

PHARMACOLOGICAL INVESTIGATION FOR ANTI-ULCER ACTIVITY OF *TERMINALIA CORIACEA* EXTRACT USING ANIMAL MODELS

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Abstract: The following study project illustrates the gastro-protective impact of *Terminalia coriacea* on aspirin-induced rat model ulcers. In both pylorus binding rats and gastric ulcerogenesis, the gastroprotective effects were contextual. The protective operation was correlated with the decrease in the gastric ulcer reports, gastric emissions and sharpness and exacerbation by NF- κ B inhibition, neutrophil identification and ROS decline due to its antioxidant properties.

Aspirin treatment, caused completely the frequency of gastric ulcerations. The combination of decided measures has no extra pain relief impact on its stratified components because the combination of TCFE medicinally induced with aspirin has an extra pain relief impact on aspirin alone and is not proved to be ulcerative.

Keywords: gastric ulcerations, *Terminalia coriacea* extract and Aspirin.

INTRODUCTION

Peptic ulcers are inferable to the inconsistency between causes which will influence the GIT mucous gastro-duodenal lining and the damage confining security components. Gastric juice (counting hydrochloric corrosive, pepsine and twofold flux bile salts), H-pylori, and NSAIDs are the hostile causes. Wrench security includes an atomic coating of bicarbonate Emitted by the surface bodily fluid cells that shape a gooey liquid over the gastric mucosa; the quality of the close interfacing between neighboring epithelial cells; and the compensation stage, through which a neighboring epithelial and mucosal stromal cells relocated quickly to fill a void and straightened them. Reasonable blood sources, as well as shaping within the stomach mucosa, depend on mucosal protections. Present day medication hence has the same hypothesis for peptic ulcer from the over physiologic prove, in which H pylori and NSAIDs play the key part. The pathogenesis of PUD is additionally questionable, in spite of the fact that. A few discoveries show that numerous causes, counting corrosive, swelling, or muscle fit, can be related to ulcer torment pathogenesis. Numerous causes, just like the composition of regular diets, are gathered to advance the release of gastric corrosive by distinctive exercises, such as cigarette admissions, lager, tea, coffee, betel nut, and fiery nourishments. PUD people are exceedingly at hazard of creating complications such as GH, puncturing and obstacle; mortality of such complications is extreme. PUD people are profoundly at hazard of death. In the cutting edge restorative world, the control and care of PUD is very relevant.

Plant Profile

Terminalia coriacea



Family Combretaceae.

Habitat Western Andhra Pradesh and Central India.

English Leathery Murdah.

Folk Tani (Andhra Pradesh)

Leathery Murdah, *Terminalia coriacea* (Roxb.) Wight and Arn. Having a place to the Combretaceae family is found in dry and warm parts of Andhra Pradesh and Tamil Nadu in India. In conventional pharmaceutical, the plant is utilized as cardiac stimulant and to treat atonic loose bowels, insensible ulcers, and incendiary conditions. Later pharmacological examinations on the methanolic extricate of *T. coriacea* clears out uncovered antinociceptive, wound mending, anticonvulsant, anti-ulcer, and hepatoprotective possibilities.

AIM & OBJECTIVES:

AIM: Chemical evaluation & Pharmacological examination of dried fruit powder of Terminalia coriacea antiulcerogenic operation Formulation of gastric ulcer.

OBJECTIVES:

1. Material analysis and verification.
2. Evaluation of ethanol extracted from organic plants against ulcers.
3. Screening of the ethanol dissolved structured Chemical
4. To evaluate the potency in research animals of extracted formulation.
5. To track intervention against ulcers in performing rats.
6. Histopathological analysis should be decided regarding the stomach and parameter measurement such as the ulcer inventory, the impact on preservation of ulcer, and the decreased stomach length.

MATERIALS & METHODS:

1. Collection of material: The extricate is ready by Maceration Method. The extricate is macerated with ethanol (99.9%) for 7 days and after that is sifted. The filtrate is vanished to get dried extricate.

MACERATION:

The powdered natural product is kept in contact with the dissolvable ethanol in proportion of 1:2 and incredible shaking is carried out, after 7 days, the extricate is sifted out at that point it is subjected to drying.

Preparation of dose: Little examining of the extricate definition was performed for administrating to the rodent.

Chemicals used: NSAIDS-example ibuprofen utilized as a toxicant; omeprazole as a common easygoing; filtered water, 10 percent formalin-as additive; anesthetic chloroform.

