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Analyzing the effects of chronic cyclooxygenase-2 inhibition in the gastrointestinal tract

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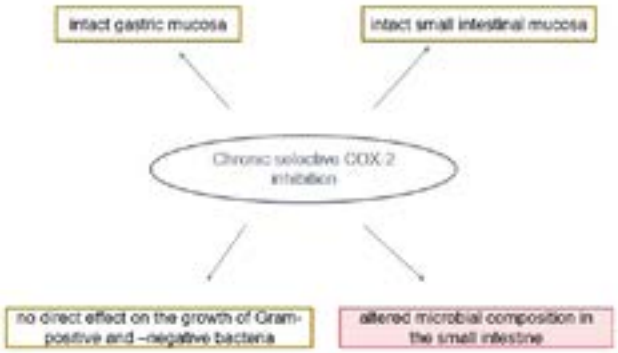
Introduction & Aim: It is well known that NSAIDs, which are among the most commonly used drugs worldwide, may cause gastric and duodenal ulceration, but in recent years it has been found that the distal parts of the small intestine are also injured. The patho-mechanism of this enteropathy is complex and insufficiently understood. Based on the literature, the inhibition of cyclooxygenase (COX) -1 enzyme and the acidic character of the compounds both play a role in the damage of intestinal mucosa, but it still remains controversial whether the selective inhibition of COX-2 enzyme can induce enteropathy. Thus, in our present experiment, the aim was to characterize the effects of chronic, selective COX-2 inhibition in the gastrointestinal tract.

Methods: Male Wistar rats (180-200 g) were treated for 1 month with either the selective, non-acidic COX-2 inhibitor rofecoxib (5 mg/kg per day, once daily) or with its vehicle (1% methylcellulose). Gastric and intestinal mucosal injury was assessed by macroscopic and histological methods. The microbial composition of the small intestinal contents was investigated by 16S rRNA Illumina sequencing, and the effect of rofecoxib on the growth of bacteria was examined by micro dilution assay.

Results: The 1-month rofecoxib treatment did not alter the body weight of the animals and did not cause significant macroscopic or histological injury in the stomach and small intestine. However, our results indicate that although rofecoxib has no direct antibacterial property, it caused significant changes in the small intestinal microbiota.

Conclusion: Based on our results, selective COX-2 enzyme inhibition, even chronically, does not cause mucosal damage in the stomach or in the small intestine, but it significantly changes the gut flora composition. Our further studies will aim to reveal the cause and consequences of this dysbiosis.



Biography

Bernadette Lazar is a PhD student at Semmelweis University, where she participates in pharmacological analysis of gastrointestinal functions in rodents by using *in vivo, ex vivo* and *in vitro* methods. The aim is to characterize the COX-2 inhibitor effects at the gastrointestinal tract, and to reveal the causes and consequences of the gut flora composition change.

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