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Colon targeted delivery of the hydroxylase inhibitor dimethyloxallogylcine (DMOG) provides enhanced protection in a murine model of colitis

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Pharmacologic hydroxylase inhibition represents a potentially important new therapeutic approach to colitis. However, because of potential side effects associated with systemic delivery of hydroxylase inhibitors including unwanted regulation of angiogenic, metabolic and erythropoeitic processes, it is desirable to develop new methods of delivery of such compounds to specific regions of the intestine in order to provide local therapeutic effects without systemic exposure. We have utilized an emulsion-based drug delivery system to attempt to achieve this goal. Initially, we demonstrated that the formulation of the hydroxylase inhibitor DMOG into a novel emulsion-based colon-specific delivery system was without effect upon the biological activity of the drug. The physical process of formulation of DMOG into the colon-specific drug delivery sphere system does not impact upon its biological activity. We next investigated whether formulated DMOG is delivered specifically to the colon when the beads are administered orally to mice. This was investigated by using transgenic mice which ubiquitously express the firefly luciferase gene under the control of a concatomer of NF-kappaB response elements (NRE) to assess NF-kappaB activity in vivo. Our results demonstrate that colon-targeted DMOG delivery resulted in an effective and selective elevation in basal NF-kappaB activity in the colon. We next investigated whether the therapeutic efficacy of colon-specific DMOG delivery in a murine model of DSS-induced colitis. Results from these experiments suggest those colon targeted DMOG beads are protective against experimental colitis in mice at a 40 fold lower dose as compared to systemic administration of DMOG. Our previous work has demonstrated that a significant proportion of the protective effects of DMOG observed in models of intestinal inflammation is a result of enhanced intestinal epithelial barrier function which diminishes the exposure of the mucosal immune system to luminal antigenic material.

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Development and evaluation of gastro retentive drug delivery system for a novel H2-receptor antagonist – Lafutidine

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Lafutidine a newly developed second generation histamine H2-receptor antagonist with its selective absorption from upper part of gastrointestinal tract and a biological half-life of 1.92±0.94 h makes it a suitable candidate for the development of gastroretentive sustained release drug delivery system in order to enhance the bioavailability. The present work explored the development of multiple unit type oral floating microspheres using Eudragit S-100 as a polymer by solvent evaporation method. The prepared microspheres were evaluated for the micromeritic properties, floating behavior, entrapment efficiency, drug release kinetics and X-ray radiographic studies. The microspheres showed good flow properties and the particle size ranging from 51.72±3.01 to 92.43±5.34 µm. Scanning electron microscopy showed spherical size with porous surface. The entrapment efficiency was found to be 56.05±5.46 to 78.56±3.17. Floating microspheres showed good buoyancy (65.12±3.57 to 94.23±3.6) up to 20 hrs. X-ray radiographic studies also proved better retention in the stomach. Thus, it may be useful for prolonged drug release in stomach to improve the bioavailability and reduced dosing frequency.

Notes:

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