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SUPPORTIVE EFFECTS OF OAT EMULSION GEL OF CURCUMIN ON DSS-INDUCED COLITIS IN MICE: IMPROVEMENTS IN ULCERATIVE COLITIS

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ABSTRACT

Ulcerative colitis (UC) is a chronic inflammatory bowel disease primarily affects the colon and rectum. Given the adverse effects of current treatments, alternatives such as turmeric, known for its anti-inflammatory properties, have been investigated. **Objective:** This study evaluated the protective effects of a turmeric-based dietary supplement in a dextran sulfate sodium (DSS)-induced colitis model in mice. **Methods**: A colitis model was used, where all mice, except the sham group, received 2.5% DSS in drinking water for 5 days. Subsequently, the mice were treated orally with turmeric at 2000 mg/kg, minocycline at 100 mg/kg, or water as a vehicle for 4 days. Histological sections of the colon were prepared and stained with hematoxylin and eosin (H&E) to assess tissue damage and inflammation. Additionally, myeloperoxidase (MPO) activity, a marker of neutrophil infiltration, was measured as an indicator of inflammation. **Results:** DSS-induced diarrhea, rectal bleeding, weight loss, an increase in disease activity index (DAI), colon weight gain, and colon shortening. Treatment with turmeric significantly reduced colon weight by 18% and colon shortening. Minocycline also showed significant improvements, reducing colon weight by 45%. **Conclusions:** The turmeric supplement demonstrated protective effects in the DSS-induced colitis model, suggesting its potential as an anti-inflammatory treatment for UC.

KEYWORDS: Anti-inflammatory, Bioavailability, Disease Activity Index, induced ulcerative colitis.

1. INTRODUCCIÓN

Ulcerative colitis (UC), a disease of the inflammatory bowel disease (IBD) group, that affects millions of people worldwide.[1–3] This pathology is mainly located in the rectum and colon, and its impact on patients quality of life is significant, compromising both their physical and social well-being due to symptoms such as weight loss, diarrhea, and rectal bleeding.[4,5]

Gut microbial dysbiosis, characterized by changes in the balance of beneficial, commensal, and pathogenic bacteria, is a typical feature of UC.[6] In inflammation, myeloperoxidase (MPO) is a pivotal enzyme produced by neutrophils, contributing to innate immune responses by generating reactive oxygen species (ROS) to combat pathogens. Elevated MPO levels are not only indicative of heightened oxidative stress but are also closely linked to the progression of inflammatory diseases like UC. As such, MPO serves as a critical biomarker in inflammation, offering insights into disease mechanisms and potential therapeutic targets.[7]

Conventional treatment for UC typically involves the use of aminosalicylates, corticosteroids, and immunosuppressive drugs. While these therapies can help manage the disease, their effectiveness is often limited, and long-term use is associated with significant side effects, including diarrhea, osteoporosis, and increased susceptibility to infections.[8]

Curcumin supplementation has been proven effective in reducing inflammation in conditions such as UC and IBD.[6,9] Curcumin, the primary active compound in turmeric—a polyphenol extracted from the root of *Curcuma longa*, a member of the *Zingiberaceae* family—has been widely studied for its broad range of biological activities.[9,10] These include anti-inflammatory, anticancer, antioxidant, antimicrobial, wound healing, and blood glucose-regulating properties.[1,10,11]

Turmeric's therapeutic effectiveness is hindered by its poor water solubility, which drastically limits its bioavailability and impairs the absorption of its active compounds.[10,11] Phytosomes are formulated to enhance

the bioavailability and absorption of turmeric. By stabilizing its active compounds, these advanced delivery systems help maximize turmeric's therapeutic benefits.[9,10] Among these materials, β-glucans, due to their hydrocolloid nature and affinity for water, can contribute to the stability of poorly soluble compounds.[12,13] Similarly, inulin derivatives can form micellar structures in solution, improving encapsulation.[14] Combining turmeric with inulin and β-glucans can increase the bioavailability of curcumin, which could result in a reduction of symptoms associated with UC.[15,16]

This study was conducted to evaluate the efficacy of a turmeric-based dietary supplement (SAC) in the treatment of dextran sodium sulfate (DSS)-induced ulcerative colitis. Key variables such as body weight, disease activity index (DAI), MPO assay, colitis index, and colonic histology were measured in mice, as these parameters are critical to assess the symptomatology of ulcerative colitis.

2. MATERIALS AND METHODS

2.1. Bromatological analysis of β-glucan and Curcumin emulsified gel: NOM 116-SSA1-1994[17] was used for moisture determination, NMX-F-608-NORMEX-20 11[18] (F=6.25) for protein, NMX-F-427-NORMEX-2019[19] for fat, NMX-F-607-NORMEX-2020[20] for ash, NOM-086-SSA1-1994[21] for dietary fiber, and NOM-051-SCFI/SSA1-2010[22] for total carbohydrates.

