Research Article

From Green Chemistry To Gastric Cytoprotection Rational Design, Characterization, And Preclinical Validation Of Biogenic Nanoparticles As Antioxidant, And Mucoadhesive Therapeutics For Gastropathy

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Abstract

Peptic ulcer disease remains a major global health concern, particularly when aggravated by non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin. It may induce multiple potential complications like gastrointestinal bleeding, stomach cancer, GERD, IBS and malabsorption of many nutrients that will leads to deficiencies. This study investigates the gastro protective potential of Acacia catechu, a polyphenol-rich medicinal plant, in indomethacin-induced gastric ulceration in wistar rats. Six groups were assigned: normal control, ulcer control, standard (famotidine), and three treatment groups of Acacia catechu (150, 250, 500 mg/kg). Following ulcer induction via indomethacin (30 mg/kg), parameters such as ulcer index, gastric pH, total acidity, TBARS, SOD, and histopathology were evaluated. In the present investigation, leaf extract and silver nanoparticles (AgNPs) of A. catechu (Ac) were subjected to various spectral (UV, Particle size, Zeta Potential, FTIR, XRD and SEM) analyses. Ac-AgNPs could be potential phyto-ulceroprotective against ulcers induced models. Results demonstrated significant dose-dependent gastro protection with A. catechu, especially at 500 mg/kg, highlighting its antioxidant and mucosal healing effects. Catechu is find to be powerhouse of antioxidants because of rich flavonoids, tannins and catechin that aid capturing of free radicals halt the oxidative stress as well as inflammatory ulcer disorder. These findings suggest that Acacia catechu is a promising natural therapeutic agent for NSAID-induced ulcers.

Keywords : Acacia catechu, Indomethacin, AgNPs, SEM, XRD, Ulcer index, TBARS, SOD, Gastro protection

1. Introduction

Peptic ulcer disease (PUD) is a prevalent gastrointestinal disorder characterized by the breakdown of the protective mucosal lining of the stomach and duodenum, resulting in localized erosions and ulcerations. The primary etiological factors include Helicobacter pylori infection and the chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin [1,2]. NSAIDs exert their ulcerogenic effect by inhibiting cyclooxygenase (COX) enzymes, leading to reduced synthesis of prostaglandins—key mediators in maintaining mucosal integrity [3]. Among NSAIDs, indomethacin is particularly potent in compromising mucosal defences and causing direct gastric irritation [4]. Although current pharmacological interventions, including proton pump inhibitors (PPIs) and H_2 receptor antagonists like famotidine, provide symptomatic relief, their use is associated with limitations such as poor bioavailability, adverse effects, and high relapse rates upon discontinuation [5,6]. This highlights the growing interest in safer, plant-derived therapeutic alternatives. Acacia catechu, a traditional medicinal plant, possesses notable anti-inflammatory, antioxidant, and gastro protective properties [7]. Its bioactive constituents—catechin, epicatechin, tannins and flavonoids—are believed to contribute in mucosal protection and healing [8,9]. Moreover components work synergistically to promote overall digestive health, antimicrobial effects, cardio protection and oral health etc. The present study investigates the ulceroprotective potential of Acacia catechu against indomethacin-induced gastric ulcers in rats.

Famotidine is a potent histamine H_2-receptor antagonist that inhibits gastric acid secretion by competitively blocking H_2 receptors on the parietal cells of the stomach lining [10]. It is commonly used in the treatment of acid-related disorders such as peptic ulcer disease, gastro esophageal reflux disease (GERD), and Zollinger-Ellison syndrome [11]. Famotidine effectively reduces both basal and stimulated gastric acid secretion, providing symptomatic relief and promoting ulcer healing. Compared to earlier H_2 blockers, it exhibits a longer duration of action and fewer adverse effects, making it a preferred choice in clinical practice [12]. Moreover famotidine is 9 times more potent than rantidine, 30% more long duration of action, less dosing required to produce sustained action on acid in stomach. Famotidine is a valuable candidate to use in preclinical experiments because of its minimal toxicity, improved bioavailability and better safety profile.

