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Multiple pharmacological effects of olive oil phenols

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Abstract

Olive oil is a unique component of Mediterranean diet and is likely to be partially responsible for the health effects of this diet. Although the medicinal potential of olive oil has been largely attributed to the antioxidant effects of bio-phenols derived from olive oil, accumulating evidence strongly suggests that, to elucidate olive oil's benefits to human health, we have to go beyond antioxidants. In this communication, through summarizing the reference-reported and database-recorded pharmacological information of olive oil phenols, we reveal that multiple pharmacological effects, other than antioxidant potential, are involved in olive oil phenols, which is of significance for understanding the health benefits of olive oil in the Mediterranean diet.

Keywords: Mediterranean diet; Olive oil; Bio-phenols; Antioxidant; Multiple pharmacological effects

Accumulating evidence indicates that adherence to Mediterranean diet (which consists of olive oil, fruits, vegetables and fish) is associated with lower prevalence of coronary heart disease, cancer and cognitive impairment, e.g., Alzheimer's disease (AD) (Scarmeas, Stern, Tang, Mayeux, & Luchsinger, 2006; Trichopoulou, Costacou, Bamia, & Trichopoulos, 2003). Since reactive oxygen species (ROS) are implicated in these diseases, the benefits of the Mediterranean diet have been largely attributed to the antioxidant potential of polyphenols contained in the diet components, especially olive oil (Owen et al., 2000b). Indeed, olive oil phenols are efficient radical-scavengers in vitro (Owen et al., 2000b) and can be well absorbed by the body (absorption >55–66 mol%) (Vissers, Zock, & Katan, 2004). However, Vissers et al. (2004) argued that the plasma concentration (<0.06 μM) of antioxidant phenols, resulting from dietary intake of olive oil, is too low to exert antioxidant effects. Moreover, increasing evidence suggests that the in vitro antioxidant potential can not necessarily be translated into in vivo therapeutic effects (Frankel & German, 2006; Halliwell, 2006; Kroon & Williamson, 2005). Therefore, it seems that, to elucidate the benefits of olive oil, we should go beyond antioxidants.

Indeed, in recent years, some pharmacological effects other than antioxidant capacity have been reported for olive oil phenols. For instance, (−)-oleocanthal (Fig. 1), a component extracted from newly-pressed extra-virgin olive oil, possesses ibuprofen-like cyclooxygenases (COX-1 and -2) inhibitory ability (Beauchamp et al., 2005); hydroxytyrosol and hydroxy-isochromans (Fig. 1) are inhibitors of platelet aggregation (Petroni et al., 1995; Togna, Togna, Franconi, Marra, & Guiso, 2003) and oleuropein (Fig. 1) can form a non-covalent complex with amyloid-β (Aβ) peptide or its oxidized form (Bazoti, Bergquist, Markides, & Tsarbopoulos, 2006). All of these effects help to explain the benefits of olive oil in preventing cardiovascular diseases, cancer and AD.

Considering the fact that tens of polyphenols have been identified from olive oil (Nikolaos, Wang, Tsimidou, & Zhang, 2005; Owen et al., 2000a), we have great interest in finding more pharmacological effects for olive oil phenols. Since natural products are usually shared by many plants, it is possible that the olive oil phenols may occur