2.2. Study design: Study design: To evaluate the histopathological changes of the colon in dextran sulfate (DSS)-induced colitis in mice, a model of inflammatory bowel disease (IBD). Thirty-two female C57BL/6 mice (8-9 weeks old) were used, divided into groups of 8 with: group 1, Sham (no DSS); group 2, Vehicle with water for injection (WFI) plus DSS 2.5%; group 3, Turmeric-based supplement (2000 mg/kg) with DSS (2.5%) and group 4, Minocycline (100 mg/kg) with DSS (2.5%). DSS was administered in drinking water for 5 days and then drinking water on the remaining days. Group 2, 3, and 4 were administered once daily (QD) by oral gavage (PO) from day 6 to day 9.

2.3. Reagents: Dextran sodium sulfate (lot no. S4140, MPBiomedicals, USA), crystalline minocycline hydrochloride (Sigma, USA), MPO mouse ELISA kit (HycultBiotech, USA), Pierce protease inhibitor mini tables (ThermoFisher, Taiwan), PMSF (Sigma-Aldrich, USA), T-PER™ tissue protein extraction reagent (ThermoFisher, Taiwan) and water for injection (Tai-Yu, Taiwan).

2.4. Histopathology: Colon tissues were collected from all animals at the end of the study. Samples were taken 4 cm from the anus, fixed in formalin, and embedded in paraffin blocks. Four-micrometer sections were cut and stained with hematoxylin and eosin (H&E) for histological analysis under light microscopy at 100X magnification (LEICA DM2700 M, USA). The histological criteria included mucosal architecture abnormalities, the degree of inflammation, erosion or ulceration, epithelial regeneration, and the extent of tissue involvement. A colitis score (Total Colitis Index) was assigned to each sample based on these criteria, resulting in a combined histological score ranging from 0 to 20, as assessed by the observer.[23]

2.5. Myeloperoxidase (MPO) assay: The tissue was homogenized and followed by centrifugation at 3,000 x g at 4°C for 15 minutes. The supernatants were stored at -80°C for subsequent cytokine analysis. To measure MPO levels, the HycultBiotech HK210 ELISA kit was used. A 96-well microtiter plate was coated with a capture antibody specific for mouse MPO. Homogenized samples, diluted 200-fold, were added along with standards, and the plate was incubated for 1 hour at room temperature. After washing and drying the plate, a diluted tracer antibody that binds to a different epitope of the MPO molecule was added and incubated for another hour. Streptavidin peroxidase, bound to the tracer, was then added and incubated for 1 hour. After a final wash, the TMB substrate was added, reacting with the enzyme for 30 minutes. The reaction was stopped with a stop solution, and MPO levels were quantified by measuring the color change in a spectrophotometer at 450 nm.

2.6. Data analysis: All data were expressed as mean ± SEM. An unpaired Student's t-test was used to compare the Vehicle group (2.5% DSS, 10 mL/kg, QD x 4, PO, T2) with the Sham group (no DSS, T1). For multiple group comparisons, one-way ANOVA followed by Dunnett's post hoc test was conducted to assess significant differences ($p<0.05$) between the Vehicle group (2.5% DSS, 10 mL/kg, QD x 4, PO, T2) and the Turmeric-based dietary supplement group (2000 mg/kg, QD x 4, PO, T3) or the Minocycline group (100 mg/kg, QD x 4, PO, T4).

3. RESULTS AND DISCUSSION

The bromatological analysis of the turmeric-based dietary supplement (SAC) is presented in Table 1. The gel form of SAC contains 90.6% moisture, providing 42.89 kcal per 100 g, with no added carbohydrates. In comparison, the bromatological analysis of turmeric, as reported by[24], indicates that turmeric contains 9.40% protein, 6.85% fat, 2.85% ash, 67.4% carbohydrates, and is a good source of fiber (4.60%). It's important to note that the amounts of protein, carbohydrates, and fat may vary depending on the curcumin extraction process. In this formulation, the product shows a higher moisture content, a 6.5% reduction in fat, and no added sugars.

As shown in Fig. 1, body weight remained stable across all groups from days 1 to 5. However, starting on day 6, group 2 (Vehicle), group 3 (SAC), and group 4 (Minocycline) experienced a significant decrease in body weight, with the most pronounced loss observed in group 2 and group 3. These changes were statistically significant, with $^{+}p < 0.05$ compared to the group 1, and $^{*}p < 0.05$ compared to the group 2. The Sham group maintained stable body weight throughout the 10 days. In contrast, the groups exposed to DSS (Vehicle, SAC, and Minocycline) showed a marked weight reduction beginning around day 6, likely due to DSS-induced intestinal inflammation.

Table 1: Bromatological analysis of the turmeric-based supplement.

Composition	%
Moisture (g/100g)	90.64±2.46
Protein (g/100g)	9.26±0.67
Fat (g/100g)	0.65±0.02
Ash (550°C) (g/100g)	0.25±0.00
Carbohydrates (g/100g)	0
Dietary fiber (g/100g)	1.69±0.372

This inflammation is associated with mucosal damage, reduced nutrient absorption, and metabolic disruption, ultimately leading to weight loss.[6] Notably, while the group 3 (SAC) experienced weight loss, it was less severe than in the vehicle group, suggesting a potential protective effect of SAC against DSS-induced colitis. This finding suggests that SAC may exert a mild protective effect in DSS induced colitis.[1]

