ABSTRACT

BACKGROUND

Nimesulide, a non-steroidal anti-inflammatory drug (NSAID), is administered orally for a variety of inflammation and pain states. The safety of Nimesulide has been a matter of public concern worldwide for some years because of its reported side effects and several countries banned or ordered Nimesulide withdraw from the market. In under developed countries and in India, Nimesulide is continuously being used as an over the counter drug. Of late there were a few reports of immunotoxicity associated with use of Nimesulide. Hence, it was considered necessary to study the toxicologic and immunotoxicologic profile of Nimesulide.

OBJECTIVES

The objective of this study was to assess the effects of a Single dose of Nimesulide in rats and mice and of Repeated dose (14-day and 28-day) in rats, to determine the Maximum Tolerable Dose (MTD), No Observed Adverse Effect Level (NOAEL) and to provide information on major toxic effects, target organs (if any) with special emphasis on Immunotoxicity.

RESULTS

Rats and mice exposed to 10, 50 and 100 mg/kg oral Nimesulide exhibited decreased body weights, decreased feed consumption, decreased locomotor activity, dizziness with lethargy, impaired gait, stupor and extension of limbs and mortality (in rats) at 100 mg/kg body weight. The severities of the clinical signs were predominant in rats. Most of the effects occurred following the single exposure during 1-4 hour observation period, except the mortalities which occurred a few days after single exposure. Rat exposed to 5, 25 and 75 mg/kg Nimesulide for 14-days, showed dullness, weakness, emaciation, decreased body weights, decreased feed consumption, changes in haematology, decreased total protein and albumin and mortality, changes in nonglandular stomach, basophilic tubules in kidneys and atrophy of thymus at the highest dose. Extension of the repeated dose study for 28-days with doses of 4, 16 and 64 mg/kg Nimesulide daily for 28 days elicited piloerection, dullness, decreased body weights, decreased body weight gains, decreased food consumption, increased reticulocyte counts, decreased albumin/globulin ratio, decreased PFC, increased liver, kidney ratios, decreased spleen, brain and heart ratio’s and changes in histology of colon and lungs (in one animal).
CONCLUSION

Oral administration of Nimesulide at higher doses (more than 8 times the human therapeutic dose) in rats induced systemic toxicity and does have effects on Humoral Immunity. It also might be inferred that Nimesulide does not have effects on Cell Mediated Immunity.

KEYWORDS

Nimesulide, Toxicity, Immunotoxicity, Cell mediated immunity, Humoral mediated immunity