Research Article

Phytotherapeutic potential of *Allium cepa* extract in dextran sodium sulfate-induced colitis

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ABSTRACT

Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by intestinal mucosal injury, oxidative stress, and excessive production of pro-inflammatory cytokines. Despite the availability of conventional therapies, long-term treatment is often associated with adverse effects, highlighting the need for safer plant-based alternatives. *Allium cepa* peel is a rich source of flavonoids, phenolic compounds, and other bioactive phytoconstituents with established antioxidant and anti-inflammatory properties. **Materials and Methods:** The ethanolic extract of *A. cepa* peel was prepared by Soxhlet extraction and subjected to preliminary phytochemical screening. UC was induced by administering 2.5% dextran sodium sulfate (DSS) in drinking water for 10 consecutive days. Animals were treated orally with *A. cepa* extract (100 and 200 mg/kg) or 5-aminosalicylic acid (5-ASA) (100 mg/kg). Therapeutic efficacy was assessed by evaluating clinical disease activity (body weight loss, stool consistency, rectal bleeding, and food and water intake), colon length, oxidative stress markers (malondialdehyde [MDA] and catalase [CAT]), pro-inflammatory cytokines (tumor necrosis factor-alpha [TNF-α], interleukin-1β (IL-1β), and interleukin-6 (IL-6)], and histopathological changes in colonic tissue. **Results:** Phytochemical screening confirmed the presence of flavonoids, glycosides, and alkaloids in the extract. DSS administration produced severe colitis, evidenced by progressive weight loss, diarrhea, rectal bleeding, reduced food and water intake, colon shortening, increased MDA levels, decreased CAT activity, elevated TNF-α, IL-1β, and IL-6 levels, and marked histopathological damage. Treatment with *A. cepa* extract significantly attenuated these alterations in a dose-dependent manner. The 200 mg/kg dose demonstrated greater efficacy than the 100 mg/kg dose by improving clinical symptoms, restoring antioxidant status, suppressing inflammatory cytokines, preserving colon length, and reducing mucosal injury, although the protective effects remained lower than those of 5-ASA. **Conclusion:** The ethanolic extract of *A. cepa* peel effectively ameliorated DSS-induced UC through antioxidant, anti-inflammatory, and mucosal protective mechanisms. The extract inhibits that *A. cepa* peel may serve as a promising phytotherapeutic candidate for the management of UC and warrants further investigation to elucidate its molecular mechanisms and clinical potential.

Keywords: *Allium cepa*, dextran sodium sulfate, inflammatory cytokines, oxidative stress, phytotherapy, ulcerative colitis

Introduction

Ulcerative colitis (UC) is a chronic relapsing inflammatory bowel disease (IBD) characterized by continuous inflammation of the colonic mucosa, leading to diarrhea, rectal bleeding, abdominal pain, weight loss, and reduced quality of life. Although the exact etiology remains unclear, UC is considered a multifactorial disorder involving genetic susceptibility, dysregulated immune responses, environmental factors, and alterations in the gut microbiota. Disruption of the intestinal epithelial barrier permits excessive penetration of luminal antigens and microorganisms, triggering chronic mucosal inflammation and progressive tissue injury.[1,2]

Oxidative stress plays a pivotal role in the pathogenesis of UC. Excessive production of reactive oxygen species (ROS) promotes lipid peroxidation, protein oxidation, DNA damage, and impairment

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of the intestinal barrier. Simultaneously, activation of inflammatory signaling pathways, particularly nuclear factor-kappa B (NF-κB), stimulates the production of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), thereby amplifying inflammatory responses and mucosal destruction. These oxidative and inflammatory events contribute significantly to disease progression and recurrence.[3,4]

Current pharmacological management of UC includes 5-aminosalicylic acid (5-ASA), corticosteroids, immunomodulators, biologic agents targeting TNF-α and integrins, and Janus kinase inhibitors. Although these therapies are effective in controlling inflammation and inducing remission, their long-term use is frequently associated with adverse effects such as gastrointestinal intolerance, immunosuppression, opportunistic infections, high treatment costs, loss of therapeutic response, and disease relapse. These limitations have stimulated increasing interest in the development of safer, cost-effective, and naturally derived therapeutic agents capable of modulating oxidative stress and inflammatory pathways.[5,6]

Medicinal plants have emerged as promising candidates for the management of inflammatory disorders due to their diverse phytochemical composition and favorable safety profile. *Allium cepa* L. (onion), particularly its outer peel, is an abundant source of quercetin, flavonoids, phenolic acids, and organosulfur compounds that exhibit potent antioxidant, anti-inflammatory, and free radical-scavenging activities. Experimental studies have demonstrated that these phytoconstituents suppress oxidative stress, inhibit NF-κB-mediated inflammatory signaling, reduce the production of pro-inflammatory cytokines, and preserve intestinal epithelial integrity, thereby protecting against experimental colitis.[7-10]

Among the available experimental models, dextran sodium sulfate (DSS)-induced colitis is one of the most widely accepted models because it closely mimics the clinical manifestations, histopathological features, epithelial barrier disruption, and inflammatory responses observed in human UC. Consequently, this model is extensively used to evaluate the therapeutic efficacy of novel anti-inflammatory and antioxidant agents.[11,12]

Therefore, the present study was designed to investigate the protective effects of the ethanolic extract of *A. cepa* peel against DSS-induced UC in Swiss albino mice by evaluating clinical disease activity, colon length, oxidative stress biomarkers, pro-inflammatory cytokines, and histopathological alterations.

