



Song Gao, PhD
Assistant Professor
Pharmaceutical and Environmental Health
Sciences

Alleviating Irinotecan-induced Diarrhea with Herbal Mixture Xiao-Chai-Hu-Tang (XCHT)

Song Gao, Ph.D. Assistant Professor, Department of Pharmaceutical and Environmental Health Sciences, TSU. Dr. Gao has broad expertise in the areas of pharmaceuticals with specific training in drug absorption using the Caco-2 cell culture model/intestinal perfusion model, metabolism using microsome-mediated models, and drug bioanalysis using LC-MS/MS. He has been working on ADME of bioactive natural products for more than 10 years and has published more than 50 publications. Dr. Gao's research has been focusing on developing recycled locally bioavailable drugs for the treatment of chronic diseases in the colon and alleviating drug induced colonic side effects. His research has been funded by CPRIT and NIH.

Abstract: Irinotecan, a prodrug of SN-38, is used to treat many types of metastatic and drug-resistant cancers, and often represents the therapy of the last resort. Unfortunately, a large percentage (up to 40%) of these patients will experience serious (Grade 2) and severe (Grade 3-4) delayed-onset diarrhea (SDOD). SDOD, which cannot be effectively managed using current therapies. SDOD may lead to prolonged hospitalization and even death in some instances. The purpose of this study is to determine the mechanism of irinotecan-induced SDOD and determine the efficacy and mechanism of Xiao-Chai-Hu-Tang (XCHT), an herbal mixture, against irinotecan-induced SDOD. In vitro and in vivo mouse and rat models were used to determine the efficacy and mechanism. The results showed that SN-38 downregulated UGT1A1, a major enzyme catalyzing SN-38's glucuronidation, in the intestine to cause SN-38 accumulation in the colon, resulting in diarrhea. Additionally, the results showed that XCHT can selectively restore UGT downregulation caused by SN-38 without affecting liver UGT expression. Intestinal perfusion showed that XCHT can also inhibit biliary secretion of SN-38. Efficacy study showed that XCHT can effectively attenuated irinotecan-induced diarrhea without affecting therapeutic efficacy. We conclude that XCHT is a promising agent to alleviate irinotecan-induced diarrhea.