoprotective effect (lipid oxidation process) on the damage of endothelial cells induced by the peroxyl radical generator AAPH (Fig. 3).

Three years later, Obied and co-workers reported a similar finding showing that the mixture of hydroxytyrosol, caffeic acid is considerably more effective in protecting DNA from oxidative damage and inhibiting the growth of cancer cells (antiproliferative agent), than any of the single constituents [31].

Following these research outcomes, a recent patent application [32] addresses the enhanced wound healing ability of olive-derived hydroxytyrosol and oleuropein added in compositions containing human umbilical cord stem cells towards reducing the time for a wound to close by 30% compared to just the cells alone, including for wounds that tend to resist healing.

The use of hydroxytyrosol for preventing bacterial infection was recently patented along with the finding that the phenol suppresses the mechanism through which bacteria in a colony interact with each other [33], adding value to the use of olive juice extract in foods not only for preventing oxidation but also bacterial contamination.

Added in small quantity (50–60-mg/L) to wine right after fermentation, olive polyphenol extracts such as Hidrox can safely replace toxic SO2, widely used worldwide to extend the shelf life of bottled wines. Successful tests carried out at an Italy-based winery, show that the addition of Hidrox did not alter the wine antioxidant profile after nine years, and also prevented the bacterial conversion of alcohol into vinegar [34], even though the taste of the wine, due to a relatively high polyphenol content, is slightly bitter.

Another bioactive biophenol contained in the olive polyphenols bouquet is the aldehyde oleocanthal whose anti-inflammatory action was readily linked to its ability to inhibit the cyclooxygenase enzymes in the prostaglandin-biosynthesis pathway [35], after Beauchamp, an expert on chemosensory, noticed that the sting felt when sipping Sicily’s olive oil, was similar to that produced when assuming non nonsteroidal anti-inflammatories such as ibuprofen.

The potential applications of oleocanthal were patented [36], claiming utilization as antioxidant (to promote wound healing, and used to provide oxidation stability in cosmetics), pain relief agent (symptom of influenza or other viral infections, headache, toothache), and preservative (anti-bacterial and antifungal agent for food packaging). Since then, two new polyphenols have been identified in olive oil. Dubbed by Magiatis and Melliou, who identified them by NMR spectroscopy, oleomissional and oleokoronal (from the names of the Greek cities Koroneiki and Messinia) [37], both are aldehydes with a similar distinctive burning taste as oleocanthal.

Remarkably, as customers aware of the health benefits of these anti-inflammatory compounds begin to ask for high phenolic extra virgin olive oils, the same scientists in Greece developed a low cost colorimetric testing kit (Aristoleo) to rapidly select high-phenolic oils at the oil mill.

3 Industrial extraction methods

Polyphenols are polar organic compounds that can be readily extracted from olive waste or from olive leaves and fruit. Current methods include elution following adsorption over selective adsorbents, extraction with water or with super-critical CO2, and nanofiltration followed by reverse osmosis. According to Frankel and co-workers, who reviewed most such methods in 2013, “the processes proposed so far are expensive and/or produce low yields.”[38]

Reflecting such variety of chemical methodologies, different extraction procedures are actually used by different companies, which generally rely on a unique source of olives, so as to minimize the variability of polyphenols in their extracts and ensure standardized production.

The method used by Creagri in the US does not use organic solvents, but rather lemon-derived citric acid in 1 wt
% concentration that, following prolonged contact with vegetation water, affords high yields of hydroxytyrosol. In detail, the vegetation water obtained from depitted olives is added with citric acid and left in incubation for several months until most of the oleuropein originally present in the vegetation water is hydrolyzed and converted to hydroxytyrosol, which is subsequently filtered and freeze-dried leaving no residues in the extracted product (Hidrox) [39].

Indena in Italy uses GRAS (generally recognized as safe) water and ethanol as the only solvents to elute the polyphenols from the olive pulp [40]. To amplify, the olive pulp is air dried and then extracted with water at a reflux temperature for 1 h. The resulting mixture, after filtration and washing with hot water, is loaded onto a resin (Amberlite XAD-7) column, eluted with ethanol, and freeze-dried affording a solid polyphenols extract (Oleasellect).

Netherlands-based DSM, on its turn, extracts the polyphenols from the olive fruit. Seppic in France manufactures the Prolivols brown powder by simply spray-drying with maltodextrin the refined oil mill wastewater [41].

Comvita in New Zealand starts from the olive leaves as source of the polyphenols. Among the different parts of the olive tree, indeed, olive leaves possess the highest oleuropein content, within a range of 1–14% compared to olive mill wastewater (0.87%) [42].

In 2005, Nunes da Ponte and co-workers in Portugal coupled supercritical fluid extraction along with nanofiltration to extract biophenols, especially hydroxytyrosol, from OMWW. The resulting natural extract comprises a minimum concentration of 15% (mass fraction), almost ten times higher compared to the industrial extracts available at that time.

