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AN OPIUM ALKALOID- PAPAVERINE AMELIORATES ETHANOL-INDUCED HEPATOTOXICITY: DIMINUTION OF OXIDATIVE STRESS

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ABSTRACT

In this communication, we show the modulatory potential of papaverine, an opium alkaloid and a well known vasodilator agent on the ethanol-induced hepatic oxidative stress in male Wistar rats. Ethanol treatment (50% v/v) enhanced lipid peroxidation significantly accompanied by a decline in the activities of glutathione peroxidase (G-Px), glutathione reductase (GR) and depletion in levels of hepatic glutathione (GSH). Ethanol administration increased hepatic glutathione-s-transferases (GST). Enhanced lipid peroxidation induced by ethanol was significantly reduced when papverine was coadministered ($P<0.05$). In addition, the depleted levels of glutathione and inhibited activities of G-Px and GR recovered significantly ($P<0.05$) levelling off to control values on co-exposure. Papaverine (200 mg/kg bw) effectively antagonised the ethanol-induced lipid peroxidation and impaired glutathione levels and glutathione dependent enzyme systems. Our results suggest that papaverine is an effective chemopreventive agent in the liver and may suppress the ethanol-induced hepatotoxicity.

KEYWORDS: Papaverine, Lipid Peroxidation, Glutathione, Ethanol, Oxidative Stress

INTRODUCTION

Lipid peroxidation mediated by free radicals is considered to be a primary mechanism of cell membrane destruction and cell damage (1). One of the most thoroughly investigated examples is the lipid peroxidation stimulated by the model hepatotoxin - ethanol. Alcoholic liver diseases may be caused by oxygen radicals such as superoxide and hydroxyl radicals, generated during the metabolism of ethanol by the microsomal oxidising system (2).

Several mechanisms against cellular lipoperoxidative injury have been outlined in which glutathione (GSH) plays an important role (3-5). In addition to being a direct free radical scavenger, GSH is known to function as a substrate of GSH-peroxidases (G-Px) and GSH-transferases (GST) (6,7). Its absence may lead to the accumulation of lipid hydroperoxides. Hepatic GSH has an especially important relationship with lipid peroxidation because of its ability to bind with free radicals that may initiate peroxidation (8,9). When xenobiotics form conjugates with hepatic GSH, the GSH level decreases and the liver cell is made more susceptible to lipid peroxidation.

Papaverine, an opium alkaloid of the Papaveraceae family, plays an important role in alteration of lipid peroxidation in rat liver. Papaverine is known for its vasodilative effect (10,11). Experiments in our laboratory have shown that

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