Previous studies have shown that certain bioactive compounds can reduce the severity of colitis by modulating the inflammatory response and maintaining the integrity of the intestinal barrier.[10] However, the protection offered by SAC was insufficient to fully prevent weight loss, suggesting its limited efficacy compared to more potent treatments such as minocycline. As an antibiotic with well-documented anti-inflammatory properties, minocycline has consistently demonstrated greater effectiveness in reducing colitis symptoms across multiple studies.[25]

Zhang *et al.*[26] demonstrated that mice treated with curcumin exhibited a significant reduction in weight loss of 15%, while those treated with micelles showed only a 5% reduction compared to the DSS-only group. This result aligns with the 14.5% reduction in weight loss observed in the present study, suggesting that combining curcumin with inulin and β-glucans may enhance its bioavailability, leading to improved stabilization of body weight. Wu *et al.*[27] reported that mice treated with a curcumin formulation experienced less weight loss associated with DSS-induced colitis, with some mice even maintaining a more stable body weight.

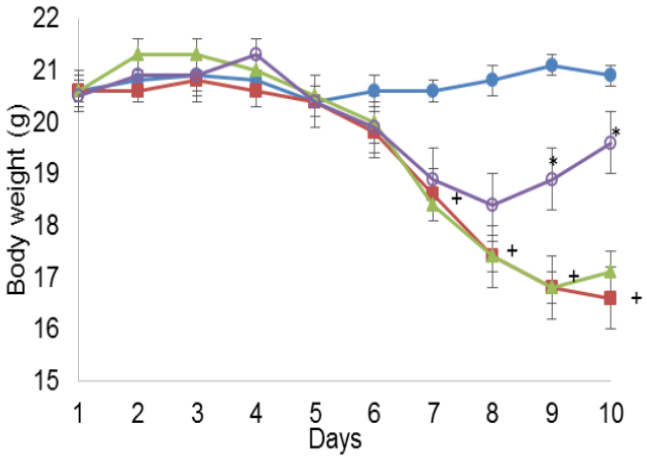


Fig. 1: Weight of mice during treatment where: (-●-) a group 1 Sham (without DSS); (-■-) group 2 Vehicle; (-▲-) group 3 with SAC (2000 mg/kg); (-○-) group 4 Minocycline (100 mg/kg). Differences are considered significant at +p< 0.05, vs sham; *p< 0.05, vs vehicle.

SAC demonstrated mild to moderate improvement in stool consistency between days 7 and 10 compared to the Vehicle (Fig. 2A). Also, SAC significantly ($p<0.05$) reduced fecal occult blood scores from day 8 to day 10 (Fig.2B). Regarding the disease activity index (DAI), led to a significant ($p<0.05$) decrease by day ten when compared to the Vehicle (Fig. 2D). The DAI was notably higher in Vehicle compared to the minocycline group, reflecting greater severity of colitis (Fig. 2D).

Histological analysis further confirmed that the SAC exhibited a significantly lower inflammatory score, suggesting that curcumin played a role in mitigating the development of DSS-induced colitis, as indicated by the reduction in histological damage.[28] Huang *et al.*,[29] tested a curcumin-loaded ginger formulation and reported a significant 32% reduction in the DAI in a DSS-induced ulcerative colitis model. Similarly, Luo *et al.*[8] found that tannic acid-coated curcumin nanoparticles (TA/Cur-NPS) reduced DAI by 55%,

bringing the levels in treated mice closer to those of healthy controls. In our study, the SAC-treated group showed a 20% reduction in IAD, indicating a moderate decrease in colitis severity, though not as pronounced as the effect observed with minocycline treatment. This suggests that SAC has a mild yet meaningful impact on mitigating colitis symptoms.