However, production on industrial scale requires technical simplicity [43]; and the supercritical fluid process originally conceived to produce the Oilhidrox extract, thus far has not been commercialized.

The solid phase extraction process using adsorption resins mentioned above has been extensively demonstrated by several research groups. Skaltsounis and co-workers passed the filtered wastewater (to eliminate suspended solids up to a limit of 25 μm) through a series of adsorbent resins (Amberlite XAD16 and XAD7HP) in order to achieve the deodorizing and decolorization of the wastewater and the removal of the polyphenol content [44].

Evaporation and recovery of the aqueous methanol used to elute and regenerate the resin affords an extract rich in polyphenols with high antioxidant activity, while the odorless yellowish wastewater with a 99.99% reduced content in polyphenols and 98% reduced COD, can be used for irrigation.

Ethanol in place of methanol, and shorter contact times, can easily be applied, with further enhancement of the efficacy and environmental and economic sustainability of the process [45].

Similarly, silica can be used to replace the Amberlite resins employed as separating column material, with similar good yields (>1 g L⁻¹) of phenolic compounds employed for example, from Jordanian OMWW [46].

### 4 Olive polyphenols market

Antioxidants are the largest category of active ingredients of the $80 billion market of anti-aging products [47]. This market expands at >10% annual growth rate, and olive polyphenols – whose hydroxytyrosol and verbascoside components share the highest level of antioxidant activity ever reported for any natural compound – can be effectively used in each of the three segments (health, appearance enhancement, and fitness) comprising the overall anti-aging products market.

The three main factors that will drive the polyphenols market growth over the next years, we argue in this study are: i) the increasing aging population in North America, Japan, and Europe with desire to defy signs of aging; ii) the consumer’s shift towards natural products for the treatment of inflammation, cardiovascular diseases, arthritis and other free-radicals mediated diseases; and iii) the consumer’s desire to replace with safe natural products the toxic chemicals such as organic peroxides, sulphites and nitrates widely used as preservatives in processed foods, wine and beverages.

In general, so far the sources of natural polyphenols have been grape seed, green tea and apple [10]. The olive polyphenols market is in its nascent stage, as extraction plants to produce high grade polyphenol extracts are eventually being installed in several Mediterranean countries, but also in China, California, New Zealand, Malaysia, and in general in all the world’s regions where olives are grown.

So far, in our views, the demand for olive polyphenols has been limited by reduced market offer. A situation that is rapidly changing. Along with pioneering company Creagri that introduced its Hidrox extract in the US market in 2003, a selection of today’s suppliers of olive polyphenols extracts includes Indena (Oleasellect and Opextan), Seppic (Prolivols), Genosa (Hytolive), Seprox Biotech (HTr), Biosearch Life (Hydrolive), Mc Cord Research (Olivamine), DSM (elaVida), Probeltebio (Mediteaxos), Certified Nutraceuticals (Olea25), Comvita (OLE), and Lachifarma (TirosoilHT). Many other companies are up to enter the market, including chemical companies making synthetic polyphenols (Wacker, e.g., since late 2014 sells synthetic hydroxytyrosol of high purity under the name HTEssence).

Most olive extracts (but not all) are based on hydroxytyrosol as the main active ingredient. Almost invariably each company has patented its extraction process, and the “novel” uses of its extract, assigning it a tradename. Herein it is relevant to notice that in 2005, Nunes and co-workers published an interesting economic analysis of the commercial natural extracts existing at that time (Table 3) [48].
Compared to the most concentrated sample, the six times higher amount of hydroxytyrosol in the extract obtained by supercritical extraction followed by nanofiltration (Oildrox), would result in a 18% lower cost of the phenol for the customer, who would also get an extract exhibiting far higher anti-oxidant, anti-microbial, and anti-inflammatory activities. The phenolic manufacturer, in its turn, would get 380% higher margin.

Accordingly, in the subsequent decade many new formulations comprising much higher phenolics and hydroxytyrosol concentration entered the market. Growing at annual rate of about 9%, the global demand for polyphenols is expected to reach 25,000 tonnes (from 14,000 tonnes in 2013) and >$1 billion in value by 2020 [10]. Followed by North America and Europe, the Asia Pacific region is already the largest and the fastest growing market for polyphenols (in terms of consumption: 41% of total market in 2013).

The market for olive polyphenols is, in order of increasing value, in the food, pharmaceutical, and cosmetics sectors (Fig. 4). Olive biophenol extracts of lower concentration are ideally suited for bakery products where they are an healthy replacement for toxic organic peroxides widely used as antimicrobial agents [49]. The brown Prolivols powder, e.g., targets this market segment since its launch.

Besides dietary supplements for the prevention of diseases and general well-being, the high valued added cosmetic applications require uncolored extracts with high concentration of the active ingredients (e.g., hydroxytyrosol and verbacoside) for easy incorporation into creams, lotions, sunscreens, deodorizers and other personal care products, which creates room for microencapsulated polyphenols [50], such as the nanoOilidrox (35 wt% in hydroxytyrosol) [48] originally developed by Nunes da Ponte and co-workers.

