Pharmacogn. Res., 2025; 17(3):801-815.
https://www.phcogres.com

Original Article

Pharmacological Investigation of *Actinidia deliciosa* Extract in NSAIDs Induced Gastric Ulcer in Rodent Model

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ABSTRACT

NSAIDs or non opoidal agents are commonly employed to treat rubor, dolor, relieve pain, but they often cause Gastrointestinal (GI) side effects, including gastritis, ulceration and bleeding. Natural products have emerged as potential alternatives or adjuncts to conventional treatments. The purpose of this study is to look at how *Actinidia deliciosa* (kiwi) extract protects against gastric ulcer brought on by NSAIDs. **Background:** NSAIDs are a group of pharmaceutical medications that are usually employed to treat rubor and dolor along with pyrexia as well as give a certain analgesic action at a certain therapeutic dose. At certain doses it is also used treat some sort of discomfort. While effective for these purposes, NSAIDs can also cause significant Gastrointestinal (GI) side effects, leading to conditions like gastritis, ulcers and even bleeding. This condition is known as NSAIDs-induced gastric ulcer. **Materials and Methods:** Rats will be divided into control, NSAIDs-induced gastric ulcer and NSAIDs-induced gastric ulcer treated with *Actinidia deliciosa* extract groups. The NSAIDs-induced gastric ulcer model will be established using indomethacin. The extract will be administered orally at various doses for a specified duration. GI damage will be assessed by measuring ulcer index, histological examination and biochemical markers (e.g., myeloperoxidase, malondialdehyde). The antioxidant activity of the extract will also be evaluated. **Results:** Preliminary findings suggest that *Actinidia deliciosa* extract significantly reduces NSAIDs-induced GI damage. It may exert its protective effects through antioxidant properties, inhibition of inflammatory mediators and mucosal barrier enhancement. **Conclusion:** *Actinidia deliciosa* extract shows promise as a potential natural agent for preventing NSAIDs-induced gastric ulcer. Further studies are warranted to elucidate the underlying mechanisms, determine the optimal dosage and administration route.

Keywords: *Actinidia deliciosa*, Antioxidant, Gastric ulcers, NSAIDs, Gastric ulcer, Diclofenac.

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Received: 17-01-2025;
Revised: 27-03-2025;
Accepted: 04-06-2025.

INTRODUCTION

A disruption in the normal integrity of the stomach mucosa that extends through the muscularis mucosa into the submucosa or deeper is referred to as a gastric ulcer. Non-opoidal agents (NSAIDs) are the most prescribed class of drugs and are also commonly used as over-the-counter preparations. Their use as anti-inflammatory, analgesic, antipyretic and, in the case of acetylsalicylic acid, antithrombotic agents make them desirable.[1] Between 15 and 40 percent of all prescriptions are for NSAIDs, according to data from both Indian and international studies. An estimated 30 million individuals use NSAIDs every day and more than 73 million prescriptions are given for them each year. According to research by Paul AD, colleagues in Mumbai, physicians often prescribed NSAIDs, with prescriptions ranging from one to fifteen per day also they prescribe only two to five NSAIDs from the plethora of the NSAIDs. The top medications prescribed by doctors are aspirin, ibuprofen, piroxicam, diclofenac, paracetamol (39.45%) and ibuprofen paracetamol FDC (Fixed Dosage Combination). However, prolonged use of them has been linked to negative effects on the liver, kidney, heart and gastrointestinal tract.[2] It was initially reported that aspirin or salicylic acid could harm the stomach based on gastroscopic observations.[3] According to numerous studies and surveys on the negative effects of NSAIDs, hospitalized patients frequently complain of stomach issues.[4] It is estimated that 1/50 to 1/150 patients are hospitalized each year due to NSAIDs-related digestive distress. The risk of upper GI bleeding is around 1 in 100, 1 in 500 patients of whereas the chances of mortality from alimentary complications is between 1 in 1000 and 1 in 5000 patient years.[5] According to 111 In-labelled leukocyte scanning, about 75% of

DOI: 10.5530/pres.20252087

long-term NSAID users experience mild intestinal irritation, which can last up to 16 months after stopping the medication. Since most of these users do not exhibit any immediate negative effects, they do not exhibit any symptoms.[6,7] Patients with GI problems who were admitted to ten general hospitals in Spain reported a progressive change in their GI status.[8]

Collection of plant

The leaves of Actinidia were collected as shown in Figure 1 from the local market near Shiva Institute of Pharmacy, Bilaspur (H.P) and authenticated at Government College, Khimlasa, Sagar Wide letter number 202345.

Plant Profile

Actinidia deliciosa is a widely spread tropical and sub-tropical broad-spectrum medicinal plant that belongs to the genus Actinidia of family of Actinidiaceae.[9] It is commonly known as Chinese gooseberry; the kiwi fruit is an eatable berry that derives from numerous types of woody vines in the genera Actinidia. It is having many properties including: heart health, digestion, skin health, sleep, immunity, cancer prevention, antioxidants.[10] Plant profile of *Actinidia deliciosa* as shown in below Table 1 are as follows.

Description of the Plant

Leaves of *Actinidia deliciosa* is oval and nearly circular in shape (Figure 1). The size of fruit is typically 2-3 inches long and 13/4-21/4 inches in diameter which is roughly the size of a large hen's egg. *Actinidia deliciosa* is high in Vitamin C and Vitamin K and additionally, it is high in dietary fiber and vitamin E (Figure 1).[12]

Phytoconstituents

Vitamin C: One of the greatest sources of Vitamin C, with a single Kiwi containing roughly 70 mg (100% DV).

Polyphenols: Flavonoids (Quercetin, Kaempferol), phenolic acids (chlorogenic acid, ferulic acid) and anthocyanins.[3]

Fiber: Both soluble, insoluble fiber, containing pectin, hemicellulose and cellulose. Carotenoids: Lutein, zeaxanthin and beta-carotene.

Actinidain: A cysteine protease enzyme with potential anti-inflammatory properties.

Polysaccharides: Arabinogalactans and rhamnogalacturonans with immunomodulatory effects.

Kiwellin: A protein with anti-microbial and anti-fungal activities.[13]

MATERIALS AND METHODS

Distilled water (Shiva Institute of Pharmacy, Laboratory), Methanol, Chloroform (Research Lab SIP), Glacial acetic acid, Ammonia, Hydrochloric acid, Ferric chloride (SIP Laboratory), Methanol, Dragendorff's Reagent, Sodium Hydroxide (SIP Laboratory), Ferric Chloride, Folin Coicalteu Reagent, Toluene, Sodium Carbonate, Gallic acid, Conc. H_2SO_4, Sodium Nitrite, Aluminum Trichloride (SIP Laboratory), Catechin, n-hexane, Ethyl Acetate, Isoflurane, Carboxy Methyl Cellulose, Diclofenac Sod. (SIP Laboratory), Potassium Chloride, Sodium Chloride, Sodium Hydrogen Phosphate (SIP Laboratory). All compounds utilized were analytical grade.

Plant Material and Collections

The leaves of *Actinidia deliciosa* were collected from Bilaspur city, on March 2023. The plant was authenticated by a taxonomist and a voucher specimen (OA/2023052) was deposited at the Government College Khimlasa, Sagar (M.P.). After collection, the leaves were initially washed using running tap water to remove dirt or dust and dried under shade in pharmacology laboratory within the Shiva Institute of Pharmacy. The leaves were then chopped into small pieces manually and ground into coarse powder mechanically using a clean mortar and pestle. The powder sample was weighed and stored in air tight container until extraction.[11]

Extraction of Plant Materials

The powdered plant material prepared using the above procedure was used for extraction process. Briefly, 108 g of the powdered material was evenly packed in a thimble and placed in the Soxhlet device' extractor and defatted by extraction with methanol for 8-10 hr. The defatted material was dried, weight and extracted with methanol at 40-60°C as the solvent until a clear solution was visible in the siphon tube of the soxhlet apparatus. To minimise the volume, the extracts underwent vacuum evaporation concentration after being filtered to eliminate any remaining undissolved material. The leftover solvents were then evaporated over a water bath that was thermostatically heated after the concentrated extracts had been transferred to a 100 mL beaker. The dried extracts were stored in desiccators until used for further investigational procedures.[14] Standard curve of gallic acid and catechin were illustrated in Graphs 4 and 5.

