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Original Article

# Protective Effect of Niosomal Gel of *Azadirachta indica* against Ulcerative Colitis induced by Dextran Sodium Sulfate (DSS) and Tri Nitro Benzene Sulfonic Acid (TNBS)

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## ABSTRACT

**Aim:** This study focuses on finding the protective action of niosomal gel of *Azadirachta indica* (neem) leaf extract in ulcerative colitis. **Materials and Methods:** The pharmacological *in vivo* model conducted here was Dextran Sodium Sulphate (DSS) model of mice colitis and Trinitro Benzene Sulfonic Acid (TNBS) induced ulcerative colitis in rats. **Results:** In DSS model, the niosomal gel of neem leaf extract at 500 mg/kg dose was found to be significant (**$p$<0.01). While in TNBS model the significance of niosomal gel containing neem leaf extract at 500 mg/kg showed highly prominent anticolitic response (***$p$<0.001). **Conclusion:** This research proved that niosomal gel of neem leaf extract had prominent effect to reverse the change in body weight and frequency of diarrhoea in treated rats. From the present study it was concluded that niosomal gel of neem leaf extract has prominent anticolitic effect on rats so it may be further use to check its effects clinically.

**Keywords:** Dextran sodium sulphate, IBD, Irritable Bowel Syndrome (IBS), Trinitro benzene sulfonic acid.

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## INTRODUCTION

Inflammatory Bowel Disease (IBD) is commonly associated with ulcerative colitis and Crohn's disease. Both Ulcerative colitis and Crohn's disease are characterized by persistent, recurrent inflammation of the GI-tract. Significant morbidity and reduced quality of life have been related to the high sickness load generated by chronic diseases like Ulcerative colitis as well as Crohn's disease. Several treatments, will have 5-ASA pharmaceuticals like sulfasalazine as well as mesalazine, may treat ulcerative colitis. Corticosteroids, like prednisone, can be utilized because of their immunosuppressive and short-term healing characteristics; however, since Corticosteroids hazards exceed their gains, they are rarely used for longer-term. Immunosuppressive drugs like azathioprine and therapies such as adalimumab and infliximab are only used while 5-ASA and corticosteroids fail to induce remission. These drugs have adverse complications, including immunosuppression, enhanced susceptibility to malignancies and autoimmune diseases and opportunistic infections.[1,2] Therefore, the development of alternative therapies that offer long term protection from the disease with no side effects would be worthy.

Nowadays more and more studies on herbal plants are conducted for alternative therapy. *Azadirachta indica*, often known as neem tree, is a species of tropical evergreen tree that is indigenous to India. It has been utilized in Ayurvedic medication for over 4000 years because of its curative actions. The parts of plant like fruits, leaves, seeds, root, as well as bark contain chemicals with medical benefits such antiviral, antipyretic, antiseptic, anti-inflammatory and anti-ulcer.[3] Numerous plant components found in neem include quercetin, azadirachtin, nimbosterol and several other limonoids. Among the compounds present in leaves are nimbin, nimbolide, ascorbic acid, n-hexacosanol and nimbiol.[4] The plant used for medicinal purposes also contains zamafaral, salannin, azadirachtin, nimbin, nimbinin and nimbin. Neem's various chemical compounds have a variety of therapeutic uses, including anti-oxidant,[5] antimicrobial, renal protective effects, cancer-fighting,[6] antifertility, liver-protective, antidiabetic and fungicidal.[7]

Niosomal dispersal showed continuous release, however developing a gel formulation greatly improved the composition's potential for topical usage. This study points to find protective action of niosomal gel of neem leaf extract in ulcerative colitis induced by DSS and TNBS in rats.

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## MATERIALS AND METHODS

### Procurement and Authentication

The plant *Azadirachta indica* was collected from Herbal Garden of NIET (Pharmacy Institute), Greater Noida and was authenticated from Botanical Garden of Indian Republic Sector-38A Noida, Uttar Pradesh. The herbarium was preserved in Pharmacognosy Division of Botanical Garden of Indian Republic with reference number BSI/BGIR/TECH/2021/13.

### Collection and Drying

The collected leaves of *Azadirachta indica* were sun dried, powdered form of dried leaves was extracted using ethanol as a solvent.