Acacia catechu (commonly known as Khadira or Black Catechu) is a highly valued medicinal tree in traditional systems like Ayurveda and Unani, renowned for treating gastric ulcers, mouth sores, and chronic skin wounds. Modern nanomedicine bridges these traditional claims by utilizing Acacia catechu extracts to green-synthesize silver nanoparticles (AgNPs), dramatically improving the plant's natural therapeutic potency. Herbal practitioners have utilized the bark, roots, and heartwood of Acacia catechu to treat various types of ulcerations. Mouth and Oral Ulcers: Formulated as mouthwashes or local applications to soothe painful aphthous ulcers and reduce gum inflammation. Gastric and Peptic Ulcers: Administered internally to shield the stomach lining, decrease bleeding (oozing), and alleviate internal inflammation. Chronic & Non-Healing Skin Ulcers: Applied externally to accelerate tissue repair and prevent the putrefaction of open wounds.

2. Material and Methods

2.1. Experimental Animals

Healthy Wistar rats weighing 150–200 g were obtained from a CPCSEA-registered animal facility. Animals were housed under standard laboratory conditions with a 12-hour light/dark cycle and had free access to a standard diet and water. All experimental protocols were reviewed and approved by the Institutional Animal Ethics Committee (IAEC).

2.2. Chemicals and Reagents

Indomethacin and famotidine were procured from certified pharmaceutical vendors. All chemicals and reagents used were of analytical grade. Plant material (leaves of Acacia catechu) was collected, authenticated, shade-dried, and extracted using hydroalcoholic extraction.

2.3. Induction of Ulcer

Gastric ulcers were induced by oral administration of indomethacin at a dose of 30 mg/kg after a 24-hour fasting period. Animals were monitored for signs of gastric distress and euthanized humanely at study termination for tissue analysis.

2.4. Plant Material and Extraction

Leaves of Acacia catechu was collected, dried, and powdered. The aqueous extract was prepared using a Soxhlet apparatus and phytochemically screened for active constituents such as tannins, flavonoids, and phenolic compounds. The extract (100g) was refluxed with the methanol. The solvent from the extract were removed under a vacuum. The extractive value was calculated by weighing. The sample was stored at 4ºC.

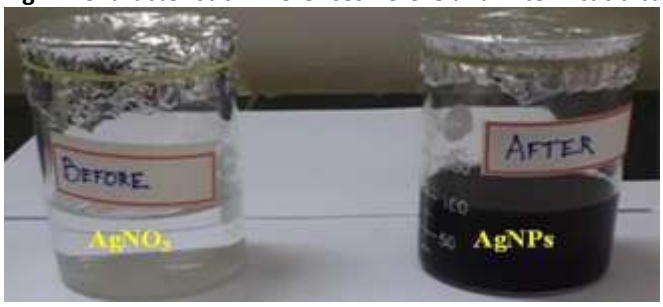
2.5 Standardized Evaluation Parameters

1. **Methanol Extractive Value: Test was performed to** determine the amount of active, polar constituents like phenols, glycosides, and alkaloids soluble in methanol.
2. **Loss on Drying (LOD):** The percentage of water and volatile matter lost upon heating, generally kept low to prevent microbial spoilage.
3. **Total Ash Value:** The total inorganic residue (earthy matter and physiological minerals) left after incineration.
4. **Acid Insoluble Ash Value:** The silica present mostly sand and soil, indicating inorganic contamination.
5. **Water Soluble Ash Value:** The portion of total ash that is soluble in water, detect the presence of water-soluble salts.
6. **Foreign Organic Matter:** The percentage of foreign matter of stems in leaf drugs, molds, or soil mixed with the target plant part.
7. **Moisture Content:** Amount of bound and free water within the sample, often measured via azeotropic distillation or Karl Fischer titration.

2.6 Biogenic Nano Preparation of extract

Polymeric nanoparticles were prepared by the solvent evaporation method. The polymeric nanoparticles were prepared by using plant extract to polymer conjugates ratio (1:2). The mixture was then subjected to Rotary evaporator for removal of the methanol. The dispersion is formed as given in **Fig. 1**. It was subjected to high speed homogenizer (10,000 RPM for 15 min) and then passed through high pressure homogenizer at pressure of 700 bars and 7 cycles. Nanoparticles solution subjected to lyophilization and dry lyophilized powder of herbal polymeric nanoparticles was formed.

