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TITLE

Exploring Novel Colon Targeting Antihistaminic Prodrug for Colitis

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Ulcerative colitis (UC) causes inflammation and ulceration of mucosa of colon and rectum. Literature reports involvement of mast cell activation & increased histamine secretion in the pathogenesis of colitis. Due to this reason, antihistaminic H_1 blocker fexofenadine is currently under investigation in the management of colitis. D-glucosamine, an anti-inflammatory nutraceutical aminosugar is involved in biosynthesis of glucosaminoglycan, a major component of intestinal mucus that maintains integrity of gut wall. Levels of N-acetyl glucosamine and glucosamine synthetase go down during the attacks of UC.

The present work was focused on design, kinetic studies & screening of colon-specific mutual prodrug of fexofenadine with D-glucosamine in TNBS-induced colitis. Fexofenadine and D-glucosamine were chemically linked through an amide linkage. Spectral analysis confirmed the structure of the prodrug (FG1).Highly hydrophilic nature of prodrug (log P: 0.046) enabled efficient delivery of fexofenadine to colon. FG1 was stable in stomach homogenates negligible release of fexofenadine in small intestinal homogenates. 82 % release of fexofenadine was observed in rat fecal matter at the end of 12 h ($t_{1/2}$: 260 min). The prodrug was twice as effective in lowering the quantifying parameters of colonic inflammation in TNBS- induced colitis than fexofenadine, D-glucosamine, their physical mixture and interestingly oral 5-amino salicylic acid while 2.7 times less effective than sulfasalazine. The prodrug restored the disrupted colonic architecture to normal and the results were comparable to sulfasalazine. Prodrug had no adverse effect on stomach, liver and pancreas. The results of the present work support the hypothesis of involvement of histamine in the pathogenesis of UC. This novel, dual acting colon- specific prodrug of fexofenadine could be used in combination with sulfasalazine as a maintenance therapy to counteract the relapse of UC.

Biography

Vriha Patel is pursuing her Masters in Pharmacy in Pharmaceutical Chemistry from Department of Pharmaceutical Chemistry, Poona College of Pharmacy, Bharati Vidyapeeth Deemed University, Pune, Maharashtra, India under the guidance of Dr. Suneela Dhaneshwar who has 40 publications, 30 conference presentations, 1 patent and 12 national/ international awards to her credit and has 20 years of teaching and research experience in the field of Pharmaceutical Sciences. She is also on the editorial board of several national journals and reviewer to more than 35 international peer-reviewed journals