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Colon-specific Celecoxib delivery: A potential strategy for repositioning the selective COX-2 inhibitor as an anti-colitic agent

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To improve the anticolitic efficacy of 5-aminosalicylic acid (5-ASA), a colon-specific mutual prodrug of 5-ASA was designed. 5-ASA was coupled to procainamide (PA), a local anesthetic, via an azo bond to prepare 5-(4-{{2-(diethylamino)ethyl}carbonyl}phenylazo)salicylic acid (5-ASA-azo-PA). 5-ASA-azo-PA was cleaved to 5-ASA and PA up to about 76% at 10 h in the cecal contents while remaining stable in the small intestinal contents. Oral gavage of 5-ASA-azo-PA and sulfasalazine, a colon-specific prodrug currently used in clinic, to rats showed similar efficiency in delivery of 5-ASA to the large intestine, and PA was not detectable in the blood after 5-ASA-azo-PA administration. Oral gavage of 5-ASA-azo-PA alleviated 2,4,6-trinitrobenzenesulfonic acid-induced rat colitis. Moreover, combined intracolonic treatment with 5-ASA and PA elicited an additive ameliorative effect. Furthermore, combined treatment with 5-ASA and PA additively inhibited nuclear factor-kappaB (NFκB) activity in human colon carcinoma cells and inflamed colonic tissues. Finally, 5-ASA-azo-PA administered orally was able to reduce inflammatory mediators, NFκB target gene products, in the inflamed colon. 5-ASA-azo-PA may be a colon-specific mutual prodrug acting against colitis, and the mutual anticolitic effects occurred at least partly through the cooperative inhibition of NFκB activity.

Biography

Seongkeun Jeong is an expert of inflammatory bowel disease (IBD) with pathological knowledge and medication. He has studied in the field of medicinal chemistry & pharmacology for a decade. He has now researched in drug delivery and repositioning of several kinds of drug candidates for the treatment of IBD with using rodent model. He is especially interested in colon-targeted drug delivery by adopting unique strategies to minimize unwanted side effects and increase large intestine drug accumulation for intensifying therapeutic effectiveness. With all of this, he is now challenging the development of new IBD treatments.

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