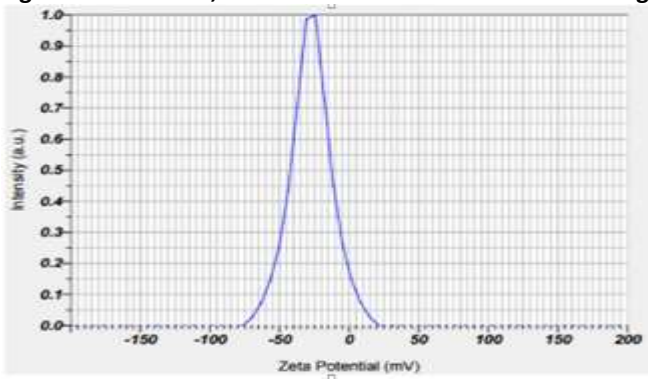
Fig. 1 : Characteristic Differences Before and After Acacia catechu Silver Nanoparticles Formation



2.7 Particle size, Zeta potential and PDI analysis

Through the use of dynamic light scattering, the particle size and PDI were determined. By measuring Brownian motion and correlating it to particle size, dynamic light scattering (also known as PCS—Photon Correlation Spectroscopy) analyzes the movement of the particles. It accomplishes this by laser-illuminating the particles and examining the variations in light intensity in the scattered light. To create an acceptable scattering intensity, double distilled water was used to dilute all samples. Using disposable polystyrene cells with a 10 mm diameter and 25°C, the zeta potential and PDI values were measured at a 90° angle as depicted in **Fig. 2.** By calculating the electrophoretic mobility, the zeta potential was calculated. For the optimized batch, the zeta potential and average particle size of the nanoparticles were calculated. (n = 3).

Fig. 2 : Particle Size, Zeta Potential of A. catechu extract AgNPs



2.8 UV, FTIR, and XRD analysis

Color change is the basic observation of Ac-AgNPs synthesis which subjected into UV and FTIR spectral analysis of of Ac-AgNPs are clearly explained in **Fig. 3, Fig. 4,** and FTIR analysis supports our hypothesis that the bio reduction of Ag^{+} ions to Ag° carried out by A. catechu leaf borne metabolite. Indeed, the FTIR spectrum showed major peaks at 3422.49, 2922.44, 2853.81, 1608.95, 1588.38, 1489.26, 1444.39, 1383.51, 1268.82, 1237.65, 1110.98, 1036.97, 888.44, 749.31, 724.33, 608.00, 539.81, 487.41, 429.37 $^{cm-1}$. Above the peak value is strong and broad, they corresponded to functional group like alcohols, phenols (O—H stretch, H-bonded, 3422.49 $^{cm-1}$). Alkanes (C-H stretch, 2922.44, 2853.81 $^{cm-1}$).

Fig. 3: UV Spectra absorption peaks of A. Catechu extract AgNPs

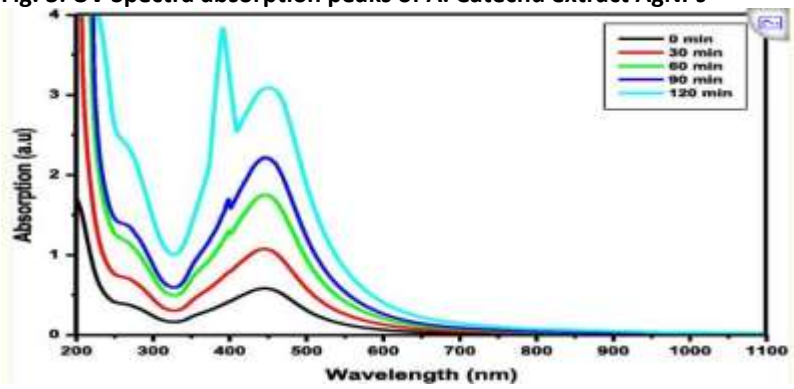
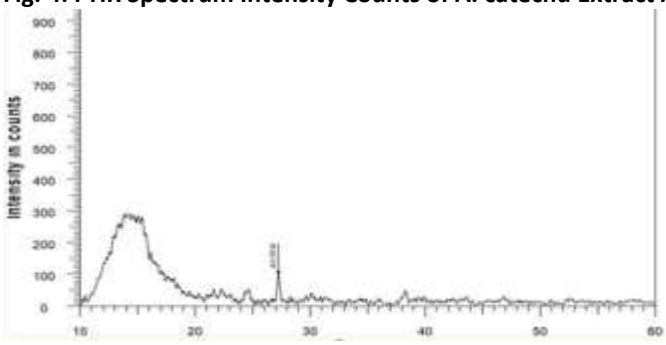


