

Dragon fruit (*Hylocereus undatus* (Haw.) Britt.) powders attenuate ulcerative disease symptoms via dextran sulfate sodium-induced mouse model

Yu-Wen Hung^{5, #}, Chia-Chi Chen^{1, #}, Yun-Xuan Chang¹, Tzu-Yun Chi¹, Ya-Peng Wang¹, Tsung-Han Wu¹, Ya-Ling Cyue¹, Pi-Hsin Chen¹, Yen-Jung Lu¹, Shih-Yi Guo¹, Suz-Ching Ke¹, Yu-Ying Fang¹, Szu-Ping Sung¹, Yan-Zhong Wu¹, Chien-Chao Chiu¹, Ching-Feng Chiu², Hsuan-Wen Chiu¹, Wei-Huang Tsai³, Yu-Hsing Lin⁴ and Shao-Wen Hung^{1, 5, *}

¹ Division of Animal Industry, Animal Technology Research Center, Agricultural Technology Research Institute, Hsinchu 300, Taiwan.

² Graduate Institute of Metabolism and Obesity Sciences, College of Nutrition, Taipei Medical University, Taipei 110, Taiwan.

³ Ministry of Agriculture, Executive Yuan, Taipei 100, Taiwan.

⁴ Department of Pet Healthcare, Yuanpei University of Medical Technology, Xiangshan, Hsinchu 300, Taiwan.

⁵ Department of Nursing, Yuanpei University of Medical Technology, Hsinchu 300, Taiwan.

Contributed equally to this work.

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Abstract

Dragon fruit is cactus based fruit that has loads of health benefits such as lowering risks of a blood sugar spike, aids in digestion etc. Its nutritional content is rich in vitamin C, vitamin E, magnesium, iron etc. Its functions on the physiological regulation are well known. Inflammatory bowel diseases (IBD) are multifactorial chronic intestinal disorders. Currently, mesalamine etc. and therapeutic strategies were suggested for IBD therapy. However, the etiology of IBD remains unclear which is an ongoing challenge and side effects of therapeutic drugs must be also considered. Thus, the aim of this study was evaluated the efficacy and therapeutic strategies investigations on the attenuated IBD symptoms via administrating three doses of dragon fruit powders in the 2% dextran sulfate sodium (DSS)-induced IBD mouse model. The female C57BL/6 mice were divided respectively the normal control group (n = 10), the negative control group (n = 10), three dose groups (n = 10 per group) of dragon fruit powders (250 mg/kg BW, 500 mg/kg BW, and 1,000 mg/kg BW). Exception of the normal control group, other groups were administrated with 2% DSS for 5 days. Later, the normal drinking water was provide to C57BL/6 mice until the end of the experiment. At the end of the experiment, the body weight (BW), the stool appearance/status, the macroscopic and microscopic colonic injuries, and myeloperoxidase (MPO) activity were monitored, measured and scored. The results were showed that BW of C57BL/6 mice in the negative control group, three dragon fruit powder groups was gradually reduced during the IBD period induced by 2% DSS, and BW of C57BL/6 mice gradually increased when the 2% DSS in drinking water was replaced with the normal drinking water. When the experiment was carried out to the 3rd to 4th week, BW of the negative control group was significantly lower than that of the normal control group. The stool appearance/status was presented that stool score in the negative control group was significantly higher than that in the normal control group ($p < 0.001$). The stool score in the high-dose dragon fruit powder group was significantly lower than that in the negative control group ($p < 0.001$). The macroscopic colons of C57BL/6 mice were performed at the end of the experiment. (1) Gut weight: It can be seen that gut weight in the normal control group is lowest and the gut weight in the negative control group is highest between all groups. The gut weight in the negative control group was higher than that in the normal control group, medium-dose dragon fruit powder group, and high-dose dragon fruit powder group were seen. (2) Gut length: It can be seen that gut length in the normal control group is longest. The gut length in the normal control group is significantly longer than that in the other groups. Exception of the normal control group, other groups were not significant difference compared to

* Corresponding author: Shao-Wen Hung

each other. (3) Gut weight-to-gut length ratio: It can be seen that gut weight-to-gut length ratio in the normal control group is lowest and the gut weight-to-gut length ratio in the negative control group is highest between all groups. The gut weight-to-gut length ratio in the negative control group was significantly higher than that in the normal control group ($p < 0.01$). The gut weight-to-gut length ratio in the high-dose dragon fruit powder group was significantly lower than that in the negative control group. The microscopic colons of C57BL/6 mice was performed at the end of the experiment. The pathological analysis items were divided into ulcer area ratio, mucosal ulcer depth, inflammatory cell infiltration, and submucosal edema. Total histopathologic scores in the 2% DSS-induced group was also significantly higher than that of the normal control group. Finally, the evaluating MPO activity was performed by using MPO activity assay kit. It can be seen that MPO activity was significant higher in the negative control group than that in the normal control group. MPO activity in the three dragon fruit powder groups were significant lower than that in the negative control group. Taken all results together, the consumption of medium-dose (500 mg/kg BW) and high-dose (1,000 mg/kg BW) dragon fruit powders has a positive improvement effect on relieving various symptoms caused by IBD via a successful 2% DSS-induced IBD mouse model.

Keywords: Dragon Fruit; Establishment of Experimental Mouse Model; Inflammatory Bowel Diseases; Dextran Sulfate Sodium; Ulcerative Disease

1 Introduction

Dragon fruit is cactus based fruit that has loads of health benefits such as lowering risks of a blood sugar spike, aids in digestion etc. Its nutritional content is rich in vitamin C, vitamin E, magnesium, iron etc. Its functions on the physiological regulation are well known that

- To reduce the risk of diabetes;
- To reduce the risks of cancer;
- Increase of immunity;
- Digestion improvement;
- To improve the cardiac vessel disorders;
- To fights the ageing skin;
- To promote the hair growth;
- To increase the healthy bones;
- To protect the eyes;
- Benefit during pregnancy [1-5].

IBD, inflammatory bowel disease is a multifactorial chronic disease involved Crohn's disease (CD) and ulcerative colitis (UC). The disease was resultant from a dysfunctional/abnormal epithelial and immune responses to intestinal microorganisms. Severe disease complications often result in surgery [6-8]. At present, IBD's etiology and pathogenesis remain unclear. The environmental and genetic factors may be considered as the etiology of IBD. Until now, the cellular and molecular insights of pathogenesis of IBD were discovered [8-12].

Clinically, patients with IBD are frequently observed clinical manifestations as nausea, abdominal pain, vomiting, diarrhea, or ileus, may be attributed to deranged gastrointestinal motility and inflammation [6-8]. Currently, 5-amino salicylic acid (5-ASA; mesalamine) is a well-established drug considered and used in the first line of treatment for the IBD's patients. 5-ASA is not free of side effects, although it is usually well tolerated [13].

