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# Activity of myricetin and other plant-derived polyhydroxyl compounds in human LDL and human vascular endothelial cells against oxidative stress

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ABSTRACT

Studies indicate that oxidative modifications of endothelium and LDL play a preeminent role in atherogenesis; therefore, the preservation of the endothelial antioxidant capacity and the inhibition of LDL oxidation by use of plant-derived compounds are an appealing strategy against several vascular disorders. On this basis, baicalein, eupatorin, galangin, magnolol, myricetin, oleuropein, silibinin and bilobalide were studied against various oxidative conditions. The radical scavenging capacity was analysed using DPPH and ORAC assays. Furthermore, the LDL oxidation was detected by measuring the formation of thiobarbituric acid reactive substances (TBARS) and by monitoring the oxidation kinetics. Further, we used cultured HUVEC to investigate the activities of the polyhydroxyl compounds towards the oxidative stress induced by $H_2O_2$. The lowest levels of TBARS were observed in the presence of oleuropein and baicalein, while myricetin, magnolol and eupatorin inhibited these ones to a lesser extent. In addition, oleuropein and myricetin exhibited higher protection in copper-induced LDL oxidation kinetics. However, only myricetin and galangin showed significant protective effects against $H_2O_2$ oxidative injury in HUVEC cells. Taken all together the results indicate myricetin as the most active agent among the selected plant-derived polyhydroxyl compounds, with prominent capacities against ox-LDL and ROS production in HUVEC.



## 1. Introduction

Inflammation, oxidative stress and endothelial dysfunction are associated with the pathogenesis of atherosclerosis [1]. Evidence supports the crucial role of oxidized low-density lipoproteins (ox-LDL) in the early inflammatory stage of atherosclerotic lesions [2,3]. Polyhydroxyl compounds are naturally occurring constituents of vegetable food and are main plant compounds with antioxidant activity. Epidemiological and clinical studies suggest that a polyphenol-rich diet may protect against cardiovascular disease and, generally, from pathological damage related to oxygen-derived free radicals (ROS) [4–6]; but the role of these plant-derived compounds in therapy is still matter of debate [7]. Generally, the epidemiological findings suggest the effectiveness of antioxidant-rich foods but, on the other hand, interventional trials with various vitamins as antioxidants, *i.e.* ß-carotene, vitamin E, ascorbic acid, folic acid, and related meta-analysis for the most part failed to demonstrate their usefulness [8,9]. In this context, it seems likely that other types of substances, as the polyphenols, may be the active compounds of vegetable foods useful against ROS-related diseases. Authors observed the necessity of proper experimental studies on single antioxidant compound, as prerequisite for clinical trials. On this basis, we selected eight polyhydroxyl compounds, mainly flavonoid derivatives, as baicalein, eupatorin, galangin, and myricetin, but also other compounds having different chemical structures, as bilobalide, magnolol, oleuropein, and silibinin (Table 1), to assess their antioxidant activities. Thus, the aim of this study was to find active compounds against oxidative stress for the potential use against atherosclerotic diseases. This study provided insight on the effects of the

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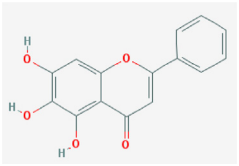
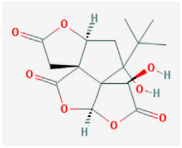
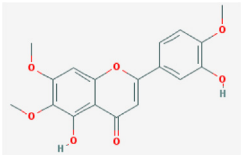
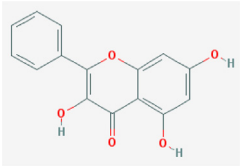
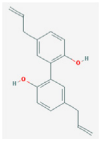
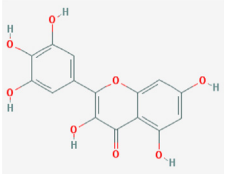
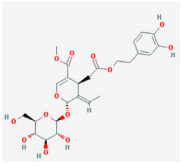
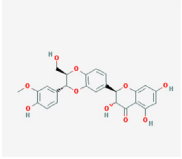
**Table 1**
Plant-derived compounds known for their presence in several botanicals.

| Compound | Chemicals | Medicinal plant[a] | Plant parts | Chemical structure[b] |
|---|---|---|---|---|
| Baicalein | Flavone | *Scutellaria baicalensis*, *Oroxylum indicum* | Herb<br>Leaf<br>Stem bark Root |  |
| Bilobalide | Sesquiterpene | *Ginkgo biloba* | Leaf |  |
| Eupatorin | Flavone | *Eupatorium* spp.<br>*Orthosiphon aristatus* | Herb<br>Rhizome Root |  |
| Galangin | Flavonol | *Alpinia* spp., *Helichrysum aureonitens*, propolis | Herb<br>Rhizome |  |
| Magnolol | Neolignan | *Magnolia officinalis* | Bark |  |
| Myricetin | Flavonol | *Myrica rubra*<br>*Tilia* spp. | Flower<br>Leaf |  |
| Oleuropein | Secoiridoid | *Olea europaea* | Fruit<br>Leaf |  |
| Silibinin | Flavanolignan | *Silybum marianum* | Fruit<br>Herb |  |

[a] Examples of plants containing the compound.
[b] The chemical structures are from PubChem.