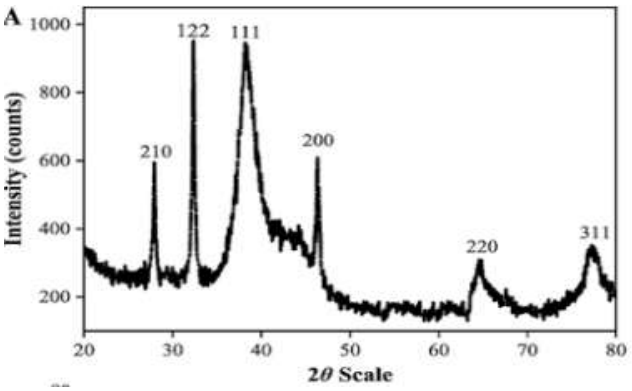
Fig. 4: FTIR Spectrum Intensity Counts of A. catechu Extract AgNPs



2.9 X-Ray Diffractometry (XRD)

Using an X-ray diffractometer with Cu as a target and a voltage of 40 kV, the powder X-ray diffraction (PXRD) patterns of BSA, Lycoat RS 720, and BSA-LYCOAT RS 720 were examined. Samples were examined at a scanning rate of 3o/2U/min in the 2θ angle range of 10-50ºC. The XRD analysis of Ac-AgNPs is obviously indicated in Fig. no. 5, the appeared peaks were likely matched, and their data were confirming with NIST chemical library.

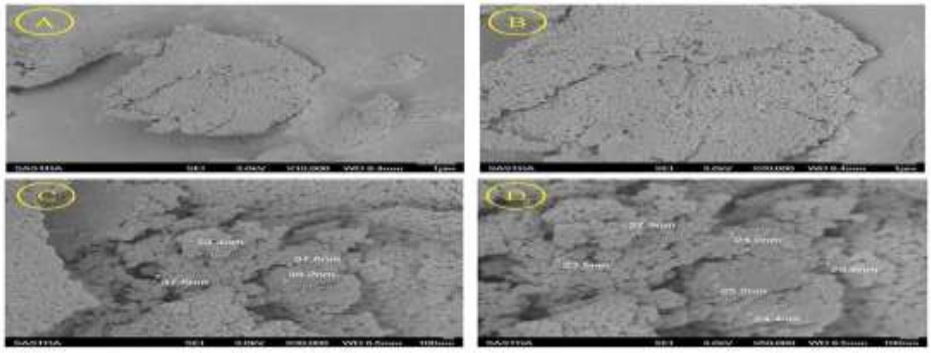
Fig. 5 : XRD Diffracted Pattern of Catechu Extract AgNPs Powder Synthesized by High Energy Ball Mill



2.10 SEM Analysis

Green synthesized of Ac-AgNPs evaluated by SEM analysis and its image has been displayed in Fig. no. 6. SEM analysis of catechu silver nanoparticles (AgNPs) typically reveals well-dispersed, predominantly quasi-spherical or spherical shapes with sizes ranging between 15 nm and 40 nm. From the image obviously declared, the Ac-AgNPs adhered with Ac-AgNPs confirmed the particle size range from 23.5 nm and 53.4 nm. SEM image has been magnified into different range, and Ac-AgNPs particles appeared like beads shaped it was indicated the category of NPs. The geometric mean diameter generally falls between 15 nm and 25 nm. However, the diameter can scale up to 50 nm depending on the ratio of silver nitrate ($AgNO_3$) to plant extract. Phytochemical capping provides high colloidal stability. While the particles often appear uniform and well-dispersed, localized clumping or clusters can occasionally occur depending on the sample preparation.