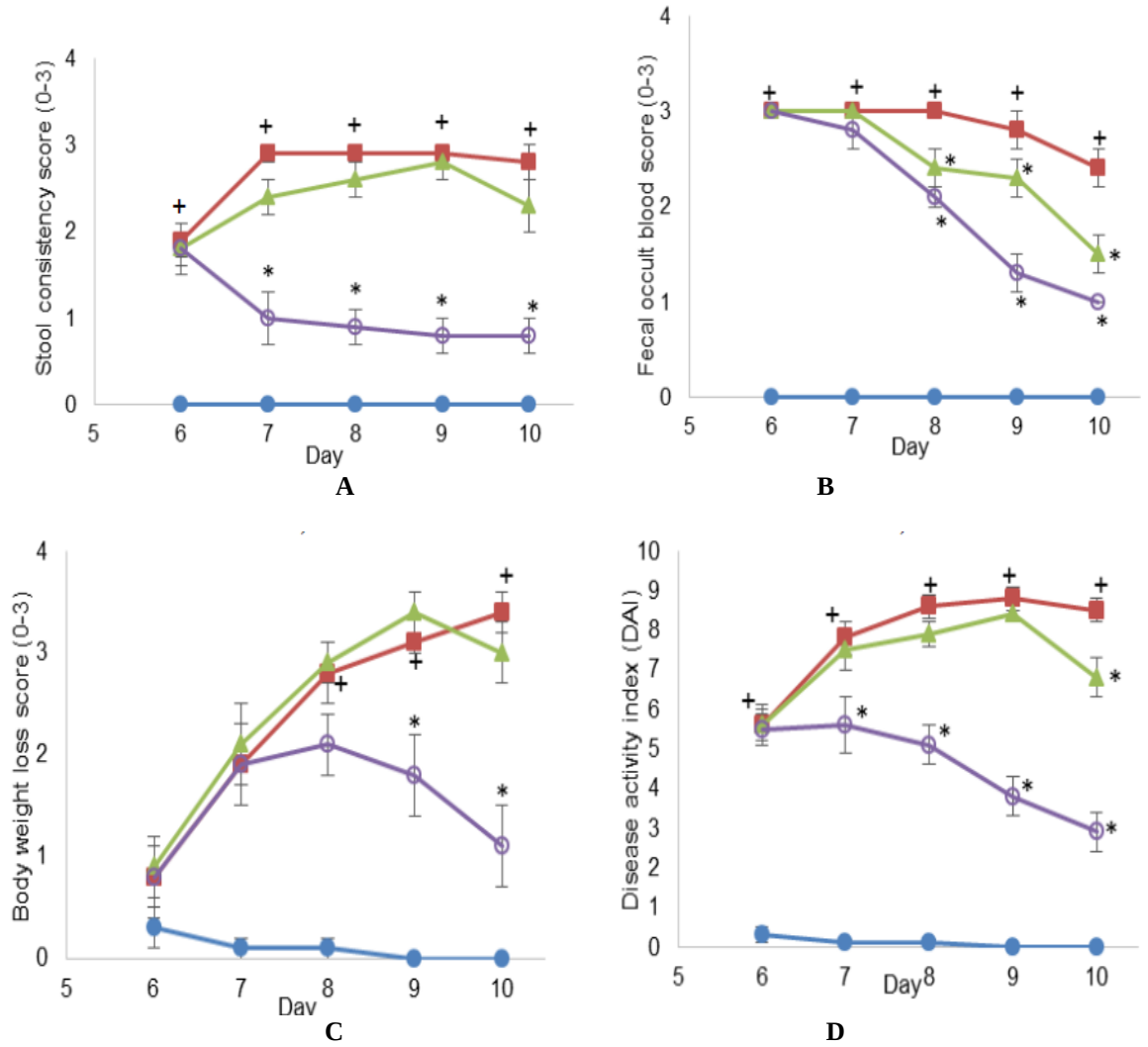


Fig. 2: A) Stool consistency score, B) Body weight loss score (0-3), C) Fecal occult blood score, D) Disease activity index. Where: (-●-) at group1 Sham (without DSS); (-■-) group 2 Vehicle; (-▲-) group 3 with SAC (2000 mg/kg); (-○-) group 4 Minocycline (100 mg/kg). Differences are considered significant at +p< 0.05, vs Sham; *p< 0.05, vs Vehicle.

Furthermore, Huang *et al*[29] demonstrated that their formulation not only reduced the severity of symptoms but also delayed the onset of key colitis indicators, such as diarrhea and blood in the stool.

Although SAC did not achieve as significant a reduction in the DAI compared to minocycline, its primary advantage is that it is a finished, market-ready product. This positions SAC as a promising option within the supplement market, particularly for products aimed at supporting intestinal health.

Fig. 3 illustrates the Total Colitis Index, which assesses the severity of DSS-induced colitis in mice. The vehicle group exhibited the highest index, indicating severe ulcerative colitis symptoms (*p < 0.05). In contrast, minocycline treatment (#) significantly reduced the colitis index compared to the vehicle group, reflecting a lower severity of the disease. The SAC also demonstrated a decrease in the colitis index, although this reduction was less pronounced than that observed in the group 4. These results reflect the reduction in mucosal architectural abnormalities, ulcerations, crypt dilatation and loss, glandular distortion, and inflammatory infiltration, with the group 4 showing significant improvement (p<0.05) versus the group 2.

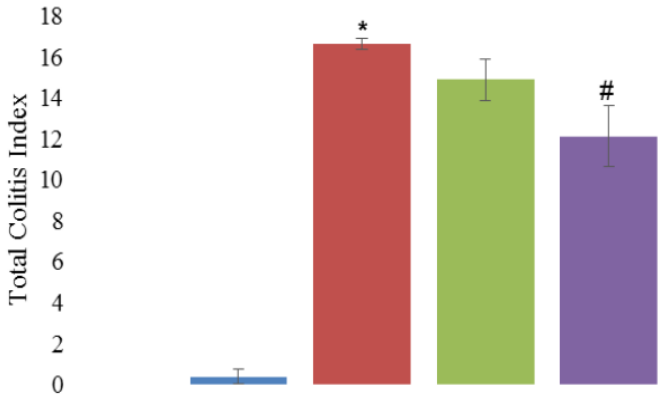


Fig. 3: Total colitis index at 9 days of treatment where: (-■-) at group1 Sham (no DSS); (-■-) group 2 Vehicle; (-■-) group 3 with SAC (2000 mg/kg); (-■-) group 4 Minocycline (100 mg/kg). Unpaired Student's t-test *p<0.05, group 2 vs. group 1. One-way ANOVA followed by Dunnett's test #p<0.05, group 2 vs. group 3 and group 4.