Materials and Methods

Plant material and authentication

Fresh red onion (*A. cepa* L.) bulbs were procured from Raj Kamal Chowk Market, Amravati, Maharashtra, India, during November 2025. The plant material was authenticated by Dr. Prashant A. Gawande, Professor and In-charge, Herbarium, Department of Botany, Sant Gadge Baba Amravati University, Amravati, Maharashtra, India. A voucher specimen (No. AM/AL/CE/510/1/28-10/2025) was deposited in the Department of Pharmacognosy, Dr. Rajendra Gode Institute of Pharmacy, Amravati, Maharashtra, India [Figure 1].

Preparation of ethanolic extract

The outer peels of *A. cepa* were separated, washed thoroughly with tap water to remove adhering impurities, shade-dried, and coarsely powdered using a mechanical grinder. Approximately 130 g of the powdered peel was extracted with 650 mL ethanol in a Soxhlet apparatus for 24 h. The extract was filtered and concentrated under reduced pressure to obtain a semisolid mass, which was stored in an airtight container at 4–8°C until further use.

Preliminary phytochemical screening

The ethanolic extract was subjected to qualitative phytochemical screening using standard methods to detect alkaloids, flavonoids, glycosides, tannins, phenolic compounds, saponins, steroids, and terpenoids.

Chemicals and reagents

DSS and 5-ASA were procured from Lab-Chem Corporation, Ahmedabad, Gujarat, India. All other chemicals and reagents used were of analytical grade.

Experimental animals

Healthy Swiss albino mice of either sex (20–25 g) were procured from the National Institute of Biosciences, Pune, India (CPCSEA Registration No. 1091/GO/Bt/07/CPCSEA). Animals were housed under standard laboratory conditions (25 ± 2°C, 55–65% relative humidity, 12 h light/dark cycle) with free access to a standard pellet diet and water. Animals were acclimatized for 1 week before the experiment.

The experimental protocol was approved by the Institutional Animal Ethics Committee of Dr. Rajendra Gode Institute of Pharmacy, Amravati, and all experimental procedures were performed in accordance with CPCSEA guidelines.

Experimental design

Animals were randomly allocated into five experimental groups ($n = 5$ per group). Group I (normal control) received the vehicle alone. Group II (DSS disease control) received DSS administration to induce colitis. Group III (positive control) received 5-ASA at a dose of 100 mg/kg (p.o.) along with DSS administration. Group IV received A. cepa extract at a dose of 100 mg/kg (p.o.) along with DSS administration, while Group V received A. cepa extract at a dose of 200 mg/kg (p.o.) along with DSS administration.

Induction of UC and treatment protocol

UC was induced by administering 2.5% (w/v) DSS in drinking water ad libitum for 10 consecutive days, except in the normal control group, which received normal drinking water. The DSS solution was freshly prepared and replaced on alternate days.

The standard drug, 5-ASA (100 mg/kg), and the ethanolic extract of *A. cepa* (100 and 200 mg/kg) were freshly suspended in carboxymethyl

cellulose solution and administered orally once daily throughout the experimental period.

Clinical assessment of DSS-induced colitis

Body weight, stool consistency, rectal bleeding, food intake, and water intake were recorded on alternate days throughout the study [Table 1].

Percentage body weight loss was calculated using the following equation:

$$\text{Body weight loss}(\%) = \left(\frac{\left[\text{Initial body weight} - \text{Body weight on observation day} \right]}{\text{Initial body weight}} \right) \times 100$$

Fresh fecal pellets were collected by placing individual animals in clean cages without bedding for approximately 15–30 min. Stool consistency and the presence of visible blood were evaluated using the clinical scoring criteria, as shown in Table 1. Food and water intake were determined by measuring the difference between the quantity supplied and the quantity remaining on each observation day.

Colon length measurement

At the end of the experimental period, animals were euthanized by cervical dislocation. The entire colon was excised, rinsed gently with normal saline, and measured from the ileocecal junction to the rectum. Colon length was recorded as an indicator of disease severity.

Biochemical estimation

Colon tissues were homogenized (10%, w/v) in 0.1 M phosphate buffer (pH 7.4) and centrifuged at 10,000 × g for 15 min at 4°C. The resulting supernatant was used for biochemical analyses.

Estimation of lipid peroxidation

Malondialdehyde (MDA), an index of lipid peroxidation, was determined using the thiobarbituric acid reactive substances assay. Absorbance was measured at 532 nm using a ultraviolet-visible spectrophotometer, and the results were expressed as nmol MDA/mg protein.

Estimation of catalase (CAT) activity

CAT activity was estimated by monitoring the decomposition of hydrogen peroxide at 240 nm and expressed as U/mg tissue.

Table 1: Clinical scoring criteria for DSS-induced colitis

Parameter	Score	Observation
Stool consistency	0	Normal
	1	Mildly soft
	2	Very soft
	3	Watery
Presence of blood in stool	0	Absent
	1	Present

DSS: Dextran sodium sulfate

Estimation of pro-inflammatory cytokines

Colon tissue concentrations of TNF-α, IL-1β, and IL-6 were quantified using commercially available GENLISA™ enzyme-linked immunosorbent assay kits according to the manufacturer's instructions. Absorbance was recorded at 450 nm using a microplate reader.