### Table 3. Hydroxytyrosol content and cost in different olive extracts

<table>
<thead>
<tr>
<th>Extract</th>
<th>Hydroxytyrosol (%)</th>
<th>Price (€/kg of extract)</th>
<th>Price (€/kg of hydroxytyrosol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hidrox</td>
<td>2.9</td>
<td>520</td>
<td>17,900</td>
</tr>
<tr>
<td>Oleoselect</td>
<td>2.2</td>
<td>350</td>
<td>15,900</td>
</tr>
<tr>
<td>Prolivols</td>
<td>1.2</td>
<td>250</td>
<td>20,900</td>
</tr>
<tr>
<td>Oildrox</td>
<td>17</td>
<td>2500</td>
<td>14,700</td>
</tr>
</tbody>
</table>

*Data of IBET laboratory (Universidade Nova de Lisboa) with Folin-Ciocalteau and ABTS tests. Values are the average of three experiments experiments (5% error).

According to Crea, an eminent biochemist [51] co-inventor of the insulin chemical synthesis and founder of Creagri, “cellular inflammation, and trying to control it, is going to be at the core of medicine for the next 20 years, and people want to manage it with natural products” [52]. After two decades of intense research on natural polyphenols applied as bioactive compounds, accumulated data support their efficacy in the prevention of free-radical-mediated degenerative diseases such as atherosclerosis, coronary heart disease, cancer, and rheumatoid arthritis [9].

Accordingly, several companies have started to commercialize olive polyphenols, formulated in different ways, with a basic common ground: the numerous health benefits and the lack of adverse effects associated to consumption and topical benefits.
application of these biochemicals. In addition, numerous functional foods and beverages [53] functionalized with olive polyphenols were lately commercialized. In 2013/2014, the world’s production of olive oil exceeded 3.2 million tonnes. Spain (1.5 million tonnes), southern Italy (500,000 tonnes), and Greece (230,000 tonnes) account for 70% of the overall output [54], whereas all together Mediterranean countries account for >90% of the world’s olive production.

In large part, the 30 million tonnes of OMWW produced yearly continue to be dealt with as “waste” and consequently landfilled or composted without having extracted the highly valued polyphenols. This eminent example of waste in modern societies is equivalent to widespread landfilling of waste orange peel containing plenty of pectin, flavonoids and limonene that continue to be discarded and landfilled as waste [3].

It is therefore somehow ironic to recognize here that Creta discovered in the early 2000s that lemon juice added to reduce the bitter taste of olive polyphenols was able to extract and at the same time to protect from rapid oxidation the hydroxytyrosol contained in vegetation water from depitted seeds.

The works of a recent international conference on polyphenol applications, were recently concluded emphasizing that “economically feasible approaches are still needed for the exploitation of biophenols by-products arising from processing of plant-derived raw materials.” [55] Focusing onto olive biophenols, the methods surveyed in this study show that the phenolics content of vegetation waters and solid olive residue can be readily extracted using a technique as simple as solid phase extraction, with full recovery of the eluting clean solvent (e.g., ethanol), co-producing large amounts of decontaminated water ready for irrigation, of high value in dry regions of the world where these trees are predominantly grown.

The global anti-aging products market is ready to absorb high and increasing amounts of high quality olive biophenols extracts, as shown by the economic success of the numerous companies cited throughout the study. Research in the field actively continues worldwide. Suffice it to mention the recent Germany’s “NeurOliv” [56] research project aimed to develop new nutraceuticals and pharmaceuticals for the prevention and treatment of neurodegenerative diseases such as the Alzheimer’s disease.

By integrating chemical, health, industrial extraction technology and market aspects into a unified picture this study will hopefully provide relevant arguments to entrepreneurs cultivating olive trees, as well as to managers of biotechnology, nutraceutical, and cosmetic companies, that the time has come to invest in economically viable extraction plants based on green chemistry technologies so as to maximize the value contained in the exquisite olive fruit, whose biophenols will benefit mankind at large, even beyond the Mediterranean basin countries where this tree has been cultivated for >5000 years [57].

This article is dedicated to Francesco Pagliaro, father of one of us, and long time maker of an exceptional olive oil in Sicily.

The authors have declared no conflict of interest.

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[13] EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to polyphenols in olive and protection of LDL particles from oxidative damage (ID 1333, 1638, 1639, 1696, 2865), maintenance of normal blood HDL-cholesterol concentrations (ID 1639), maintenance of normal blood pressure (ID 3781), “anti-inflammatory properties” (ID 1882), “contributes to the upper respiratory tract health” (ID 3468), “can help to maintain a normal function of gastrointestinal tract” (3779), and “contributes to body defences against external agents” (ID 3467) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA J.* 2011, 9, 2033.

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