Table 1: Plant profile of *Actinidia deliciosa*.[11]

Kingdom	Plantae
Family	*Actinidiceae*
Class	*Magnoliopsida*
Division	*Magnoliophyta*
Genus	*Actinidiceae*
Species	*deliciosa*

Preliminary Phytochemical Testing

All the extracts were subjected to qualitative phytochemical testing procedures for determining if typical plant secondary metabolites are present or absent showed (Table 4).[15]

Experimental animals and protocol

Wistar rats (aged 4-6 months, weighing 250-300 g) were sourced from the ITM University, School of Pharmacy, Animal House Facility, Gwalior, MP, India. These 30 rats were housed in groups of three in clean polypropylene cages, acclimating for a week prior to the study. The animal facility (Reg. No. SOP/IAEC/23/04) maintained a controlled environment with a 12 hr light-dark cycle, 60±5% relative humidity, 25-30°C temperature and 10% air exhaust conditioning. All procedures adhered to Good Laboratory Practice guidelines set by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA). The rats were provided with ad libitum access to balanced rat diet pellets. The Institutional Animal Ethics Committee approved all experimental protocols (IAEC/2023/04) before the study commenced.

Acute oral toxicity test

Both Aqueous Extract (AQ) and 80% Methanolic Extract (ME) was evaluated for toxicity based on internationally accepted protocol drawn by OECD guidelines-425.[16]

EXPERIMENTAL DESIGN

Preparation of drugs for administration

All the animals were given the doses according to their body weights. Required quantity of diclofenac was suspended in 1% CMC for oral administration. Test drug (MEPA) was also suspended in 1% CMC. Drugs were given in a volume of 0.1 mL/100 g animal and were prepared just before the experiment (1% CMC solution was used as a vehicle).

Induction of Gastric Ulcer

The study model was of 10 days. All the animals were divided into 5 groups:

The experimental groups were subjected to two distinct treatment regimens.

Group 1: The first group, designated as the NC group, received a 1% Carboxymethyl Cellulose (CMC) vehicle solution for a duration of ten days.

Group 2: The second group, labeled as the DCF group, also received the vehicle solution for ten days, but additionally underwent a four-day course of Diclofenac treatment, administered orally twice daily at a dosage of 9 mg per kilogram of body weight. This Diclofenac regimen was initiated on the sixth day and concluded on the tenth day of the experiment.

Groups 3, 4, 5: Groups 3, 4 and 5 were subjected to a 10-day oral treatment regimen with Methanolic Extract of *Actinidia deliciosa* (MEAD) at doses of 200, 400 and 800 mg/kg body weight respectively. MEAD was administered 30 min prior to Diclofenac (DCF) administration. On the 12th hr post-final MEAD dose, rats were anesthetized with isoflurane, blood samples were collected and animals were euthanized via CO_2 asphyxiation. The entire Gastrointestinal (GI) tract was excised, the stomach and small intestinal contents were collected separately. The GI tissues were opened longitudinally, rinsed with Phosphate-Buffered Saline (PBS) and fixed in formalin. To assess the extent of gastric, ulcerative damage, the total length of mucosal lesions in each rat was measured and quantified. The luminal pH of the stomach and small intestine contents was determined using a digital pH meter. To confirm the presence or absence of gastric ulcerative lesions and to evaluate the impact of MEAD on DCF-induced damage, histopathological analysis was conducted. Representative GI tissue sections were processed, stained and examined under a microscope. Microscopic examination allowed for the identification and documentation of any morphological alterations, including inflammatory cell infiltration, mucosal erosion, ulceration and other signs of tissue injury. By comparing

Figure 1: *Actinidia deliciosa.*

the histological findings between the treatment groups, the control group, the protective effects of MEAD on DCF-induced gastrointestinal damage could be assessed.[8]

Changes in Body Weight and Food Intake

When Diclofenac treatment was started on the sixth day, b.i.d., there was a noticeable decrease in the average daily food intake and body weight of the rats in the DC group. The DC group experienced a more severe decline than the other groups, NC, because treatment with a methanolic extract of *Actinidia deliciosa* stopped the decline in food intake and body weight.

Evaluation of Gastrointestinal Damage

Rats administered diclofenac for four days b.i.d. experienced significant abdominal and small intestinal hemorrhage. While the ulcerative lesion indices were 0.00±0.00, 29.33±3.82, 6±3.89 and 2.83±2.98 respectively, the gastric lesion indices in the NC, DC, T-400 and T-800 groups were 0.00±0.00, 17±2.89, 4±3.89 and 2.67±2.82 respectively (Graph 7). In the NC group, no gastric ulcerative damage was seen. The gastric and intestinal lesion index in the DC group was noticeably higher than that of the NC, T-400 and T-800 groups (Still). The methanolic extract of *Actinidia deliciosa* dose-dependently reduced the ulcerative damage caused by Diclofenac, even though there was no significant difference in the intestinal lesion indices of the NC, T-400 and T-800 groups ($p<0.005$).[12]

Effect of Drugs on Gastrointestinal Luminal pH

Gastric and luminal pH significantly decreased after taking diclofenac. The gastrointestinal luminal pH in the DC group was significantly lower than that of the other groups being evaluated ($p<0.05$) (Graph 8). The gastrointestinal pH of NC, T-400 and T-800 was significantly the same ($p<0.05$). This indicates that by preserving the pH of the gastrointestinal lumen, the methanolic extract of *Actinidia deliciosa* dose-dependently reduced the gastric ulcerative damage caused by Diclofenac.

Haematological and Serum Biochemical Parameters

Gastrointestinal bleeding is one of the most dangerous and common side effects of NSAID-induced gastric ulcers. The GI lumen of the DC group showed obvious blood and ulcers, but not that of the NC group. When compared to T-400 and T-800, GI bleeding significantly reduced the DC group's Hb, HCT, albumin and total protein levels ($p<0.05$) (Graph 9). These findings implied that *Actinidia deliciosa* methanolic extract can lessen blood loss and stop the gastric ulcerative damage brought on by DC. Since the study found no increase in the serum level of ALT, the effects of the methanolic extract of *Actinidia deliciosa* were not limited to the stomach and intestine; it also had a positive effect on the liver (no hepatic dysfunction).

Estimation of Lipid Peroxidation

Rats in the DC group had significantly higher MDA levels in their stomach and small intestine than rats in the NC, T-400 and T-800 groups ($p<0.05$) (Graph 10). The GI MDA levels in the NC, T-400 and T-800 groups did not differ significantly ($p<0.05$). According to these findings, the administration of diclofenac caused oxidative damage and inflammation in the stomach and intestinal mucosa, while the methanolic extract of *Actinidia deliciosa* reduced the risk of gastric ulcers.

Histopathological Study

The gastric and intestinal sections of rats in the DC group showed focal erosions of superficial epithelium, epithelial stratification, perforations and basal lamina degeneration, according to histopathological photomicrographs of the GI tissues of the rats (Figures 3 and 4). This histopathological investigation made it clear that taking *Actinidia deliciosa* methanolic extract concurrently with Diclofenac can lessen the gastrointestinal harm that Diclofenac causes.

Statistical Analysis

The data was statistically analyzed using GraphPad Prism 8. The *p*-value for the multiple comparisons of groups was determined using the one-way ANOVA test.

RESULTS

Acute toxicity test

During the 14-day observation period after oral administration of a single dose of 2000 mg/kg, rats did not exhibit any visible signs of behavioral (alertness, restlessness, irritability and fearfulness), neurological (spontaneous activity, reactivity, touch response, pain response and gait), autonomic (defecation and urination), or physical changes (lacrimation, loss of appetite, tremors, hair erection, salivation, diarrhea, or morbidity or mortality. Additionally, during the 2-week follow-up, there was no decrease in the amount of food or water consumed.