Histopathological examination

Colon tissues were fixed in 10% neutral buffered formalin for 48–72 h, dehydrated through graded ethanol, cleared in xylene, and embedded in paraffin wax. Sections of 4–5 μm thickness were prepared using a rotary microtome and stained with hematoxylin and eosin (H&E). Histological examination was performed under a light microscope to evaluate epithelial damage, crypt distortion, goblet cell depletion, inflammatory cell infiltration, submucosal edema, ulceration, and vascular congestion.

Statistical analysis

Data are presented as mean ± standard error of the mean ($n = 5$). Statistical analysis was performed using one-way analysis of variance followed by Tukey's multiple comparison test using GraphPad Prism version 10. Differences were considered statistically significant at $P < 0.05$.

Results

Preliminary phytochemical screening of *A. cepa* extract

Preliminary phytochemical screening of the ethanolic extract of *A. cepa* peel confirmed the presence of flavonoids, glycosides, and alkaloids. Flavonoids were identified by the Shinoda, lead acetate, alkaline reagent, and zinc-HCl tests, whereas alkaloids were confirmed using Dragendorff's, Mayer's, and Hager's reagents. The presence of these phytoconstituents suggests that the extract possesses potential antioxidant and anti-inflammatory properties [Figure 3].

Clinical assessment of DSS-induced colitis

Body weight loss

DSS administration produced progressive body weight loss throughout the experimental period compared with the normal control group [Table 2]. Treatment with *A. cepa* extract significantly attenuated body weight loss in a dose-dependent manner. The 200 mg/kg dose produced greater protection than the 100 mg/kg dose, although the standard drug (5-ASA) showed the greatest improvement.

Clinical disease activity

Clinical manifestations of DSS-induced colitis progressively worsened in the disease control group, as evidenced by deterioration in stool consistency and the presence of rectal bleeding from Day 7 onward [Table 3]. Treatment with 5-ASA and *A. cepa* extract attenuated the clinical severity of colitis, resulting in improved stool consistency and reduced rectal bleeding compared with the DSS disease control

group. The high-dose *A. cepa* extract (200 mg/kg) demonstrated greater improvement than the low-dose group (100 mg/kg), with clinical scores approaching those observed in the 5-ASA-treated group. Overall, the extract inhibits that *A. cepa* extract dose-dependently alleviated the clinical manifestations of DSS-induced colitis, with the 200 mg/kg dose providing superior protection against disease progression.

Food and water intake

DSS administration markedly reduced food and DSS water intake in the disease control group throughout the experimental period, reflecting progressive disease severity compared with the normal control group [Table 4]. Treatment with 5-ASA and *A. cepa* extract attenuated these reductions, resulting in improved food and DSS water intake relative to the DSS disease control group. The high-dose *A. cepa* extract (200 mg/kg) demonstrated greater improvement than the low-dose group (100 mg/kg), with food and DSS water intake approaching the levels observed in the 5-ASA-treated animals by the end of the study [Table 4]. This indicates a dose-dependent beneficial effect of *A. cepa* extract on maintaining nutritional status and fluid consumption during DSS-induced colitis [Figure 2].

Colon length

Colon shortening was markedly evident in DSS-treated animals, confirming severe colonic inflammation [Table 5]. The normal control group exhibited a mean colon length of 10.0 cm, whereas the disease control group showed a significant reduction to 3.3 cm. Treatment with 5-ASA restored colon length to 9.4 cm, while *A. cepa* extract

Table 2: Effect of *Allium cepa* extract on body weight loss (%) in DSS-induced colitis

Groups	Day 3	Day 5	Day 7	Day 9	Day 11
Normal control	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
Disease	0.96±0.20	6.88±0.34$^{\#\#\#\#}$	12.00±0.46$^{\#\#\#\#}$	16.88±0.34$^{\#\#\#\#}$	18.88±0.65$^{\#\#\#\#}$
Standard	0.96±0.20	4.40±0.47***	6.64±0.66****	7.00±0.64****	6.30±0.48****
Treatment 1	1.36±0.20	6.64±0.43	9.84±0.47*	12.80±0.96**	12.60±0.72**
Treatment 2	1.12±0.20	6.20±0.47	7.45±0.66***	8.90±0.64***	8.00±0.54****

DSS: Dextran sodium sulfate, ANOVA: Analysis of variance, SEM: Standard error of the mean. **Values are expressed as mean±SEM (n=5). Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple comparison test. $^{\#\#\#\#}P$<0.0001 versus Normal Control; $^{*}P$<0.05, $^{**}P$<0.01, $^{***}P$<0.001, $^{**}P$<0.0001 versus DSS disease control

Table 3: Effect of *Allium cepa* extract on clinical disease activity in DSS-induced colitis

Groups	Day 3		Day 5		Day 7		Day 9		Day 11	
	SC	BS	SC	BS	SC	BS	SC	BS	SC	BS
Normal control	0	0	0	0	0	0	0	0	0	0
DSS disease control	0	0	1	0	2	1	3	1	3	1
DSS+5-ASA (100 mg/kg)	0	0	0	0	1	1	1	0	0	0
DSS+*Allium cepa* extract (100 mg/kg)	0	0	1	0	2	1	2	1	2	0
DSS+*Allium cepa* extract (200 mg/kg)	0	0	1	0	1	0	2	1	1	0

