

**ANTIULCER ACTIVITY OF METHANOLIC EXTRACT OF LEAF OF
TYLOPHORA INDICA ON HISTAMINE AND NAPROXEN INDUCED
GASTRIC LESIONS IN RATS**

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Summary

The objectives of the present study was to evaluate anti-ulcer activity of methanolic extract of *T. indica* leaf as using experimental models in order to justify its traditional use. *Tylophora indica* Burn. (*T. indica*) (Family Asclepiadaceae) is a shrub distributed in Africa, Asia, Australia and Oceanic Islands. The dried leaves of *T. indica* used as folk remedy in the treatment of dysentery, bronchial asthma, ulcers and allergic rhinitis. The methanolic extract of *T. indica* leaves at dose (50, 100, 200 mg/kg) produced 9.66%, 16.09%, 47.53% ulcer inhibition and 6.57%, 8.95%, 18.68% ulcer inhibition in naproxen and histamine induced ulcer respectively. At different dose methanolic extract of *T. indica* showed antiulcer activity against naproxen and histamine induced ulcer probably due to decrease in lipid peroxide level and by blocking H₂ receptor respectively.

Keywords: *Tylophora indica*, Asclepiadaceae, Antiulcer, Histamine, Naproxen.

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Introduction

Several plants and herbs are used in medicine to treat different types of gastrointestinal disorders, including peptic ulcer. Ulcerative lesions of gastrointestinal (GI) tract are one of major side effects associated with the use of non-steroidal anti-inflammatory drugs (NSAIDs), alcohol, stress and ischemic reperfusion (1). Therefore there is an urgent need to identify novel antiulcer agents derived from plant sources.

Tylophora indica (*T. indica*, Family Asclepiadaceae) Burn. (Hindi, Antamul), is an endangered medicinal plant distributed in Africa, Asia, Australia and Oceanic Islands (2). Traditionally the dried leaves are used as an expectorant, emetic, anti-dysenteric, anti-asthmatic, ulcers and allergic rhinitis. A decoction of the leaves 1 in 10 and an infusion of root bark were used in dysentery, asthma, and bronchitis. The root juice of other species *T. fasciculata* is given in milk as tonic; the leaves are pounded and used as an application to unhealthy ulcers (3). Similarly leaf extracts of *T. conspicua* exhibits antiulcer activity on indomethacin induced gastric ulceration and gastric acid secretion in male albino rats (4). This plant already has been reported in the treatment of bronchial asthma and immunomodulatory activity, anti-diarrhoeal, anti-inflammatory, anti-arthritic and hepatoprotective (5-9). The different medicinal uses for *T. indica* in folk medicine stimulated an ethnopharmacological evaluation for anti-ulcer activity. There has been no systematic study until now to show the anti-ulcer activity of *T. indica*. Hence the objective of present study was to investigate anti-ulcer activity of *T. indica* leaf using histamine and naproxen induced ulcer in rat.

Methods

Plant material

T. indica leaves were collected from the Botanical Garden of Bharati Vidyapeeth University, Erandawane campus, Pune, India in the month of March. The samples were authenticated by Regional Research Institute, Pune and voucher specimen (F. 3-1/2006/RRI) was kept at departmental herbarium of RRI.

Preparation of extracts

T. indica leaves were dried at room temperature and powdered by using mechanical grinder, approximately 500 gm powder material was extracted with sufficient amount of methanol in soxhlet apparatus. The extracts at the different doses of 50, 100, 200 mg/kg were suspended in 1% CMC (carboxyl methyl cellulose) solution and used for study.

Animals and Treatments

Male wistar rats were (200-230 gm) procured from National Institute of Bioscience Pune, India and fed with standard laboratory chew. The animals were kept in standard environmental conditions (21°C, 60-70% humidity) under 12 h light/dark cycles.

