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Original Article

Influence of Schisandrin A on Serum TNF-α, IL-1β, D-Lactic Acid, Diamine Oxidase and Colonic Tissue Oxidative Stress Markers in a Murine Model of Ulcerative Colitis

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ABSTRACT

Introduction: This study was to demonstrate the potential roles and effects of Schisandrin A in the therapy of Ulcerative Colitis (UC). **Materials and Methods:** 60 mice from the China Experimental Animal Center were purchased and the mice were assigned to Group A (normal control), Group B (UC model), Group C1 (80 mg/kg Schisandrin A), Group C2 (40 mg/kg Schisandrin A), Group C3 (20 mg/kg Schisandrin A) and Group D (sulfasalazine), each comprising 10 individuals. An UC model was established and various parameters including colonic mass, colon length, colon weight index, spleen index and disease activity index were compared across groups. **Results:** The results revealed marked decreases in colonic mass, colon weight index and spleen index in Group B mice versus Group A. Conversely, colon length, disease activity index, TNF-α, IL-1β, DAO, D-LA and colonic tissue Oxidative Stress (OS) markers showed substantial elevation ($p<0.05$) in Group B. Comparing Group B with Groups C1, C2, C3 and D indicated varying degrees of improvement in colonic mass, colon length, colon weight index, spleen index, disease activity index, colonic tissue TNF-α, IL-1β levels, as well as serum DAO and D-LA levels and colonic tissue OS markers ($p<0.05$). **Conclusion:** In summary, Schisandrin A exhibited the ability to alleviate inflammatory reactions, suppress OS responses and improve symptoms and inflammation severity in UC mice.

Keywords: Inflammatory factors, Oxidative stress, Schisandrin A, Ulcerative colitis.

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INTRODUCTION

Ulcerative Colitis (UC) is a chronic inflammatory bowel disease affecting the mucosa and submucosa of the colon. Its characteristic symptoms include abdominal pain, diarrhea and rectal bleeding.[1,2] The pathogenesis of this disease is intricate, involving factors such as immune dysregulation, aberrant Oxidative Stress (OS) responses and disturbances in the intestinal microbiota.[3] The incidence of UC is progressively rising, making it a significant global health concern.[4,5] Currently, the therapy of UC relies primarily on anti-inflammatory drugs, immunosuppressants and biologics.[6] Nevertheless, not all patients respond effectively to these therapeutic approaches and long-term use might entail certain side effects. Consequently, the exploration of novel treatment strategies and therapeutic agents has emerged as a pivotal research direction.

Traditional Chinese Medicine (TCM) serves as an ancient therapeutic modality with a longstanding history in the management of inflammatory disorders, garnering significant attention in recent years.[7] Schisandrin A, as a principal active constituent of Schisandra chinensis, has found extensive application in TCM-based clinical practices for UC treatment.[8,9] Preliminary investigations have indicated that Schisandrin A possesses a multifaceted pharmacological profile encompassing antioxidant, anti-inflammatory and immunomodulatory properties, thereby positioning it as a potential candidate for UC therapy.[10-13] Nevertheless, the precise mechanistic underpinnings of the role of Schisandrin A in UC treatment, as well as its impact on OS markers within serum and colonic tissues, remain incompletely elucidated. The present study evaluated the therapeutic effects of Schisandrin A in UC via a murine model, while exploring its regulatory effect on serum Tumor Necrosis Factor-alpha (TNF-α), Diamine Oxidase (DAO), D-Lactic Acid (D-LA) and colonic tissue OS markers. Through an in-depth examination of pharmacological mechanisms of Schisandrin A,

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this research endeavors to offer novel insights and theoretical foundations for the therapy of UC.

In summary, UC is a chronic inflammatory bowel disease with a complex pathological mechanism. Current therapeutic approaches are limited by efficacy and side effects, thus highlighting the urgent need for the development of novel treatment strategies. Schisandrin A, an important bioactive compound derived from *Schisandra chinensis*, exhibits a range of pharmacological properties, including antioxidant, anti-inflammatory and immunomodulatory effects, suggesting its potential therapeutic value in the treatment of UC within the context of traditional Chinese medicine. However, its precise mechanism of action and impact on oxidative stress markers in serum and colon tissues remain unclear. Therefore, this study aimed to investigate the potential therapeutic effects of Schisandrin A in UC, particularly focusing on its regulatory effects on oxidative stress markers in serum and colon tissues. Using a UC mouse model, the study examined the therapeutic effects of Schisandrin A at different doses by assessing its impact on parameters such as colon weight index and spleen index. Additionally, changes in serum levels of TNF-α, IL-1β, D-Lactic Acid (D-LA) and Diamine Oxidase (DAO) were measured, along with alterations in oxidative stress-related markers in colon tissue. This study sought to elucidate the anti-inflammatory and antioxidant mechanisms of Schisandrin A. The findings not only provide scientific evidence for the application of Schisandrin A in UC treatment but also offer theoretical support for the further exploration of traditional Chinese medicine in the management of inflammatory bowel diseases.