5-ASA is rapidly and extensively absorbed before reaching the colon in most clinical cases. Rectal or oral corticosteroids are also commonly administrated but appear to be less effective than 5-ASA administration in inducing and maintaining remission [13]. Taken the informations together, the search for novel therapeutic IBD drugs and the development of therapeutic strategies for IBD is an ongoing challenge. Therefore, there has been an urgent need for alternative medicine with high efficacy and fewer adverse effect [13-15]. The aim of this study was to apply an optimal IBD animal model for the researches of therapeutic IBD candidate drugs and novel therapeutic strategy developments.

2 Material and methods

2.1 Chemicals and Reagents

Phosphate-buffered saline (PBS; Sigma-Aldrich, Cat. No. P3813), saline (Taiwan Biotech Co., LTD, Cat. No. 100-120-1101), Zoletil 50 (Virbac, Carros, France), myeloperoxidase (MPO) activity assay kit (abcam, Cat. No. ab105136), dextran

sulfate sodium salt (Spectrum Chemical, Cat. No. DE136), hexadecyltrimethylammonium bromide (HTAB; Sigma-Aldrich, Cat. No. H6269), KH_2PO_4 (Sigma-Aldrich, Cat. No. P5655), Na_2HPO_4 (Sigma-Aldrich, Cat. No. S9763), horseradish peroxidase (Sigma-Aldrich, Cat. No. 77332), and tetramethylbenzidine (TMB; Sigma-Aldrich, Cat. No. 860336) were used in this experiment.

2.2 Experimental Animals and Experimental Design

Adult female 50 C57BL/6 mice [6 weeks old; body weight (BW) between 20-22 g] with specific pathogen-free conditions were used for this study, were purchased from BioLASCO Taiwan Co., Ltd. (Yilan, Taiwan). The environment was maintained room temperature (24-27°C) and 60%-70% humidity with a photoperiod of 12-hr light/12-hr dark cycle. The study will begin after a week acclimation. The Institutional Animal Care and Use Committee (IACUC) of Agricultural Technology Research Institute inspected all animal experiments and this study comply with the guidelines of protocol IACUC 111053 approved by the IACUC ethics committee. The female 50 C57BL/6 mice were divided respectively the normal control (n = 10), the negative control (n = 10), three dose groups (n = 10 per group) of dragon fruit (*Hylocereus undatus* (Haw.) Britt.) powders (250 mg/kg body weight, 500 mg/kg body weight, and 1,000 mg/kg body weight). All C57BL/6 mice were fed with standard laboratory diet (No. 5053, LabDiet®; PMI Nutrition International, St. Louis, MO, USA) ad libitum during the experimental period. The change of C57BL/6 mice' BW, C57BL/6 mice' stool appearance/status, the observation of C57BL/6 mice' behaviors, and MPO expression of the collected C57BL/6 mice' intestine tissues were monitored, scored, and detected during the experiment (Fig. 1).

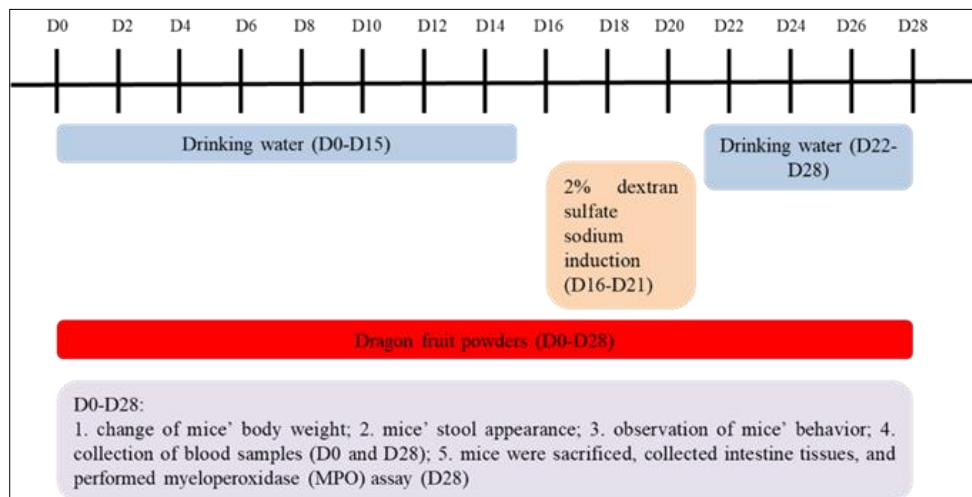


Figure 1 Experimental designs: Dragon fruit powders attenuate ulcerative disease symptoms via dextran sulfate sodium-induced mouse model

2.3 Induction of Colitis and Determination of Scores of Stool Consistency

Briefly, the dragon fruit powders (250 mg/kg body weight, 500 mg/kg body weight, and 1,000 mg/kg body weight) were orally administrated by gavage in the three dose groups of dragon fruit powders at the beginning of the experiment. Except the normal control group, C57BL/6 mice in other four groups were administrated with 2% DSS involved drinking water for 5 days in 3rd week. Later, the normal drinking water was provided to C57BL/6 mice until the end of the experiment. Finally, C57BL/6 mice were sacrificed after overdose anaesthetized. During the study, C57BL/6 mice' BW and stool consistency were recorded daily. Scores of stool consistency was defined as followed score 0, normal stool; score 1, soft stool; score 2, watery stool.

2.4 Assessment of the Severity of Colitis

The colon was removed, opened with longitudinal incision, cleaned, and rinsed with PBS to remove fecal material. Gross damage lesion of the colonic mucosa was assessed by a senior veterinary pathologist. The length, weight, and weight/length ratio of C57BL/6 mice' colons were measured. The individual damage features of colitis were graded according the method described [13, 15]. Colonic tissue samples were taken form macroscopic damage area and processed for subsequent MPO activity measurement.

2.5 Histological Assessment of Colitis

Colonic tissue samples of C57BL/6 mice were fixed in 10% neutral buffered formalin and embedded in paraffin blocks. Four to five μm sections were stained with hematoxylin and eosin. The slides were then evaluated by a senior veterinary pathologist. The scores of colon injury were defined according to the method described [13, 15] as score 0, normal; score 1, one area of inflammation or no ulcer; score 2, one area of ulcer; score 3, one area of inflammation or one or two one area of ulcers; score 4, one area of inflammation, ulcers > 2 area; score 5, two area of inflammation, ulcers > 2 area; score 6, ulceration > 2 cm.

