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DUAL MECHANISM OF MANGIFERIN PROTECTION AGAINST IRON-INDUCED DAMAGE TO 2-DEOXYRIBOSE AND ASCORBATE OXIDATION

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Introduction

Iron is vital in life because it is an important component of molecules that undergo intracellular redox reactions. However, this property also makes iron potentially toxic, since redox reactions may generate reactive oxygen species (ROS)[1].

Iron-chelating agents were introduced in the 1960s for the treatment of iron overload related diseases like hemochromatosis and β- thalassemia, where iron can accumulate at high hepatic levels[2]. Currently, deferoxamine (DFO) is the only iron chelator still clinically used. However, the cost of the treatment and lack of intestinal absorption of DFO have prompted research in the pursuit of alternatives[3].

We have recently shown that mangiferin, a naturally occurring glucosylxanthone, causes rapid oxidation of Fe (II) and prevents Fe (III) reduction by ascorbate, diminishing the availability of Fe (II) for the Fenton reaction and thus preventing ferrous iron-induced lipid peroxidation in isolated rat liver mitochondria[4].

The antioxidant activity of several polyphenols, involving prevention of $^{\bullet}$OH formation and ascorbate oxidation, has been correlated with their iron-chelating properties; however, as far as we know, this has not been established with mangiferin, so the aim of the present work is to further document the action of mangiferin as an antioxidant, mainly through its Fe (III) -chelating properties and its ability to induce Fe (II) oxidation and not merely due to OH scavenging activity.

Materials and methods

The formation of OH radicals was measured using 2-deoxyribose oxidative degradation. The principle of the assay is the quantification of the main 2-deoxyribose degradation product, malonaldehyde (MDA), by its condensation with TBA[5]. The rate of ascorbate oxidation was followed at 265 nm[6] in a Hitachi U-2001 spectrophotometer at 28 °C.

Oxygen concentration was polarographically determined with a Clark-type electrode (Yellow Springs Instruments Co.) in a 1.3-ml glass chamber equipped with a magnetic stirrer at 28°C. Absorption spectra from 300 to 700 nm were obtained using a Hitachi U-2001 spectrophotometer at 28°C.

Results and discussion

Results revealed that mangiferin was equally effective in preventing degradation of both 15 mM and 1.5 mM 2-deoxyribose. At a fixed Fe (III) concentration, increasing the concentration of ligands (either EDTA or citrate) caused a significant reduction in the protective effects of mangiferin. Interestingly, mangiferin strongly stimulated Fe (III)-EDTA ascorbate oxidation, but inhibited it when citrate was used as iron co-chelator. Mangiferin stimulated O_2 consumption due to Fe (II) (formed by Fe (III) ascorbate reduction) autoxidation when the metal ligand was EDTA, but inhibited it when citrate was used. These results suggest that mangiferin removes iron from citrate, but not from EDTA, forming an iron-mangiferin complex that cannot induce ascorbate oxidation effectively, thus inhibiting iron-mediated oxyradical formation. Taken together, these results indicate that mangiferin works mainly by a mechanism different from the classical hydroxyl radical scavengers, keeping iron in its ferric form, by complexing Fe (III), or stimulating Fe (II) autoxidation.

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