Phytochemical analysis of *Actinidia deliciosa*

Actinidia deliciosa's methanolic extract yield was 9.68%. Following standard protocol, a preliminary phytochemical assay of the methanolic extract of *Actinidia deliciosa* showed the absence of alkaloids and saponins but the presence of flavonoids, glycosides, tannins, steroids, terepenoids and phenolic compounds. These constituents' qualitative presence was assessed using TLC and HPTLC, with n-hexane, ethyl acetate and glacial acetic acid as the solvent system (9: 3: 0.3). Subsequent quantitative analysis of the extract's flavonoid and total phenolic content revealed that it contained 0.638 g of quercetin and 71.21 g of gallic acid, respectively. Graphs 1-5 represented phytochemical analysis of extracts.

Phytochemical Fingerprinting by TLC and HPTLC

Concentration of Total Phenolic Compounds

Straight Line Equation: y = bx+c

y=0.0023x+0.0177

x=y-0.0177/0.0023

Concentration Of Flavonoids

Straight line equation: y=bx+c

y=0.0023x+0.0177

x=y-0.0177/0.0023

In vivo Study

Changes in Body Weight and Food Intake

The effects of methanolic extract of **Actinidia deliciosa** and Diclofenac (DC) treatment on the average daily food intake and body weight of rats are shown in Graph 6. After starting twice-daily (b.i.d.) Diclofenac treatment on the sixth day, the DC group's food intake and body weight significantly decreased. In comparison to the Normal Control (NC) group and the groups treated with 400 mg/kg (T-400) and 800 mg/kg (T-800) of the **Actinidia deliciosa** extract, the DC group experienced a significantly greater (p<0.05) steep decline. The DC group's average food intake and body weight continued to decline over the next nine days. On the other hand, the NC group showed an upward trend in daily food consumption and body. In Graphs 6-10 these *in vivo* studies were showed.

Evaluation of Gastrointestinal Damage

Diclofenac administration over a period of 4 days b.i.d resulted in high levels of stomach and small intestinal hemorrhagic damage in rats. Gastric lesion indices in NC, DC, T-400, T-800 groups were 0.00±0.00, 17±2.89, 4±3.89, 2.67±2.82 respectively (Graphs 6-10), whereas, ulcerative lesion indices were 0.00±0.00, 29.33±3.82, 6±3.89, 2.83±2.98 respectively (Graph 7). No gastric ulcerative injury was observed in NC group. In DC group gastric and intestinal lesion index was significantly more than the lesion index of other groups- NC, T-400, T800 (Figure 2). While there was no significant difference between gastric and intestinal lesion indices of NC, T-400, T800 groups, (p<0.005) showing that methanolic extract of *Actinidia deliciosa* dose dependently attenuated Diclofenac induced ulcerative damage.

Effect of Drugs on Gastrointestinal Luminal pH

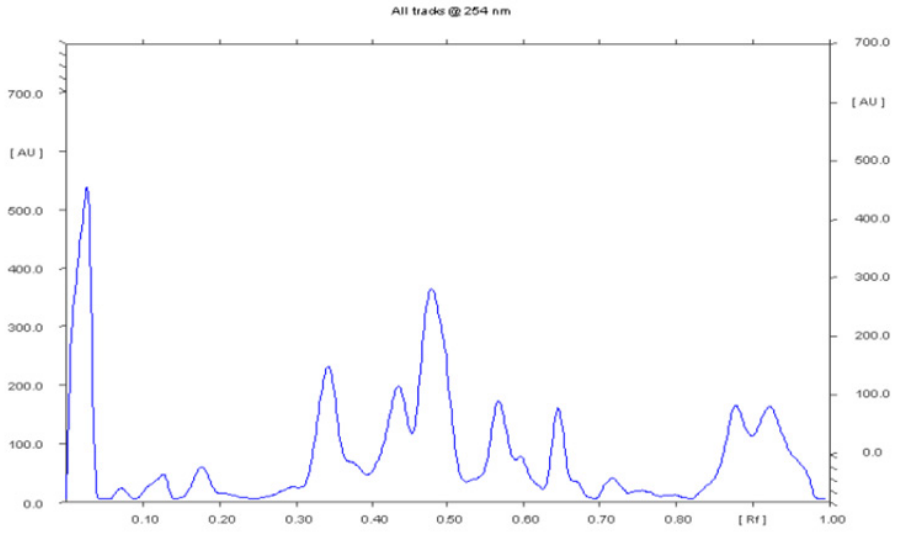
Administration of diclofenac caused a marked decrease in both luminal and stomach pH. When compared to the other groups being evaluated, the gastrointestinal luminal pH in the DC group was significantly lower (p<0.05) (Graph 8). The gastrointestinal pH levels of NC, T-400 and T-800 were significantly identical (p<0.05). This implies that *Actinidia deliciosa* methanolic extract, by preserving the pH of the gastrointestinal lumen, dose-dependently reduced the gastric ulcerative damage caused by Diclofenac. Figure 3 showed ulcerative damage of drugs on different treatments.

Haematological and Serum Biochemical Parameters

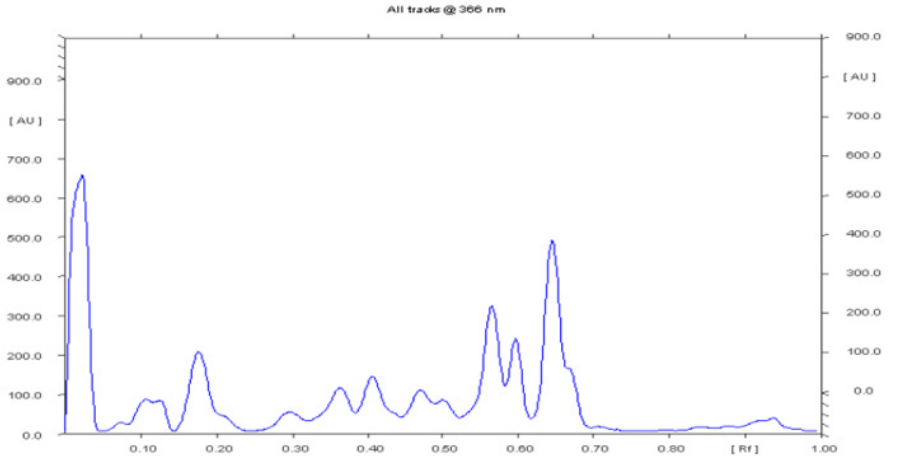
Gastrointestinal bleeding is one of the most dangerous and common side effects of NSAID-induced gastric ulcers. The GI lumen of the DC group showed obvious blood and ulcers, but not that of the NC group. When compared to T-400 and T-800, GI bleeding significantly reduced the DC group's Hb, HCT, albumin and total protein levels (p<0.05) (Graph 7c.4). These findings implied that *Actinidia deliciosa* L. methanolic extract can lessen blood loss and stop the gastric ulcerative damage brought on by DC. The study found no increase in the serum level of ALT, indicating that the methanolic extract of *Actinidia deliciosa* had a

Table 2: Phytochemical Screening of *Actinidia deliciosa*.

Sl. No.	Name of Test	Procedure	Observation	Inference
1	Test for Phenolics	Extract (1 mL) + $FeCl_3$ (few drops)	Greenish Yellow Colour	Phenolics present
2	Test for Flavonoids	Extract (1 mL) + 10% NaOH	Reddish orange colour	Flavonoids present
3	Test of Alkaloids	Extract (1 mL) + Dragendorff's Reagent	-	Alkaloids absent
4	Test for Saponins (Foam Test)	Extract (1 mL) + water	No foam observed	Saponins Absent
5	Test for Glycosides	Extract (1 mL) + water + 10% NaOH	Greenish Yellow Colour	Glycosides Present
6	Test for Tannins	Extract (1 mL) + $FeCl_3$ + water	Green Colour	Tannins Present
7	Test for Steroids/Terpenoids	Extract (1 mL) + $CHCl_3$ (1 mL) + H_2SO_4 (1 mL). Shake and allow to stand.	Reddish brown colour	Steroids/terpenoids absent



Graph 1: Qualitative Analysis of Phytoconstituents present in Methanolic extract of *Actinidia deliciosa* using HPTLC under CAMAG HPTLC system at 254 nm. Solvent used: n-Hexane: ethyl acetate: glacial acetic acid (9:3:0:3).



