The role of mangiferin in the prevention of liver Fe accumulation and fibrosis in experimentally induced iron overload in rats

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Background: Iron overload due to genetic abnormalities or repeated blood transfusions in patients with thalassemia can cause irreversible organ damage because of hemosiderosis and hemochromatosis and result in death. Standard chelating agents for the treatment of iron overload are expensive, the mode of administration sometimes is invasive, and they can cause various unwanted side effects. The study investigates mangiferin, the active compound from the leaves of *Mangifera indica* as a preventive treatment of iron overload.

Methods: Thirty rats were divided into 5 groups: normal control (N), iron overload (IO), and iron overload with mangiferin doses of 50 mg (IOM50), 100 mg (IOM100) or 200 mg (IOM 200) / kg BW. Iron overload in our rat model was induced by means of 15 mg intraperitoneal iron dextran given twice a week for 4 weeks. After 4 weeks, blood and liver samples are taken from the rats. Mangiferin serum concentration was measured with HPLC. Liver hemosiderin measurement was accomplished with iron-Prussian blue reaction in hepatocytes and in Kupffer cells with Le Sage scoring method (score 0-4). METAVIR method was used for trichrome coloring to determine fibrosis in the liver (score 0-4). Statistical analysis was conducted with Kruskal Wallis and Mann Whitney for post hoc test.

Results: The levels of mangiferin after administration of dose 50 mg, 100 mg and 200 mg/kg BW for 4 weeks were 416.10, 310.55 and 450.11 ng/mL, respectively. Iron overload induced for 4 weeks showed significant difference Fe accumulation in Kupffer cells for IO compare to N groups, score 2.7 vs 0 ($p=0.006$). Mangiferin therapy gave no significant results. Fe accumulation in hepatocyte and fibrosis analysis showed no significant difference among groups ($p=0.063$ and $p=0.086$ respectively). Fe hepatocyte scores for N, IO, IOM50, IOM100, and IOM200 were 0, 0.7, 0, 0.5, 0.17, respectively. Fibrosis score for N, IO, IOM50, IOM100 and IOM200 were 0.25, 1.17, 0.4, 0.75, and 0.67, respectively.

Conclusion: Oral administration of mangiferin showed non-linear pharmacokinetics and low bioavailability. Mangiferin could not prevent the accumulation of Fe in liver and fibrosis.