**Values are expressed as median clinical scores (n=5). SC: Stool consistency, BS: Blood in stool, DSS: Dextran sulfate sodium

Table 4: Effect of *Allium cepa* extract on food and water intake

Groups	Day 3		Day 5		Day 7		Day 9		Day 11	
	FI (g)	DWI (mL)	FI (g)	DWI (mL)	FI (g)	DWI (mL)	FI (g)	DWI (mL)	FI (g)	DWI (mL)
Normal control	10.40±0.24	—	10.60±0.20	—	10.80±0.24	—	10.80±0.20	—	11.00±0.00	—
DSS disease control	9.60±0.24	8.00±0.00	7.30±0.20	6.00±0.00	6.30±0.24	5.20±0.20	5.80±0.24	4.80±0.20	5.10±0.24	3.60±0.24
DSS+5-ASA (100 mg/kg)	10.00±0.00	8.60±0.24	9.40±0.24	7.00±0.00	8.80±0.20	6.20±0.20	8.20±0.20	5.60±0.24	9.00±0.00	5.40±0.24
DSS+A*llium cepa* extract (100 mg/kg)	9.80±0.20	8.00±0.00	9.00±0.00	6.20±0.20	8.20±0.20	5.60±0.24	7.60±0.24	5.40±0.24	7.20±0.20	4.60±0.24
DSS+A*llium cepa* extract (200 mg/kg)	10.00±0.00	8.40±0.24	9.20±0.20	6.80±0.20	8.60±0.24	6.00±0.00	8.00±0.00	5.40±0.24	8.40±0.24	5.20±0.20

FI: Food intake, DWI: Drinking water intake, SEM: Standard error of the mean, DSS: Dextran sodium sulfate. Values are expressed as mean±SEM (n=5)