Fig. 6: SEM Report of A. catechu extract AgNPs



2.11. Grouping and Treatment Design

Multiple treatment designs can be implemented like Dose Response study (Evaluate Famotidine Effects at different doses), Time course study (Assess Drug Effects at various timings) and combination Therapy (Investigation of Standard drug with another one). Animals were randomly divided into six groups (n = 6 per group)

Table-1: Experimental Protocol Design of Animals Separated into Six Group with Six Animals In Each Group

Sr. No.	Groups	Treatment	Dose (mg/kg)
1.	Group 1	Normal Control	Water
2.	Group 2	Ulcer Control	Indomethacin 30 mg/kg
3.	Group 3	Standard Drug (Famotidine)	40 mg/kg
4.	Group 4	Acacia catechu Low Dose	150 mg/kg
5.	Group 5	Acacia catechu Medium Dose	250 mg/kg
6.	Group 6	Acacia catechu High Dose	500 mg/kg

Treatments were administered orally once daily for 7 days post-induction.

Evaluation Parameters

Gastric juice was collected post-euthanasia to determine pH, volume, and total acidity. Ulcer index and percentage protection were calculated macroscopically. Mucosal content was estimated gravimetrically. Biochemical analysis included TBARS (lipid peroxidation marker) and SOD (superoxide dismutase) levels. Histopathology of the gastric mucosa was performed using hematoxylin and eosin staining.

3. Results

3.1 Physicochemical screening

These physicochemical tests are standard pharmacognostic parameters used to evaluate the purity, quality, and adulteration of botanical drugs. Values vary by plant species and geographical location. The following methods determine the percentage value for the various physicochemical tests which are given below.

Table-2: Physicochemical Parameters of Acacia catechu Extract

Sr. No.	Solvent	Value
1.	Methanol Extractive value	4.6%
2.	Loss on drying (%w/w)	3.7%
3.	Total Ash value (%w/w)	6.5%
4.	Acid insoluble ash value (%w/w)	1.7%
5.	Water soluble ash value (%w/w)	3.6%
6.	Foreign organic matter (%w/w)	0.8%
7.	Moisture content (%w/w)	6.4%

3.2. Ulcer Index and Protection

Acacia catechu significantly reduced ulcer index in a dose-dependent manner ($p < 0.01$), with the highest inhibition observed at 500 mg/kg. This group exhibited a protective effect comparable to famotidine. Acacia catechu extracts have demonstrated up to

a 71.14% inhibition of gastric ulcers. When green-synthesized AgNPs are utilized, they lower the ulcer index by inhibiting inflammation and linear breaks in the gastric mucosa

3.3. Gastric pH, Volume, and Total Acidity

Treatment with Acacia catechu increased gastric pH and reduced volume and total acidity significantly compared to the ulcer control group ($p < 0.05$). Gastric pH Treatment with the extract significantly elevates the gastric pH, reducing the highly acidic environment that leads to ulceration Gastric Volume as depicted in **Table-3**. The total volume of gastric secretions is reduced, limiting the damaging contact of acid on the stomach lining. Total and Free Acidity Both free and total acidity levels decrease, demonstrating the extract's anti secretory properties.

Table -3: Effect of Acacia catechu on Ulcer Index, Percentage Ulcer Protection, Volume and P_H and Total Acidity in Indomethacin Induced Ulcer in Rats