Acute toxicity studies: A solid sound-related, harmful check, as characterized by the Organization of Money related Co-operation and Advancement, agreeing to the controls, will be decided on secure verbal estimations of depleted homes. In arrange to avoid coprophagy, they are set exclusively in apportioned cages with wide wired feet within the to begin with put. They must be fasted at this organize overnight (but require water) some time recently dosing. After this expansion of the remove measurements so that the determination of extend animals is as it were doable.

The programs have been following the generation of restorative (or toxicological) side impacts for 48-72 hours after amassing and searching for the side effects of hurtfulness and mortality. [8]

PRELIMINARY PHYTOCHEMICAL SCREENING:

Standard screening tests of the plants extricate will be carried out for different plants constituents. The unrefined extricates are screened for the nearness and nonappearance of auxiliary metabolites such as Alkaloids, steroids, phenols, flavanoids, saponins, glycosides, terpenoids, tannins and antraquinone etc.

EXPERIMENTAL ANIMALS:

The test ponders will be carried out at Shadan college of Pharmacy, Hyderabad, rats (180-250gms) of either sex housed in standard conditions of temperature ought to be (24-27°C) or light (12 hours light/dark cycles) is set. Creatures ought to be nourished with standard pellet count calories and water advertisement libitum. Creatures are haphazardly chosen for gathering. All tests are to be performed concurring to the shapes of moral conditions (CPCSEA)⁵.

CHEMICALS AND REAGENTS:

- Distilled water - as solvent to dissolve the test and standard drugs.
- Omeprazole² - standard drug for ulcer
- Aspirin - standard drug for inducing ulcer
- Ethanol 99% v/v - preparation of plant extract

EXPERIMENTAL DESIGN: The rats will be haphazardly separated into 6 bunches (n = 6) for each of the 2 models utilized within the study. Each rodent within the particular gather gotten typical Distilled water (control), or Omeprazole 20 mg/kg (reference standard), TCFE 125, 250, 500gm p.o for 7 days.

GROUPS	DRUGS	DOSES
GROUP 1	Distilled water	1ml/kg-p.o
GROUP 2	Control	500mg/kg-p.o
GROUP 3	Control + standard drug	20mg/kg-p.o
GROUP 4	Control +TCFE	125mg/kg-p.o
GROUP 5	Control +TCFE	250mg/kg-p.o
GROUP 6	Control + TCFE	500mg/kg-p.o

SCREENING METHODS:**A) INVIVO MODELS:****1. PYLORUS LIGATION IN RATS⁸:**

This strategy was portrayed by Shay et al. The premise for this demonstrate is that aggregation of unbuffered gastric juice over a certain length of time leads to peptic ulceration in rats whose pylorus will be ligated.

GROUPS	DRUGS	DOSES
GROUP1	Distilled water	1ml/kg-p.o
GROUP2	Control	150mg/kg-p.o
GROUP3	Control + standard drug	20mg/kg-p.o
GROUP4	Control +TCFE	125mg/kg-p.o
GROUP5	Control +TCFE	250mg/kg-p.o
GROUP6	Control + TCFE	500mg/kg-p.o

PROCEDURE: Wistar rats (150 to 200g) will be utilized for the try. The creatures will be fasted for 48hrs some time recently the agent method. Be that as it may, they will be given free get to to water advertisement libitum. To avoid cannibalism and coprophagy, the creatures will be housed separately in cages with raised bottoms of wide wire work. Beneath ether anesthesia, one-inch midline stomach entry point is given underneath the xiphoid handle. The pylorus will be carefully lifted out with negligible taking care of and footing and ligated without harming its blood supply. The stomach will presently be supplanted and the stomach divider closed with sutures. The test compound will be managed either orally or subcutaneously and the creatures will be put in plastic barrels. Approximately 17-19hrs after pyloric ligation, the creatures will be yielded and the stomach dismembered out. The substance of the stomach will be depleted into a graduated centrifuge tube and their causticity decided by titration with 0.1N NaOH. The stomach will be opened along its more noteworthy ebb and flow, stuck on a plug plate and internal surface inspected for ulceration with a binocular magnifying lens. The ulcer list will be calculated and ulcer seriousness evaluated as specified underneath.

Ulcer severity is graded as:

0-No Ulcer, 1-Superficial ulcer, 2-Deep ulcer, 3-Perforation

The ulcer index (U_i) is calculated by the following equation:

$$U_i = U_N + U_S + U_P \times 10^{-1}$$

Where U_N = Average of number of ulcer/animals; U_S =Average of severity scores;

U_P = Percentage of animals with ulcers.

Ulcer index and acidity of gastric content of the treated animals will be compared with the control.