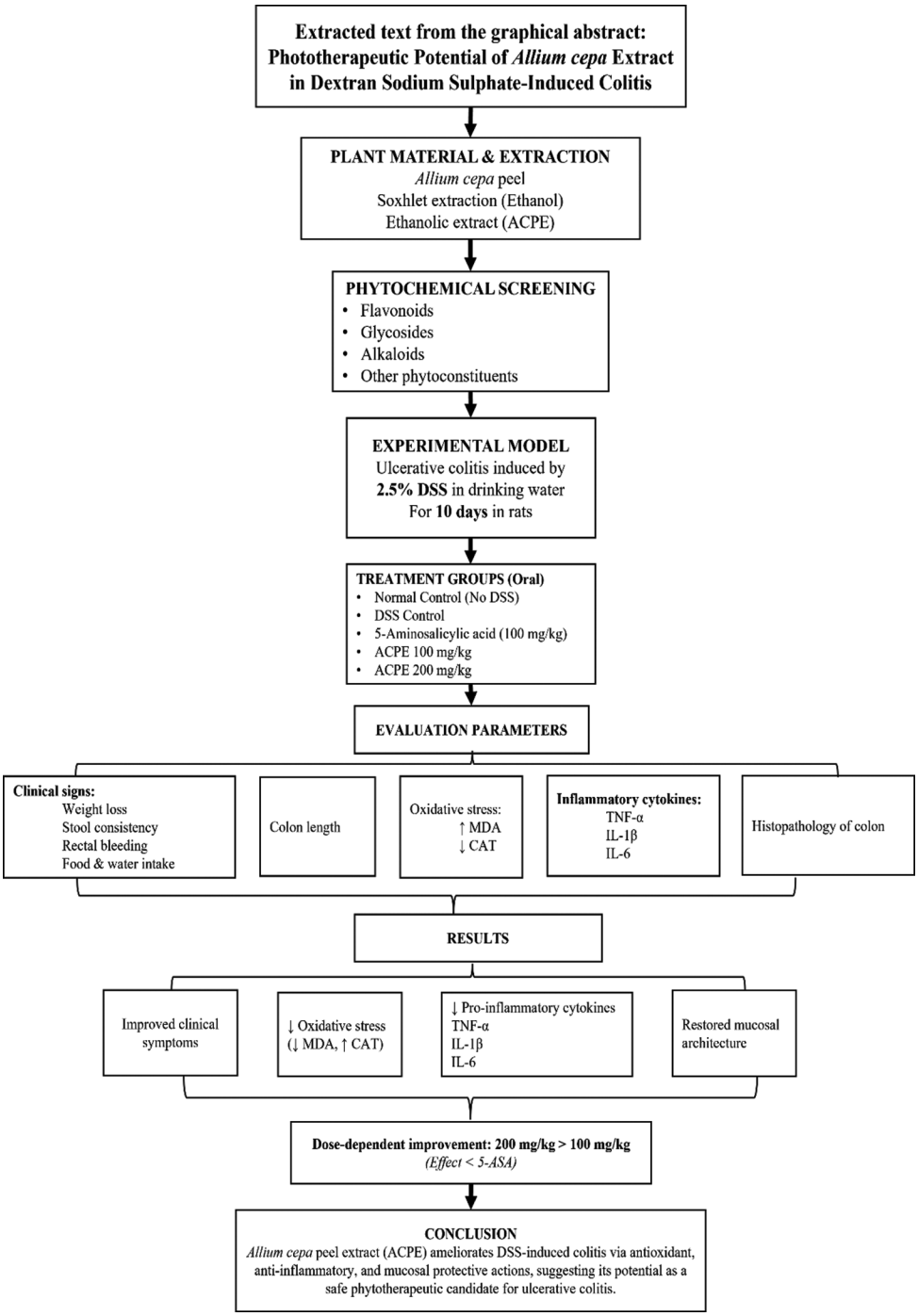

Figure 1: Schematic representation of the experimental design and phytotherapeutic. Effects of *Allium cepa* peel extract in dextran sodium sulfate-induced ulcerative colitis

Table 5: Effect of *Allium cepa* extract on colon length

Group	Colon length (cm)
Normal control	10.0±0.2
Disease control	3.3±0.2####
5-ASA	9.4±0.2****
Extract 100 mg/kg	5.6±0.3*
Extract 200 mg/kg	6.7±0.3**

SEM: Standard error of the mean, DSS: Dextran sodium sulfate, 5-ASA: 5-aminosalicylic acid. **Values are expressed as mean±SEM (n=5). ####P<0.0001 versus normal control; *P<0.05, **P<0.01, ***P<0.001, **P<0.0001 versus DSS disease control

increased colon length to 5.6 cm and 6.7 cm at doses of 100 and 200 mg/kg, respectively, indicating dose-dependent protection against DSS-induced colonic injury.

Biochemical parameters

Oxidative stress and pro-inflammatory cytokines

DSS administration markedly increased oxidative stress, as evidenced by elevated MDA levels and reduced CAT activity, together with a significant increase in TNF-α, IL-1β, and IL-6

levels [Table 6]. Treatment with *A. cepa* extract significantly restored antioxidant status and suppressed inflammatory cytokine production in a dose-dependent manner. The 200 mg/kg dose demonstrated greater efficacy than the 100 mg/kg dose, although the standard drug produced the most pronounced protective effect [Figures 4-8].

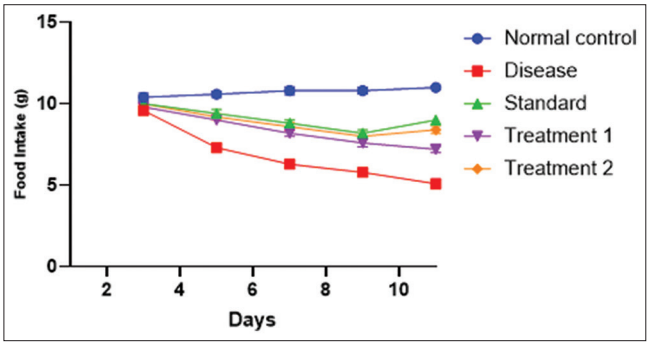

Figure 2: Effect of Allium cepa extract on food intake in experimental animals during the study period. Data are presented as mean ± standard error of the mean ($n = 5$). One-way analysis of variance followed by Dunnett's multiple comparison test versus disease control

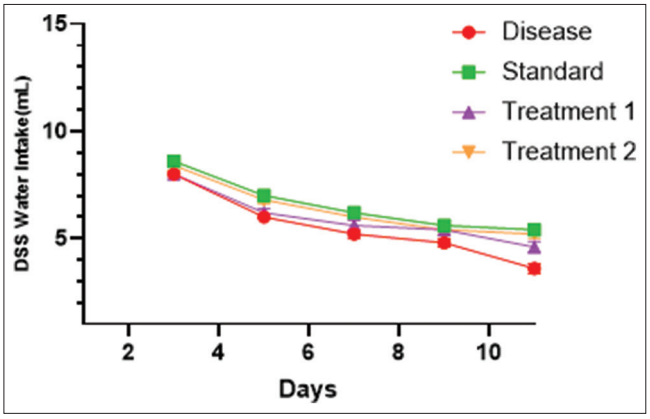

Figure 3: Effect of Allium cepa extract on dextran sodium sulfate-induced water intake in experimental animals during the study period. Data are presented as mean ± standard error of the mean ($n = 5$). One-way analysis of variance followed by Dunnett's multiple comparison test versus disease control

Histopathological evaluation

Representative H&E-stained sections of colonic tissue are shown in Figure 9. The normal control group exhibited intact mucosal architecture with well-organized crypts and no evidence of inflammatory infiltration. In contrast, DSS-treated animals showed severe epithelial erosion, crypt distortion, inflammatory cell infiltration, submucosal edema, and ulceration. Treatment with 5-ASA markedly restored normal colonic architecture. Administration of *A. cepa* extract attenuated DSS-induced histopathological alterations in a dose-dependent manner, with the 200 mg/kg dose showing greater preservation of mucosal integrity, reduced inflammatory infiltration, and improved crypt architecture compared with the 100 mg/kg dose [Figure 9].