### Extraction of Plant Materials

In a round bottom flask, 250 mL ethanol (solvent) was added, which was fixed to a Soxhlet condenser and extractor on a heating mantle. The powdered leaves (100 g) are loaded in thimble that is fixed inside Soxhlet extractor. The solvent was heated using the heating mantle and began to evaporate, passing through the apparatus to the condenser. The condensate then drops into the reservoir, which holds the thimble. When the solvent level reaches the syphon, it is poured back into the flask and the cycle begins again. This procedure is repeated for four days.[8]

### Experimental Animals

The Wistar Albino rats (male) of body weight 180 to 200 g were used. The animals were procured from the animal House at the NIET (Pharmacy Institute) in Greater Noida. The animals were housed in a controlled setting that maintained a steady 25.2°C and a 12 hr day night cycle and the rodents were given a pellet *ad libitium* feed according to CPCSEA guidelines. The experimental protocol was approved by an institutional animal care and use committee vide reference number IAEC/NIET/2022/01/02.

### Preparation of Niosomal gel of *Azadirachta indica* leaf extract

#### *Shaking Hand Method (Thin Film hydration Technique)*

In a round bottom flask, surfactants and lipid (cholesterol) were mixed in an organic volatile solvent (methanol) with extract of neem leaves. The organic solvent was evaporated using a rotary evaporator under vacuum at room temperature, leaving a thin film of heterogeneous substances deposited on the flask wall. With moderate film was rehydrated with aqueous phase at moderate temperature just above transition temperature of the surfactants employed.

This process formed large multilamellar niosomes. After the formation of niosomes, the gelling agent (1% carbopol and polyethylene glycol) was incorporated this noisome suspension.

The use of sonication helped to bring this niosomal gel to required nano particle range.[9]

### Experimental Set-Up

- Male Wistar albino rats were used because of their ability to reduce inflammation.
- The duration of the study was 15 days for both anti-inflammatory activity experimental models.
- Each group of six rat was randomly assigned to one of five anti-inflammatory groups.

### Trinitrobenzene Sulfonic Acid Model (TNBS)

Male wistar albino rats weighing between 180 and 200 g were divided into 5 groups of 6.

- Group I-Control (Positive), TNBS (10 mg/kg Intra-rectally) + 50% Ethanol (v/v).
- Group II- Negative control CMC (2 mg/kg, p.o).
- Group III-TNBS+Niosomal gel of *Azadirachta indica* extract (250 mg/kg, rectal).
- Group IV-TNBS+Niosomal gel of *Azadirachta indica* extract (500 mg/kg, rectal).
- Group V-TNBS+Sulphasalazine (30 mg/kg, rectal).

### Experimental Procedure

The positive control group received 10 mg/kg TNBS diluted in 0.25 mL of 50% ethanol (v/v) and injected rectally once daily using a Teflon polyurethane catheter inserted 4-8 cm into the anus. The negative control group received 2 mg/kg Carboxymethyl Cellulose (CMC) soaked in distilled water and delivered daily via oral gavage. Further, two groups, designated as Test compound (I) and Test compound (II), were given the corresponding concentration of the API *Azadirachta indica* Extract (i.e. 250 mg/kg and 500 mg/kg rectal) as well as 10 mg/kg TNBS diluted in 50% ethanol (v/v) via a Teflon polyurethane catheter implanted 4-8 cm via the rectum. The final group was given daily Sulphasalazine at a dose of 30 mg/kg via rectal route, along with TNBS, which served as the standard group.[10] On the seventh day, the animals were sacrificed after receiving an overdose of halothane. We monitored the animals' weight, diarrhoea rate and food and water intake regularly during the experiment. The colons were removed from the murdered animals, placed on a dish of ice, then dissected hygienically before being opened longitudinally and rinsed in cold saline to eliminate any leftover luminal secretions. The colon was viewed under a microscope very away and any obvious damage was graded on a scale of 0 to 5. For histological evaluation, small slices of the colon were removed from two different locations of each colon and put in 10% formalin.[1]

### DSS (Dextran Sodium Sulfate) Model of Rat Colitis

Wistar male rats weighing approximately (180-200 g) were divided into 5 groups of 6 animals each.