2. GASTRIC ULCER-INDUCTION BY ETHANOL:

The try will be performed agreeing to the strategy of Morimoto et al 10. After 12 hour of fasting, the rats will be haphazardly separated into six bunches of six creatures each. To begin with bunch will be given 1ml of vehicle (Distilled water), and the moment bunch will be treated with Omeprazole 20 mg/kg. bunch III (control) IV, V, VI gotten ethanolic extricate (125,250mg/kg, 500mg/kg), individually.

All the medicines will be managed orally. One hour after treatment, all the rats will get 1ml of 99.5% ethanol to initiate gastric ulcer. One hour afterward, the creatures will be yielded by cervical disengagement, and the stomach evacuated and opened along the more noteworthy ebb and flow. The stomachs will be delicately flushed with water to expel the gastric substance and blood clots, for consequent checking. The ulcers will be classified as – Ordinary stomach, 1- spot ulceration, 1.5- Hemorrhagic streaks, 2- Ulcer.

B) INVITRO MODEL:**1) H⁺/K⁺ - ATPase Inhibition Activity:**

Proton potassium ATPase will be arranged from mucosal scrapings of rodent will be decided as por detailed strategy. Stomachs of solid rats will be washed delicately with tap water. The mucosal layer of fundus will be rejected and homogenized in ice-cold phosphate buffer, pH 7.4. The homogenate will be centrifuged for 20 min at 18,000 rpm. The supernatant so gotten will be recentrifuged for 60 min at 100,000 rpm. The pellet would be resuspended in homogenization buffer. Ficoll-sucrose spasmodic thickness angle centrifugation will be utilized to get ready H⁺ + K⁺ ATPase. Protein will be decided by the strategy of Bardford.

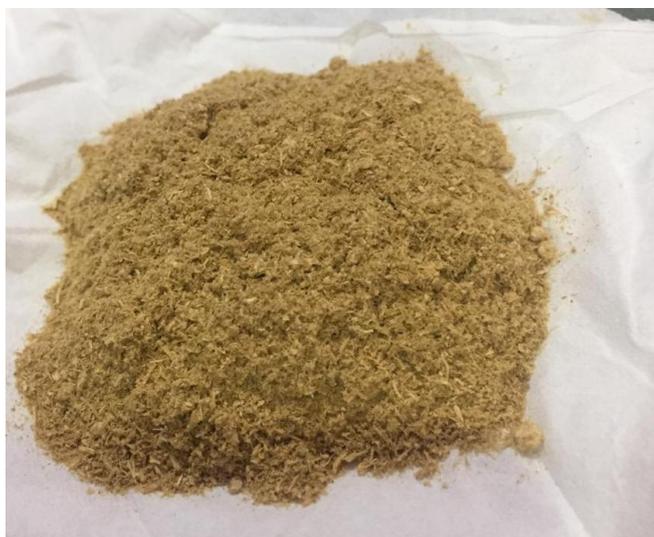
HISTOPATHOLOGICAL EVALUATION PARAMETERS:

- Determination of gastric p^H
- Free and total acidity determination
- Volume of gastric secretion
- Ulcer index, Ulcer scores, Size of ulcers, Number of gastric ulcers

RESULT AND DISCUSSION**PRELIMINARY QUALITATIVE CHEMICAL SCREENING.**

Specific chemical experiments have been performed in line with conventional techniques to differentiate between the respective constituents. The outcome is the unusual event of this chemical analysis.

Chemical constituent	Test	Extract
Tannins	Ferric chloride test	+
	Lead acetate test	+
	Acetic acid sol.	-
	Dil. Iodine sol.	+
Alkaloids	Mayer's test	+
	Dragendroff's test	+
	Hager's test	+
	Wagner's test	+
Glycoside		
A. Cardiac glycosides	Baljet's test	+
	Legal's test	+
	Keller-killiani test	+
	Liebermann's test	+
B. Steroids	Salkowski test	+
	Liebermann-burchard test	+
	Liebermann's test	+
C.Saponins	Foam test	+
D. Flavonoids	Schinoda test	-
	Lead acetate test	-
	NaOH test	-
E. Anthraquinones	Borntrager's test	-
	Modified-borntrager's test	+
Carbohydrates	Molisch test	+
	Fehling's test	-
	Benedict's test	-
Proteins	Biuret's test	-
	Millon's test	-



Extract Formulation, filtered through ethanol



PHARMACOLOGICAL STUDY ACCUTE TOXICITY STUDIES

The table shows a dose of Extricates subordinate effects. The antiulcer benefits of modern medications have improved with rising doses. In 2 ml / kg body weight, the maximum effect was observed. Ethanol structure happens in extreme collapse.