MATERIALS AND METHODS

Mice grouping and model induction

The 60 mice used in this experiment were purchased from the China Experimental Animal Center (Beijing Vital River Laboratory Animal Technology Co., Ltd.), with a body weight range of 18-22 g. All mice were housed under standard environmental conditions, with a temperature of 22±2°C, humidity of 50-60% and a 12-hr light/dark cycle. They were provided with *ad libitum* access to water and standard chow. After a one-week acclimatization period, the mice were used for subsequent experiments.

Mice were randomly assigned to the following 6 groups: Group A (normal control), Group B (UC model), Group C1 (Schisandrin A high-dose group, 80 mg/kg), Group C2 (Schisandrin A medium-dose group, 40 mg/kg), Group C3 (Schisandrin A low-dose group, 20 mg/kg) and Group D (sulfasalazine), with 10 mice per group. A 2.5% solution of trinitrobenzene sulfonic acid was prepared by dissolving 500 mg of trinitrobenzene sulfonic acid in 50% ethanol. Mice were fasted for 24 hr to ensure emptying of the gastrointestinal tract and reduce potential interference. Urethane injection was administered in accordance with specified dosages to anesthetize mice, ensuring a painless state. The mice were placed in an inverted position and a catheter of a venous indwelling needle was gently inserted through the anus into the colon, with its tip approximately 3 cm away from the anus. Using a syringe, a pre-prepared solution of trinitrobenzene sulfonic acid in ethanol was slowly injected into the colon, administering 60 µL. After removal of the catheter, the mice were maintained in an inverted position for 60 sec, facilitating optimal contact of the drug with the colonic mucosa. Subsequently, the mice were placed back into their cages to recover. For Group A, mice were administered a 50% ethanol solution of equivalent volume instead of trinitrobenzene sulfonic acid. After 24 hr, the aforementioned procedure was repeated, administering the same drug or solution to induce UC model.

Effects on colonic mass, colonic length, colon weight index and spleen index in mice

On the morning following the completion of treatment, mice were anesthetized with 3% pentobarbital sodium. The abdominal skin was incised to expose the lower abdomen, and the colon was carefully excised from the anus to the cecum. The length of the colon was measured along the longitudinal axis. Subsequently, the colon was longitudinally dissected, flushed with Phosphate-Buffered Saline (PBS) and its contents were removed before weighing. The colon weight index was calculated using the equation [(colon mass/body mass of the mouse)×100%]. Additionally, the spleen was dissected from the mice and the spleen index was calculated.

Detection of colonic tissue OS levels

The Superoxide Dismutase (SOD), Glutathione Peroxidase (GSH-PX), eNOS and iNOS activities, as well as the Total Antioxidant Capacity (T-AOC), Nitric Oxide (NO) and Myeloperoxidase (MPO) expression levels in colonic tissues of colitis-induced rats were assessed. Colonic samples were retrieved from frozen storage vials and combined with tissue lysis buffer. Homogenization was performed using an ultrasonic homogenizer and the resulting supernatant was collected and stored in 2 mL Eppendorf tubes with corresponding labels. The SOD levels were determined using the WST-1 methodology, NO levels were assessed using a microplate-based approach and the remaining tissue indicators' concentrations were measured using chemical colorimetric assays.[14]

Disease Activity Index (DAI) assessment in mice

The DAI of each mouse group was evaluated to assess the symptoms of UC by considering alterations in fecal characteristics and the presence of rectal bleeding.[15] 0 points were awarded for fecal consistency rates of 0% to 19%, 1 point for 20% to 39%, 2 points for 40% to 59%, 3 points for 60% to 79% and 4 points for 80% to 100%. Hemoccult grading was allocated as: 0 points for negative, 1 point for weak positive, 2 points for positive, 3 points

for strong positive and 4 points for visible gross rectal bleeding. The DAI score was calculated as the sum of fecal consistency score and hemoccult grading.[16,17]

Measurement of serum DAO and D-LA levels in mice

The quantification of serum DAO and D-LA levels were conducted in adherence to the operational guidelines of the ELISA kit (Thermo Fisher Scientific, USA). Two duplicate wells were designated for each sample and sample concentrations were calculated using the standard curve. The results were averaged for subsequent statistical analysis.

Measurement of colonic tissue MPO, TNF-α and IL-1β levels in mice

MPO activity assay was implemented as follows. Approximately 50 mg of colonic tissue was weighed and homogenized to a 10% tissue slurry in PBS containing 0.5% hexadecyltrimethylammonium bromide solution. The homogenate was subjected to low-temperature centrifugation at 14,000 rpm for 15 min. An aliquot of the supernatant of 80 liters was mixed with a sodium phosphate buffer (50 mmol/L, pH 6.0) containing 0.0005% o-dianisidine and 0.1% H_2O_2 and absorbance readings were taken at 460 nm wavelength over 2 min at 30-min intervals. The average rate of change in absorbance values within 2 min was calculated to determine enzyme activity, expressed as units of enzyme activity per gram of colonic tissue.[18,19] For TNF-α and IL-1β determination, colonic tissue was homogenized to a 10% tissue slurry and subjected to low-temperature centrifugation at 14,000 rpm for 10 min. The measurement procedures for TNF-α and IL-1β were performed according to the instructions of the respective kits and the results were expressed as pg/g tissue.

Statistical methodologies

Data entry and statistical analysis were conducted using *SPSS 22.0*. Descriptive statistics were employed for categorical data presentation, using frequencies and percentages, while continuous data were presented as mean±standard deviation. $p<0.05$ indicated statistically significant.

