POLYPHENOLIC DERIVATIVES AND METAL COMPLEXATION IN THE IMPROVEMENT OF THEIR PHARMACOLOGICAL ACTIVITY

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ABSTRACT

Flavonoids, such as flavones and flavonols, are plant polyphenolic compounds, which are found in many natural plant species, especially fruits and vegetables [1]. As the most common natural flavonoid, quercetin and its derivatives are widely present in nuts, beverages, and Chinese herbal medicine. Flavonoids have proven to be potent antioxidant agents, due to their ability to prevent injury, caused by free radicals, through mechanisms such as direct scavenging of reactive oxygen and nitrogen species (ROS and RNS), activation of antioxidant enzymes, and sequestering chelation of metals. Their ability to chelate metal ions is very important, since metal complexes of several flavonoids, like morin and quercetin, have shown potent antioxidant activity in *in vitro* studies [1]. A significant problem, however, of flavonoids in potential applications in health, arises due to its low solubility in aqueous media. To that end, a challenge emerges to increase the solubility and bioavailability of flavonoids so that its biological activity reaches effectively all engaging targets in (sub)cellular media. To that end, sulfonic derivatives of quercetin have been reported, albeit with no significant detail, to exhibit antibacterial and antitumor activities to go along with their antioxidant properties [2]. Based on the existing literature, our research tried to focus on flavonoid bioavailability and in so doing develop well-defined methodologies providing soluble flavonoids in aqueous media. Furthermore, enhancement of bioavailability of derivatized flavonoids was sought after through reactivity of sulfonic derivatives of quercetin and their complexes with metal ions [3,4]. To meet the challenge of improving flavonoid solubility, quercetin-5'-sulfonic acid was synthesized reproducibly and crystallized in order to confirm its X-ray structure. The well-defined flavonoid was subsequently used for the synthesis of complexes with metal ions, including divalent-trivalent metal ions of metabolic importance (Zn(II)), Cr(III), Ga(III)). The nature and properties of such novel binary and ternary metal-flavonoid complexes (with auxiliary aromatic chelators) was confirmed using elemental analysis, FT-IR spectroscopy, 1D-2D NMR spectroscopy, and luminescence studies. The collective properties set the basis for further inquiry into the biological role of the derivatized flavonoids and hybrid metalloforms thereof, thus meriting future applications in health and theranostics.

KEYWORDS: Flavonoid, Quercetin, Metal complex, Antioxidant activity, bioavailability

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