Discussion

The present study demonstrated that the ethanolic extract of *A. cepa* peel significantly ameliorated DSS-induced UC by improving clinical symptoms, restoring colon length, attenuating oxidative stress, suppressing inflammatory cytokine production, and preserving colonic histoarchitecture. The protective effects were dose-dependent, with the 200 mg/kg dose exhibiting greater efficacy than the 100 mg/kg dose, although the standard drug, 5-ASA, produced the greatest therapeutic response.[13]

DSS-induced colitis is one of the most widely accepted experimental models of UC because it closely reproduces the clinical manifestations, epithelial barrier disruption, inflammatory cell infiltration, and histopathological changes observed in human disease. Administration of DSS damages the intestinal epithelial barrier, facilitating bacterial translocation and activation of innate immune responses, which subsequently trigger excessive oxidative stress and inflammatory cytokine production. Consequently, this model has been extensively used for evaluating potential anti-inflammatory agents and phytotherapeutics for IBD.[11,14]

Preliminary phytochemical screening of the ethanolic extract confirmed the presence of flavonoids, glycosides, and alkaloids.

Table 6: Effect of *Allium cepa* extract on oxidative stress markers and pro-inflammatory cytokines

Groups	MDA (nmol/mg protein)	CAT (U/mg protein)	TNF-α (pg/mL)	IL-1β (pg/mL)	IL-6 (pg/mL)
Normal control	0.59±0.02	2.90±0.03	79.05±0.51	75.85±1.93	82.66±0.86
Disease control	2.02±0.00$^{\#\#\#\#}$	1.52±0.01$^{\#\#\#\#}$	179.06±0.58$^{\#\#\#\#}$	176.46±1.50$^{\#\#\#\#}$	179.26±0.52$^{\#\#\#\#}$
5-ASA	1.09±0.02****	2.80±0.04****	122.97±0.39****	119.65±0.87****	125.57±0.57****
Extract 100 mg/kg	1.79±0.02*	2.22±0.04**	152.59±1.19**	152.66±0.68**	166.99±0.48*
Extract 200 mg/kg	1.44±0.02***	2.47±0.03***	136.89±0.35***	128.69±0.70***	152.89±0.44***

MDA: Malondialdehyde, CAT: Catalase, TNF-α: Tumor necrosis factor-alpha, IL-1β: Interleukin-1β, IL-6: Interleukin-6, 5-ASAL: 5-aminosalicylic acid, SEM: Standard error of the mean, DSS: Dextran sodium sulfate, ANOVA: Analysis of variance. **Values are expressed as mean±SEM (n=5). Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple comparison test. $^{\#\#\#\#}P<0.0001$ versus normal control; $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$, $^{**}P<0.0001$ versus DSS disease control

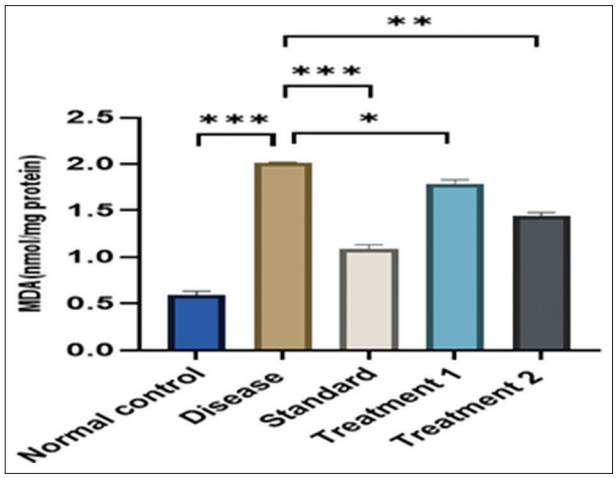

Figure 4: Effect of *Allium cepa* extract on oxidative stress and inflammatory biomarkers (malondialdehyde [MDA], catalase, tumor necrosis factor-alpha, interleukin-1β, and interleukin-6) in experimental animals MDA. Data are presented as mean ± standard error of the mean ($n = 5$). One-way analysis of variance followed by Dunnett's multiple comparison test. *$P < 0.05$, **$P < 0.01$, *$P < 0.001$ versus disease control

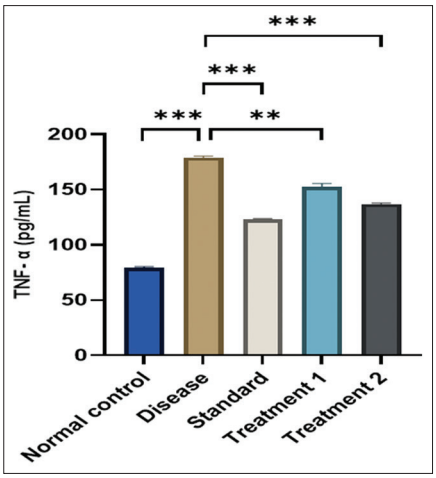

Figure 6: Effect of *Allium cepa* extract on oxidative stress and inflammatory biomarkers (malondialdehyde, catalase, tumor necrosis factor-alpha, interleukin-1β, and interleukin-6) in experimental animals tumor necrosis factor-alpha. Data are presented as mean ± standard error of the mean ($n = 5$). One-way analysis of variance followed by Dunnett's multiple comparison test. *$P < 0.05$, **$P < 0.01$, *$P < 0.001$ versus disease control