Histological changes of the colon in group 2, were characterized by multifocal to diffuse dropouts of whole crypts, moderate to severe transmural alteration of typical architecture, diffuse ulceration, altered crypt architecture, and multifocal to diffuse lesions, and mucosal to submucosal inflammatory cell infiltration of the colon compared to group 1 ($p<0.05$; unpaired Student's t-test), reflecting successful induction of 2.5% DSS-induced colitis in female C57BL/6 mice (Figure 4 A-B).In Fig. 4A, colon tissue shows normal architecture with well-organized crypts and preserved mucosa. The epithelium is intact, representing a healthy, undamaged colon, typical of an untreated control group 1. The histological score is low (group 1. 0.38±0.38), indicating the absence of damage. In the colon of an animal treated with 2.5% DSS (Fig. 4B), clear signs of damage are observed, with moderate ulcerations and considerable infiltration of inflammatory cells (*) in the mucosa and submucosa. There is loss of normal crypt architecture and possible submucosal edema. The epithelium has been severely affected, and the elevated score (group 2. 16.63±0.2) reflects significant damage. SAC treatment demonstrated a moderate effect (Fig. 4C). Inflammatory cells (*) were still present, extending into the submucosa, but ulceration and tissue damage were less severe than in the group treated with DSS alone. The crypt structure remained largely intact, though with some areas showing alterations. The histological damage score (group 3: 14.38±1.03) indicates that SAC partially reduced the severity of inflammation.

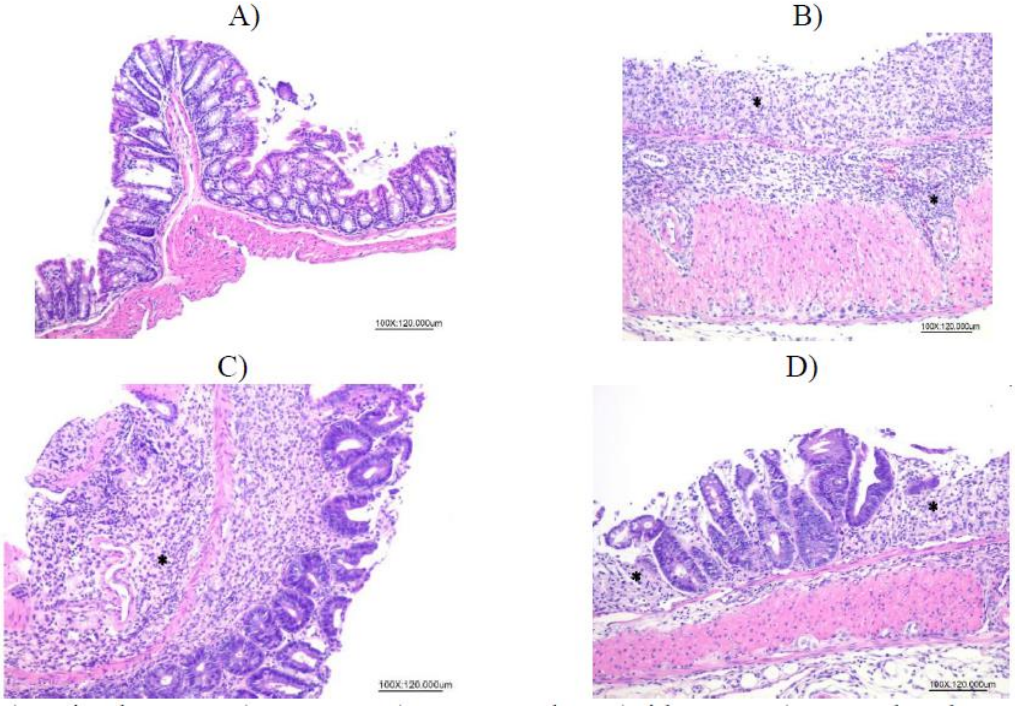


Fig. 4. A) Animal ID: 1-1 (100X, H&E) group 1, Sham (without DSS), normal, colon. group 1. 0.38±0.38 B) Animal ID: 2-1 (100X, H&E) group 2, Vehicle (2.5% DSS), 10 mL/kg, QD x 4, PO, moderate ulceration, and inflammatory cell infiltration (*), colon. group 2. 16.63±0.2. C) Animal ID: 3-1 (100X, H&E) group 3, SAC, 2000

mg/kg, QD x 4, PO, moderate inflammatory cells spreading to submucosa (*), colon. group 3. 14.38±1.03 D) Animal ID: 4-2 (100X, H&E) group 4, Minocycline, 100 mg/kg, QD x 4, PO, focal ulceration and cystic dilatation (*), colon. group 4. 12.13±1.51

In contrast, minocycline treatment (Fig. 4D) had a more pronounced effect, though not entirely curative. Focal areas of ulceration (*) and cystic dilatations in the mucosa were observed, suggesting partial protection from damage. Cellular infiltration was less extensive compared to untreated DSS groups, and the overall architecture of the colon showed signs of partial repair. However, the damage was not completely reversed.