2.6 Assessment of MPO Activity

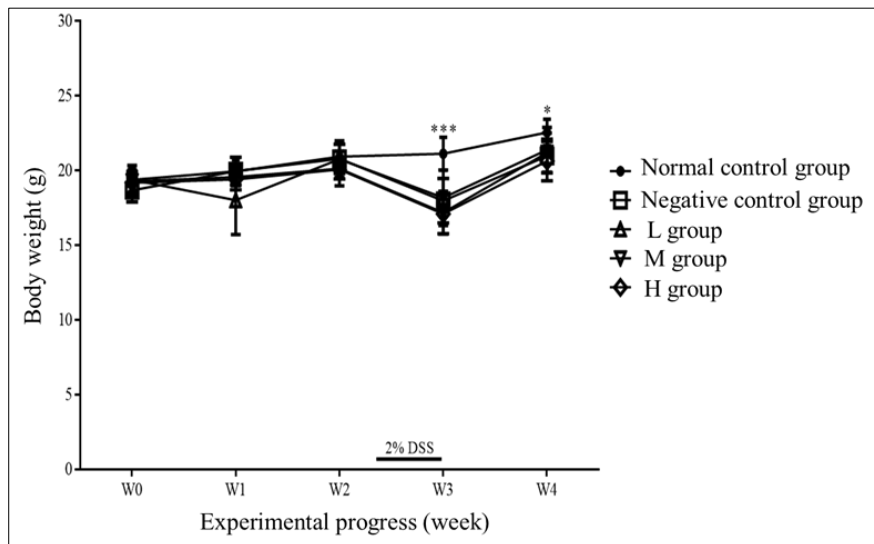
MPO activity was assessed as a marker of neutrophil infiltration slightly modified to the method described [13, 15]. Briefly, storage colonic tissue samples were removed from -80°C and allowed to thaw on ice. When the samples thawed, 1 mL of 0.5% HTAB containing 50 mM KH_2PO_4 and 0.1 M Na_2HPO_4 was added per 100 mg tissue for homogenization. Homogenates was centrifuged at $12,000 \times g$ for 10 minutes at 4°C after freeze/thaw for four times. The supernatant was collected for MPO activity assay. The stock solution of horseradish peroxidase was 0.5 mg/mL and used as a standard. The substrate of MPO activity assay was TMB to show up the reaction. In the reaction, 10 μL of standard and sample were added to appropriately labeled tubes. TMB was added at a volume of 100 μL to initiate the reaction, and 100 μL 0.1 M H_2SO_4 was added after 10 minutes of initiation to terminate MPO reaction. The absorbance changes were measured by a spectrophotometer at 450 nm and MPO activity was expressed as nanograms per milligram of tissue.

2.7 Statistical Analysis

SPSS (Statistical package for the social sciences) statistical software (version 28.0) were used for statistical analysis. Measurement data were expressed as mean \pm standard deviation (SD). All comparisons were made by one-way ANOVA (Analysis of Variance). All significant differences are reported at * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

3 Results

3.1 Change of BW of C57BL/6 Mice



Data presented mean \pm SD. * $p < 0.05$; *** $p < 0.001$

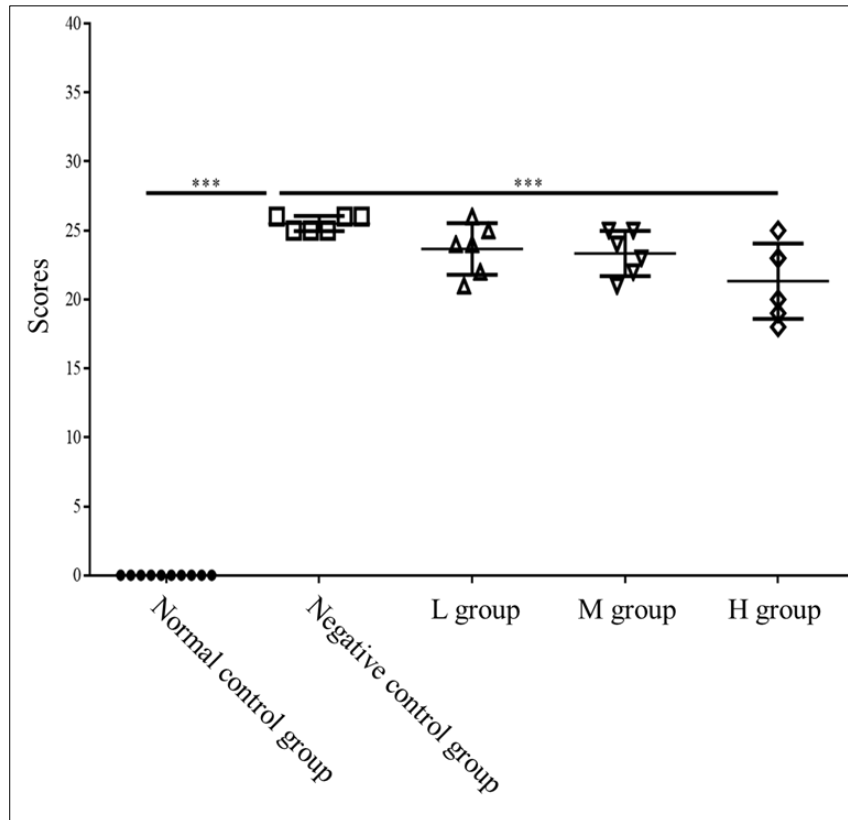
Figure 2 Change of BW of C57BL/6 mice during the experiment. The female C57BL/6 mice were divided respectively the normal control group (n = 10), the negative control group (n = 10), three dose groups (n = 10 per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight). Exception of the normal control group, C57BL/6 mice in other groups were administrated with 2% DSS involved drinking water for 5 days. Later, the normal drinking water was provide to C57BL/6 mice until the end of the experiment

Change of BW of C57BL/6 mice was monitored every day. The results showed that BW of C57BL/6 mice in the negative control group, three dragon fruit powder groups was gradually reduced during the IBD period induced by 2% DSS, and BW of C57BL/6 mice gradually increased when the 2% DSS in drinking water was replaced with the normal drinking

water. When the experiment was carried out to the 3rd to 4th week, BW of the negative control group was significantly lower than that of the normal control group. Although three dragon fruit powder groups showed a trend of BW loss, but there was no statistical difference from the normal control group (Fig. 2).

3.2 The Stool Appearance/Status of C57BL/6 Mice

The stool appearance/status of C57BL/6 mice was monitored and scored every day. Data showed that stool appearance/status was presented that stool score in the negative control group was significantly higher than that in the normal control group ($p < 0.001$). The stool score in the high-dose dragon fruit powder group was significantly lower than that in the negative control group ($p < 0.001$) (Fig. 3).