RESULTS

Effects of Schisandrin A on colonic mass, colonic length, intestinal weight index and spleen index in UC mice

The study analyzed colon tumors, colon length, colon weight index and spleen index in the Groups A, B, C1, C2, C3 and D of mice. One-way Analysis of Variance (ANOVA) followed by *post-hoc* multiple comparisons revealed that, compared to the Groups B, C1, C2, C3 and D, mice in the Group A exhibited significantly lower colon mass, colon weight index and spleen index and a significantly greater colon length ($p<0.05$). In comparison to Group B, the Groups C1, C2, C3 and D displayed lower colon tumor mass and spleen index, along with longer colon lengths. Additionally, the colon weight index was lower in Groups C1, C3 and D, while the colon tumor mass and spleen index increased sequentially across Groups C1, C2 and C3, with a corresponding decrease in colon length. The colon weight index in the Group C3 was significantly higher than in the Group C1 ($p<0.05$). Detailed results are shown in Figure 1.

Effects of Schisandrin A on DAI in UC mice

The study observed and compared the DAI of mice in the Groups A, B, C1, C2, C3 and D. One-way ANOVA followed by *post-hoc* Tukey's test was used to compare the mean values between groups. The results showed that the DAI of the Group A was consistently lower than that of all other groups. Furthermore, the DAI of the Groups C1, C2, C3 and D was significantly lower than that of the Group B. Additionally, the DAI values of the Group C1, C2 and C3 progressively increased and these differences were statistically significant ($p<0.05$). Detailed results are presented in Figure 2.

Effects of Schisandrin A on TNF-α and IL-1β levels in colonic tissues of UC mice

The study quantified the levels of TNF-α and IL-1β in the colon tissues of mice from the Groups A, B, C1, C2, C3 and D. One-way ANOVA followed by *post-hoc* Tukey's test was used to compare the mean values between groups. The results showed that, compared to the Groups B, C1, C2, C3 and D, the Group A had significantly lower levels of TNF-α and IL-1β. Furthermore, the levels of TNF-α and IL-1β in the Groups C1, C2, C3 and D were significantly lower than those in the Group B, with a progressive reduction in TNF-α and IL-1β levels in the Groups C1, C2 and C3. These differences were statistically significant ($p<0.05$). Detailed results are shown in Figure 3.

Effects of Schisandrin A on serum DAO and D-LA levels in UC mice

A comparison of serum levels of DAO and D-LA after Schisandrin A treatment among different groups of mice was conducted. Serum levels of DAO and D-LA in Group A were consistently less than those in the other groups. A decrease in Schisandrin A concentration was associated with a gradual reduction in serum DAO and D-LA levels in Groups C1, C2, C3 and D. Furthermore, a decrease in Schisandrin A concentration was also associated with a gradual decrease in serum DAO and D-LA levels and these variations were remarkable with a *p*-value of less than 0.05. Specific details are presented in Figure 4.

The study measured the levels of DAO and D-LA in the serum of mice from the Groups A, B, C1, C2, C3 and D. One-way ANOVA followed by *post-hoc* Tukey's test was used to compare the mean values between groups. The results showed that, compared to Group B, Groups C1, C2, C3 and D, the Group A had significantly lower levels of DAO and D-LA. Furthermore, the levels of DAO and D-LA in the Groups C1, C2, C3 and D were significantly