- Group I-Control (Positive) dextran sodium sulphate (30 mg/mL, p.o.).
- Group I-Negative control CMC (2 mg/kg p.o.).
- Group III-DSS+Niosomal gel of *Azadirachta indica* extract (250 mg/kg rectal).
- Group IV-DSS+Niosomal gel of *Azadirachta indica* extract (500 mg/kg rectal).
- Group V-Sulphasalazine (30 mg/kg rectal).

### Experimental Procedure

To induce colitis, DSS (30 mg/ kg) was added to safe drinking water at a concentration of 3% for 5 days. After that, the Wistar albino rats were divided into 5 groups of 6. For the sake of comparison, one group received a dose of DSS (30 mg/mL) via oral gavage. The placebo group received 2 mg/kg of Carboxymethyl Cellulose (CMC) dissolved in sterile water once a day. Participants in the Test Compound (I) group were given DSS (30 mg/mL) in water, while those in the Test Compound (II) group were given either 250 mg/kg or 500 mg/kg of API *Azadirachta indica* Extract through rectal route. The third and final group received DSS (30 mg/mL) in their drinking water and Sulphasalazine (30 mg/kg) by rectal route. The sulfated polysaccharide DSS was injected into the drinking water of rats to induce ulcerative colitis, which resulted in weight loss, bloody diarrhoea, ulcer formation, epithelial cell death and neutrophil infiltration.[11] After 7 days, we overdosed the animals with ether to put them to sleep. Weight, food and water intake were only some of the indicators of animal health that were constantly recorded. At the end of the seventh day, the animals were slain and their colons were dissected aseptically, placed in an plate, opened longitudinally and rinsed with cold saline to eliminate luminal secretions. With the aid of the standards set forth by Morris *et al.*, (1989) and were able to assign a score from 0 to 5 (Table 1) to the degree of damage to the colon. In order to conduct a histological analysis, researchers removed two little sections of colon from each animal and preserved them in 10% formalin.[12]

### Histopathological Study

At the end of the 21$^{st}$ day, food was taken away from the Wistar albino rats and they fasted overnight but the animals had easy access to water. Under strong ether anaesthesia, the animal was killed and slaughtered through cervical dislocation. Surgically, colon was removed. After, following that, the tissues were immersed in 10% formalin for 1 hr (diluted to 10% with normal wine) to avoid shrinking of the organ for histological investigations. Colon was taken out and stored in the containers separately filled with formalin (10% v/v). It was incubated at 37°C under aseptic conditions for histopathological evaluation under the microscope.

## RESULTS AND DISCUSSION

### Trinitrobenzene Sulfonic Acid (TNBS) Model of Colitis

In the trinitrobenzene sulfonic acid model, inflammation was induced by intrarectal administration of TNBS. The result of this experiment showed changes in the weight of test group rats at both the doses of *Azadirachta indica* extract 250 mg/kg (17.64±0.436) (**$p$<0.01) and 500 mg/kg (18.69±0.537) (*$p$<0.05) in comparison to positive control group rats (21.57±0.412) which was comparable to the standard group (20.62±0.626) as shown in Table 2. For stool consistency in the Positive Control group, bloody diarrhoea was observed (0.75±0.012) in the test groups the frequency of diarrhoea reduced at both the doses of *Azadirachta indica* extract 250 mg/kg and 500 mg/kg (0.65±0.012) (***$p$<0.001) and (0.50±0.007) (****$p$<0.0001) respectively, which was comparable to the standard group (0.32±0.011). The colon weight and length increased in the test group which was (0.206±0.0049) and in the standard group (0.2383±0.006) (*$p$<0.05) in comparison to the positive control group (0.34±0.009) (Table 2).

Colonic variables were evaluated in a control group of 6 people who were given CMC. 6 rats were given TNBS intra-rectally in a 50% (v/v) ethanol vehicle. To compare the control and TNBS groups, one-way ANOVA and Tukey's multiple comparison post hoc tests were used and the results are presented as the mean standard error of the mean (Figure 1).

Colonic variables were evaluated in a control group of 6 rats who were given CMC. Six rats were given TNBS intra-rectally in a 50% (v/v) ethanol vehiclecompare the control and TNBS groups, one-way ANOVA and Tukey's multiple comparison post hoc tests were used and the results are presented as the mean standard error of the mean (*$p$<0.01, **$p$<0.001, **$p$<0.001).