Group	Ulcer Index (Mean ± SEM)	% Ulcer Protection	Gastric Volume (mL)	Gastric pH	Total Acidity (mEq/L)
Group I – Normal Control	0.45 ± 0.05		1.25 ± 0.08	3.85 ± 0.10	38.25 ± 1.10
Group II – Ulcer Control	14.60 ± 0.40^{a}	$0.00\%^{a}$	3.90 ± 0.12^{a}	1.62 ± 0.08^{a}	89.60 ± 1.50^{a}
Group III – Standard (Famotidine 30 mg/kg)	3.20 ± 0.22^{b}	$78.08\%^{b}$	2.10 ± 0.10^{b}	3.25 ± 0.12^{b}	45.70 ± 1.20^{b}
Group IV – Acacia catechu 150 mg/kg	7.90 ± 0.30^{bc}	$48.56\%^{bc1}$	2.90 ± 0.14^{bc1}	2.40 ± 0.10^{bc1}	71.40 ± 1.35^{bc1}
Group V – Acacia catechu 250 mg/kg	4.80 ± 0.25^{bc}	$72.01\%^{bc2}$	2.40 ± 0.11^{bc2}	2.85 ± 0.13^{bc2}	53.20 ± 1.25^{bc2}
Group VI – Acacia catechu 500 mg/kg	2.95 ± 0.18^{bc}	$76.02\%^{bc3}$	2.15 ± 0.09^{bc3}	3.10 ± 0.12^{bc3}	48.95 ± 1.10^{bc3}

Superscripts in Table 10 indicates a is disease control, b is standard Group, bc1 is 150mg/kg, bc2 is 250mg/kg and bc3 is 500 mg/kg. In which per activity 3 values mean were calculated and values are expressed as mean ± S.D, $p<0.01$.

3.4. Gastric Mucus and Biochemical Markers

Acacia catechu increased mucus content significantly and showed a notable decrease in TBARS and increase in SOD levels, indicating antioxidant potential. Studies on Acacia catechu utilize its phytochemically rich extracts for the green synthesis of silver nanoparticles (AgNPs) to evaluate their gastro protective, antioxidant, and anti-inflammatory efficacy as demonstrated in Fig. no. 7 and Table no. 4.

Fig. 7: Gastric Mucus and Biochemical Markers in Various Grouped Animals

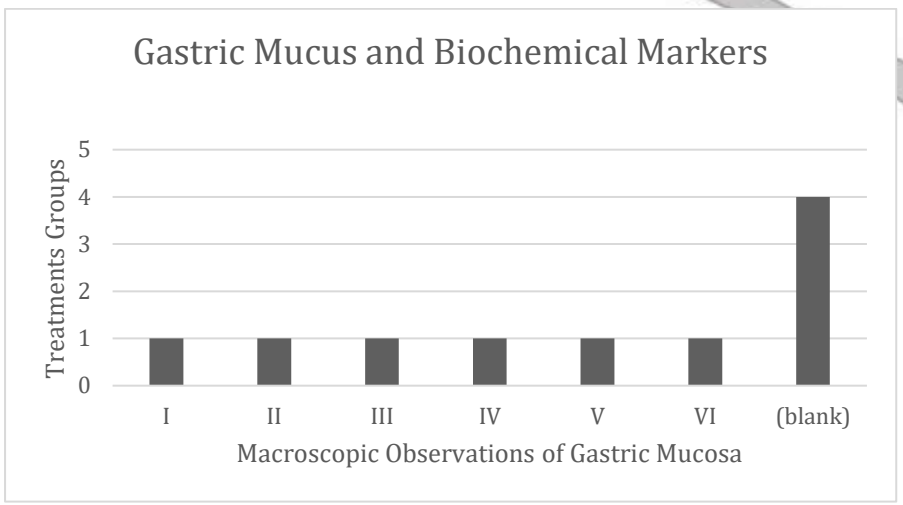
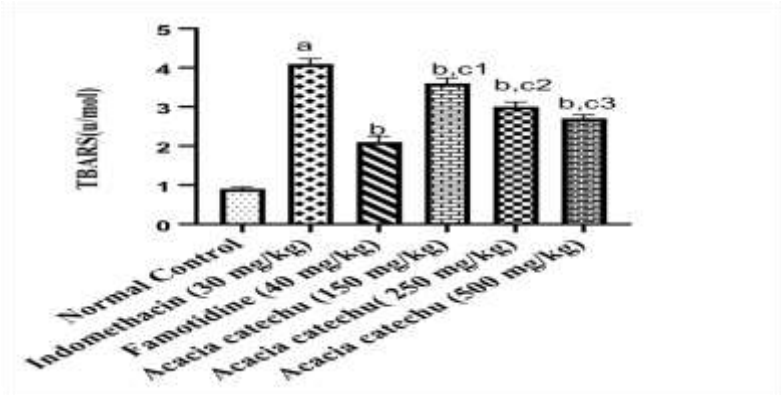