Data presented mean \pm SD. *** $p < 0.001$

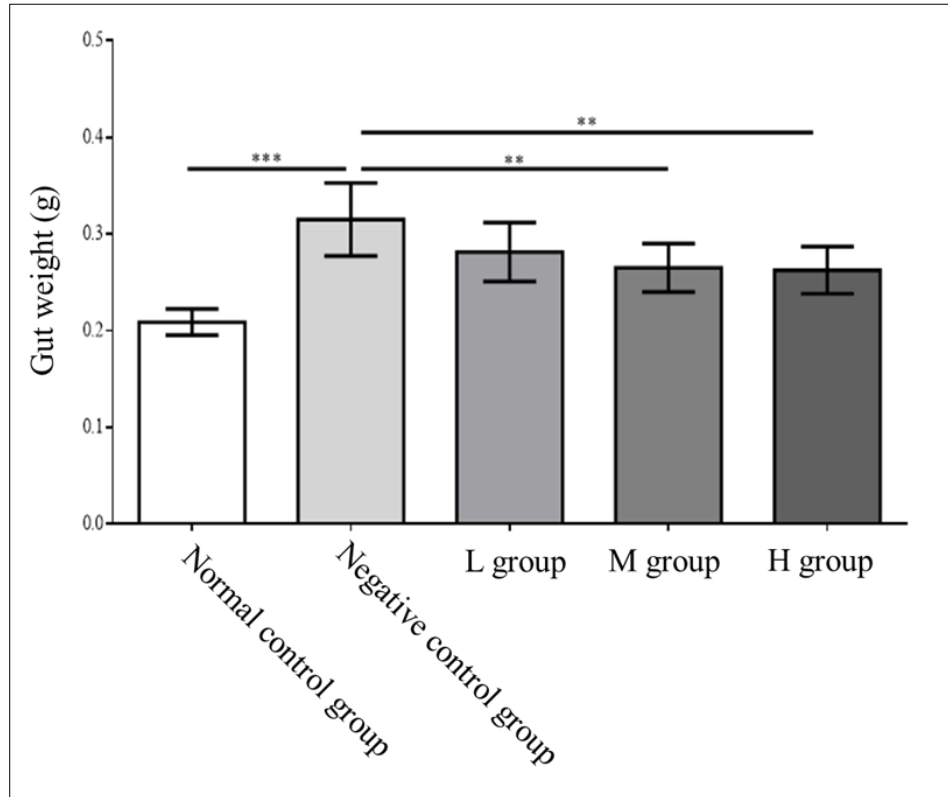
Figure 3 Stool appearance/status and scoring of C57BL/6 mice during the experiment. The female C57BL/6 mice were divided respectively the normal control group ($n = 10$), the negative control group ($n = 10$), three dose groups ($n = 10$ per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight). C57BL/6 mice were administrated with 2% DSS involved drinking water for 5 days.

Later, the normal drinking water was provide to C57BL/6 mice until the end of the experiment. Scores of stool consistency was defined as followed score 1, normal stool; score 2, soft stool; score 3, watery stool

3.3 The Macroscopic Colonic Injuries of C57BL/6 Mice

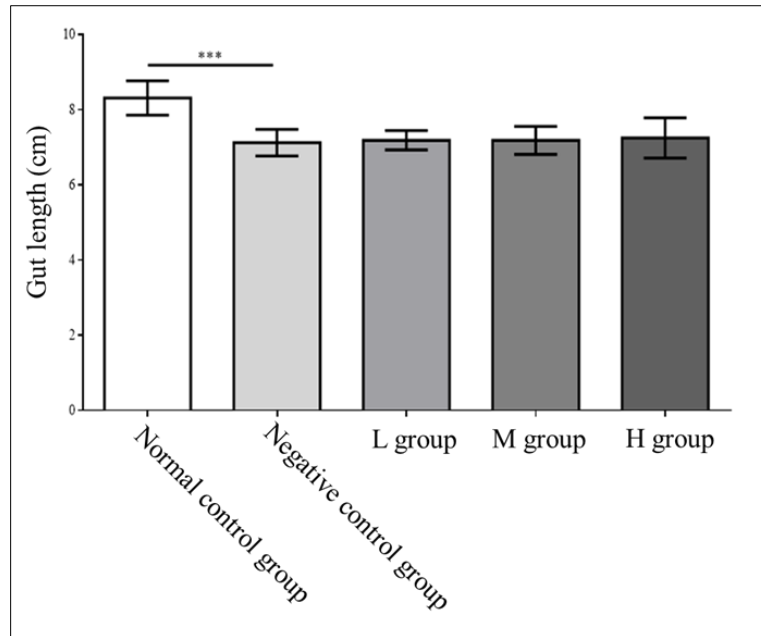
The macroscopic colons of C57BL/6 mice were performed at the end of the experiment. The results showed that (1) Gut weight: the gut weight of each group was 0.21 ± 0.01 g for the normal control group, 0.32 ± 0.04 g for the negative control group, 0.28 ± 0.03 g for the low-dose dragon fruit powder group, 0.27 ± 0.03 g for the medium-dose dragon fruit powder group, and 0.26 ± 0.02 g for the high-dose dragon fruit powder group. It can be seen that gut weight in the normal control group is lowest and the gut weight in the negative control group is highest between all groups. The gut weight in the negative control group was higher than that in the normal control group, medium-dose dragon fruit powder group, and high-dose dragon fruit powder group were seen ($p < 0.01$) (Fig. 4). (2) Gut length: the gut length of each group was 8.31 ± 0.46 cm for the normal control group, 7.13 ± 0.35 cm for the negative control group, 7.19 ± 0.26 cm for the low-dose dragon fruit powder group, 7.19 ± 0.37 cm for the medium-dose dragon fruit powder group, and 7.25 ± 0.53 cm for the high-dose dragon fruit powder group. It can be seen that gut length in the normal control group is longest. The gut length in the normal control group is significantly longer than that in the other groups ($p < 0.001$).

Exception of the normal control group, other groups were not significant difference compared to each other (Fig. 5). (3) Gut weight-to-gut length ratio: the gut weight-to-gut length ratio of each group was 0.03 ± 0.01 g/cm for the normal control group, 0.05 ± 0.01 g/cm for the negative control group, 0.04 ± 0.00 g/cm for the low-dose dragon fruit powder group, 0.04 ± 0.00 g/cm for the medium-dose dragon fruit powder group, and 0.04 ± 0.01 g/cm for the high-dose dragon fruit powder group. It can be seen that gut weight-to-gut length ratio in the normal control group is lowest and the gut weight-to-gut length ratio in the negative control group is highest between all groups. The gut weight-to-gut length ratio in the negative control group was significantly higher than that in the normal control group ($p < 0.01$). The gut weight-to-gut length ratio in the high-dose dragon fruit powder group was significantly lower than that in the negative control group ($p < 0.05$) (Fig. 6).