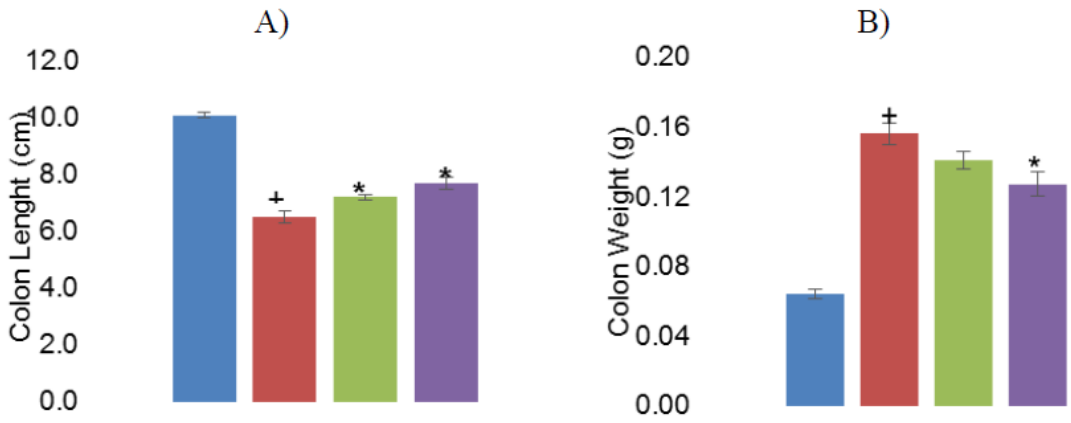
The histological score (group 4: 12.13±1.51) reflects an improvement compared to the DSS group, though residual tissue damage remains evident.

Salem & Wadie[30] observed that high-dose niacin significantly reduced inflammation and preserved colonic tissue structure, showing less epithelial necrosis and moderate inflammatory infiltration, indicating a dose-dependent protective effect. In this study, both minocycline and SAC treatments demonstrated moderate protective effects. Minocycline reduced ulceration and inflammatory infiltration, though some side effects, such as cystic dilatation and residual tissue damage, were noted. SAC treatment also reduced cellular infiltration, but the colon's structural integrity was not fully restored. These findings are relevant to the development of new anti-inflammatory therapies for the treatment of colitis.

Treatment with DSS caused a significant shortening of colon length compared to SAC and minocycline, as shown in Figure 5A. This effect was particularly marked in the group 2, where colon shortening was one of the most obvious signs of severe inflammation associated with DSS-induced colitis.

Concordantly, the ratio of colon weight to colon length, a key marker of tissue edema, was also significantly higher in the DSS group 2 compared to the treated groups 3 and 4, as seen in Figure 5C. The curcumin nanoparticle-treated group 3 showed a significant reduction in this ratio compared to the vehicle group, indicating less fluid accumulation and a possible decrease in inflammatory edema. On the other hand, treatment with minocycline, considered as a positive control, showed the most remarkable results, with a 45% decrease in colon weight and a significant improvement in colon length, reflecting its potent anti-inflammatory action and its ability to preserve the structural integrity of colonic tissue (Figures 5A-B).

As for neutrophil infiltration, assessed through colonic MPO levels (a marker of inflammatory activity), a significant increase was observed in the DSS group 2 compared to the healthy control group 1. However, treatment with SAC failed to significantly reduce MPO levels compared to the vehicle group (Figure 5D). This finding suggests that, although SAC contributed to improving some indicators of colonic inflammation and edema, its effect on overall inflammatory activity, as measured by MPO, was limited. In contrast, treatment with minocycline was more effective in reducing both inflammation and structural damage in the colon, which reinforces its therapeutic potential in models of colitis-induced.



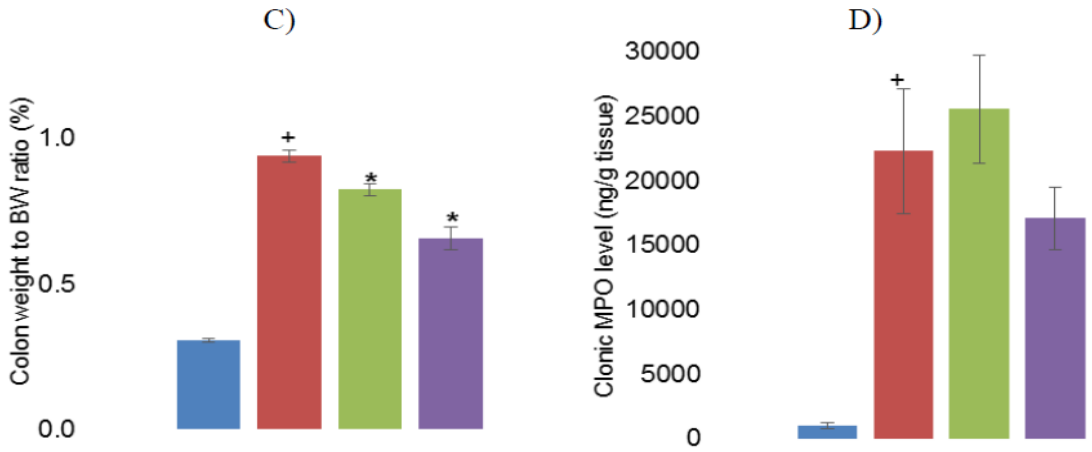


Fig. 5: Anti-inflammatory activity of SAC in vivo. A) Colon size, B) colon weight, C) colon weight to body weight ratio and D) MOP activity, where: (-■-) at group 1 Sham (without DSS); (-■-) group 2 Vehicle; (-■-) group 3 with SAC (2000 mg/kg); (-■-) group 4 Minocycline (100 mg/kg) E) Representative photographs of the colon. Mean values ± SEM were determined, and one-way ANOVA followed by Dunnett's test was applied for comparison between vehicle and treated groups. Differences are considered significant at +p< 0.05, vs sham; *p< 0.05, vs vehicle.