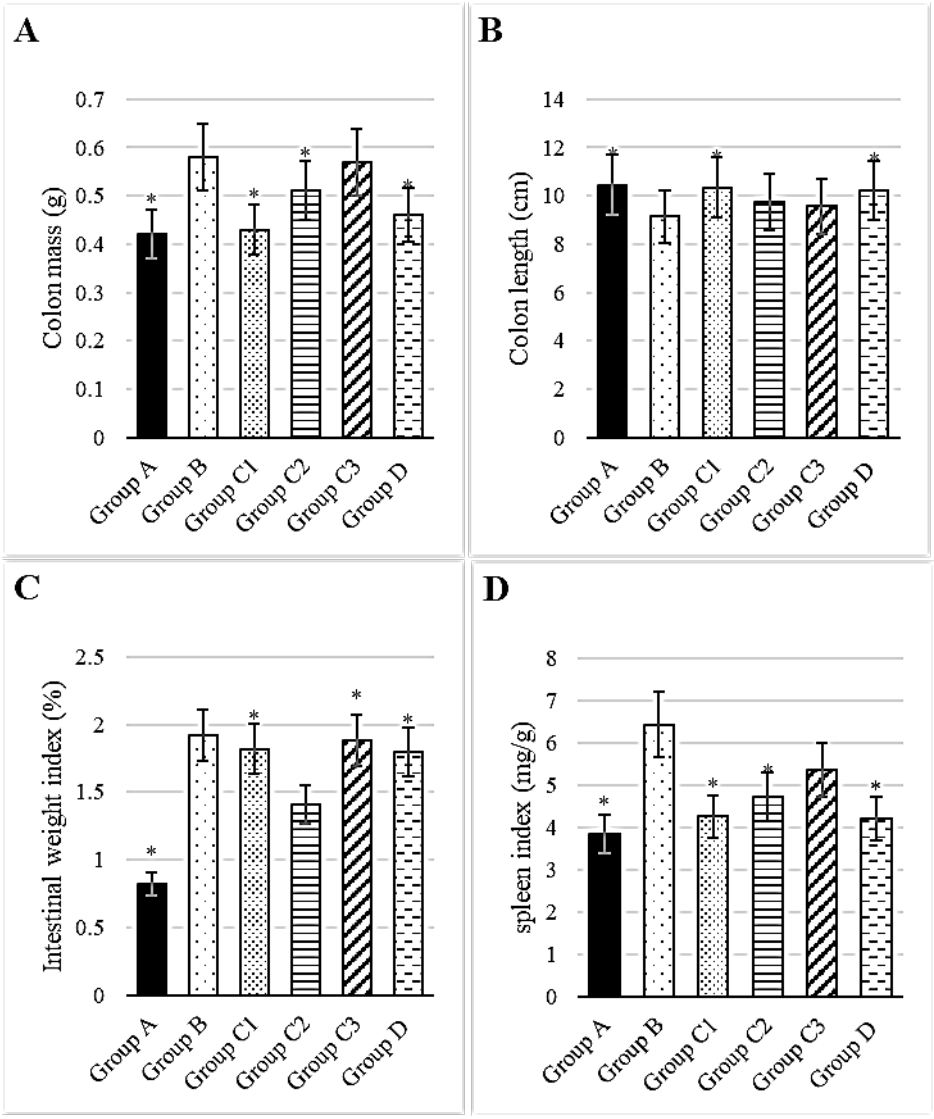

Figure 1: Comparison of colonic mass (A), Colonic length (B), Intestinal weight index (C) and Spleen index (D) in various mouse groups. Note: *p<0.05 vs. Group B.

lower than those in the Group B, with a progressive decrease in DAO and D-LA levels across the Groups C1, C2 and C3. These differences were statistically significant (p<0.05). Detailed results are presented in Figure 4.

Effects of Schisandrin A on OS markers in UC mice

The impact of Schisandrin A on the activities of SOD, GSH-PX, eNOS and iNOS, as well as levels of T-AOC, NO and MPO in tissue among different groups of mice was observed and compared. The results indicated that the activities of SOD, GSH-PX, eNOS and iNOS, as well as expression levels of T-AOC, in Group A mice were all substantially superior to in Group B. Conversely, the expression levels of NO and MPO in Group A mice were markedly inferior to in Group B. In Groups C1, C2, C3 and D mice, the activities of SOD, GSH-PX, eNOS, iNOS and T-AOC were all greatly superior to Group B and these discrepancies were substantial with a p-value of less than 0.05. Moreover, in Groups C1, C2, C3 and D mice, the expression levels of NO and MPO were all remarkably inferior to Group B and these differences were considerable with a p-value of less than 0.05. Specific details are depicted in Figures 5 and 6.

The study measured the levels of SOD, GSH-PX, eNOS, iNOS, T-AOC, NO and MPO in the serum of mice from the Groups A, B, C1, C2, C3 and D. One-way ANOVA followed by *post-hoc* Tukey's test was used to compare the mean values between groups. The results indicated that, compared to Group B, mice in the Groups A, C1, C2, C3 and D had significantly higher levels of SOD, GSH-PX, eNOS, iNOS and T-AOC and significantly lower levels of NO and MPO. Additionally, the levels of SOD, GSH-PX and T-AOC decreased progressively in the Groups C1, C2 and C3, while eNOS, iNOS, NO and MPO levels increased

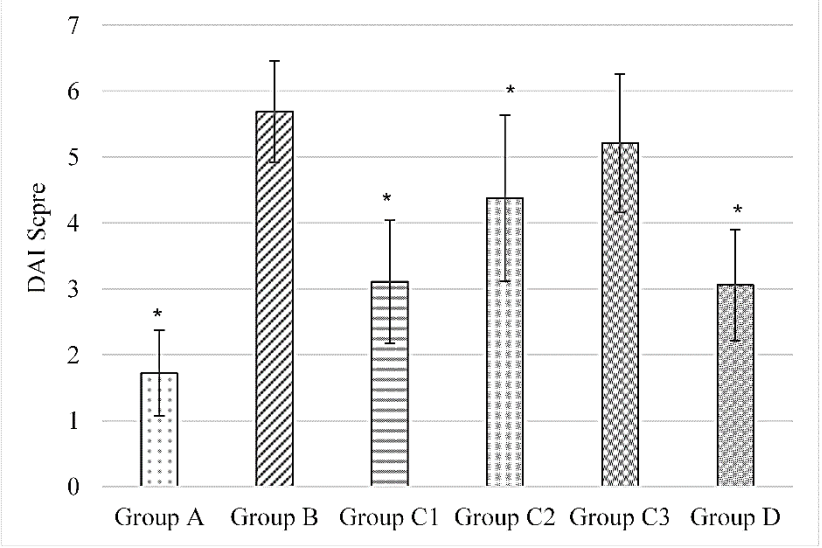

Figure 2: Effects of Schisandrin A on DAI in various mouse groups. Note: *p<0.05 vs. Group B.