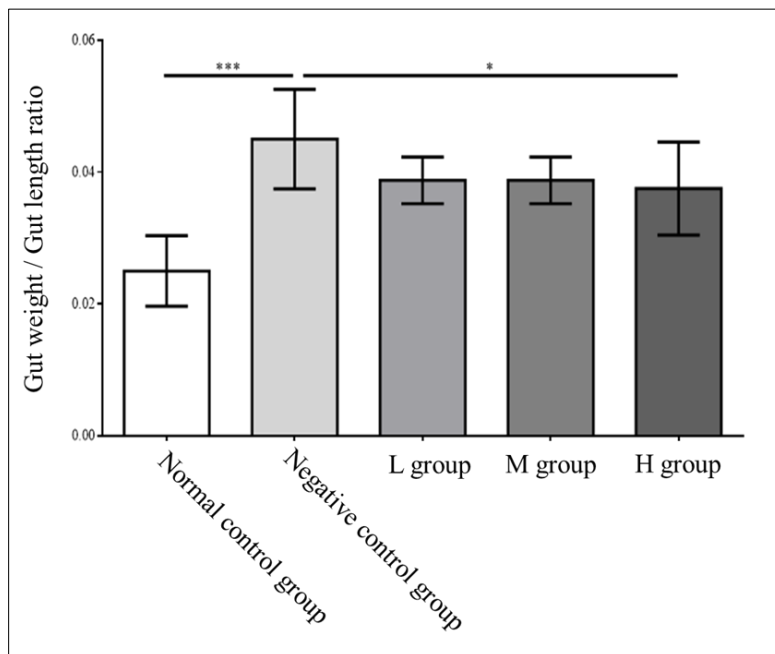
Data presented mean \pm SD. ** $p < 0.01$; *** $p < 0.001$

Figure 4 Gut weight of C57BL/6 mice with and without the administration of dragon fruit powders. The female C57BL/6 mice were divided respectively the normal control group (n = 10), the negative control group (n = 10), three dose groups (n = 10 per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight). The gut weight (g) in all C57BL/6 mice were measured



Data presented mean \pm SD. *** $p < 0.001$

Figure 5 Gut length of C57BL/6 mice with and without the administration of dragon fruit powders. The female C57BL/6 mice were divided respectively the normal control group (n = 10), the negative control group (n = 10), three dose groups (n = 10 per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight). The gut length (cm) in all C57BL/6 mice were measured



Data presented mean \pm SD. * $p < 0.05$; *** $p < 0.001$

Figure 6 Gut weight / gut length ratio (g/cm) of C57BL/6 mice with and without the administration of dragon fruit powders. The female C57BL/6 mice were divided respectively the normal control group (n = 10), the negative control group (n = 10), three dose groups (n = 10 per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight). The gut weight / gut length ratio (g / cm) in all C57BL/6 mice were measured

3.4 The Microscopic Colonic Tissue Injuries of C57BL/6 Mice

The microscopic colons of C57BL/6 mice was performed at the end of the experiment. After C57BL/6 mice were sacrificed, the intestinal tissue was collected for pathological analysis (Fig. 7). The pathological analysis items were divided into ulcer area ratio (Area), mucosal ulcer depth (Ulceration), inflammatory cell infiltration (Inflammation), and submucosal edema (Edema). The score of ulcer area ratio of intestinal mucosal epithelium in the negative control group was significantly higher than that in the normal control group ($p < 0.001$), the medium-dose dragon fruit powder group ($p < 0.01$), and the high-dose dragon fruit powder group ($p < 0.01$) (Fig. 8A). The severity of ulcers in the crypts and mucosal surfaces of the colorectum was scored. The severity of ulcers in the crypts and mucosal surfaces of the colorectum in the negative control group was a significant higher than that in the normal control group ($p < 0.001$) (Fig. 8B). The severity of inflammatory cell infiltration in the colorectal lesion was scored. The severity of inflammatory cell infiltration in the negative control group was a significant higher than that in the normal control group ($p < 0.001$). The severity of inflammatory cell infiltration in the medium-dose dragon fruit powder group and high-dose dragon fruit powder group was a significant lower than that in the negative control group ($p < 0.01$ - $p < 0.001$) (Fig. 8C). The severity of edema fluid in the lymphatic vessels in the submucosa was scored. The severity of edema fluid in the lymphatic vessels in the submucosa in the negative control group was a significant higher than that in the normal control group ($p < 0.001$) (Fig. 8D). According to the scores of ulcer area ratio, mucosal ulcer depth, inflammatory cell infiltration, and submucosal edema. The comprehensive score in the negative control group was significantly higher than that in the normal control group ($p < 0.001$), the medium-dose dragon fruit powder group ($p < 0.01$), and the high-dose dragon fruit powder group ($p < 0.01$) (Fig. 8E).

