

RESEARCH ARTICLE

Effect of *Yang*-activating and stasis-eliminating decoction from Traditional Chinese Medicine on intestinal mucosal permeability in rats with ulcerative colitis induced by dextran sulfate sodium

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Supported by National Natural Science Foundation of China Project: the Effect and Mechanism of Ulcerative Colitis Rats in the Intestinal Barrier Permeability by Huayutongyang Formula (No. 81373848)

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Accepted: March 1, 2017

medicinals from Traditional Chinese Medicine (TCM) on the intestinal mucosal permeability in rats with ulcerative colitis induced by dextran sulfate sodium (DSS).

METHODS: Totally 55 male Wistar rats (body weight of 170-190 g) were randomly divided into the blank group ($n = 10$) and the model duplication group ($n = 45$). The blank group was not intervened, while the other was modeled with 5% dextran sulfate sodium by gavaging in a dosage of 4 mL per day to induce ulcerative colitis, a total of 7 days. Then, the model rats were divided into model blank group, mesalazine group and TCM group, and each group was consisted of 15 rats. They were given retention enema 10 min with normal saline, mesalazine enema (0.036 g/mL), and *Yang*-activating and stasis-eliminating decoction [0.54 g/mL of a decoction boiled by Puhuang (*Pollen Typhae*), Xiebai (*Bulbus Allii Macrostemonis*) and Wulingzhi (*Faeces Trogopteri*)] for 10 days respectively. Afterwards, all of the rats were evaluated by disease activity index (DAI), histological changes of distal colon, expression of occludin protein and ultrastructure of intestinal epithelial cells. Furthermore, ratio of lactulose to mannitol (L/M) discharged in urine was evaluated.

RESULTS: Comparing the results between TCM and model control groups, scores of DAI and histological lesions decreased significantly ($P = 0.000 < 0.01$), ultrastructures of intestinal epithelial cells and tight junctions were more complete. The expression of occludin protein ($P = 0.001 < 0.01$) increased while the L/M value decreased significantly

Abstract

OBJECTIVE: To evaluate the effect of decoction prepared with *Yang*-activating and stasis-eliminating

($P = 0.000 < 0.01$) in TCM group. There was no statistical difference between the TCM and mesalazine groups in results of each item ($P > 0.05$).

CONCLUSION: The decoction prepared with Yang-activating and stasis-eliminating TCM medicinals can restore intestinal mucosal epithelial cells and tight junctions the model rats with ulcerative colitis; it can reduce histological lesions and protect the permeability of intestinal mucosa barrier in the rats as well.

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Keywords: Colitis, ulcerative; Epithelial cells; Intestinal mucosa; Permeability; Occludin; Dextran sulfate; Removing blood stasis; Activating Yang; Medicine, Chinese Traditional

INTRODUCTION

The pathogenesis of ulcerative colitis (UC) is not totally clear, but it is often considered to be associated with the damage of intestinal mucosa and dysfunction of intestinal barrier. Permeability may reflect the integrity of intestinal mucosal barrier, which acts as a measurable feature of the barrier's function.¹⁻³ Because the intestinal permeability will change in many diseases including inflammatory bowel disease (IBD), some scholars have treated IBD as a kind of disease related to altered permeability.^{4,5} Moreover, tight junctions (TJs), between epithelial cells, play an important role in IBD because of the altered structure and pathological expression.^{6,7}

5-amino salicylic acid (5-ASA) is a general medication for UC. Previous studies have shown that basalazine or mesalazine orally could decrease the abnormal permeability in UC rats,^{8,9} however, the effect on permeability by mesalazine enema has rarely been reported. Besides, corticosteroids, immunosuppressant treatment, biological agents and fecal microbiota transplantation (FMT) have different efficiencies. Shixiaosan [Puhuang (*Pollen Typhae*) and Wulingzhi (*Faeces Trogopterpri*)] is a classic formula in TCM, combining with Xiebai (*Bulbus Allii Macrostemonis*), which are used in this experiment. We want to assess the functionality of Yang-activating and stasis-eliminating TCM enema with diverse indexes in UC model rats.

Precious study shows that dextran sulfate sodium (DSS) has an explicit mechanism to induce UC models. It can not only strengthen the resistance between intestinal epithelial cells to increase permeability, but also exhaust the mucus, induce bacteria permeating and decrease function of intestinal barrier.^{10,11} This study aimed to observe the decoction prepared with Yang-activating and stasis-eliminating medicinal of TCM, on

rats with UC induced by DSS. It will also detect the histological and ultrastructural changes of intestine, meanwhile, detect the content of two kinds of sugar probe in urine in order to observe the change of I/m indirectly.

MATERIALS AND METHODS

Materials

Totally 55 male Wistar rats [specific pathogen free level, two-month-old, weighting (180 ± 10) g] were supplied by Beijing Bioscience Co., Ltd. (Certificate of quality No. SCXK [jing] 2014-0004). They were fed in the Animal Center and the study was approved by the experimental animal ethics committee of Tianjin University of TCM. Anti-Occludin antibody (ab31721, British Abcam Company, concentration was 1:400); Gas chromatograph (7890A, American Agilent, Santa Clara, CA, USA); Transmission electron microscope (H-7500, Japanese Hitachi); Dextran sodium sulfate (MW 36000-50000, American MP Bio, CA, USA); Mesalazine enema (H20080353, Germany Salofalk); Yang-activating and stasis-eliminating decoction [10 g of Puhuang (*Pollen Typhae*), 10 g of Xiebai (*Bulbus Allii Macrostemonis*) and 10 g of Wulingzhi (*Faeces Trogopterpri*), which were decocted into the decoction equivalent to 2.7 g/kg of crude drugs] by pharmaceutical department in the First Teaching Hospital of Tianjin University of TCM.

Methods

Totally 55 rats were randomly selected by random number method and divided into two groups: blank group ($n = 10$) and model duplication group ($n = 45$). All the rats were given ordinary pellet fodder during experimental period. The blank group drank distilled water freely while the model duplication one was lavaged by 5% DSS solution (4 mL once daily for each rat) 7 days.¹² After modeling, with exception of 10 rats in the blank group, the rest rats were randomly divided into model blank group ($n = 15$), TCM group ($n = 15$) and mesalazine group ($n = 15$). The blank group was not intervened, while the model control, TCM and mesalazine groups were given retention enema respectively with normal saline, 0.54 g/mL decoction of Yang-activating and stasis-eliminating and 0.036 g/mL mesalazine enema. Reserved time of enema was 10 min and dosage was 2 mL for each rat every time, which maintained 10 days in total.

Recording DAI scores of rats

The body weight, character of feces, fecal occult blood test (FOBT) and gentle conditions were observed and recorded, furthermore, scores of DAI was evaluated on the 3rd, 5th and 7th during model duplication period and on the 4th, 7th and 10th among intervene time. The standard for scores of DAI¹³ was presented (Table 1).

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