

Endogenous antioxidant and LOX-mediated systems contribute to the hepatoprotective activity of aqueous partition of methanol extract of *Muntingia calabura* L. leaves against paracetamol intoxication

ABSTRACT

Methanol extract of *Muntingia calabura* L. (family Muntingiaceae) leaf has been reported to exert various pharmacological activities including hepatoprotection. The present study was carried out to identify the most effective hepatoprotective partition derived from the extract and to determine the mechanisms of action involved. The extract was partitioned using solvents with different polarity to yield petroleum ether (PEMC), ethyl acetate (EAMC), and aqueous (AQMC) extracts. Each extract, at 250 mg/kg, was subjected to the paracetamol (PCM)-induced hepatotoxic assay and several parameters such as liver weight, liver/body weight ratio, serum liver enzymes' level, and histopathological examinations were determined. Each partition was also tested for their antioxidant and anti-inflammatory potentials. The most effective extract (AQMC) was prepared in additional dose of 50 and 500 mg/kg, and then subjected to the same liver toxicity test in addition to the endogenous antioxidant enzymes assay. Moreover, AQMC was also subjected to the phytochemical screening and HPLC analysis. Overall, from the results obtained: AQMC exerted significant ($p < 0.05$): (i) antioxidant activity when assessed using the DPPH, SOD and ORAC assays with high TPC detected; (ii) anti-inflammatory activity via LOX, but not XO pathway; (iii) hepatoprotective activity indicated by its ability to reverse the effect of PCM on the liver weight and liver/body weight ratio, the level of serum liver enzymes (ALT, AST, and ALP), and activity of several endogenous antioxidant enzymes (SOD and CAT). Phytochemicals analyses demonstrated the presence of several flavonoid-based bioactive compounds such as gallic acid and quercetin, which were reported to possess hepatoprotective activity. In conclusion, AQMC exerts hepatoprotective activity against the PCM-induced toxicity possibly by having a remarkable antioxidant potential and ability to activate the endogenous antioxidant system possibly via the synergistic action of its phytoconstituents.

Keyword: *Muntingia calabura* leaves; Anti-inflammatory activity; Endogenous antioxidant activity; Hepatoprotective activity; Paracetamol-induced hepatotoxicity