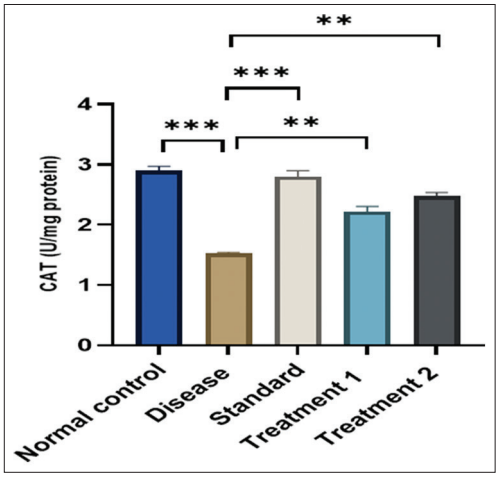

Figure 5: Effect of *Allium cepa* extract on oxidative stress and inflammatory biomarkers (malondialdehyde, catalase, tumor necrosis factor-alpha, interleukin-1β, and interleukin-6) in experimental animals' catalase. Data are presented as mean ± standard error of the mean ($n = 5$). One-way analysis of variance followed by Dunnett's multiple comparison test. *$P < 0.05$, **$P < 0.01$, *$P < 0.001$ versus disease control

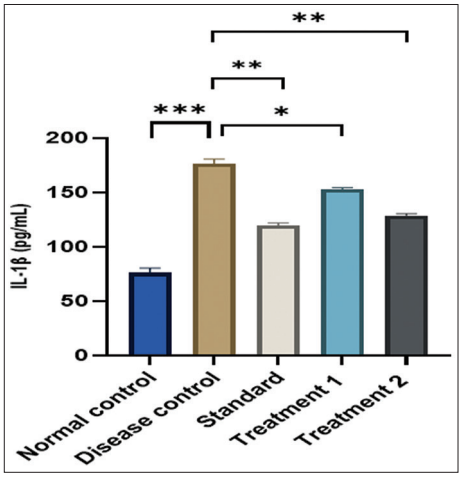

Figure 7: Effect of *Allium cepa* extract on oxidative stress and inflammatory biomarkers (malondialdehyde, catalase, tumor necrosis factor-alpha, interleukin-1β, and interleukin-6) in experimental animals Interleukin-1 beta. Data are presented as mean ± standard error of the mean ($n = 5$). One-way analysis of variance followed by Dunnett's multiple comparison test. *$P < 0.05$, **$P < 0.01$, *$P < 0.001$ versus disease control

Onion peel is particularly rich in quercetin and other flavonoids, which possess potent antioxidant, anti-inflammatory, and free radical-scavenging activities. Ethanol has been reported to be an effective extraction solvent for recovering these phenolic constituents, thereby enhancing the biological activity of *Allium cepa* extracts. The beneficial effects observed in the present study are therefore likely attributable to the synergistic action of these phytoconstituents.

Oxidative stress plays a central role in the pathogenesis of UC. Excessive production of ROS during DSS-induced inflammation promotes lipid peroxidation, resulting in elevated MDA levels and depletion of endogenous antioxidant enzymes such as CAT. In the present study, the treatment with *A. cepa* extract significantly reduced MDA levels, indicating attenuation of oxidative stress through scavenging of ROS and inhibition of lipid peroxidation, thereby protecting cellular membrane integrity. Simultaneously, CAT activity was significantly restored, suggesting enhancement of endogenous antioxidant defense mechanisms. Although the underlying molecular pathways were not directly investigated, these findings are consistent with previous reports indicating that quercetin-rich onion extracts activate the Nrf2 signaling pathway, leading to increased expression of antioxidant enzymes and improved detoxification of ROS.[15]

Inflammatory cytokines are major mediators of intestinal injury in UC. Activation of pattern-recognition receptors, particularly Toll-like receptor-4 (TLR4), stimulates the NF-κB signaling pathway,

resulting in increased production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which promote leukocyte recruitment, epithelial injury, and chronic mucosal inflammation. In the present study, *A. cepa* extract significantly reduced the tissue levels of these cytokines, suggesting suppression of inflammatory signaling. Previous studies have demonstrated that quercetin inhibits TLR4/NF-κB activation, suppresses cyclooxygenase-2 and inducible nitric oxide synthase expression, reduces macrophage activation, and consequently limits the production of pro-inflammatory mediators in experimental models of IBD.[16]

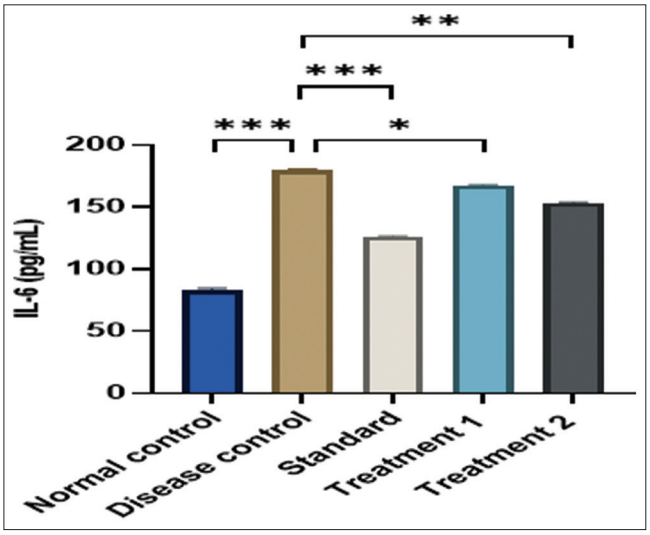

Figure 8: Effect of *Allium cepa* extract on oxidative stress and inflammatory biomarkers (malondialdehyde, catalase, tumor necrosis factor-alpha, interleukin-1β, and interleukin-6) in experimental animals interleukin-6 Data are presented as mean ± standard error of the mean ($n = 5$). One-way analysis of variance followed by Dunnett's multiple comparison test. *$P < 0.05$, **$P < 0.01$, *$P < 0.001$ versus disease control