Graph 2: Qualitative Analysis of Phytoconstituents present in Methanolic extract of *Actinidia deliciosa* using HPTLC under CAMAG HPTLC system at 366 nm. Solvent used: n-Hexane: ethyl acetate: glacial acetic acid (9:3:0:3).

beneficial effect on the liver (no hepatic dysfunction) in addition to the stomach and intestine.

Estimation of Lipid Peroxidation

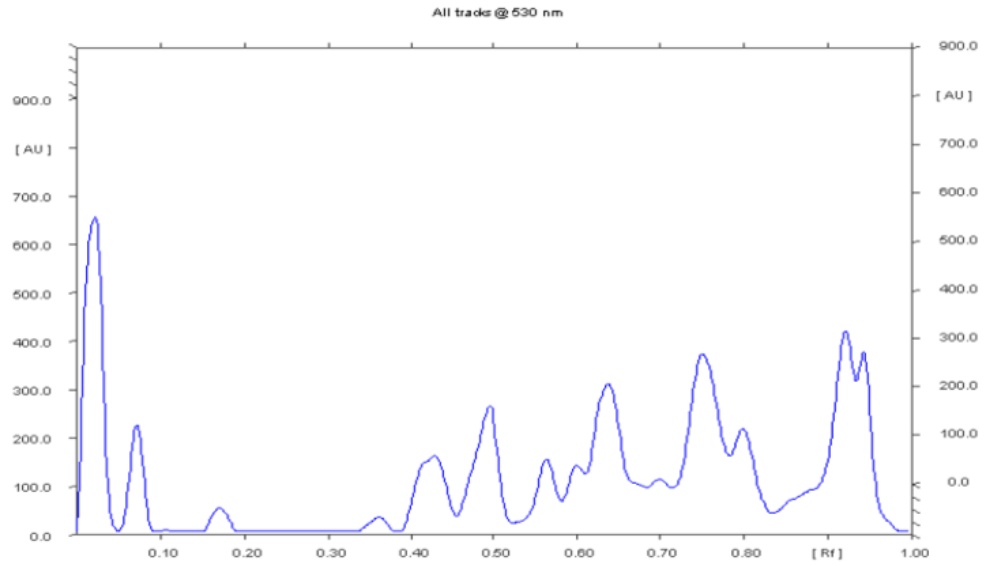
When compared to the NC, T-400 and T-800 groups, the rats in the DC group had significantly higher MDA levels in their stomachs and small intestines ($p<0.05$) (Graph 7). The NC, T-400 and T-800 groups' GI MDA levels did not differ significantly ($p<0.05$). These findings implied that the administration of diclofenac caused oxidative damage, intestinal mucosal inflammation and a methanolic extract of *Actinidia deliciosa* that reduced the risk of gastric ulcers.

Histopathological study

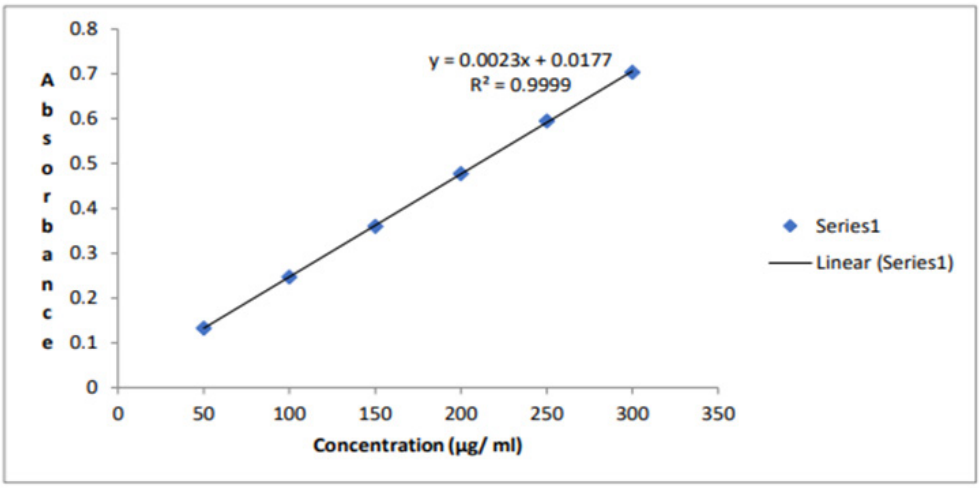
The gastric and intestinal sections of rats in the DC group showed focal erosions of superficial epithelium, epithelial stratification, perforations and basal lamina degeneration, according to histopathological photomicrographs of the GI tissues of the rats (Figure 4). This histopathological investigation made it clear that taking *Actinidia deliciosa* methanolic extract concurrently with Diclofenac can lessen the gastrointestinal harm that Diclofenac causes.

DISCUSSION

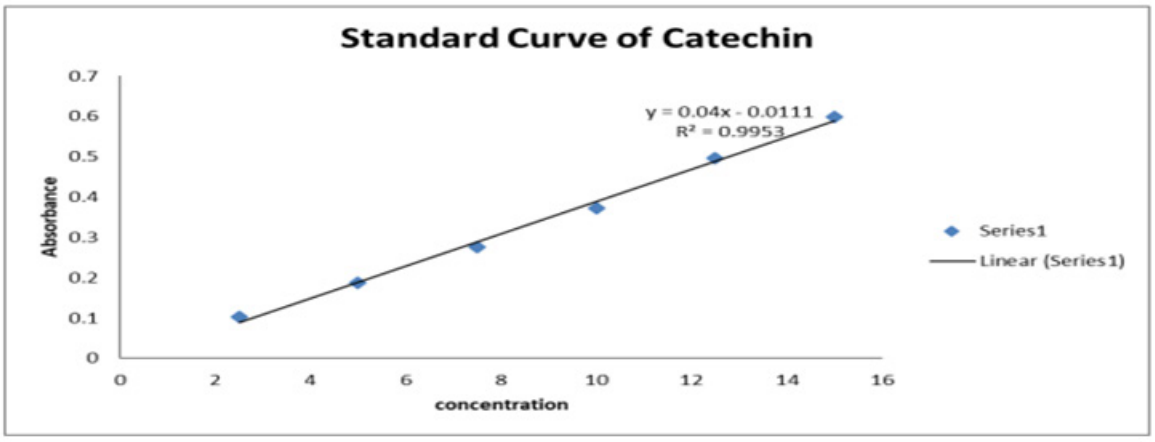
In the treatment of inflammatory, analgesic, antipyretic and antithrombotic (acetylsalicylic acid in low dose) conditions, patients take NSAIDs, the most popular class of medications.



Graph 3: Qualitative Analysis of Phytoconstituents present in Methanolic extract of *Actinidia deliciosa* using HPTLC under CAMAG HPTLC system at 530 nm. Solvent used: n-Hexane: ethyl acetate: glacial acetic acid (9:3:0:3). Phytochemical Qualitative Analysis Using Hptlc (High Performance Thin Layer Chromatography).



Graph 4: Standard Curve of Gallic Acid.



Graph 5: Standard Curve of Catechin.

Table 3: R_f values of Different Phytoconstituents.

Sl. No.	Peak No.	R_f values		
		254 nm	366 nm	530 nm
1.	1	0.03	0.03	0.01
2.	2	0.06	0.08	0.06
3.	3	0.12	0.11	0.11
4.	4	0.17	0.17	0.38
5.	5	0.31	0.27	0.43
6.	6	0.33	0.35	0.48
7.	7	0.41	0.40	0.65
8.	8	0.47	0.46	0.62
9.	9	0.56	0.51	0.63
10.	10	0.61	0.56	0.72
11.	11	0.66	0.61	0.74
12.	12	0.71	0.66	0.82
13.	13	0.87	0.72	0.91
14.	14	0.92	0.93	0.93

Table 4: Absorbance of Gallic Acid.