UC is a type of IBD that causes symptoms such as diarrhea, abdominal pain, and blood in the stool.

These findings suggest that curcumin acts not only as an anti-inflammatory, but also as a protective agent that improves the integrity of the colon and allows the recovery of body weight, which could be critical in the management of clinical symptoms of UC.[21]

4. CONCLUSION

Treatment with turmeric-based dietary supplement (SAC) showed a moderate effect in mitigating the symptoms of DSS-induced colitis in mice. Although SAC did not reach the effectiveness of minocycline, it demonstrated a significant impact on reducing DAI by 20%, colon weight, and preserving colon length compared to the control group. And improved parameters such as fecal consistency and the presence of occult blood, suggesting a therapeutic potential in the management of colitis.

At the histological level, both SAC and minocycline reduced inflammatory infiltration and tissue damage, suggesting that SAC has anti-inflammatory properties. However, SAC did not significantly decrease MPO levels, indicating its limited ability to inhibit MPO activity compared to minocycline. While SAC shows promise in mitigating inflammation, its overall impact on MPO activity appears to be limited.

Treatment with SAC offers a viable alternative to reduce the severity of colitis symptoms. Combining SAC with other therapeutic agents could be a promising strategy to enhance outcomes in future preclinical and clinical studies.

5. CONTRIBUTION OF THE AUTHORS

Flores-Méndez and Flores-Berrios designed the product.
Flores-Méndez designed the study, worked on the experimental work and analyzed the data.
Estrada-Alvarado read and reviewed content.
Vera-García wrote the article, analyzed data.
All authors read and approved the final version of the manuscript.

6. CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

7. REFERENCES

1. Mirhadi E, Tasbandi A, Kesharwani P, Sahebkar A. Curcumin: historical background, introduction, structure, and physicochemical attributes. In: *Curcumin-Based Nanomedicines as Cancer Therapeutics*. Elsevier, 2024; 3-22. doi:10.1016/B978-0-443-15412-6.00005-2
2. Vezza T, Molina-Tijeras JA, González-Cano R, et al. Minocycline Prevents the Development of Key Features of Inflammation and Pain in DSS-induced Colitis in Mice. *J Pain*, 2023; 24(2): 304-319. doi:10.1016/j.jpain.2022.09.016
3. Yamamoto-Furusho JK, Bosques-Padilla FJ, Charúa-Guindic L, et al. Inflammatory bowel disease in Mexico: Epidemiology, burden of disease, and treatment trends. *Rev Gastroenterol México Engl Ed*, 2020; 85(3): 246-256. doi:10.1016/j.rgmxen.2019.07.005
4. Kaenkumchorn T, Wahbeh G. Ulcerative Colitis. *Gastroenterol Clin North Am*. 2020;49(4):655-669. doi:10.1016/j.gtc.2020.07.001
5. Nascimento R de P do, Machado AP da F, Galvez J, Cazarin CBB, Maróstica Junior MR. Ulcerative colitis: Gut microbiota, immunopathogenesis and application of natural products in animal models. *Life Sci*, 2020; 258: 118129. doi:10.1016/j.lfs.2020.118129