Table - Dosage subordinate considers of Extricates utilizing initiated ulcer shown rodent

Treatment	No of animal	Ulcer Index	Total Acidity (mEq/L)	Acid Volume (ml)	Ph
GROUP-1	6	6.74	57.25	3.75	4.7
GROUP-2	6	11.50	126.15	8.15	2.2
GROUP-3	6	8.45	88.43	6.05	3.6
GROUP-4	6	5.60	53.51	3.09	4.8
GROUP-5	6	3.75	47.21	2.85	5.3
GROUP-6	6	2.43	42.65	2.46	5.4
SD		3.278	3.3832	2.240	1.225
SEM		1.338	1.2787	0.9144	0.5004

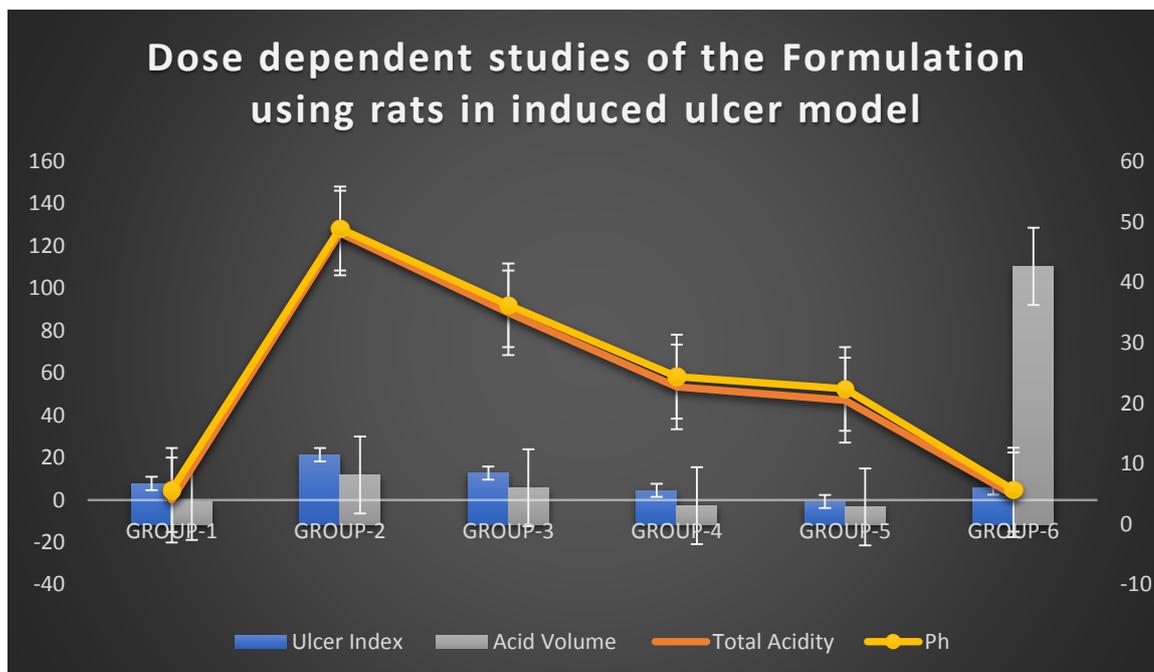


Figure - Dose dependent studies of the Unani Formulation using rats induced ulcer model

Pyloric ligation induced ulceration in rats.