Sl. No.	Concentration (µg/mL)	Absorbance at 750 nm			Mean Absorbance
1	50	0.123	0.144	0.312	0.132
2	100	0.242	0.252	0.248	0.248
3	150	0.356	0.362	0.363	0.361
4	200	0.475	0.477	0.476	0.476
5	250	0.597	0.598	0.592	0.596
6	300	0.692	0.703	0.716	0.703

Table 5: Concentration of Total Phenolic Compounds.
Estimation of Flavonoids

Plant Extract (methanolic)	Absorbance			Mean Absorbance	Concentration (w/w)			Standard Deviation	Mean Concentration
Actinidia deliciosa	0.325	0.378	0.405	0.367	30.47	30.47	30S.47	3.6	71.13

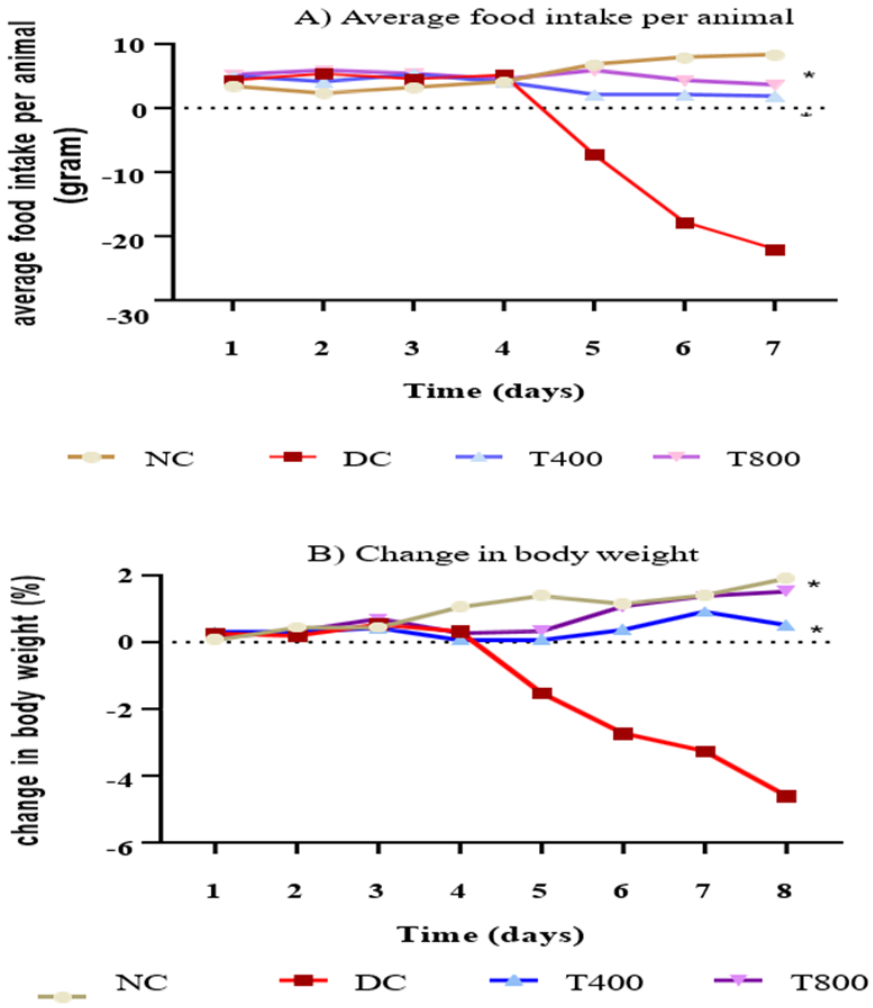
Table 6: Absorbance of Catechin.

Sl. No.	Concentration	Absorbance at 510			Mean
1	2.6	0.103	0.107	0.103	0.103
2	5.3	0.184	0.186	0.195	0.191
3	7.4	0.268	0.287	0.281	0.292
4	11.1	0.381	0.383	0.362	0.372
5	13.3	0.482	0.504	0.488	0.400
6	16.1	0.588	0.607	0.596	0.500

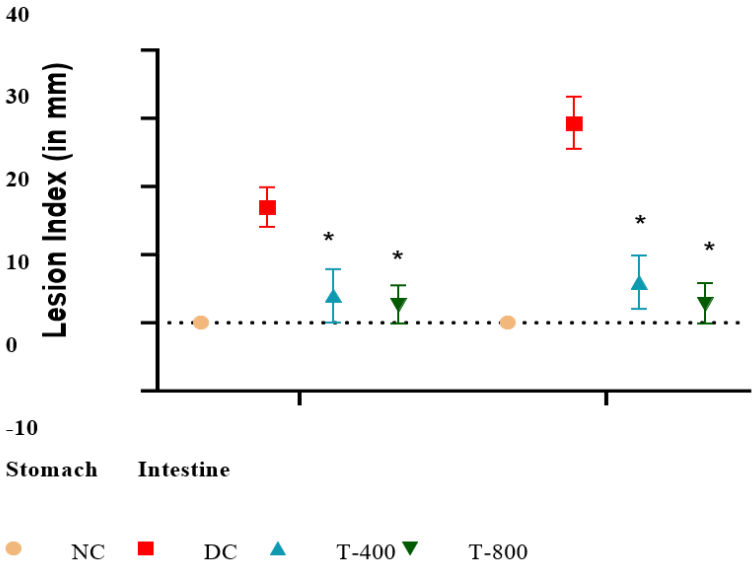
PPIs or H2RAs are recommended for patients to lower their risk of bleeding and stomach ulcers brought on by NSAIDs. Although this method is logical, it is dubious as a means of achieving positive results in the small intestine.[17] Recent developments in endoscopic procedures, such as capsule and double balloon endoscopy, have shown that NSAID-induced small intestinal ulcerations in people are more common and more severe than gastropathy.[13] There are currently no approved therapeutic approaches to stop ulcerative damage caused by NSAIDs. Therefore, it's critical to identify the best therapeutic approaches that are both GI safe and effective in preventing the ulcerative and gastric damage caused by NSAIDs. Therefore, the scientific community is searching for a medication or combination of medications that could stop NSAID enteropathy and the clinically significant worsening of ulcerative lesions caused by NSAIDs by antisecretory drugs.[14] Great results have been obtained from the use of medicinal plants in traditional medical systems for the management or treatment of illnesses, indicating that herbal remedies may be useful in the treatment of a variety of illnesses and conditions. A significant percentage of people worldwide have been persuaded to switch to this alternative medical approach due to its accessibility, affordability and capacity to cause minimal side effects when taken. Furthermore, several studies have indicated that medicinal plants use multi-target strategies, which reduce

Table 7: Concentration of Flavonoids.

Plant Extract (methanolic)	Absorbance			Mean Absorbance	Concentration (w/w)			Standard Deviation	Mean Concentration
Actinidia deliciosa	0.243	0.238	0.251	0.244	0.635	0.623	0.655	0.02	0.638



Graph 6: The effects of various treatments on rats' body weight in different groups and (A) average food intake. Rats' average daily food intake and body weight decreased the most in the DC group when compared to the NC, T-400 and T-800 groups. The NC, T-400 and T-800 groups did not significantly correlate with one another ($p<0.05$). Mean±SD is used to express the data ($n=6$).



Graph 7: The impact of different treatments on the rats' gastrointestinal lesion index across different groups. The DC group's gastricularative lesion index was significantly higher than that of every other group evaluated (*p<0.05). The GI lesion indices of the NC, T-200 and T-800 groups did not differ significantly, suggesting that the *Actinidia deliciosa* extract considerably reduced the gastrointestinal damage brought on by diclofenac. The data is presented as mean±standard deviation (n=6).