Table - 4: Physical Macroscopic Observations in Ulcerated Mucosa

Group	Treatment	Macroscopic Observations of Gastric Mucosa
I	Normal Control	Intact mucosa, no visible lesions or congestion
II	Ulcer Control (Indomethacin 30 mg/kg)	Severe mucosal damage, deep ulcers, hemorrhagic Streaks
III	Standard – Famotidine (40mg/kg)	Mild superficial ulcers, reduced congestion
IV	Acacia catechu 150 mg/kg	Moderate ulcers, localized mucosal thickening
V	Acacia catechu 250 mg/kg	Few small ulcers, improved mucosal integrity
VI	Acacia catechu 500 mg/kg	Nearly normal mucosa, minimal erosion, preserved architecture

Fig 8: TBARs Biochemical Estimation among all grouped animals

TBARS



This assay evaluates the antioxidant efficacy of herbal silver nanoparticles by measuring their ability to inhibit lipid peroxidation (cellular damage) TBARS (Thiobarbituric Acid Reactive Substances) assay measures malondialdehyde (MDA), a primary biomarker for lipid peroxidation and oxidative stress. In animal studies evaluating Acacia catechu silver nanoparticles (AgNPs), TBARS levels typically spike during oxidative damage (e.g. toxicity or disease models) and are significantly reduced upon treatment with the antioxidant-rich AgNPs. Plant extracts (rich in polyphenols and flavonoids) act as reducing and capping agents for nanoparticles.

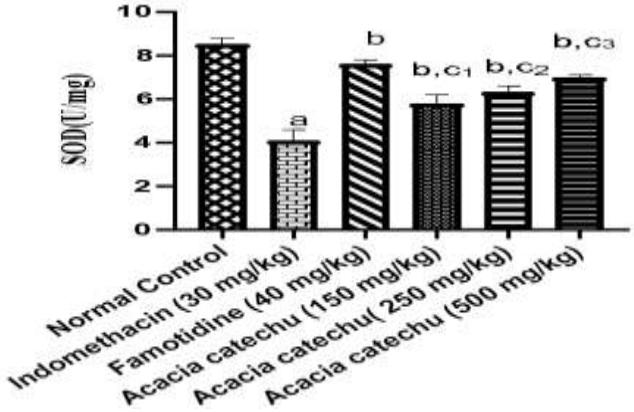
The TBARS test confirms if the nano-formulation enhances or retains the extract's ability to neutralize free radicals and protect lipids.

Superscripts in Fig No.01 indicates a is disease control, b is standard Group, bc1 is 150mg/kg, bc2 is 250mg/kg and bc3 is 500 mg/kg. In which per activity 3 values mean were calculated and values are expressed as mean ± S.D, $p<0.01$.

3.5 SOD Assay

This assay measures SOD by evaluating its ability to inhibit the reduction of a tetrazolium salt to water-soluble formazan dye by superoxide anions generated by xanthine oxidase. Ensure herbal AgNPs are dissolved or suspended in the assay buffer. Since some herbal extracts and metal nanoparticles exhibit their own background absorbance, prepare blank controls containing only the nanoparticle suspension to subtract background interference. Assay results shows the size, stability, and therapeutic properties as depicted in **Fig. no. 9**. Typically, these assays confirm nanometer-scale particle sizes, crystalline structures, and potent antioxidant and antimicrobial activities, making them highly effective as therapeutic agents.