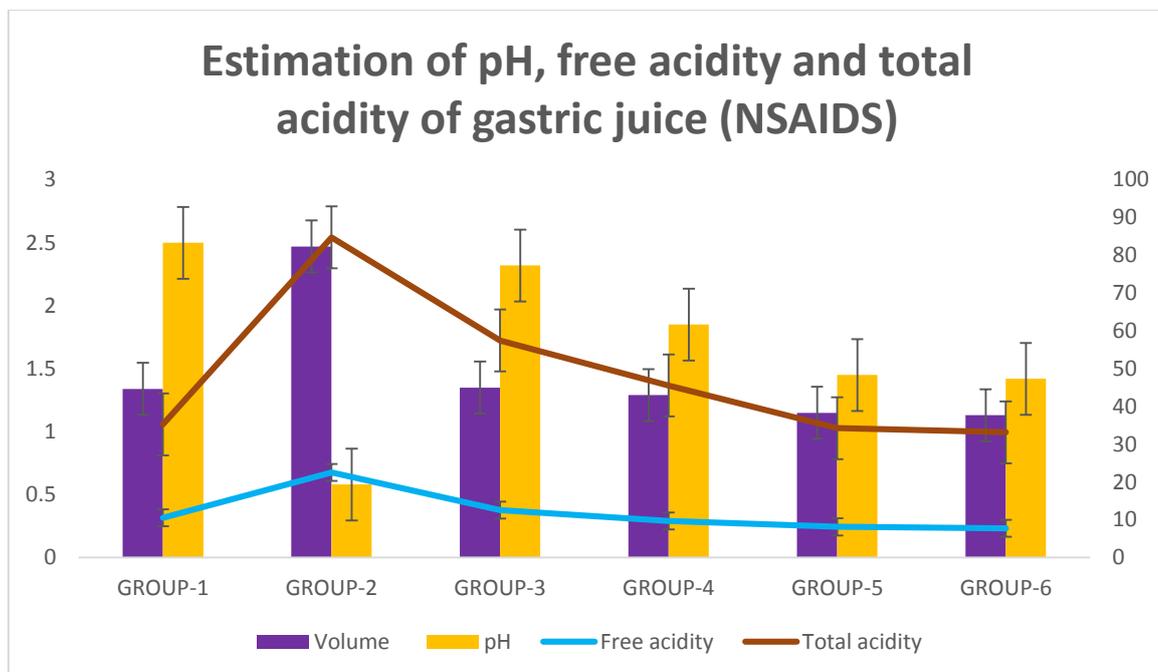


Determination of free and total acidity

Two or three droplets of Topfer's reagent were applied and the titration was 0.01 N sodium hydroxide before the colour ruded was all extracted, and the appearance of the mixture became yellowish and white. It is a piper of 1 milliliter of gastric juice. There was a popular amount of soluble foundation. This relates this amplitude to free sharpness. There have been two to three declines in phenolphthalein structure and titration before an unmistakable ruddy ting emerged. The whole antacid quantity was well established.

Estimation of pH, free acidity and total acidity of gastric juice (NSAIDS)

Grouping of animals	Volume of gastric juice (ml)	% Inhibition	Free acidity (meq/l/100 g)	Total acidity (meq/l/100 g)
GROUP-1	1.34	2.50	10.54	35.25
GROUP-2	2.47	0.58	22.50	84.75
GROUP-3	1.35	2.32	12.55	57.45
GROUP-4	1.29	1.85	9.65	45.54
GROUP-5	1.15	1.45	8.12	34.26
GROUP-6	1.13	1.42	7.76	33.17
SD	0.506	0.698	0.549	2.008
SEM	0.206	0.285	0.244	0.891