**Table 1: Parameters for determining the severity of morphological deterioration in colon segments.**

| Rating | Gross morphology |
|---|---|
| 0 | No damage |
| 1 | There is no ulceration and hyperaemia. |
| 2 | Liner ulcers that aren't inflamed at all. |
| 3 | Liner ulcers with a single site of inflammation. |
| 4 | More ulcers and inflammatory regions, including ulcers up to 1 cm in diameter. |
| 5 | Several ulcers and inflammation, including ulcers measuring more than 1 cm in diameter. |

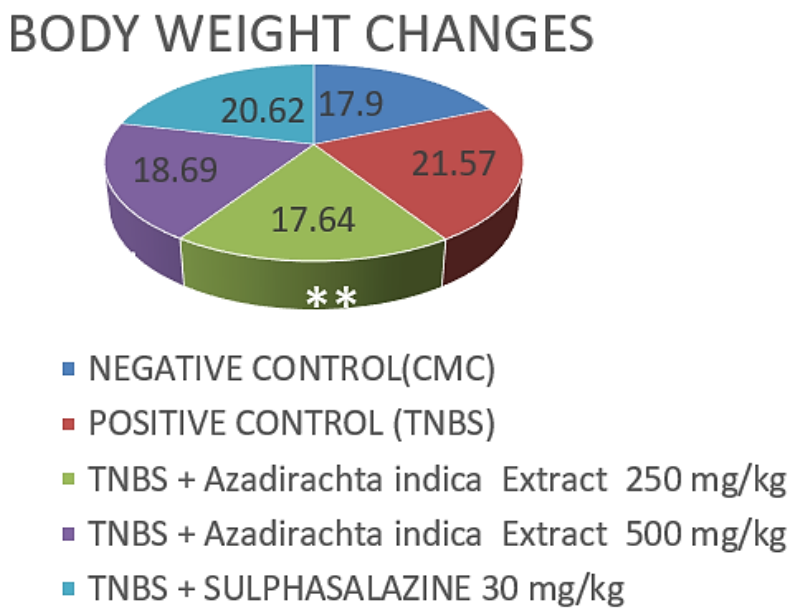


**Figure 1:** Effect of Niosomal gel of *Azadirachta indica* extract in body weight change in TNBS-induced rat colitis model. *n*=6 for each group, data was recorded as mean±SEM. ANOVA was used for statistical analysis. The maximum response was observed at 500 mg/kg (****$p<0.0001$). *=Showed less significance, **=Showed more significance than single star, ***=Showed more significance single and double star, ****=Showed higher significance.

**Table 2: Effect of Niosomal gel of *Azadirachta indica* extract in TNBS-induced rat colitis model.**

| Groups | Number of Animals (n) | Body weight changes(g) (Final weight-Initial weigh) | Stool Consistency (rating0-1) | Colon weight/length (g/cm) |
|---|---|---|---|---|
| Negative Control (CMC). | 6 | 17.90±0.436 | 0 | 0.34±0.009 |
| Positive Control (TNBS). | 6 | 21.57±0.412 | 0.75±0.012 | 0.201±0.006 |
| TNBS+Niosomal gel of *Azadirachta indica* leaf Extract 250 mg/kg. | 6 | 17.64±0.508** | 0.65±0.012*** | 0.206±0.0049 |
| TNBS+Niosomal gel of *Azadirachta indica* leaf Extract 500 mg/kg. | 6 | 18.69±0.537* | 0.50±0.007**** | 0.2383±0.006* |
| TNBS+Sulphasalazine 30 mg/kg (Standard). | 6 | 20.62±0.626 | 0.32±0.011 | 0.266±0.006 |

The no. of animals *n*=6 for each group, data was recorded as mean±SEM. ANOVA was used for statistical analysis. The maximum response was observed at 500 mg/kg (****$p<0.0001$).

Histopathological observations of colon tissue after the treatment with *Azadirachta indica* extract (500 mg/kg and 250 mg/kg) in TNBS rat colitis: (A) Negative Control (CMC), the mucosa is normal. (B) Positive Control (TNBS 10 mg/kg), inflammatory cell infiltration, apoptosis of epithelium at luminal interface and gross ulceration and proliferous granulomas. (C) TNBS (10 mg/kg)+*Azadirachta indica* extract (250 mg/kg), epithelial ulceration, inflammatory effusion, proliferous granulomas and cell infiltration were are all symptoms of mucosal ulcers. (D) TNBS (10 mg/kg)+*Azadirachta indica* extract (500 mg/kg), Crypto abscess development and minor mucosal ulceration. (E) TNBS (10 mg/kg)+Standard (Sulphasalazine 30 mg/kg), the architecture of mucosal lining was intact, no epithelial damage and ulcers were seen (Figure 2).