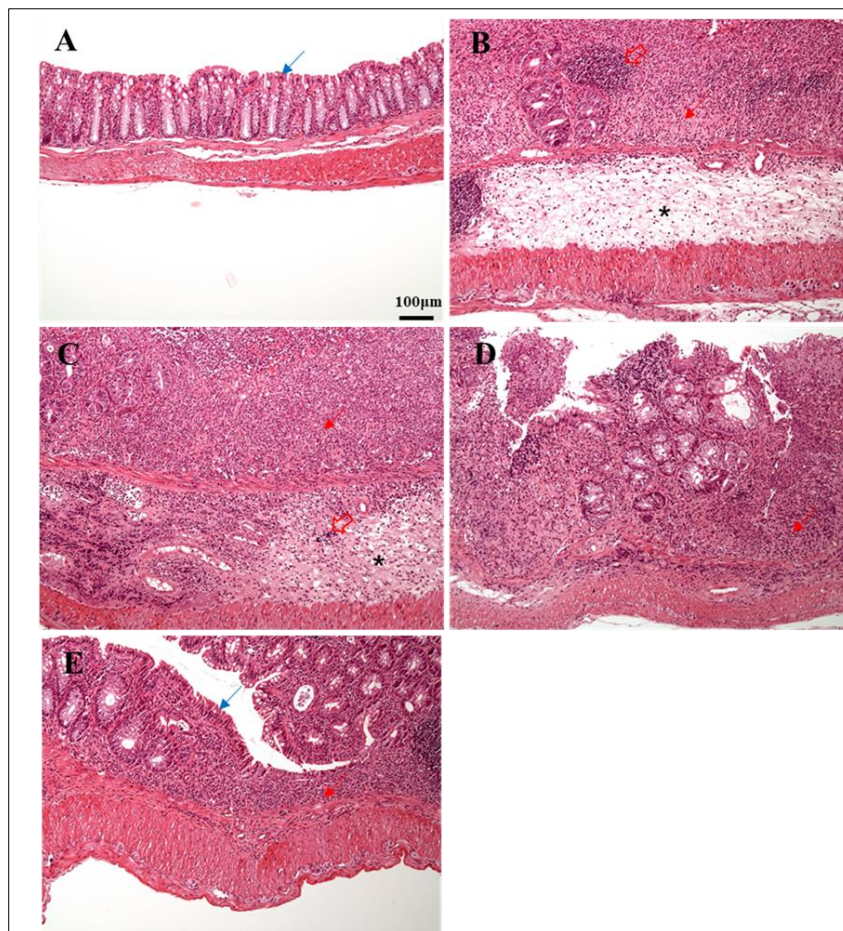
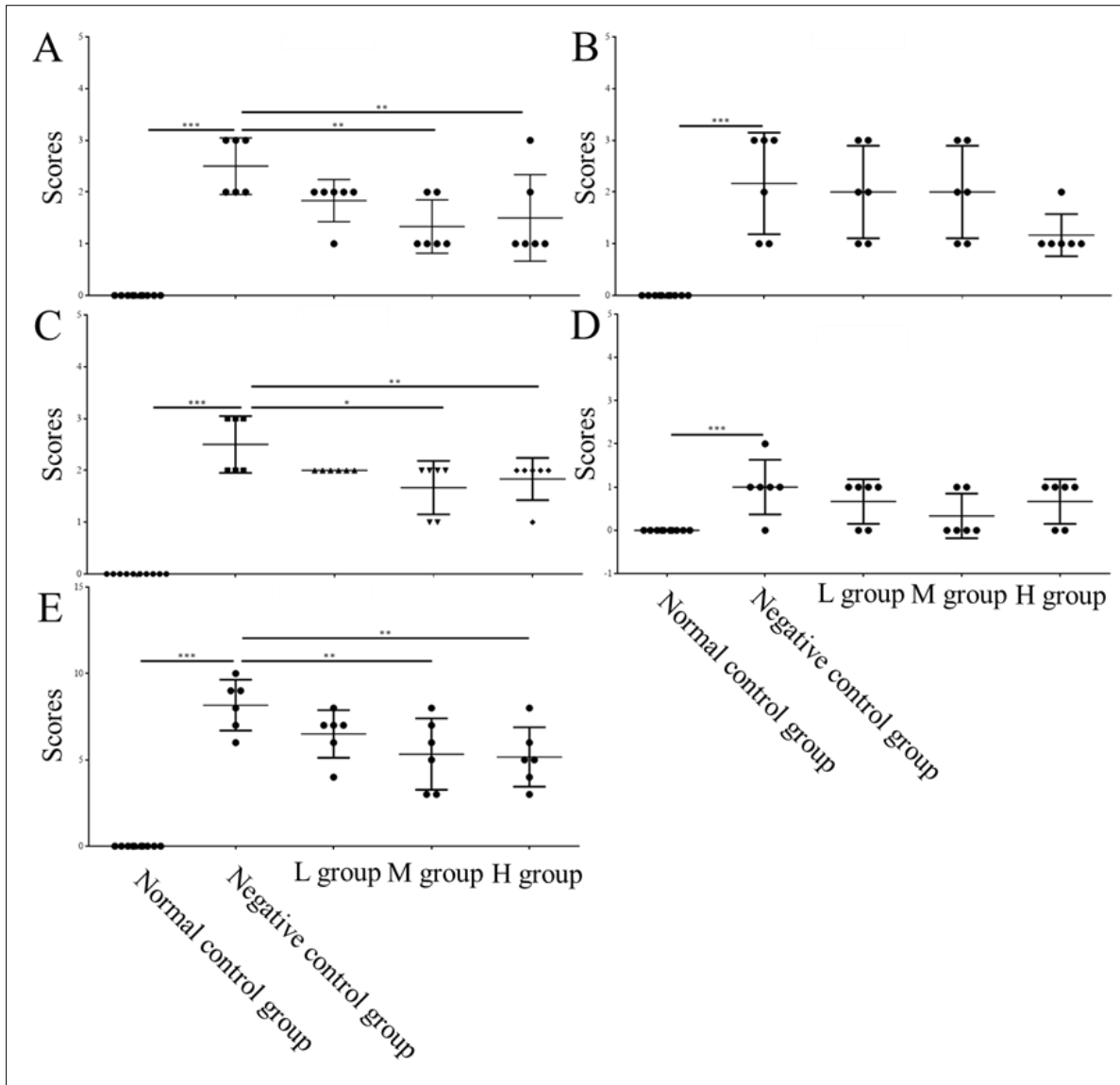


Figure 7 Microscopic inner appearance of colon tissues of C57BL/6 mice. The female C57BL/6 mice were divided respectively the normal control group ($n = 10$), the negative control group ($n = 10$), three dose groups ($n = 10$ per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight). (A) Normal control group. (B) Negative control group. (C) Low-dose dragon fruit powder group. (D) Medium-dose dragon fruit powder group. (E) High-dose dragon fruit powder group. The blue arrows represent the normal intestinal mucosal tissue. The red arrows represent mucosal ulcers. The black asterisks represent submucosa edema. The red hollow arrows represent inflammatory cell infiltration. H&E staining, 100 \times magnification



Data presented mean \pm SD. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Figure 8 Microscopic inner appearance of colon tissues of C57BL/6 mice. The female C57BL/6 mice were divided respectively the normal control group (n = 10), the negative control group (n = 10), three dose groups (n = 10 per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight). (A) Area. (B) Ulceration. (C) Inflammation. (D) Edema. (E) Total scores. The scores of colon injury were performed as score 0, normal; score 1, one area of inflammation or no ulcer; score 2, one area of ulcer; score 3, one area of inflammation or one or two one area of ulcers; score 4, one area of inflammation, ulcers > 2 area; score 5, two area of inflammation, ulcers > 2 area; score 6, ulceration > 2 cm

3.5 MPO Activity in the Colon Tissues of C57BL/6 Mice

Evaluating MPO activity was performed by using MPO activity assay kit. The results showed that the MPO activity of each group was 92.17 ± 23.06 pg/g for the normal control group, 408.12 ± 198.69 pg/g for the negative control group, 173.10 ± 65.69 pg/g for the low-dose dragon fruit powder group, 104.14 ± 62.23 pg/g for the medium-dose dragon fruit powder group, and 126.14 ± 62.15 pg/g for the high-dose dragon fruit powder group. It can be seen that MPO activity was significant higher in the negative control group than that in the normal control group ($p < 0.001$). MPO activity in the three dragon fruit powder groups were significant lower than that in the negative control group ($p < 0.01$ - $p < 0.001$) (Fig. 9).