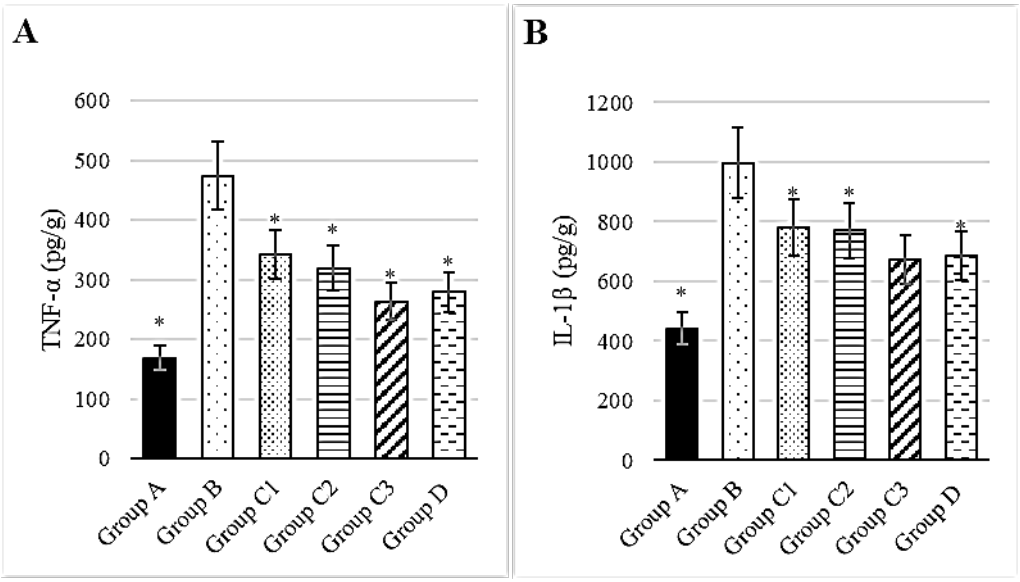

Figure 3: Effects of Schisandrin A on TNF-α (A) and IL-1β (B) Levels in colonic tissues of various mouse groups. Note: *p<0.05 vs. Group B.

sequentially. All these differences were statistically significant (p<0.05). Detailed results are presented in Figures 5 and 6.

DISCUSSION

UC is a chronic gastrointestinal disorder characterized by symptoms such as abdominal pain, diarrhea and rectal bleeding, which significantly impair the quality of life of affected individuals.[20] In recent years, the incidence of UC has been steadily increasing, likely due to changes in lifestyle and dietary habits. Hence, the search for effective treatment methodologies is of paramount importance to alleviate the suffering of UC patients and enhance their overall well-being. Currently, the therapy of UC primarily relies on anti-inflammatory drugs, immunosuppressants and biologics, but not all patients respond favorably to these therapies.[21,22] Thus, the pursuit of novel treatment modalities and therapeutic agents remains a critical research direction. In the realm of traditional Chinese medicine theory, Schisandra chinensis is a commonly used herbal remedy, often employed to regulate the spleen and stomach and enhance physical constitution.[23] Research reports have shown that Schisandrin A possesses anti-inflammatory, antioxidant, hepatoprotective and anti-gastric smooth muscle spasm effects. However, its potential role in UC has not yet been investigated.[24] Building upon this premise, this study embarked on exploring the potential role and plausible therapeutic effects of Schisandrin A in UC treatment, aiming to offer scientific insights for the

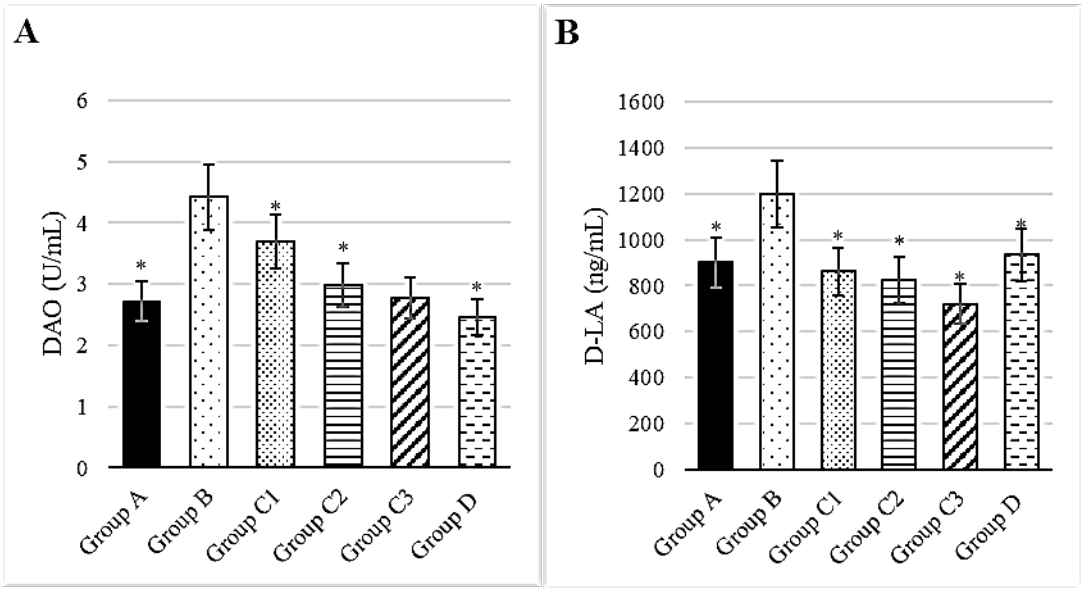

Figure 4: Effects of Schisandrin A on serum DAO (A) and D-LA (B) Levels in various mouse groups. Note: **p*<0.05 vs. Group B.