The antioxidant and anti-inflammatory activities of *Allium cepa* extract were further supported by histopathological findings. DSS-treated animals exhibited extensive epithelial erosion, crypt distortion, inflammatory cell infiltration, submucosal edema, and ulceration, whereas treatment with the extract markedly preserved mucosal architecture and reduced inflammatory cell infiltration, particularly at the higher dose. Preservation of goblet cells, restoration of the protective mucus layer, maintenance of crypt architecture, and reduction in submucosal edema suggest improved epithelial regeneration and protection of intestinal barrier integrity. These protective effects likely reduce antigen penetration, limit neutrophil infiltration, decrease epithelial apoptosis, and promote mucosal healing, thereby contributing to restoration of normal colonic architecture. Similar histological improvements have been reported with quercetin-rich plant extracts in experimental models of UC.[8-10]

Overall, the findings of the present study demonstrate that the ethanolic extract of *A. cepa* peel confers significant protection against DSS-induced UC through coordinated antioxidant, anti-inflammatory, and mucosal protective mechanisms. Although molecular signaling pathways were not directly evaluated, the observed reduction in oxidative stress, restoration of antioxidant defenses, suppression of pro-inflammatory cytokines, and improvement in histopathological features collectively suggest that modulation of the Nrf2 antioxidant pathway and inhibition of TLR4/NF-κB-mediated inflammatory signaling may contribute to the therapeutic effects of the extract. Further mechanistic investigations are warranted to confirm these

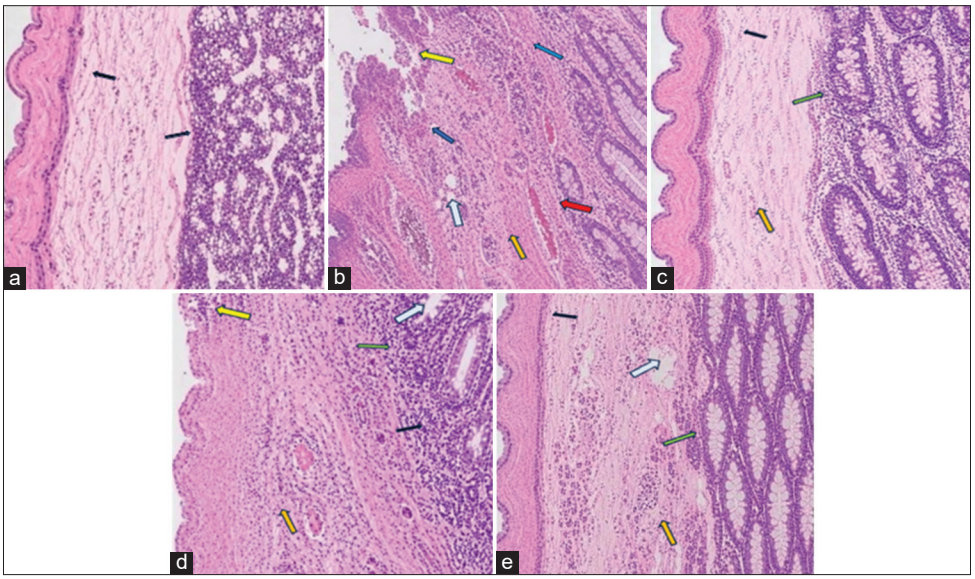

Figure 9: Representative hematoxylin and eosin-stained colonic sections showing the protective effect of *Allium cepa* extract against dextran sodium sulfate (DSS)-induced ulcerative colitis. (a) Normal control; (b) DSS disease control; (c) Standard control (5-aminosalicylic acid-treated group); (d) *A. cepa* extract (100 mg/kg); and (e) Treatment 2 *A. cepa* extract (200 mg/kg). Higher-dose *A. cepa* extract demonstrated improved preservation of colonic architecture and reduced inflammatory changes

molecular targets and identify the specific bioactive phytoconstituents responsible for the observed pharmacological activity.[15]

Conclusion

The present study demonstrates that the ethanolic extract of *A. cepa* peel effectively protects against DSS-induced UC by improving clinical manifestations, restoring colon length, reducing oxidative stress, suppressing pro-inflammatory cytokines, and preserving colonic histological architecture. The higher dose (200 mg/kg) produced greater therapeutic efficacy than the lower dose, although 5-ASA remained the most effective treatment. The extract inhibits that *A. cepa* peel possesses considerable potential as a phytotherapeutic candidate for UC due to its antioxidant and anti-inflammatory properties. Further studies focusing on bioactive compound isolation, molecular mechanisms, pharmacokinetic evaluation, and clinical validation are necessary to establish its therapeutic potential for the management of IBD.

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