## Dextran Sodium Sulfate (DSS) Model of Rat Colitis

In the DSS model, the inflammation was induced by administering DSS. The result of this experiment showed changes in the

weight of test group rats at both the doses of *Azadirachta indica* extract 250 mg/kg (13.17±0.6381) (**$p$<0.001) and 500 mg/kg (17.87±0.4183) (**$p$<0.001) in compare to positive control group rats (19.97±0.4318) which was comparable to the standard group (21.77±0.9817) (***$p$<0.0001). For stool consistency in the Positive Control group, bloody diarrhoea was observed (0.57±0.016) in the test groups the frequency of diarrhoea reduced at both the doses of *Azadirachta indica* extract 250 mg/kg and 500 mg/kg (0.48±0.029) (*$p$<0.05) and (0.38±0.007) (**$p$<0.005) respectively, which was comparable to the standard group (0.31±0.008) (****$p$<0.0001). The colon weight and length increased in the test group which was (0.18±0.006) (**$p$<0.001) and (0.17±0.006) and in the standard group (0.25±0.003) (***$p$<0.001) in compare to the positive control group (0.17±0.006) (***$p$<0.001) (Figure 3).

Colonic variables were evaluated in a control group of 6 rats who were given CMC. For the DSS group, six rats took the drug for five days via oral gavage after it had been diluted in water. Means and Standard Errors of Means (SEM) were reported and to determine

**Table 3: The Effect of Niosomal gel of *Azadirachta indica* extract in DSS-induced colitis rat model.**

| Groups | Number of Animals (*n*) | Body weight changes (g) | Stool Consistency (rating 0-1) | Colon weight/length (g/cm) |
|---|---|---|---|---|
| Negative Control (CMC). | 6 | 11.64±0.5353 | 0 | 0.29±0.007 |
| Positive Control (DSS). | 6 | 19.97±0.4318 | 0.57±0.016 | 0.17±0.006 |
| DSS+Niosomal gel of *Azadirachta indica* leaf Extract 250 mg/kg. | 6 | 13.17±0.6381** | 0.48±0.029* | 0.18±0.006** |
| DSS+Niosomal gel of *Azadirachta indica* leaf Extract 500 mg/kg. | 6 | 17.87±0.4183 | 0.38±0.007** | 0.17±0.006 |
| DSS+Sulphasalazine 30 mg/kg (Standard). | 6 | 21.77±0.9817 | 0.31±0.008 | 0.25±0.003 |

The No. of animals $n$=6 for each group, data was recorded as mean±SEM. ANOVA was used for statistical analysis. The maximum response was observed at both 250 mg/kg as well as 500 mg/kg dose (**$p$<0.001).