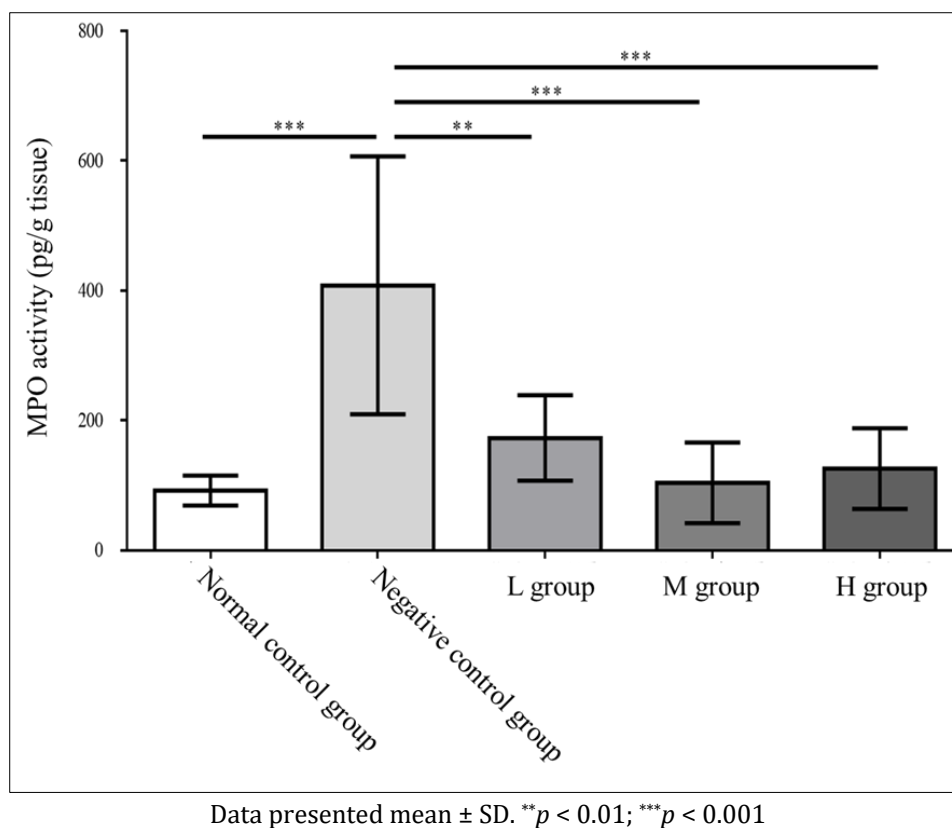


Figure 9 Expression of MPO activity in the colon tissues of C57BL/6 mice. The female C57BL/6 mice were divided respectively the normal control group (n = 10), the negative control group (n = 10), three dose groups (n = 10 per group) of dragon fruit powders (L group: 250 mg/kg body weight, M group: 500 mg/kg body weight, and H group: 1,000 mg/kg body weight)

4 Discussion

Dragon fruit contains high amounts of fiber that maintains blood sugar levels (glycaemic control) and reduces risk of diabetes, and aids in digestive health. They also contains anti-cancer and improvement of cardio vessel properties that can reduce the risks of colon cancer and cardiovascular diseases. It contains vitamin C, a powerful antioxidant plays an important role in the boost of the immune system and prevents from contracting chronic diseases such as diabetes, Alzheimer's and Parkinson's disease, cancer, fights ageing skin etc. Additionally, its tiny dark black seeds are rich in omega-3 and omega-9 fatty acids that are good for the heart and reduce the risks of cardiovascular diseases. In addition, the dragon fruit contains beta-carotene prevents eye problems such as cataracts and macular degeneration. It also contains vitamin B, folate, and iron that making it an ideal fruit for pregnancy. B vitamins and folate prevents birth defects and boosts energy during pregnancy. Its calcium and magnesium contents are responsible for the bone development of the fetus and help fight postmenopausal complications in women [1-5].

The main benefit of dragon fruit antioxidants (betalains, hydroxycinnamates, flavonoids etc) is to capture and get rid of free radicals. Dragon fruit with red pulp contains betalains that reduces LDL (low-density lipoprotein) cholesterol. It prevents LDL from oxidation and damage. Hydroxycinnamates is the anti-cancer benefits in the dragon fruit. They have been shown to prevent or decrease cancer growth. Flavonoids are associated with improved brain health and function as well as a lower risk of developing cardiovascular diseases [1-5].

IBD (mainly covers CD and UC) is a group of idiopathic, chronic, and relapsing inflammatory conditions mainly affecting colon and small intestine and characterized by severe abdominal pain and diarrhea. CD and UC are chronic and progressive inflammatory diseases that may affect GI tract and might be associated with an increased risk for colon cancer [14, 16-25]. Currently, several animal models of IBD have been developed. These animal models of IBD were provided to help out in identification of novel drug targets and therapeutic strategies. Although these animal models have lot of shortcomings but still some promising new drugs have been developed by utilization of these preclinical animal models [26-37].

In this study, the aim of this study was evaluated the efficacy and therapeutic strategies investigations on the attenuated IBD symptoms via administrating three doses of dragon fruit powders in the 2% dextran sulfate sodium (DSS)-induced IBD mouse model [38]. Taken all results together, the consumption of medium-dose (500 mg/kg BW) and high-dose (1,000 mg/kg BW) dragon fruit powders has a positive improvement effect on relieving various symptoms caused by IBD via a successful 2% DSS-induced IBD mouse model.

5 Conclusion

IBD are multifactorial chronic intestinal disorders. Currently, mesalamine etc. and therapeutic strategies were suggested for IBD therapy. However, the etiology of IBD remains unclear and side effects of therapeutic drugs must be considered. Thus, the aim of this study was evaluated the efficacy and therapeutic strategies investigations on the attenuated IBD symptoms via administrating three doses of dragon fruit powders in the 2% dextran sulfate sodium (DSS)-induced IBD mouse model. Taken all results together, the consumption of medium-dose (500 mg/kg BW) and high-dose (1,000 mg/kg BW) dragon fruit powders has a positive improvement effect on relieving various symptoms caused by IBD via a successful 2% DSS-induced IBD mouse model.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

The Institutional Animal Care and Use Committee (IACUC) of Agricultural Technology Research Institute inspected all animal experiments and this study comply with the guidelines of protocol IACUC 111053 approved by the IACUC ethics committee.

References

- [1] Montiel-Sánchez M, García-Cayuela T, Gómez-Maqueo A, García HS, Cano MP. *In vitro* gastrointestinal stability, bioaccessibility and potential biological activities of betalains and phenolic compounds in cactus berry fruits (*Myrtillocactus geometrizans*). Food Chem. 2021; 342: 128087.
- [2] Saenjum C, Pattananandecha T, Nakagawa K. Antioxidative and anti-inflammatory phytochemicals and related stable paramagnetic species in different parts of dragon fruit. Molecules. 2021; 26: 3565.
- [3] Thaiudom S, Oonsivilai R, Thaiwong N. Production of colorant powder from dragon fruit (*Hylocereus polyrhizus*) peel: Bioactivity, heavy metal contamination, antimutagenicity, and antioxidation aspects. J Food Process Preserv. 2021; 45: e15044.
- [4] Utpott M, de Araujo RR, Vargas CG, Paiva ARN, Tischer B, Rios ADO, Flôres SH. Characterization and application of red pitaya (*Hylocereus polyrhizus*) peel powder as a fat replacer in ice cream. J Food Process Preserv. 2020; 44: e14420.
- [5] Joshi M, Prabhakar B. Phytoconstituents and pharmaco-therapeutic benefits of pitaya: A wonder fruit. J Food Biochem. 2020; 44: e13260.
- [6] Strober W, Fuss IJ, Blumberg RS. The immunology of mucosal models of inflammation. Annu Rev Immunol. 2002; 20: 495-549.
- [7] Bouma G, Strober W. The immunological and genetic basis of inflammatory bowel disease. Nat Rev Immunol. 2003; 3: 521-533.
- [8] Waldner MJ, Neurath MF. Novel cytokine-targeted therapies and intestinal inflammation. Curr Opin Pharmacol. 2009; 9: 702-707.