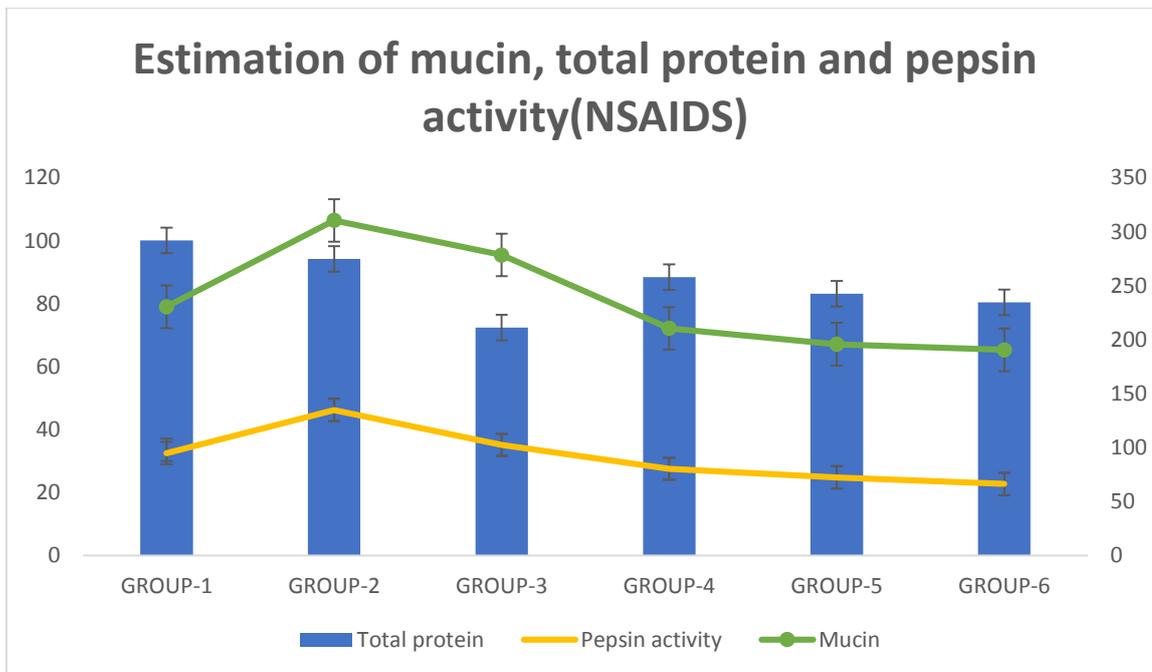
Estimation of total proteins

The degradation of protein in gastric juice was measured by 90 percent of gastric juice liquor in 9:1 amounts within the alcoholic acceleration. The distilled gastric juice has been split up to a limit of 0.1 ml in 1 liter of 0.1 NaOH, 0.5 liter of which have been put through a separate measuring tank. Included and held for 10 min 4 ml of soluble mix. 0.4ml of phenol reagent was applied after that and production of it was begun again after 10 minutes of color.

A test was performed using Hitachi 15-20 spectrophotometer against a simple arrangement of purified water at 610 nm. A regular bent with Bovine Egg White was used to measure the protein content and it was distributed as microgram / milliliter gastric juice. The t-test of the pupil was used for the objective analysis.

Estimation of mucin, total protein and pepsin activity(NSAIDS)

Grouping of animals	Mucin	Total protein ($\mu\text{g/ml}$)	Pepsin activity ($\mu\text{mole/ml}$)
GROUP-1	230.55	100.08	32.56
GROUP-2	310.50	94.25	46.25
GROUP-3	278.50	72.45	35.15
GROUP-4	210.55	88.45	27.55
GROUP-5	195.78	83.15	24.85
GROUP-6	190.56	80.47	22.73
SD	4.8047	0.9324	0.8587
SEM	1.9762	0.4054	0.3505



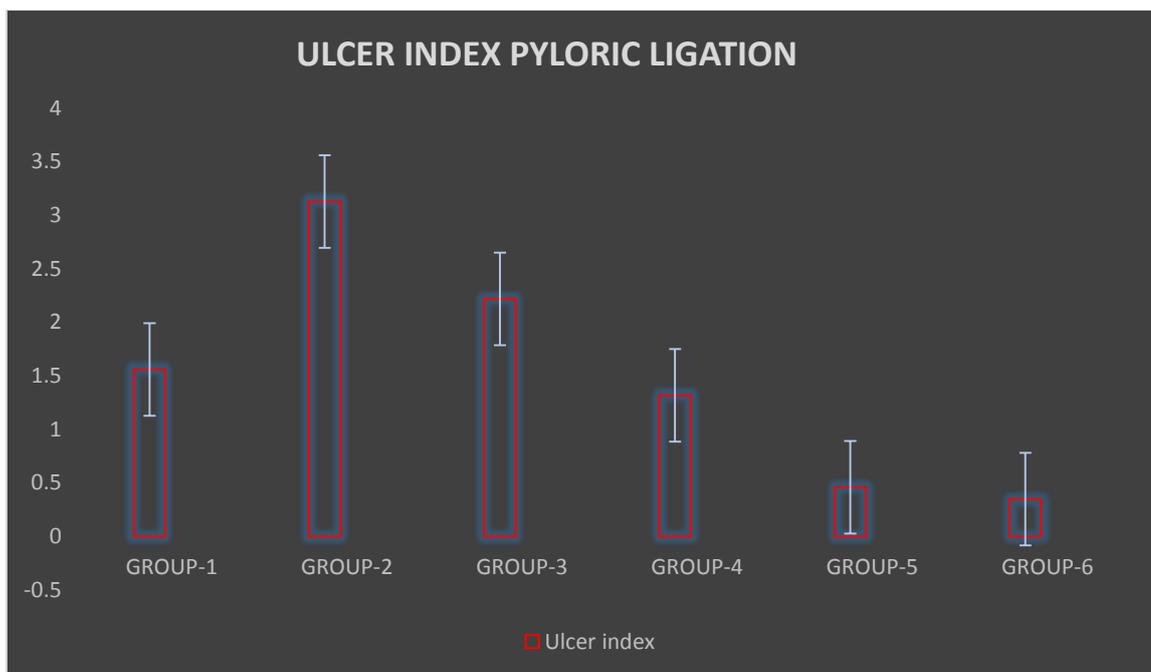
Estimation of mucin

The glandular parcel cutting that revealed the lower ebb and flow was removed after the processing of gastric juices. Ever-long tumors were tossed for 2 hour in 0.1% Alcian 8GX broken down to 0.16 M sucrose tamponed to a pH of hydrochloric corrosive sodium acetic acid derivation of 0.05 M. Two incremental washings of 15 and 45 min in 0.25 M sucrose arrangements were removed to uncomplexed light. A submersion in 10 ml aliquots of 0,5 M magnesium chloride for 2 h at Color Complex with Body Fluid was improved.