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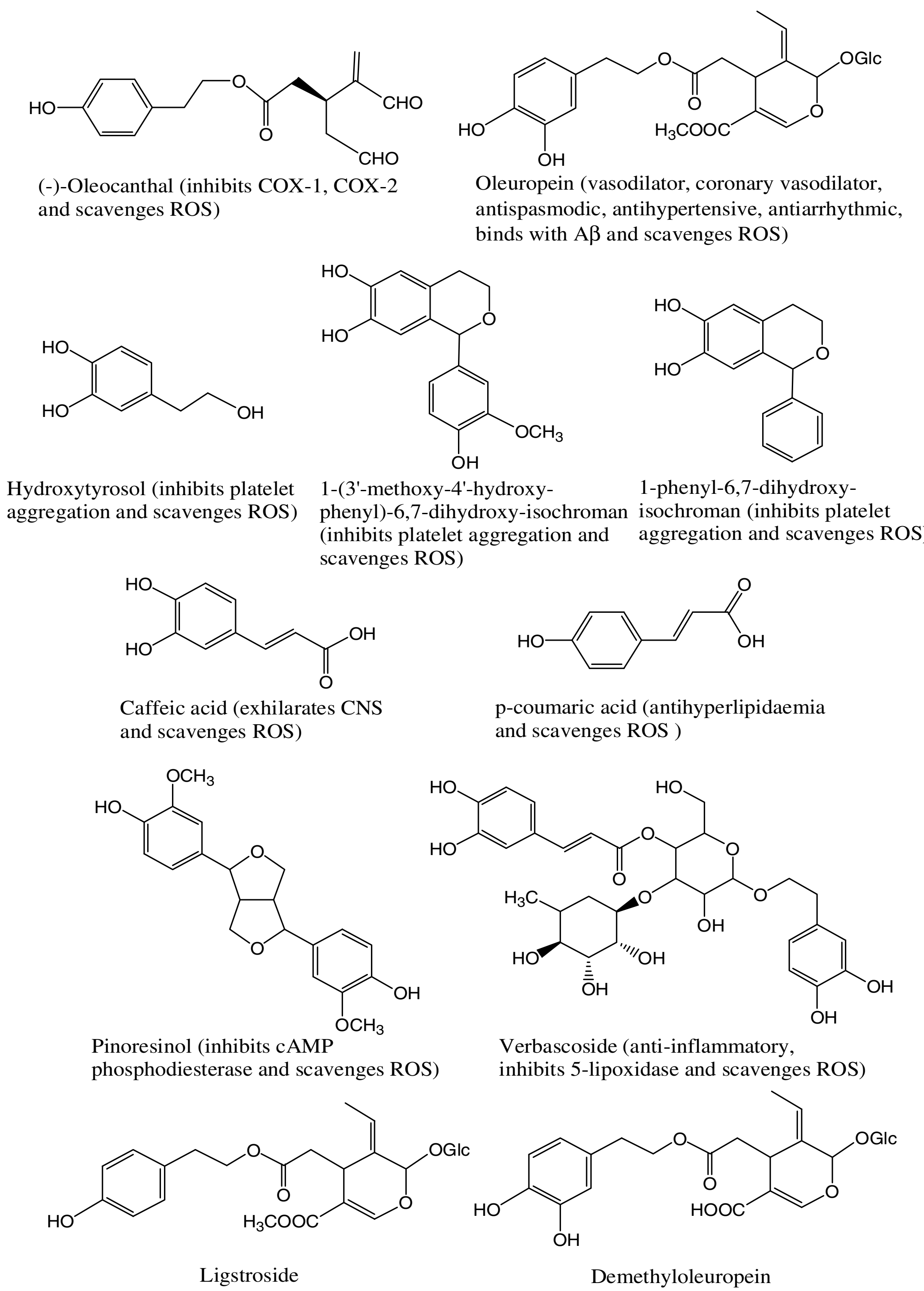

Fig. 1. Structures and multiple pharmacological effects of olive oil phenols.

in other plants and some of them may have been recorded in drug databases or natural medicine databases. Therefore, we searched a comprehensive medicinal chemistry (CMC) database (which contains 8659 drugs) and a traditional Chinese medicine database (TCMD) (which contains 10,458 components) by using CMC-3D Finder and ChemFinder, respectively, to hunt for olive oil phenols (or their congugates) and corresponding activities.

It was found that three (benzoic acid, gallic acid, oleuropein) and 13 olive oil phenols (benzoic acid, caffeic acid, catechol, cinnamic acid, dihydroxybenzoic acid, gallic acid, hydroxytyrosol, oleuropein, *p*-coumaric acid, *p*-hydroxybenzoic acid, pinoresinol, syringic acid, verbascoside) had been recorded in the CMC and TCMD, respectively. Some pharmacological activities associated with anti-cancer, anti-cardiovascular diseases and anti-AD were identified for caffeic acid (CNS exhilarant), oleuropein (vasodilator, coronary vasodilator, antispasmodic, antihypertensive, antiarrhythmic), *p*-coumaric acid (antihyperlipidaemia), pinoresinol (cAMP phosphodiesterase inhibitor) and verbascoside (anti-inflammatory, 5-lipoxidase inhibitor) (Fig. 1). The structural similarity search also provided some clues to finding new pharmacological effects for olive oil phenols. For instance, it was found that olive oil phenols ligstroside and demethyloleuropein (Fig. 1) are highly structurally similar to oleuropein (with similarity of >95%), implying that both phenols may hold pharmacological effects as diverse as oleuropein. Besides, magnolin, a platelet aggregation inhibitor recorded in TCMD, was identified as a cognate of the olive oil phenol pinoresinol (with >95% similarity), which strongly suggests that the latter holds anti-platelet-aggregation potential. These findings deserve further experimental investigations.

In conclusion, through summarizing the reference-reported and database-recorded pharmacological information of olive oil phenols, we provided a relatively comprehensive pharmacological profile of olive oil phenols which goes far beyond antioxidant activity. With the rapid progress in pharmacological research on olive oil phenols, it can be expected that we will fully understand the health benefits of olive oil and even Mediterranean diet in the not-very-distant future. In addition, the present analyses offer further evidence to support the finding that many natural antioxidants are multipotent agents (Zhang, Yang, & Tang, 2006), which implies that it would be better to look further than antioxidants when developing functional foods.

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