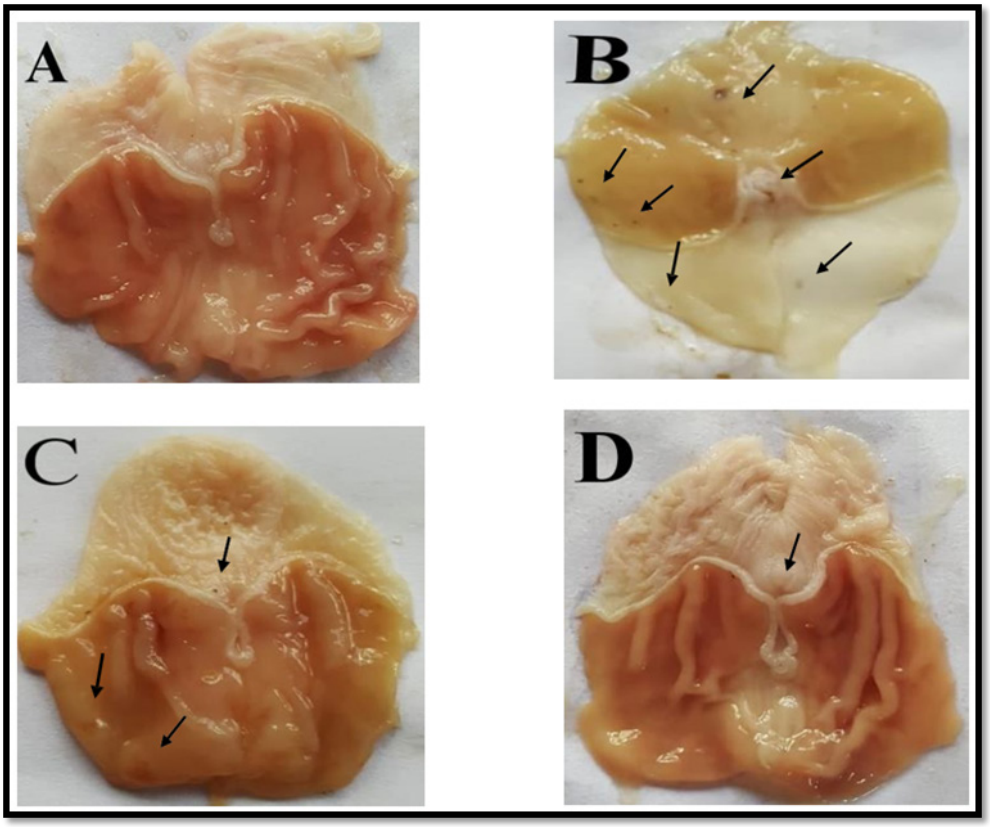
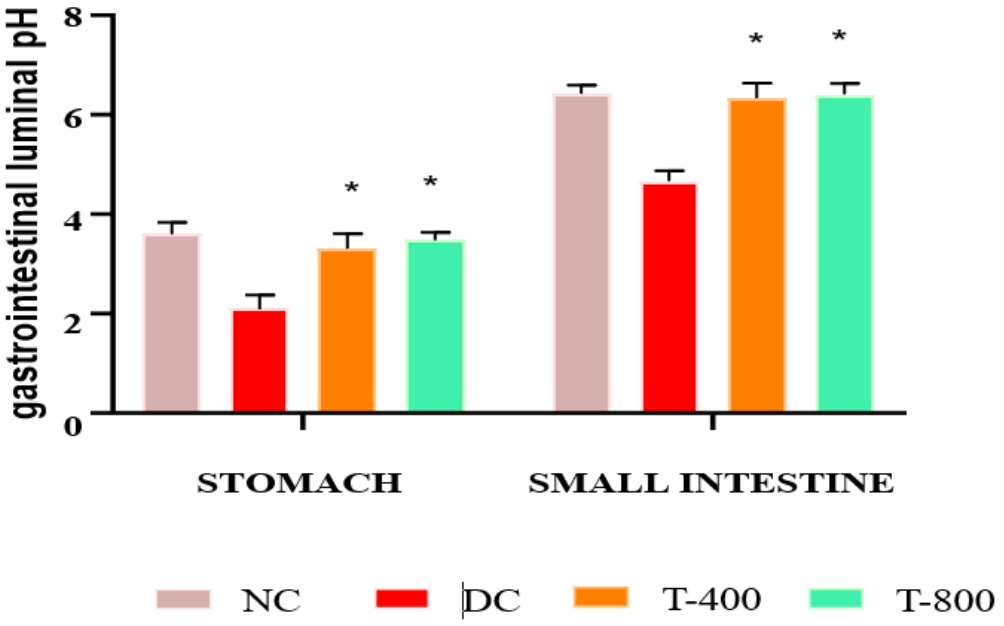
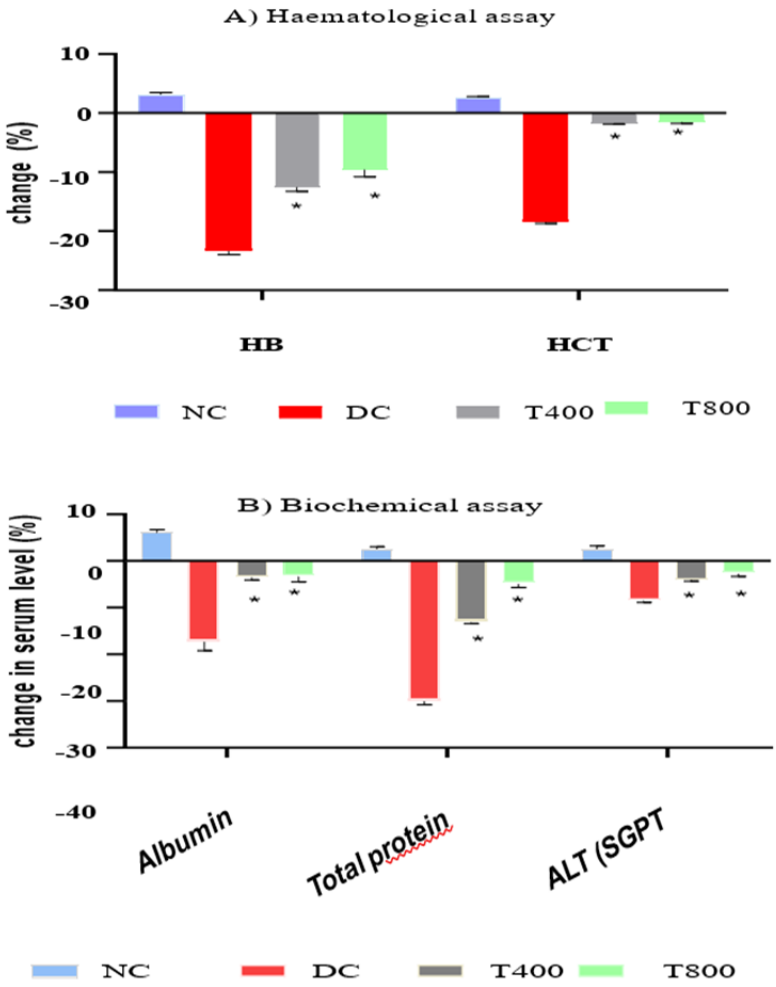


Figure 2: Macroscopic assessment of gastropathic damage across treatment groups (illustrative pictures) (A) NC (B) DC (C) T-400 (D) T-800. When DC was administered twice daily for five days at a dose of 9 mg kg-1, it caused significant hemorrhagic damage to both the small intestine and stomach. Gastricularative damage was attenuated in a dose-dependent manner when DC and CUR were administered together. Hemorrhagic damage is indicated by arrows (n=6).

Figure 3: The observation of ulerative damage under a microscope in different treatment groups (representative images). (A) T-400; (B) DC; (C) T-800. DC treatment for five days (9 mg kg-1 twice daily) caused significant hemorrhagic damage to the small intestine and stomach. The attenuation of gastricularative damage was dose dependent when DC and CUR were administered together. Damage from hemorrhage is indicated by arrows (*n*=6).



Graph 8: The impact of different treatments on the rats' gastrointestinal luminal pH across different groups. The GI luminal pH was markedly raised when *Actinidia deliciosa* extract and Diclofenac were administered together, dose dependently. The GI luminal pH of the DC group was significantly lower than that of the NC, T-400 and T-800 groups, as well as the intestinal luminal pH of the rats in the NC group ($p<0.05$). Furthermore, the rats in the T-400 and T-800 groups had significantly higher gastric luminal pH values than the NC group ($p<0.05$). Nevertheless, the intestinal luminal pH of the NC, T-400 and T-800 groups did not differ significantly and the data was presented as mean±S.D (*n*=6).