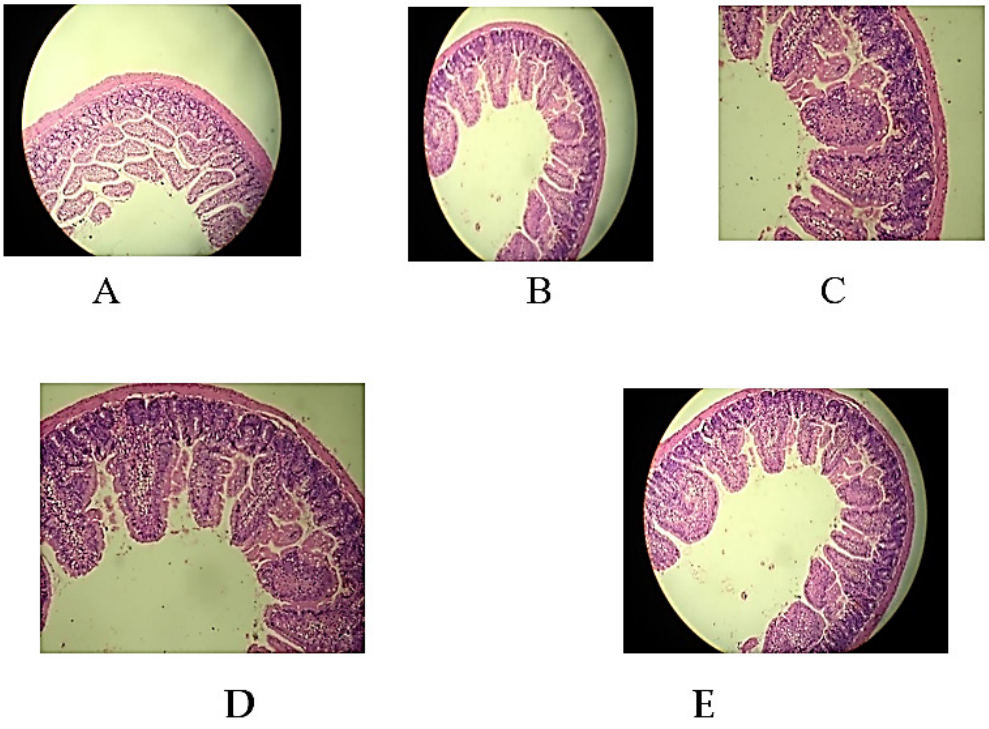


**Figure 2:** Photomicrographs showing Hematoxylin and Eosin-stained segments of rat colons in TNBS-induced rat colitis model.

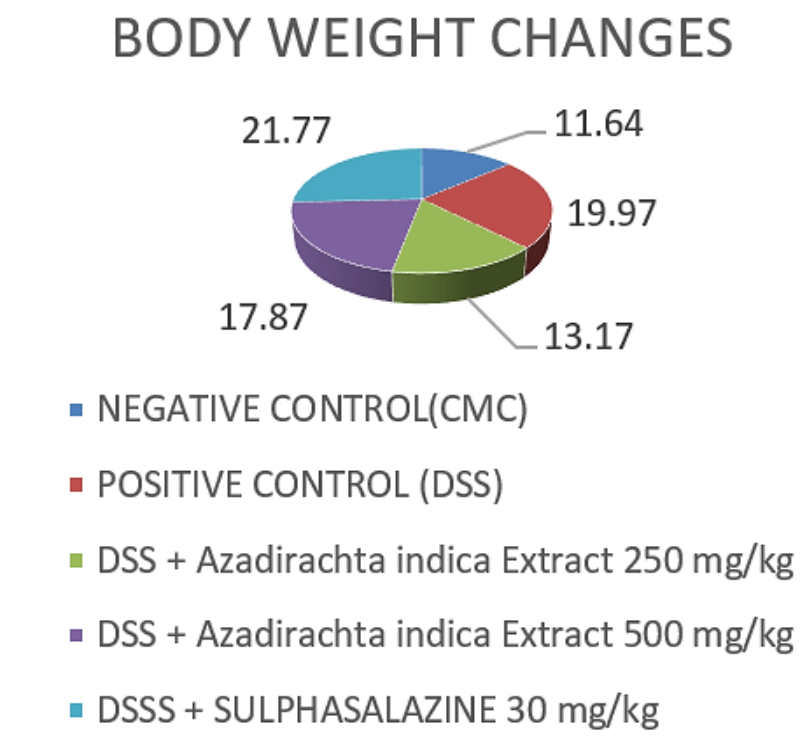


**Figure 3:** Effect of Niosomal gel of *Azadirachta indica* extract in body weight change in DSS-induced rat colitis. The no. of animals *n*=6 for each group, data was recorded as mean±SEM. ANOVA was used for statistical analysis. The maximum response was observed at both 250 mg/kg as well as 500 mg/kg dose (**$p$<0.001).

