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Effect of a Non-Steroidal Anti-Inflammatory Agent with Beneficial Effect on Ulcerative Colitis and Anti-oxidant Properties on Drug Metabolizing Enzymes

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AIM

In the design and the safety evaluation of drugs there is concern to determine their potential to cause induction or inhibition of metabolic enzymes. It has been documented that the compound {5-(2-hydroxy-ethylamino) 1 phenyl-3 hexanone} (HEPH) has significant antioxidant properties by inhibiting carrageenan rat paw oedema by 78%. It has been also shown that this compound can reduce the extent of tissue damage on the ulcerative colitis on an experimental model of experimental colitis in rats. HEPH was also found to be a potent free radical scavenger as determined by its significant hydroxyl radical scavenging activity. The aim of the present study was to investigate the influence of the compound on drug metabolizing enzymes.

MATERIALS-METHODS

We investigated the effect of the tested compound *in vivo* after a single administration on zoxazolamine induced paralysis. We also investigated the effect of a prolonged treatment of the tested compound (5 days) on aminopyrine N-demethylation, on P450 total concentration and on protein concentration (post-mitochondrial and microsomal). The effect of the tested compound on *in vitro* aminopyrine N-demethylation was also investigated using postmitochonrial fraction from untreated rats.

RESULTS

It was found that the examined compound had no effect on the metabolism of zoxazolamine and aminopyrine. In contrast, the tested compound caused a significant decrease in total P450, had no effect on protein concentration and inhibited the *in vitro* aminopyrine N-demethylation on a concentration–dependent way. From the structural characteristics of the tested compound it can be concluded that it interacts with CYP2D.

CONCLUSIONS

Inflammation is a pathologic situation that results in reduced microsomal metabolism of drugs The manifested lack of any effect of HEPH or zoxazolamine and aminopyrine metabolism car be considered as a favorable characteristic of the compound. Since the knowledge of individua differences in the metabolism of drugs shoulc improve the efficiency of drug therapy, the results of this study may contribute to a further evalua tion of the mechanism of action of this compound