Graph 9: The impact of different treatments on rats' (A) haematological and (B) serum biochemical parameters across different groups. When diclofenac was administered, serum levels of albumin, total protein, Hb and HCT levels significantly decreased in comparison to all other groups ($p<0.05$). The DC group's haematological and biochemical parameters declined more than those of the NC, T-400 and T-400 groups' rats ($p<0.05$). The NC T-400 and T-800 groups' levels of Hb, HCT, serum albumin and total protein did not, however, differ significantly. The data ($n=6$) is presented as mean±S.D.

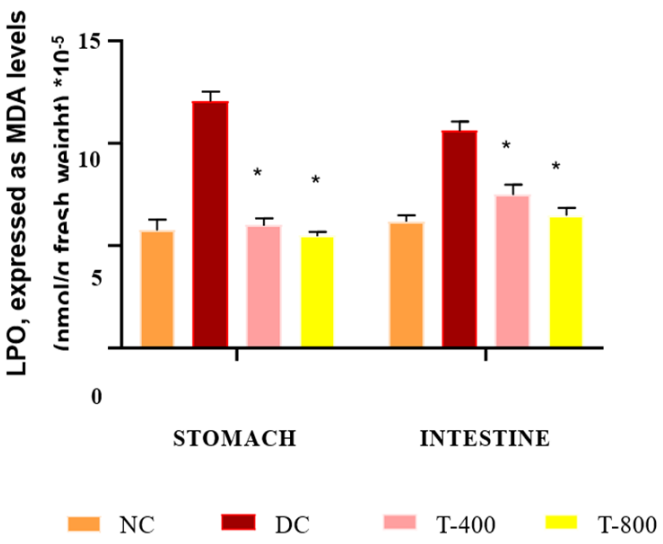
the likelihood of treatment failure. Numerous phytoconstituents that have been extracted from plants have proven to be effective anti-inflammatory, gastroprotective and antioxidant agents. These compounds are also commonly used to treat stomach ulcers. Chinese gooseberry, or *Actinidia deliciosa*, is a well-liked medicinal plant. It has been widely used historically to treat a number of conditions, such as inflammation, hepatoprotection and gastroprotection.[15] In both *in vitro* and *in vivo* tests, the plant extract demonstrated outstanding antioxidant and anti-inflammatory properties.[11] It is anticipated that the plant has significant anti-gastric ulcer activity based on the literature review conducted on the plant's known activities. to assess *Actinidia deliciosa* extract's effectiveness in treating gastric ulcers brought on by NSAIDs. As indicated in Table 2, phytochemical screening of the methanolic extract of *Actinidia deliciosa's* aerial parts revealed the presence of phenols, flavonoids, triterpenoids, tannins, glycosides and steroids.

Phytochemical fingerprinting

The methanolic extract's TLC and HPTLC analysis revealed several bands when viewed at different wavelengths, including 254 nm, 366 nm and 530 nm (Figure 5, Graphs 1-3). Numerous peaks and areas under HPTLC analysis were also found in a related study by Awasthi *et al.*, and Rakhi *et al.*, indicating the presence of several distinct phytoconstituents in the extract.

Total phenolics estimation by Photometry

A significant amount of phenolics was found in the plant extract, according to photometric estimation (Table 3). Estimation of total flavonoids by using photometry. A significant amount of flavonoids was found in the plant extract according to photometric estimation (Table 7). Rats in this study experienced significant gastric ulcerative damage after receiving oral Diclofenac for four days. It was observed that pretreatment with *Actinidia deliciosa* methanolic extract reduced the gastric ulcerative damage caused by Diclofenac in a dose-dependent manner. Changes



Graph 10: In the Gastrointestinal (GI) tissues of rats from various experimental groups, the study investigated the impact of different treatments on Lipid Peroxidation (LPO), specifically measured as Malondialdehyde (MDA) levels. According to the results, the Diclofenac (DC) group had significantly higher intestinal and gastric MDA levels than any other group ($p<0.05$), suggesting that Diclofenac treatment significantly increased lipid peroxidation. In contrast, there were no discernible variations in the GI MDA levels between the groups treated with 400 mg/kg of the extract (T-400), 800 mg/kg of the extract (T-800) and the Normal Control (NC) group. For each group, the data are shown as the mean±standard deviation (S.D.) for 6 rats.

in food intake and body weight. The DC group experienced a symbolic decrease in food intake and body weight throughout the study. At doses of 400 and 800 mg/kg body weight, as shown in (Graph 6), *Actinidia deliciosa* methanolic extract, however, inhibited the decrease in body weight and average food intake in Diclofenac-induced gastric ulcerative rat models.

Changes in haematological and serum biochemical assay

There is evidence that NSAIDS increase the risk of gastrointestinal bleeding.[15] Hb, HCT, serum albumin, serum total protein and serum levels all decreased in this study. In order to assess the effectiveness of *Actinidia deliciosa* extract in NSAID-induced gastric ulcers, ALT was observed in the DC group, suggesting that the small intestine is the primary site of GI bleeding. Both the T-400 and T-800 groups demonstrated that methanolic extract of *Actinidia deliciosa* prevents gastric ulcerative damage and displayed slight changes in hematological and biochemical analysis (Graph 9).

Evaluation of gastrointestinal luminal pH

Analysis of the effects of drug treatments in different groups on GI luminal pH was done in light of the fact that acid has been found to be a significant factor in the pathophysiology of

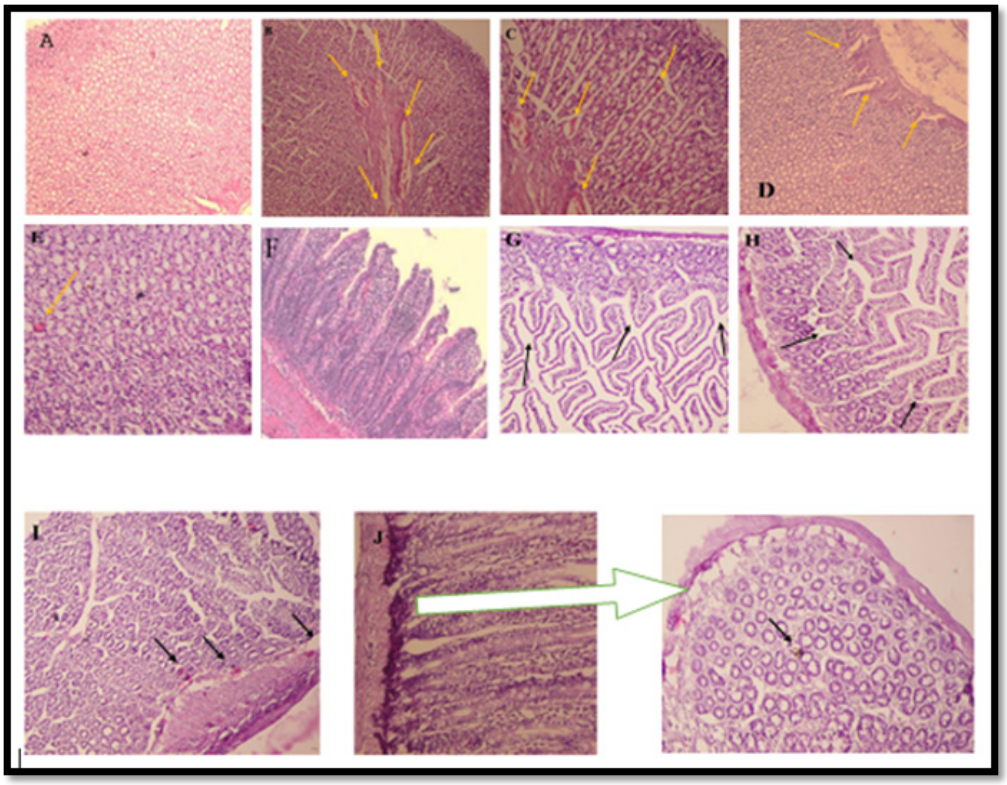


Figure 4: Microscopic analysis of representative histological sections of the small intestine and stomach of rats in various treatment groups, arranged from F to J (intestine) in the following order: NC, DC, T-200, T-400 and T-800, respectively. sections of the stomach and intestines stained with H&E and magnified 10 times. Histology of the intestinal sections of rats in the DC and T-200 groups showed neutrophil infiltration, perforations, basal lamina degeneration, focal erosions of the superficial epithelium and epithelial stratification. Administration of *Actinidia deliciosa* extract reduced the dose-dependent gastric damage caused by Diclofenac. Mucosal erosions and ulceration are indicated by arrows ($n=6$).