Fig. 9: SOD Estimation in Grouped Animal



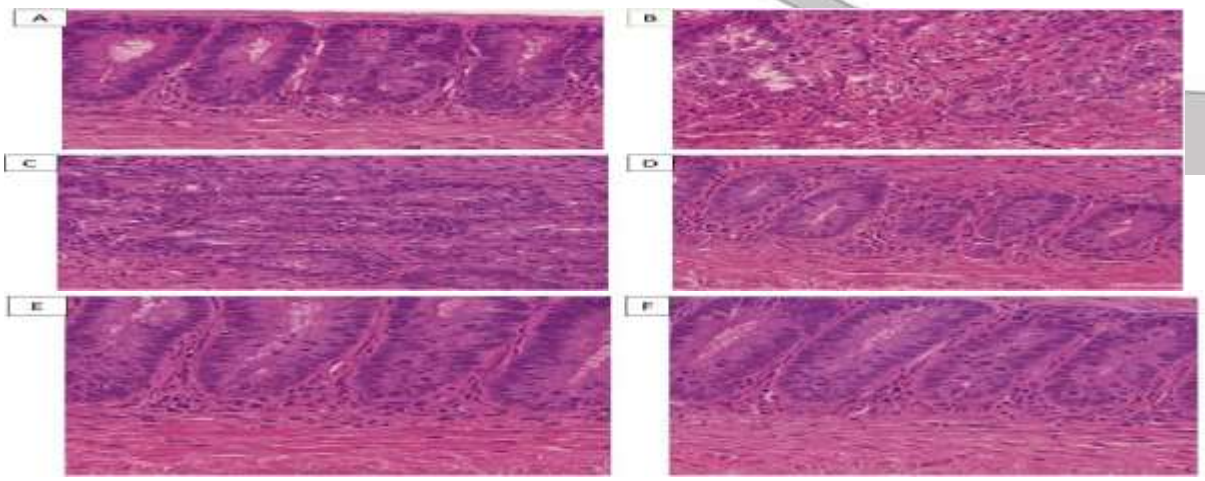
Superscripts in Fig No.01 indicates a is disease control, b is standard Group, bc1 is 150mg/kg, bc2 is 250mg/kg and bc3 is 500 mg/kg. In which per activity 3 values mean were calculated and values are expressed as mean ± S.D, $p<0.01$.

3.6. Histopathological Findings

Microscopic examination revealed preserved mucosal architecture in treated groups, especially at 500 mg/kg. Epithelial regeneration and reduced inflammatory infiltrates were the evidences that support and reveal the gastro protective mechanism in Indomethacin induced Peptic ulceration Model. Histopathological evaluation of stomach tissue following exposure to herbal (green-synthesized) silver nanoparticles (AgNPs) generally reveals one of two outcomes**:** gastro protective effects or dose-dependent cytotoxicity as shown in Fig. 10. When used as a therapeutic agent (often in ulcer models induced by ethanol or aspirin), the histopathology of the stomach shows:

- **Preserved Mucosa:** Intact gastric glands and columnar epithelial cells.
- **Reduced Lesions:** Significant reduction in hemorrhagic spots, sub-epithelial edema, and necrosis.
- **Decreased Inflammation:** Less leucocyte (white blood cell) infiltration in the sub mucosa, confirming anti-inflammatory and antioxidant activities.
- **Biochemical Backing:** Studies show an increase in tissue antioxidant enzymes (like SOD and CAT) and improved mucus secretion, validating the protective architecture.

Fig. 10: Histopathology of Stomach



4. Conclusion

Antiulcer standard (famotidine) and test drugs doses (150, 250 and 500 mg/kg) were estimated during experimental protocols likewise Ulcer index, ulcer score, gastric acid volume, gastric fluid P_H, SOD, TBARS, histopathological observations. Acidic juice was collected post-euthanasia to determine pH, volume, and total acidity. Ulcer index and percentage protection were calculated macroscopically. Mucosal content was estimated gravimetrically. Biochemical estimations revealed TBARS (lipid peroxidation marker) and SOD (superoxide dismutase) levels. Histopathology of the gastric mucosa was performed using hematoxylin and eosin staining. Acacia catechu demonstrate the significant ulcer protective effects against indomethacin-induced gastric ulcers in rats, supporting its traditional use as a natural remedy for gastric ailments. Plant active components shows promising potential in managing ulcer. This eco-friendly method produces biocompatible, stable nanoparticles known for targeted antimicrobial and ulcer-protective therapeutic applications.

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