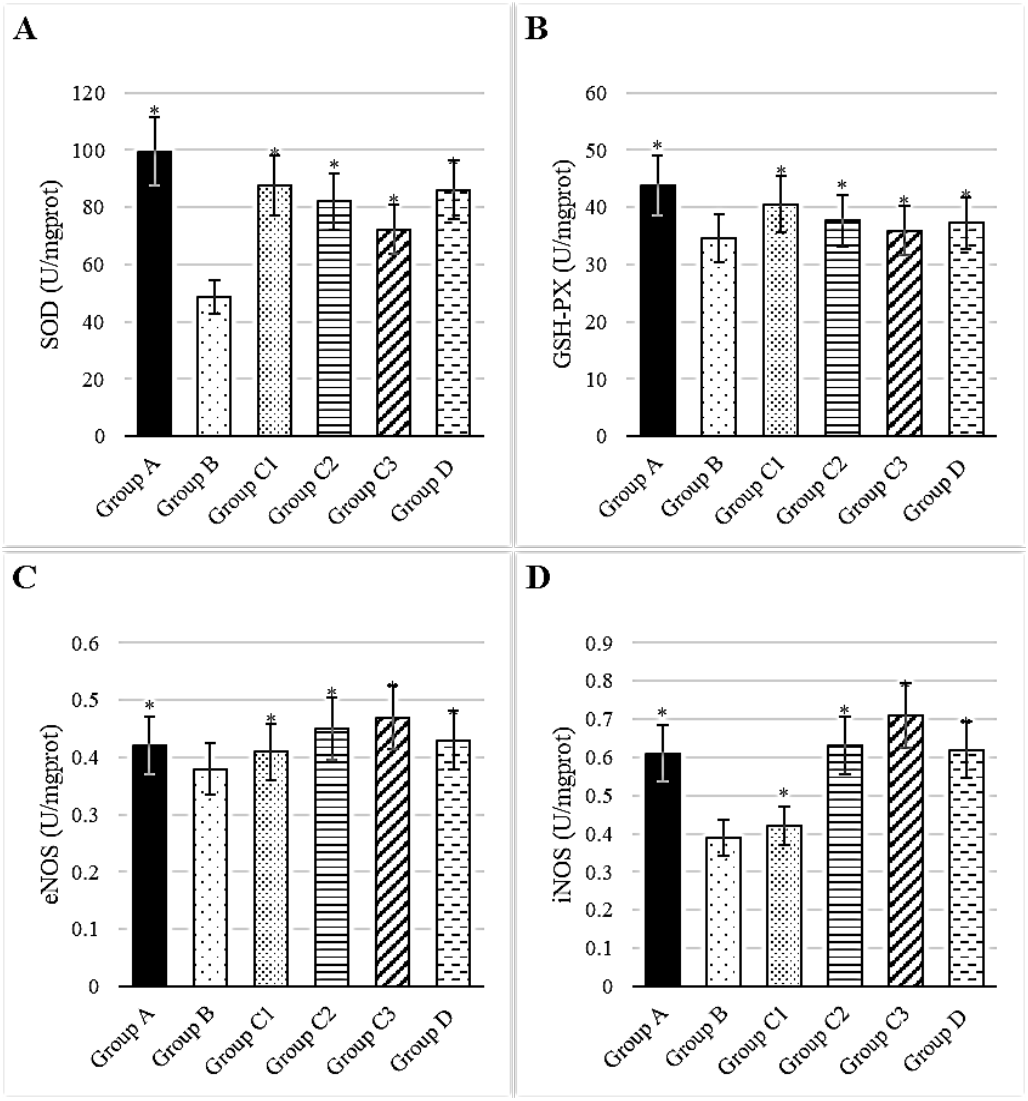

Figure 5: Effects of Schisandrin A on SOD (A), GSH-PX (B), eNOS (C) and iNOS (D) Activities in various mouse groups. Note: **p*<0.05 vs. Group B.