The blues were trembling slightly, when diethyl ether volume increased, and a Hitachi 15-20 spectrophotometer calculated the optical thickness of the watery phase at 605 nm. The mucin material from the regular mucin cord, which is conveyed by microgram / gram of wet organ tissue, was selected.

Table: The relative area and corresponding ulcer index.

Groups	Relative area/mm ²	Ulcer index
GROUP-1	11–20	1.56
GROUP-2	91–100	3.13
GROUP-3	41–50	2.22
GROUP-4	21–30	1.32
GROUP-5	5–10	0.46
GROUP-6	1-5	0.35
	Perforation	1.0



In addition, the seriousness of mucosal injuries may be measured using the technique mentioned by Dekanski et al., and the ulcer record is as follows:

0 = no injury.

1 = lumen blood,

2 = pinpointed erosions.,

3 = 1 to 5 minor disintegrations < 2 mm,

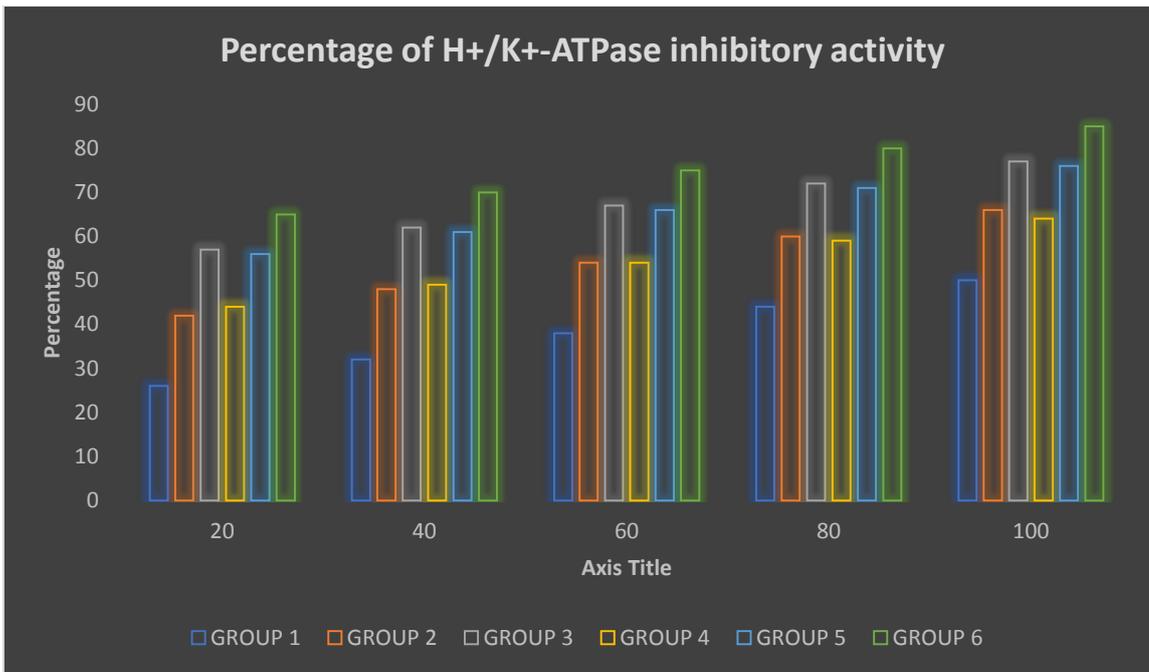
4 = more than five tiny < 2 mm disintegrations,

5 = 1 to 3 large > 2 mm disintegrations.

H⁺/K⁺ - ATPase Inhibition Activity:

Proton potassium ATPase will be prepared from mucosal scrapings of rat will be determined as por reported method [21,22]. Stomachs of healthy rats will be washed gently with tap water. The mucosal layer of fundus will be scrapped and homogenized in ice-cold phosphate buffer, pH 7.4. The homogenate will be centrifuged for 20 min at 18,000 rpm. The supernatant so obtained will be recentrifuged for 60 min at 100,000 rpm. The pellet would be resuspended in homogenization buffer. Ficoll-sucrose discontinuous density gradient centrifugation will be utilized to prepare H + K + ATPase. Protein will be determined by the method of Bardford.