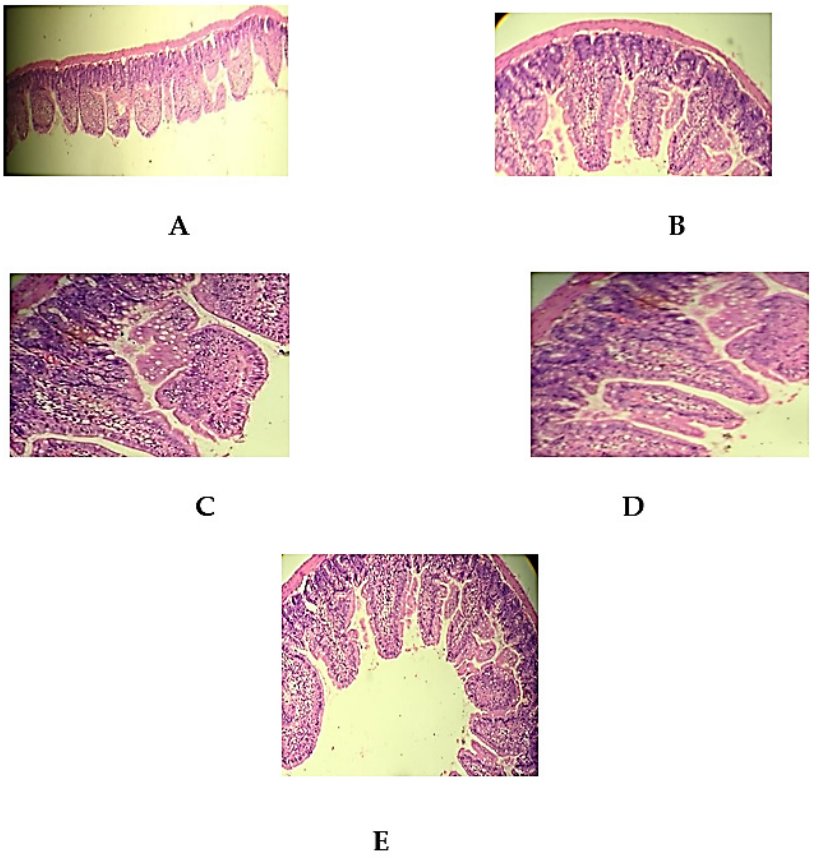


**Figure 4:** Histological studies of Dextran Sodium Sulfate (DSS) Rat Colitis.

statistical significance between the control and DSS groups, a one-way Analysis of Variance (ANOVA) with Tukey's multiple comparison post hoc testing was used. It had been watered down. When comparing the control and DSS groups, the results are given as means with standard errors (*$p$<0.01), (**$p$<0.05) and (***$p$<0.001) (Table 3).

Histopathological observations of colon issue after the treatment with *Azadirachta indica* extract (250 mg/kg and 500 mg/kg) in dextran sodium sulfate rat colitis: (A) Negative Control (CMC), displaying the histology of a normal rat owel. (B) Positive Control (DSS 30 mg/kg), revealing a substantial inflammatory cell infiltration in the basal lamina and submucosa, as well as moderate colonic ulcers. (C) DSS (30 mg/kg)+*Azadirachta indica* extract (250 mg/kg), with no inflammatory cell infiltrate in the basal lamina and submucosa, the rat has the fewest colon ulcers. (D) DSS (30 mg/kg)+*Azadirachta indica* extract (500 mg/kg), the inflamed response in the rat has recovered without ulceration of the gut wall; only modest infiltration can be seen in the basal lamina. (E) DSS (30 mg/kg)+Standard (Sulphasalazine 30 mg/kg), rat showing no intestinal ulcerations intact mucosal lining with very good histology of lamina propria and submucosa (Figure 4).

## CONCLUSION

The current study investigated the potential use of *niosomal gel* in the treatment of intestinal inflammation in the first instance. In this study, 2 different experimental models of colitis (IBD) were used: Trinitro benzene sulfonic acid and dextran sodium sulfate induced colitis. For 7 days, trinitro benzene sulfonic acid and dextran sodium sulfate were administered. The trinitro benzene sulfonic acid model and dextran sodium sulfate model of experimental colitis on rats are the most commonly used models for experimental colitis. They are strikingly similar to the most common IBD symptoms. The trinitro benzene sulfonic acid rat colitis model, on the other hand, results in a transmural lesion with clinical features similar to Crohn's disease. In the dextran sodium sulfate model in rats, which is more closely related to human ulcerative colitis, inflammation is limited to the intestinal epithelium.

The pharmacological efficacy of *niosomal gel* was amply demonstrated by a notable improvement in the inflammatory response and even a reduction in cellular infiltration, both experimentally and histopathologically. There was severe colonic mucosal and submucosal injury following trinitro benzene sulfonic acid and dextran sodium sulfate treatment, which was characterized by inflammatory cell infiltration and growth of epithelial ulcerations. Significant invasion of inflammatory cells was the primary characteristic of the acute phase. Inflammatory granulomas and ulcers caused by trinitro benzene sulfonic acid made up the majority of the chronic phase.