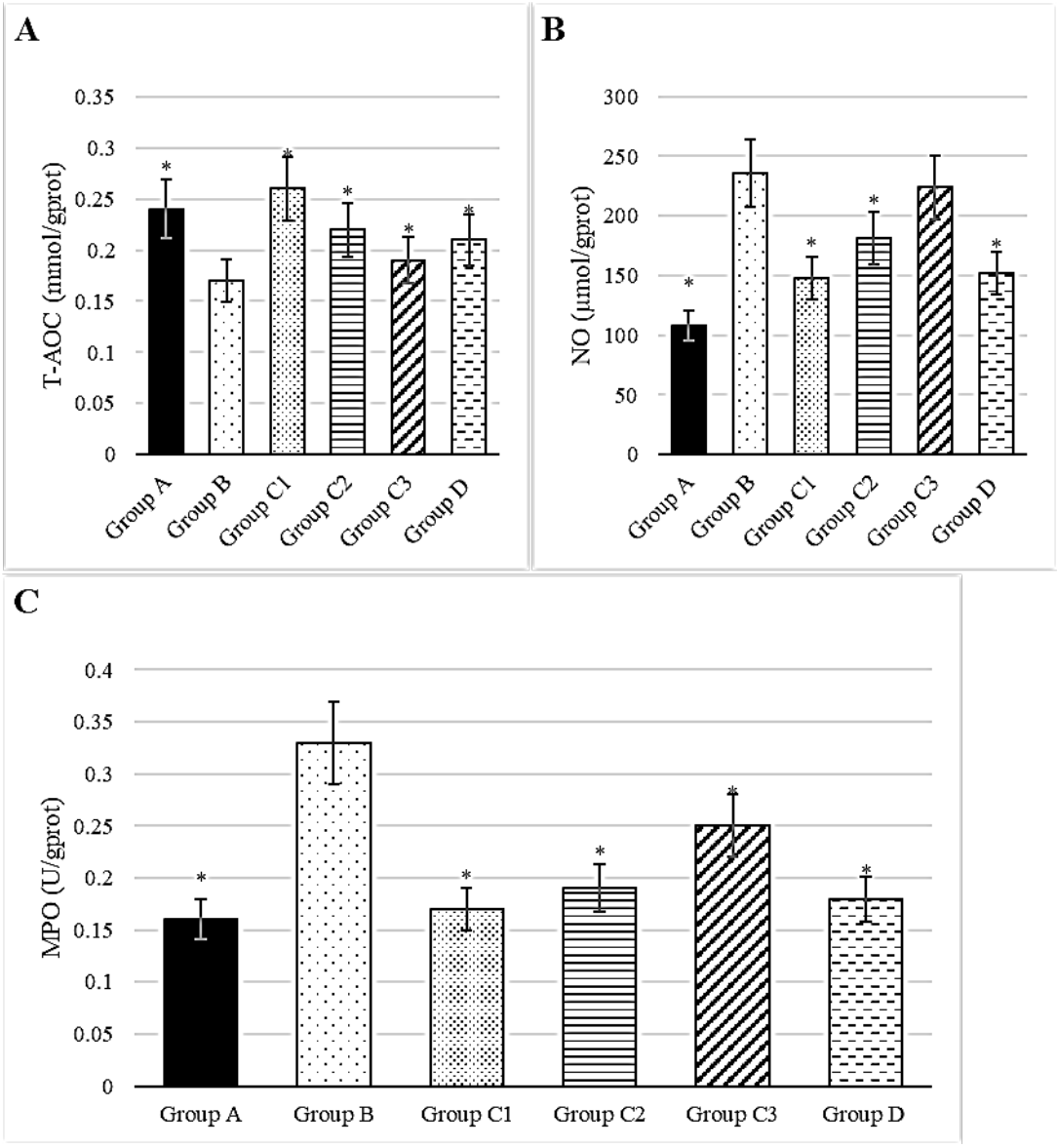

Figure 6: Effects of Schisandrin A on T-AOC (A), NO (B) and MPO (C) Levels in various mouse groups. Note: *p<0.05 vs. Group B.

development of new treatment strategies and medications, ultimately providing patients with improved therapeutic options. The research involved the administration of varying doses of Schisandrin A to mice, observing changes in colonic quality, length, intestinal weight index and spleen index, while also assessing alterations in inflammation-related and OS markers to evaluate its therapeutic efficacy.

In the UC model group (Group B), the colonic quality, colonic weight index and spleen index of mice were markedly higher versus Group A, while the colonic length was markedly lower. This observation confirms the successful establishment of the UC model and the severity of the disease. Subsequently, different doses of treatment were administered to the high-dose Schisandrin A group (Group C1), medium-dose Schisandrin A group (Group C2), low-dose Schisandrin A group (Group C3) and sulfasalazine group (Group D). The results showed that as the Schisandrin A concentration decreased, the mice exhibited a gradual increase in colonic quality, a decrease in colonic length, an increase in colonic weight index, an increase in spleen index and a progressively rising disease activity index, all demonstrating statistically significant differences. This indicates that Schisandrin A, at various doses, effectively improved the symptoms and inflammation severity in mice with UC. Further analysis revealed that the TNF-α and IL-1β in colonic tissues of the Schisandrin A treatment groups were inferior to those in the UC model group and these levels progressively decreased with decreasing Schisandrin A concentration. Additionally, the serum levels of DAO and D-LA in the Schisandrin A treatment groups were inferior to those in the UC model group and these levels also gradually decreased with decreasing Schisandrin A