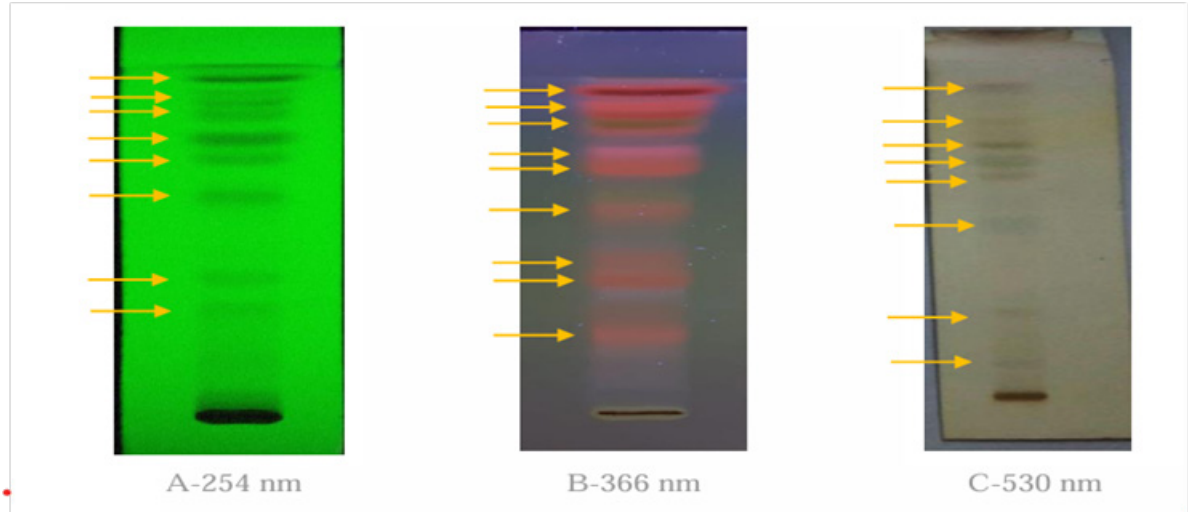


Figure 5: Qualitative Analysis of Figure Phytoconstituents present in Methanolic extract of *Actinidia deliciosa* using TLC Bands under UV/visible Spectrophotometer at 254 and 366 nm and 530 nm respectively. Solvent used: n-Hexane: ethyl acetate: glacial acetic acid (9:3:0:3).

NSAID gastropathy and that changes in gut pH may also affect NSAID enteropathy by changing the composition of the gut microbiota. The luminal pH of the stomach and the intestines was significantly lowered by the administration of Diclofenac alone. Co-administration of *Actinidia deliciosa* methanolic extract and Diclofenac, however, eliminated the effects of NSAIDs on the intestinal luminal pH in the T-400 and T-800 groups while leaving the gastric luminal pH unchanged when compared to the DC group (Graph 8).

Lipid peroxidation estimation

The most mutagenic byproduct of lipid peroxidation is MDA, which is produced when lipid hydroperoxides break down. When evaluating the role of free radicals in damaging membranes, MDA levels are helpful because they show damage caused by these free radicals. It was shown that giving diclofenac raised the amount of MDA in the GI tissues. Nevertheless, the T-400 and T-800 groups' GI MDA levels were significantly lowered when *Actinidia deliciosa* methanolic extract and diclofenac were administered together (Graph 10). Increased MDA levels have been correctly linked to increased Reactive Oxygen Species (ROS) in GI tissues, which may lead to mitochondrial dysfunction, inflammation of the epithelial barrier and increased intestinal permeability. It has been correctly identified as a major contributor to the etiopathogenesis of NSAID-induced GI damage. Enhanced IP may expose the already stressed, ulcerated GI mucosa to harmful agents like bile, bacteria and NSAIDs, resulting in severe GI damage. One thing to note, though, is that even though pharmacodynamically it seems like there isn't a problem with herb-drug interactions and histological evidence backs up this opinion, more research is necessary given the potential complications that could result from pharmacokinetic herb-drug interactions. to assess the extract from *Actinidia deliciosa's* ability to prevent gastric ulcers caused by NSAIDs.

CONCLUSION

Actinidia deliciosa aerial's pharmacological and phytochemical analysis verifies the plant's legitimacy. MOLE was found to have an extractive value of 9.68%. Upon evaluation, several classes of phytoconstituents that were separated from *Actinidia deliciosa* demonstrated strong anti-oxidant, anti-inflammatory, anti-tumor, gastroprotective and hepatoprotective properties. The phytochemical analysis of the methanolic extract of *Actinidia deliciosa* in this study revealed the presence of triterpenoids, flavonoids, glycosides, tannins and phenolic phytoconstituents (Figure 5). 14 peaks can be seen under 254, 366 and 530 nm in the HPTLC fingerprint profile of the methanolic extract of *Actinidia deliciosa* leaves (Tables 5 and 6). Chromatograms under 254 nm, 366 nm and 530 nm had corresponding R_f values in the range of 0.03-0.92, 0.02-0.94 and 0.02-0.94 (Table 2). Total phenolic in MOLE was estimated to be 71.12 g, or the equivalent of gallic acid. According to Tables 3 and 7, the estimated total flavonoids were 0.638 g of catechin equivalent. The current investigation's initial pharmacological studies demonstrated that the extract of *Actinidia deliciosa* and all of its parameters have anti-inflammatory, anti-oxidant and gastroprotective properties. In rats, the methanolic extract of *Actinidia deliciosa* showed protection against gastrointestinal damage brought on by diclofenac. The extract's complex mechanisms of action are probably what cause this protective effect. The extract was effective in reducing the effects of diclofenac on changes in intestinal permeability brought on by oxidative stress, lipid peroxidation, gastrointestinal blood loss and changes in gastric luminal pH.

ACKNOWLEDGEMENT

I would highly like to thank and appreciate all my students and colleagues that have helped me throughout this project without which I would not have completed this project. With extreme pleasure, I would also like to thank my colleagues Ms. Manisha Dhiman, Ms. Arushi, Ms. Anshul, Ms. Risha and Ms. Seema for their continued support throughout this experiment. I would like to thank my students Nidhika and Prince that have helped me throughout with the documentation as well as experimentation of this project.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs; **HPTLC:** High Performance Thin Layer Chromatography; **ANOVA:** Analysis of Variance; **FC:** Folin-Ciocalteu's; **COX;** Cyclooxygenase.

AUTHOR'S CONTRIBUTIONS

AC, AS, PS, SD performed whole experimental procedures. All authors read and approved the final manuscript.

SUMMARY

A common side effect of nonsteroidal anti-inflammatory drugs, gastric ulcers caused by NSAIDs are discussed in this response. It describes risk factors, clinical signs, prevention techniques and the mechanisms underlying GI damage. Through the inhibition of prostaglandins, direct damage to the mucosa and an increase in oxidative stress, NSAIDs can result in gastrointestinal harm. Age, GI issues in the past, high NSAID dosages and concurrent medication use are risk factors. From minor stomach discomfort to severe bleeding, symptoms can vary widely. Lower doses of NSAIDs, selective COX-2 inhibitors, taking NSAIDs with food, proton pump inhibitors, abstaining from alcohol and quitting smoking are some prevention techniques.

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Cite this article: Chaudhuri A, Arushi, Dhiman M, Thakur A, Kumari R, Devi S, *et al*. Pharmacological Investigation of *Actinidia deliciosa* Extract in NSAIDs Induced Gastric Ulcer in Rodent Model. Pharmacog Res. 2025;17(3):801-15.