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An anti-colitic mutual colon-specific prodrug of 5-aminosalicylic acid : Procainamide conjugated to 5-aminosalicylic acid via an azo bond

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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]carbamoyl} 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

Wooseong Kim is a researcher with expert knowledge of inflammatory bowel disease (IBD) and colorectal cancer. He published several academic studies through the IBD model using rodent. His main field of interest is the cause and treatment of IBD. Through his research and training, he has the knowledge and experience of chemical knowledge and experimental techniques, biological research techniques and even animal experiments. With all of this, he is now challenging the development of new IBD treatments.

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