Animals were divided into five groups containing six animals in each group. Group 1 was control administered with 1% CMC (1 ml), group 2 treated with standard, for histamine induced ulcer standard was ranitidine (100 mg/kg p.o.) and for naproxen induced ulcer omeprazole (30 mg/kg p.o.) were used. Other three groups were administered with different doses (50, 100, 200 mg/kg) of test drug (10, 11). Experimental work was approved by Institutional Animal Ethics Committee with

CPCSEA number CPCSEA/59/08. Acute oral toxicity was done according to OECD 425 guidelines.

Experimental procedure

Histamine induced ulcer

Different doses of control, standard and test drug were given to animals. One hour after drug administration, Ulcer was induced using 300 mg/kg histamine hydrochloride was given intraperitoneally. Animals were sacrificed after 6 hr of ulcer induction. Stomach was isolated and opened along the greater curvature to expose inner surface. Inner surface was washed thoroughly with normal saline. Each stomach was scanned in scanner UMAX 5600 and the image was stored for lesion area measurement. Area was measured by using image analysis software. The ulcer index and % inhibition was determined by using following formula (12-14).

$$UI = [\text{Ulcerated area (mm}^2\text{)} / \text{total stomach area (mm}^2\text{)}] \times 100$$

$$\%I = \text{Ulcer index of control} - \text{Ulcer index of test} / \text{Ulcer index of control} \times 100$$

Naproxen induced ulcer

Different doses of control, standard and test drug were given to animals. One hour after drug administration Gastric ulcer was induced by using naproxen 80 mg/kg p.o. After six hours of naproxen administration animals were sacrificed by cervical dislocation, stomach was isolated and opened along greater curvature to expose inner surface. Inner surface was washed thoroughly with normal saline. The ulcer area, ulcer index and the percentage inhibition were calculated as described above.

Statistical analyses

Statistical analysis was performed using ANOVA followed by dunnetts multiple comparison test and significance of difference between treatments was accepted at $p < 0.05$.

Results

The result showed that methanolic extract of *T. indica* leaf possesses an anti-ulcer activity against histamine and naproxen induced gastric ulceration in rats. At different doses methanolic extract of *T. indica* leaves exhibited 6.57%, 8.95% and 18.68% inhibition while ranitidine exhibited 71.76 % inhibition against histamine induced gastric ulcer. The results were shown in Table 1.

In naproxen induced ulcer methanolic extract of *Tylophora* leaf showed 9.66%, 16.09% and 47.53% ulcer inhibition while ulcer inhibition in case of omeprazole was 56.59%. The results were shown in Table 2. Figure 1 and 2 showed that the ulcer index was decreased with increasing dose in both histamine and naproxen induced ulcer as compared to control.

Table 1: Effect of *T. indica* leaf extract on gastric ulcer induced by histamine in rats.

Treatment	Dose	US (mm ²)	UI	% I
Control 1% CMC	1ml/animal	10.08 ± 0.21	2.06 ± 0.15	-
Ranitidine	100mg/kg	2.84 ± 0.14**	0.54 ± 0.04	71.76
TL extract	50mg/kg	9.41 ± 0.15	1.85 ± 0.08	6.57
TL extract	100mg/kg	9.17 ± 0.19	1.82 ± 0.07	8.95
TL extract	200mg/kg	8.19 ± 0.37**	1.59 ± 0.06	18.68

Value represent the mean ± S.E.M. of gastric lesion area the result was analyzed by ANOVA followed by Dunnetts multiple comparison test *p<0.05; **p<0.01, TL: *T. indica* leaf and, US: ulcer surface, UI: ulcer index, % I: percent inhibition.

Table 2: Effect of *T. indica* leaf extract on gastric ulcer induced by naproxen in rats.