- [9] James SL, Irving PM, Geary RB, Gibson PR. Management of distal ulcerative colitis: frequently asked questions analysis. *Intern Med J.* 2008; 38: 114-119.
- [10] Papadakis KA, Targan SR. Current theories on the causes of inflammatory bowel disease. *Gastroenterol. Clin. North Am.* 1999; 28: 283-296.
- [11] Chidlow JH, Jr., Shukla D, Grisham MB, Kevil CG. Pathogenic angiogenesis in IBD and experimental colitis: new ideas and therapeutic avenues. *Am J Physiol Gastrointest Liver Physiol.* 2007; 293: G5-G18.
- [12] Okayama M, Hayashi S, Aoi Y, Nishio H, Kato S, Takeuchi K. Aggravation by selective COX-1 and COX-2 inhibitors of dextran sulfate sodium (DSS)-induced colon lesions in rats. *Dig Dis Sci.* 2007; 52: 2095-2103.
- [13] Siddiqui A, Ancha H, Tedesco D, Lightfoot S, Stewart CA, Harty RF. Antioxidant therapy with N-acetylcysteine plus mesalamine accelerates mucosal healing in a rodent model of colitis. *Dig Dis Sci.* 2006; 51: 698-705.
- [14] Mizoguchi A. 2012. Animal models of inflammatory bowel disease. *Prog Mol Biol Transl Sci.* 2012; 105: 263-320.
- [15] Chiu CT, Kuo SN, Hung SW, Yang CY. Combined treatment with hyaluronic acid and mesalamine protects rats from inflammatory bowel disease induced by intracolonic administration of trinitrobenzene sulfonic acid. *Molecules.* 2017; 22: 904.
- [16] Arthur K, Zeissig S, Blumberg RS. Inflammatory bowel disease. *Annu Rev Immunol.* 2010; 28: 573-621.
- [17] Beisner J, Stange EF, Wehkamp J. Innate antimicrobial immunity in inflammatory bowel diseases. *Expert Rev Clin Immunol.* 2010; 6: 809-818.
- [18] Bhattacharyya S, Borthakur A, Anbazhagan AN, Katyal S, Dudeja PK, Tobacman JK. Specific effects of BCL10 serine mutations on phosphorylations in canonical and noncanonical pathways of NF- κ B activation following carrageenan. *Am J Physiol Gastrointest Liver Physiol.* 2011; 301: G475-G486.
- [19] Boismenu R, Chen Y. Insights from mouse models of colitis. *J Leukoc Biol.* 2000; 67: 267-278.
- [20] Burisch J. Crohn's disease and ulcerative colitis. Occurrence, course and prognosis during the first year of disease in a European population-based inception cohort. *Dan Med J.* 2014; 61: B4778-B14778.
- [21] Goyal N, Rana A, Ahlawat A, Bijjem KRV, Kumar P. Animal models of inflammatory bowel disease: a review. *Inflammopharmacology.* 2014; 22: 219-233.
- [22] Joshi SV, Vyas BA, Shah PD, Shah DR, Shah SA, Gandhi T.R. Protective effect of aqueous extract of *Oroxylum indicum* Linn. (root bark) against DNBS-induced colitis in rats. *Indian J Pharmacol.* 2011; 43: 656.
- [23] Jurjus AR, Khoury NN, Reimund JM. Animal models of inflammatory bowel disease. *J. Pharmacol. Toxicol. Methods.* 2004; 50: 81-92.
- [24] Kawada M, Arihiro A, Mizoguchi E. Insights from advances in research of chemically induced experimental models of human inflammatory bowel disease. *World J Gastroenterol.* 2007; 13: 5581.
- [25] Lees CW, Barrett JC, Parkes M, Satsangi J. New IBD genetics: common pathways with other diseases. *Gut.* 2011; 60: 1739-1753.
- [26] Low D, Nguyen DD, Mizoguchi E. Animal models of ulcerative colitis and their application in drug research. *Drug Des Devel Ther.* 2013; 7: 1341-1357.
- [27] McGuckin MA, Eri R, Simms LA, Florin TH, Radford-Smith G. Intestinal barrier dysfunction in inflammatory bowel diseases. *Inflamm Bowel Dis.* 2009; 15: 100-113.
- [28] Mitrovic M, Shahbazian A, Bock E, Pabst MA, Holzer P. Chemo-nociceptive signalling from the colon is enhanced by mild colitis and blocked by inhibition of transient receptor potential ankyrin 1 channels. *Br J Pharmacol.* 2010; 160: 1430-1442.
- [29] Modi HK. A review on: screening models of inflammatory bowel disease. *J Global Pharm Technol.* 2012; 4: 01-09.
- [30] Ordas I, Eckmann L, Talamini M, Baumgart DC, Sandborn WJ. Ulcerative colitis. *Lancet.* 2012; 380: 1606-1619.
- [31] Patel SH, Rachchh MA, Jadav PD. Evaluation of anti-inflammatory effect of anti-platelet agent-clopidogrel in experimentally induced inflammatory bowel disease. *Indian J Pharmacol.* 2012; 44: 744.
- [32] Rath HC, Wilson KH, Sartor RB. Differential induction of colitis and gastritis in HLA-B27 transgenic rats selectively colonized with *Bacteroides vulgatus* or *Escherichia coli*. *Infect Immun.* 1999; 67: 2969-2974.

- [33] Rosenstiel P, Fantini M, Bräutigam K, Kühbacher T, Waetzig GH, Seegert D, Schreiber S. TNF- α and IFN- γ regulate the expression of the NOD2 (CARD15) gene in human intestinal epithelial cells. *Gastroenterology*. 2003; 124: 1001-1009.
- [34] Siegmund B, Zeitz M. Innate and adaptive immunity in inflammatory bowel disease. *World J Gastroenterol*. 2011; 17: 3178-3183.
- [35] Stadnicki A, Colman RW. Experimental models of inflammatory bowel disease. *Arch Immunol Ther Exp (Warsz)*. 2003; 51: 149-156.
- [36] Wallace KL, Zheng LB, Kanazawa Y, Shih DQ. Immunopathology of inflammatory bowel disease. *World J Gastroenterol*. 2014; 20: 6-21.
- [37] Wilk JN, Bilsborough J, Viney JL. The *mdr1a*^{-/-} mouse model of spontaneous colitis. *Immunol Res*. 2005; 31: 151-159.
- [38] Lin YH, Chang YX, Chi TY, Wu TH, Wang YP, Lu YJ, Lin CY, Huang PM, Chen GH, Chiu CC, Chiu CF, Chiu HW, Tsai WH, Chen CC, Hung SW. 2022. Establishment of a dextran sulfate sodium-induced ulcerative disease mouse model. *Int J Front Life Sci Res*. 2022; 3: 30-38.