6. Zhong YB, Kang ZP, Wang MX, et al. Curcumin ameliorated dextran sulfate sodium-induced colitis via regulating the homeostasis of DCs and Treg and improving the composition of the gut microbiota. *J Funct Foods*, 2021; 86: 104716. doi:10.1016/j.jff.2021. 104716
7. Siraki AG. The many roles of myeloperoxidase: From inflammation and immunity to biomarkers, drug metabolism and drug discovery. *Redox Biol*, 2021; 46: 102109. doi:10.1016/j.red ox.2021.102109
8. Luo R, Lin M, Zhang C, et al. Genipin-crosslinked human serum albumin coating using a tannic acid layer for enhanced oral administration of curcumin in the treatment of ulcerative colitis. *Food Chem*, 2020; 330: 127241. doi:10.1016 /j.foodchem.2020.127241
9. Varma, Karthik, Jude, Shintu, Varghese, Bincicil, Kuttappan, Sasikumar, Amalraj, Augustine. Curcuma Longa. In: Amalraj, Augustine, ed. *Herbs, Spices and Their Roles in Nutraceuticals and Functional Foods*. Elsevier, 2023; 1, 14: 15-23. doi:10.1016/C2020-0-04193-9
10. Kour, Jasmeet, Ahmad, Gulzar, eds. Curcumin. In: *Nutraceuticals and Health Care*. Vol 1. Academic Press. Elsevier, 2022; 159-175.
11. Mirzaei H, Shakeri A, Rashidi B, Jalili A, Banikazemi Z, Sahebkar A. Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies. *Biomed Pharmacother*, 2017; 85: 102-112. doi:10. 1016/j.biopha.2016.11.098
12. Luiza Koop B, Nascimento Da Silva M, Diniz Da Silva F, et al. Flavonoids, anthocyanins, betalains, curcumin, and carotenoids: Sources, classification and enhanced stabilization by encapsulation and adsorption. *Food Res Int*, 2022; 153: 110929. doi:10.1016/j.foodres .2021.110929
13. Paul B. *An Evaluation of the Role of PromOat® on the Stability of Oil-in-Water Emulsions*. Lund University, 2020.
14. Usman M, Zhang C, Patil PJ, et al. Potential applications of hydrophobically modified inulin as an active ingredient in functional foods and drugs - A review. *Carbohydr Polym*, 2021; 252: 117176. doi:10.1016/j.carbpol.2020.117176
15. Clímaco GN, Gonçalves RFS, Fernandes JM, Pinheiro AC, Vicente AA, Fasolin LH. Simultaneous vehiculation of curcumin and riboflavin in bigels produced through WPI cold-set gelation. *Food Hydrocoll*, 2025; 158: 110460. doi:10.1016/j.foodhyd.2024.110460
16. Zhan S, He M, Wu Y, Ouyang J. Improved light and ultraviolet stability of curcumin encapsulated in emulsion gels prepared with corn starch, OSA-starch and whey protein isolate. *Food Chem*, 2024; 446: 138803. doi:10.1016/j.foodche m.2024.13880
17. NOM-116-SSA1-1994, Bienes y servi- cios. Determinación de humedad en alimentos por tratamiento térmico. Método por arena o gasa. https://dof.g ob.mx/nota_detalle.php?codigo=4728942&fecha=15 /08/1994&print=true.
18. NMX-F-608-NORMEX-201. Alimentos, Determinación de Proteínas en alimentos. Método de ensayo (prueba). https://nor mex.com.mx/producto/nmx-f-608-norme x-2011/
19. NMX-F-427-NORMEX-2019. Alimen- tos. Determinación de grasa (método gra- vimétrico por hidrólisis ácida). Método Mojonnier. Método de prueba. https://no rmex.com.mx/producto/nmx-f-427-norme x-2019/
20. NMX-F-607-NORMEX-2020. Alimen- tos. Determinación de cenizas en alim- entos. Método de prueba. https://normex .com.mx/producto/nmx-f-607-normex-2020/
21. NOM-086-SSA1-1994. Bienes y servi- cios. Alimentos y bebidas no alcohólicas con modificaciones en su composición. Especificaciones nutrimentales. https://fa olex.fao.org/docs/pdf/mex17734.pdf
22. NOM-051-SCFI/SSA1-2010. Especifi- caciones generales de etiquetado para alimentos y bebidas no alcohólicas preenvasados-Información comercial y sanitaria. https://www.dof.gob.mx/norm asOficiales/4010/seeco11_C/seeco11_C.htm
23. Dieleman LA, Palmen MJHJ, Akol H, et al. Chronic experimental colitis induced by dextran sulphate sodium (DSS) is characterized by Th1 and Th2 cytokines. *Clin Exp Immunol*, 1998; 114(3): 385-391. doi:10.1046/j.1365-2249.1998.00728.x
24. Hanif Mughal M. Turmeric polyphenols: A comprehensive review. *Integr Food Nutr Metab*, 2019; 6(6). doi:10.15761 /IFNM.1000269
25. Asadi A, Abdi M, Kouhsari E, et al. Minocycline, focus on mechanisms of resistance, antibacterial activity, and clinical effectiveness: Back to the future. *J Glob Antimicrob Resist*, 2020; 22: 161-174. doi:10.1016/j.jgar.2020.01.022
26. Zhang C, Wang X, Xiao M, et al. Nano-in-micro alginate/chitosan hydrogel via electrospray technology for orally curcumin delivery to effectively alleviate ulcerative colitis. *Mater Des*, 2022; 221: 110894. doi:10.1016/j.matdes. 2022.110894
27. Wu M, Ping H, Wang K, et al. Oral delivery of pectin-chitosan hydrogels entrapping macrophage-targeted curcumin-loaded liposomes for the treatment of ulcerative colitis. *Int J Pharm*, 2023; 647: 123510. doi:10.1016/ j.ijpharm.2023.123510
28. Ohno M, Nishida A, Sugitani Y, et al. Nanoparticle curcumin ameliorates experimental colitis via modulation of gut microbiota and induction of regulatory T cells. Singh UP, ed. *PLOS ONE*, 2017; 12(10): e0185999. doi:10.1371/jour nal.pone.0185999
29. Huang S, Zhang M, Li X, et al. Formulation, Characterization, and Evaluation of Curcumin-Loaded Ginger-Derived Nanovesicles for Anti-Colitis Activity. *J Pharm Anal*. Published online May, 2024; 101014. doi:10.1016/j.jpha 2024.101014

30. Salem HA, Wadie W. Effect of Niacin on Inflammation and Angiogenesis in a Murine Model of Ulcerative Colitis. *Sci Rep*, 2017; 7(1): 7139. doi:10.1038/s4 1598-017-07280-Y