concentration. These findings suggest that Schisandrin A exerts its therapeutic effects through multiple mechanisms, particularly by inhibiting the production of inflammatory cytokines and alleviating oxidative stress. Schisandrin A significantly reduces the levels of TNF-α and IL-1β in intestinal tissues, thereby mitigating intestinal inflammation and improving the symptoms of UC. Furthermore, the antioxidant effect of Schisandrin A may be associated with the modulation of the Nuclear factor erythroid 2-related factor 2 (Nrf2) pathways. Activation of Nrf2 promotes the expression of antioxidant enzymes such as SOD and GSH-PX, which help neutralize free radicals, reduce oxidative damage and attenuate inflammatory responses. Further studies could explore the specific role of Schisandrin A in the Nrf2 pathway, providing scientific evidence for its potential as a therapeutic agent in UC treatment. These mechanisms underscore the significance of Schisandrin A as a natural compound in the fields of anti-inflammatory and antioxidant therapy. SOD is a crucial antioxidant enzyme in mitochondrial OS, acting to scavenge ROS generated during mitochondrial metabolism, thus inhibiting lipid oxidation and stabilizing cell membranes. The combined action of GSH-PX and SOD extends a wider antioxidant defense against oxidative damage to the colonic mucosa by effectively removing peroxides.[25,26] T-AOC reflects the overall antioxidative capacity of the organism, encompassing both enzymatic and non-enzymatic components. The former mainly includes SOD and GSH, while the latter includes vitamins C and E. T-AOC reflects the content and activity of antioxidant-related enzymes, the functional state of antioxidant systems and indirectly reflects the degree of lipid peroxidation. Greater tissue T-AOC content indicates a faster rate of free radical clearance.[27] The activities of SOD, GSH-PX, eNOS, iNOS and T-AOC in the colonic tissues of groups C1, C2 and C3 were all notably superior to those in the B group, while NO and MPO were markedly lower. Studies have shown that NO can lead to the infiltration of a large number of inflammatory cells and simultaneously induce vasodilation and increased vascular permeability in colonic tissues, facilitating the delivery of more nutrients to the inflammatory site through blood vessels, thereby providing ample material support for the division, proliferation and infiltration of inflammatory cells.[28,29] Following modeling, NO levels markedly increase, whereas they decrease markedly after Schisandrin A treatment, suggesting that the alleviation of intestinal inflammation in mice by Schisandrin A may be related to the reduction in NO content. eNOS and iNOS are endothelial nitric oxide synthase and inducible nitric oxide synthase, respectively, with eNOS having anti-inflammatory and protective effects, including the prevention of bacterial translocation.[30] The influence of iNOS on intestinal inflammation remains contentious, although relevant studies suggest that iNOS has various biological effects, such as bactericidal activity and a critical role in the healing of skin and intestinal mucosa.[31] The eNOS and iNOS in Group B were greatly inferior to those in Group A and they notably increased after treatment, indicating that the mechanism of Schisandrin A therapy for UC is associated with the upregulation of eNOS and iNOS levels. This observation also partially validates the positive role of eNOS and iNOS in colonic inflammation healing. The findings collectively suggest that Schisandrin A alleviates OS damage in UC mice by enhancing the activity of antioxidant enzymes, reducing the expression of oxidative damage indicators NO and MPO, thereby mitigating OS injury.

In summary, the experimental outcomes collectively demonstrated that Schisandrin A can remarkably ameliorate the symptoms and inflammatory severity in UC mice across different dosages, with the therapeutic effect positively correlated with the dosage. Further research is required to explore the mechanisms of action of Schisandrin A at different dosages and treatment durations, thereby uncovering its potential therapeutic value in the treatment of UC. The potential therapeutic mechanism of Schisandrin A may involve the inhibition of inflammatory factor generation, alleviation of OS response and enhancement of antioxidant enzyme activity. Nevertheless, this study still harbors certain limitations, such as the absence of in-depth mechanistic investigations and comparative analyses involving other dosages and treatment durations. Hence, further research endeavors are warranted to gain a deeper understanding of Schisandrin A's mechanistic role and potential value in the therapy of UC.

CONCLUSION

Schisandrin A, as a potential herbal component, holds promise for the therapy of UC. Across various dosages, Schisandrin A effectively ameliorates the symptoms and inflammatory severity in UC mice, with its therapeutic efficacy positively correlated with the dosage. Therapeutic effects of Schisandrin A are likely mediated through the inhibition of inflammatory cytokine production, attenuation of OS response and enhancement of antioxidant enzyme activity. These findings offer valuable insights for further research and development of Schisandrin A as a therapeutic agent for UC, while also suggesting new avenues for the adoption of traditional Chinese medicine in the therapy of inflammatory bowel diseases. Nevertheless, further investigations are needed to validate these findings and delve into the mechanisms of action of Schisandrin A and its safety profile to fully realize its clinical potential.

ACKNOWLEDGEMENT

Not applicable.

ABBREVIATIONS

UC: Ulcerative colitis; **OC:** Oxidative stress; **TCM:** Traditional Chinese medicine; **DAO:** Diamine oxidase; **PBSB:** Phosphate-buffered saline; **T-AOC:** Total antioxidant capacity; **NO:** Nitric oxide; **MPO:** Myeloperoxidase; **DAI:** Disease activity index.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

CONSENT FOR PUBLICATION

The manuscript is approved by all authors for publication.

AVAILABILITY OF DATA AND MATERIALS

The data and materials of this experiment are available.

SUMMARY

The manuscript investigates the potential therapeutic effects of Schisandrin A on Ulcerative Colitis (UC) using a murine model. The study examines various doses of Schisandrin A and its impact on key inflammatory markers, oxidative stress indicators and the severity of UC symptoms. The results suggest that Schisandrin A significantly alleviates UC symptoms by reducing inflammation and oxidative stress in a dose-dependent manner, indicating its promise as a potential treatment for UC. Further research is recommended to explore the mechanisms of action and validate the therapeutic potential of Schisandrin A in clinical settings.

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