When given to both trinitro benzene sulfonic acid and dextran sodium sulfate models after the induction of colonic damage, *niosomal gel* had the beneficial effect. The results in both cases suggested that promoting the healing of inflamed tissues is dose dependent. As a result, *niosomal gel* can be considered a good candidate for the treatment of human IBD because traditional medicine prolongs the course of treatment, which supports its low toxicity.

In the model, Trinitro benzene sulfonic acid was administered intrarectally, which caused the inflammation. The results of this experiment revealed changes in the weight of test group rats at the *niosomal gel* doses of 250 mg/kg (*$p$<0.001) and 500 mg/kg (***$p$<0.001) in comparison to rats in the positive control group, which were like the standard group (***$p$<0.001). Bloody diarrhoea was seen in the Positive Control group's stool (***$p$<0.001), but in the test groups, the frequency of diarrhoea was decreased at both the 250 mg/kg and 500 mg/kg doses of *niosomal gel* (*$p$<0.05) and (**$p$<0.01), which was comparable to the standard group (***$p$<0.001). In the test group, which was (***$p$<0.001) (*$p$<0.05) and in the control group, which was (**$p$<0.01), the colon's weight and length increased.

In the Dextran sodium sulphate model, changes in the weight of test group rats at both the doses of *Azadirachta indica* extract 250 mg/kg (*$p$<0.05) and 500 mg/kg (**$p$<0.01), the stool consistency in the test groups and the frequency of diarrhoea were reduced at both the doses and colon weight and length were increased.

Ulcerative Colitis (UC), which affects many people, has a significant financial and social burden on the healthcare system. There are numerous ailments known as UCs, none of which have a known cause. According to the gut-brain axis theory, altered gut physiology and psychological variables interact to cause brain and gut problems, which have an impact on each other's expression.

The research demonstrated the impact of leaf extract of *Azadirachta indica* was clearly indicated to have significant action against ulcerative colitis. Overall activity *Azadirachta indica* against ulcerative colitis is due to presence of nimbidin and other phytoconstituents like antioxidants, flavonoids. For the targeted drug delivery of *Azadirachta indica* leaf extract an updated formulation was prepared that is niosomal gel in which the herbal extract was incorporated into formulation for the enhancement of availability of drug at the site of action. The main objective was to select niosomes as a targeted drug delivery as it has improved stability and provide high as well as sustained drug concentration.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**IBD:** Inflammatory Bowel Disease; **DSS:** Dextran Sodium Sulfate; **TNBS:** Trinitrobenzene Sulfonic Acid; **CMC:** Carboxymethyl Cellulose; **SEM:** Standard Errors of Mean; **ANOVA:** Analysis of Variance; **CD:** Crohn's Disease; **UC:** Ulcerative Colitis.

## SUMMARY

Inflammatory Bowel Disease (IBD), encompassing ulcerative colitis and crohn's disease, leads to chronic gastrointestinal inflammation, significantly impacting patients' quality of life. traditional treatments include 5-asa drugs like sulfasalazine, corticosteroids, and immunosuppressants; however, these can have severe side effects. consequently, there is a growing interest in alternative therapies, particularly herbal remedies. one such candidate is *Azadirachta indica*, or neem, which has been used in ayurvedic medicine for over 4,000 years due to its diverse therapeutic properties. This study explored the protective effects of a niosomal gel formulation of neem leaf extract against ulcerative colitis induced by Dextran Sodium Sulfate (DSS) and Trinitrobenzene Sulfonic Acid (TNBS) in rat models. Neem's active compounds, including quercetin and azadirachtin, possess anti-inflammatory and antioxidant properties. the study involved extracting neem leaves using ethanol and preparing a niosomal gel for rectal administration.

Results indicated that the neem extract significantly reduced weight loss and diarrhea frequency in treated rats compared to controls. histopathological evaluations showed improved colon health with reduced inflammation and ulceration in the neem-treated groups. the findings suggest that neem's niosomal gel formulation could be a promising alternative for managing ulcerative colitis, offering therapeutic benefits without the adverse effects associated with conventional medications. further research is warranted to confirm these results and explore clinical applications.

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