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# Conjugation of with Dextran is a potential strategy to control colonic distribution of the drugs susceptible to metabolism by colonic microbes

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Metronidazole (MTDZ), the drug of choice for the treatment of protozoal infections such as luminal amebiasis, is highly susceptible to colonic metabolism, which may hinder its conversion from a colon-specific prodrug to an effective anti-amebic agent targeting the entire large intestine. Thus, in an attempt to control the colonic distribution of the drug, a polymeric colon-specific prodrug, MTDZ conjugated to dextran via a succinate linker (Dex-SA-MTDZ), was designed. Upon treatment with dextranase for 8 h, the degree of Dex-SA-MTDZ depolymerization (%) with a degree of substitution (DS, mg of MTDZ bound in 100 mg of Dex-SA-MTDZ) of 7, 17, and 30 was 72, 38, and 8 respectively, while that of dextran was 85. Depolymerization of Dex-SA-MTDZ was found to be necessary for the release of MTDZ, because dextranase pretreatment ensures that de-esterification occurs between MTDZ and the dextran backbone. In parallel, Dex-SA-MTDZ (DS 17) was found not to release MTDZ upon incubation with the contents of the small intestine and stomach of rats, but released MTDZ when incubated with rat cecal contents (including microbial dextranases). Moreover, Dex-SA-MTDZ exhibited prolonged release of MTDZ, which contrasts with drug release by small molecular colon-specific prodrugs, MTDZ sulfate and *N*-nicotinoyl-2-{2-(2-methyl-5-nitroimidazol-1-yl)ethyloxy}-D,L-glycine. These prodrugs were eliminated very rapidly and no MTDZ was detected in the cecal contents. Consistent with these *in vitro* results, we found that oral gavage of Dex-SA-MTDZ delivered MTDZ [as MTDZ conjugated to (depolymerized) dextran] to the distal colon. However, upon oral gavage of the small molecular prodrugs, no prodrugs were detected in the distal colon. Collectively, these data suggest that dextran conjugation is a potential pharmaceutical strategy to control the colonic distribution of drugs susceptible to colonic microbial metabolism.

## Biography

Dohoon Kim is a researcher with knowledge based on Chemistry and Biology. He is researching and studying about prodrugs which is targeting to large intestine and cause and treatment of intestinal bowel disease(IBD). He has the experiences of chemical and biological knowledge and experimental techniques through his research. He is now keep studying and researching to extend chemical and biological knowledge and experimental techniques.

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