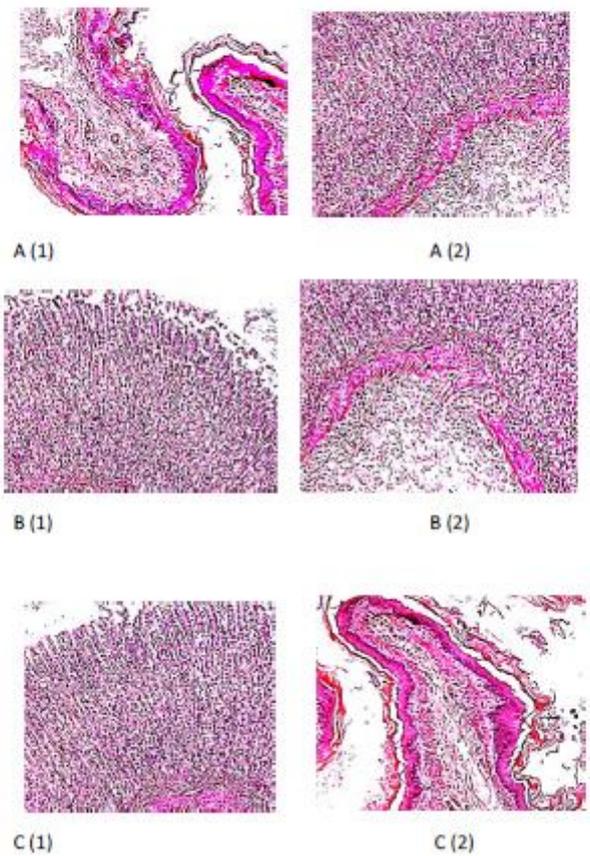
Groups	Percentage of H ⁺ /K ⁺ -ATPase inhibitory activity					
	Concentration of Extract	20	40	60	80	100
GROUP 1		26	32	38	44	50
GROUP 2		42	48	54	60	66
GROUP 3		57	62	67	72	77
GROUP 4		44	49	54	59	64
GROUP 5		56	61	66	71	76
GROUP 6		65	70	75	80	85
SD		1.392	1.351	1.311	1.272	1.233
SEM		0.5684	0.5176	0.5354	0.5194	0.5037



Histopathological Studies

DIAGNOSIS:

- A. **BIOPSY AT 6:00: Sub mucosal infiltration**
- B. **BIOPSY AT 8:00: Proliferation of granulation tissue noticed in glandular stomach.**
- C. **ENDOSCOPIC Result: No ulceration or inflammation noticed**



INFERENCES

The 6:00 biopsy reveals slight submucosal invasion and proliferation of connective tissue of the non-glandular stomach in inflammatory cells. However, at 8:00 (figures above) the biopsy indicates inflammatory sub-mucosal invasion cells and granulation

tissue proliferation in the glandular stomach. The glandular stomach had usual mucosal coating found and there was no ulceration or inflammation.

DISCUSSION

The following study project illustrates the gastro-protective impact of Terminalia coriacea on aspirin-induced rat model ulcers. In both pylorus binding rats and gastric ulcerogenesis, the gastroprotective effects were contextual. The protective operation was correlated with the decrease in the gastric ulcer reports, gastric emissions and sharpness and exacerbation by NF- κ B inhibition, neutrophil identification and ROS decline due to its antioxidant properties.

With Group 6 (High Dose), Group 6 reveals not only a lower acid volume but also the maximum degree of antiulcer behavior attributable to lowest ulcers. These findings are important.

The level of gastric juice inhibition in extract classes (Group 4, Group 5, and Group 6) was found to be less moderate.

CONCLUSION:

The above results can be inferred that the TCFE -detailed formulation against induced ulcer in the rat model can be called an adjuvant in ulcer care that can greatly reduce the need for standard measures by oral NSAIDS operators such as Aspirin. The efficacy and feasibility of the long-term usage of this sedate as a potential antiulcer agent have been demonstrated in planned clinical procedure in the assistance of lower measurements of the detailing TCFE formula.

Aspirin treatment, caused completely the frequency of gastric ulcerations. The combination of decided measures has no extra pain relief impact on its stratified components because the combination of TCFE medicinally induced with aspirin has an extra pain relief impact on aspirin alone and is not proved to be ulcerative.

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