Treatment	Dose	US (mm ²)	UI	% I
Control 1% CMC	1ml/animal	5.86 ± 0.191	1.16 ± 0.05	-
Omeprazole	30mg/kg	2.54 ± 0.090**	0.50 ± 0.02	56.59
TL. Extract	50mg/kg	5.29 ± 0.24	1.01 ± 0.06	9.66
TL. Extract	100mg/kg	4.92 ± 0.15*	0.94 ± 0.06	16.09
TL. Extract	200mg/kg	3.08 ± 0.19**	0.60 ± 0.04	47.53

Value represent the mean ± S.E.M. of gastric lesion area the result was analyzed by ANOVA followed by Dunnetts multiple comparison test *p<0.05; **p<0.01.

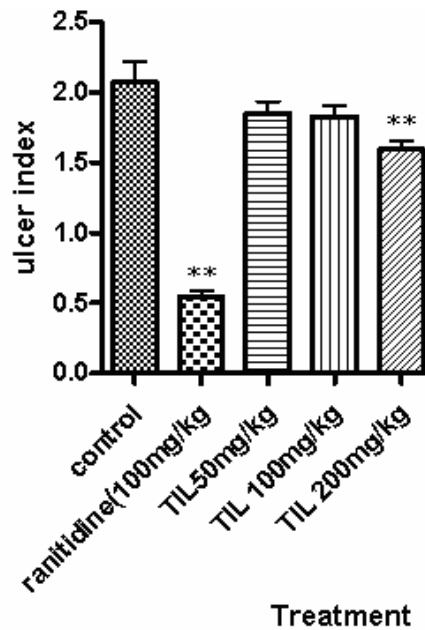


Fig 1: Effect of *T. indica* leaf extract on gastric ulcer induced by histamine in rats.

Value represent the mean \pm S.E.M. * $p < 0.05$, and *** $p < 0.001$ considered significant compared to control and standard. TIL: *T. indica* leaf.

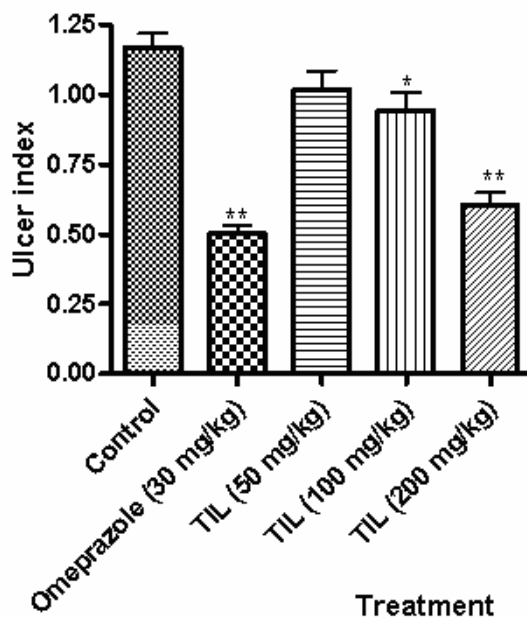


Fig 2 Effect of *T. indica* leaf extract on gastric ulcer induced by naproxen in rats.

Value represent the mean \pm S.E.M. * $p < 0.05$ and *** $p < 0.001$ considered significant compared to control and standard.

Discussion

In the present investigation various animal models were used to evaluate antiulcer potential of *T. indica* and distinguish the probable mechanism. It is well known that nonsteroidal anti-inflammatory drugs (NSAIDs) induce severe gastric mucosal damage in rat (15). Naproxen induce ulcer by increasing the level of lipid peroxides. *T. indica* probably provide protection against lipid peroxide induced ulceration by enhancing the activity of anti-oxidant enzymes glutathione peroxidase and catalase (16).

The induction of gastric ulcers by histamine administration has long been recognized and is mediated through stimulation of H₂ receptor results in enhanced gastric acid secretion and vasodilation. *T. indica* probably block H₂ receptor and exhibited better therapeutic efficacy against histamine induced ulcer (17).

Conclusion

It may be concluded that the results of present study confirm the ethnobotanical claim of *T. indica* for the treatment of gastric ulcer.

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