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The effect of ethanol extract of *Morinda tinctoria* Roxb leaves on antiulcer activity in rats

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ABSTRACT

The main Objective of the study is to screen the antiulcer activity of ethanol extract of *Morinda tinctoria* Roxb leaves using different experimentally induced gastric ulcer models in rats. Gastric ulcer was induced in rats by pylorus ligation, 80% ethanol (1ml/ rat) and aspirin (200mg/kg). In pylorus ligation induced ulcer model the parameters studied were gastric volume, free acidity, total acidity and ulcer index. Lesion index and percentage inhibition of ulcer were determined in ethanol induced ulcer model and in aspirin induced ulcer model the ulcer index was determined. In pylorus ligation model, MTE (*Morinda tinctoria* extract) pretreatment caused significant reduction in gastric volume, free acidity, total acidity and ulcer index as compared to control group. In ethanol induced and aspirin induced ulcers, MTE was effective in reducing the lesion index. The results suggest that MTE posses significant ($p<0.001$) antiulcer activity. This may be the presence of flavanoid in the plant.

KEYWORDS

Morinda tinctoria roxb;
Antiulcer activity;
Pylorus ligation.

INTRODUCTION

Morinda tinctoria Roxb commonly called as Nuna or manganatti belonging to Rubiaceae is a moderate sized deciduous tree with spongy deeply cracked yellowish bark cultivated throughout the hotter parts of India[1]. The leaves of *Morinda tictoria* Roxb are traditionally used to cure diarrhoea, ulcerative stomatitis, gastropathy, wounds, gout, hernia and fever[2]. The leaves are reported to posses antimicrobial activity[3].

Peptic ulcer is a circumscribed ulceration of mucous membrane penetrating through muscularis mucosa and occurring in areas bathed by acid in stomach. The gastric ulcer is produced due to abnormality in gastric secretion or abnormal mucosal defense. To regain the balance different therapeutic agents like plant extract are used to inhibit the acid secretion or to boost up the mucosal defense mechanism. In this context, study of the alcoholic extract of *Morinda tinctoria* Roxb against pylorus ligation, ethanol and aspirin induced ulcers were under taken in rat models.

MATERIALS AND METHODS

Preparation of extract

The fresh leaves of *Morinda tinctoria* Roxb were collected from the Tampcol garden, Chennai in the month of December 2004 and authenticated by Dr. Jayaraman, plant anatomy and Research center, Chennai. A voucher specimen is deposited in our labo-

Full Paper

ratory for reference. The leaves were shade dried, powdered and extraction was carried out by continuous percolation in soxhlet apparatus using 90% ethanol. The extract was evaporated under vacuum. The extractive value of the alcoholic extract was (5.2%).

Animals

Male albino rats weighing between 150-200g were used for the study. The animals were housed under standard condition of temperature (23±1°C), 12hours light/dark cycle and fed with standard died and water ad libitium. Before performing the experiment, ethical clearance was obtained from Institutional Animal Ethics Committee.

Antiulcer studies

1. Pylorus ligation induced gastric ulcers

The rats were divided in to 3 groups of each consisting of 6 animals and fasted for 48 hours with free access of water. Pyloric ligation was performed under light ether anaesthesia to each animal[5]. Animals were given normal saline (2ml/kg), MTE (300mg/kg) and Ranitidine (20mg/kg), orally immediately after pylorus ligation. Animals were sacrificed after 4 hours. The stomach was carefully removed and the gastric contents were collected. The gastric juice was centrifuged at 3000 rpm for 30 min and the volume of gastric juice was measured. Free and total acidity in the supernatant were determined by titration with 0.1N NaoH and expressed as mEq/L/100g[6]. The stomach was cut open along the greater curvature and pinned on a soft board for evaluating gastric ulcers and ulcer index was calculated[7]..

2. Ethanol induced gastric ulcers

The rats were divided in to 3 groups of each consisting of 6 animals and fasted for 24 hours with free access of water. Animals were given normal saline (2ml/kg), MTE (300mg/kg) and Ranitidine (20mg/kg). 1 hour later 1ml of 80% ethanol was administered to each animal[8]. Animals were sacrificed 1 hour after ethanol administration, stomachs were isolated and cut open along the greater curvature and pinned on a soft board. The length of each gastric lesion was measured and the lesion index was expressed as sum of the length of the entire lesion in mm[9]. The percentage inhibition was calculated.

3. Aspirin induced gastric ulcers

18 Rats were randomly divided in to 3 groups of 6 each and fasted for 24 hours with free access of water. Animals were given normal saline (2ml/kg), MTE (300mg/kg) and Ranitidine (20mg/kg) orally. After 1 hour 200mg/kg of aspirin was orally given to each animal[10]. Animals were sacrificed 4 hours later, stomachs were isolated and ulcer index and percentage inhibition of ulcer was determined.

Statistical analysis

The values are expressed as mean ± SEM (n=6). Data analysis was carried out using student's t test. Discrepancies with ($p<0.05$) were considered to be statistically significant.

RESULTS

Effect of pylorus ligation induced gastric ulcers

The MTE 300mg/kg treated animals showed ulcer index score value 1.5±0.05 which was statistically significant ($p<0.001$) when compared to solvent control group (2.2±0.034). The MTE treated group showed significant reduced values of free and total acidity ($p<0.001$)when compared to solvent control group. There was also significant reduction in gastric volume for MTE treated groups (3.9±0.13) ($p<0.001$) when compared to solvent (TABLE 1).

Effect of ethanol induced gastric ulcer

Oral administration of 80% ethanol produced gastric lesions in stomach. Treatment with the extract (300mg/kg) and ranitidine(20mg/kg) significantly ($p<0.001$) protected the gastric mucosa and the lesion

TABLE 1 : Effect of MTE on Pylorus ligation induced gastric ulcers in rats

Design of treatment	Dose (mg/kg)	Gastric volume (ml/100mg)	Free acidity (mEq/L)	Total acidity (mEq/L)	Ulcer score
Control (Normal saline)	2ml/kg	5.6±0.15	18.7±0.20	25±0.2	2.2±0.03
Ranitidine	20	2.3±0.26[c]	O8.6±0.15[a]	15±0.18[a]	1.0±0.01[a]
alcoholic extract of MTE	300	3.9 ± 0.13[a]	15.7 ± 0.33[a]	20 ± 0.3[a]	1.5±0.05[a]

Values are mean ± S.E.m. n= number of animals in each group. Significant differences with respect to solvent control group were evaluated by student's-test. ([a]p<0.001)

TABLE 2: Effect of MTE on ethanol induced gastric ulcer in rats

Treatment	Dose (mg/kg)	Lesion index	%Inhibition of ulcer
Control (Normal saline)	2ml/kg	5.62 ± 0.13	-
Ranitidine	20	1.96 ± 0.35[a]	65.12
Extract	300	2.45 ± 0.15[a]	56.41

Values are mean ± S.E.M. n= number of animals in each group; Significant differences with respect to solvent control group were evaluated by student's-test. ([a]p<0.001).

TABLE 3: Effect of MTE on Aspirin induced gastric ulcer in rats

Treatment	Dose (mg/kg)	Lesion index	%Inhibition of ulcer
Control (Normal saline)	2ml/kg	2.0 ± 0.89	-
Ranitidine	20	0.26 ± 0.26[a]	87
Extract	300	0.67 ± 0.41[a]	66.5

Values are mean ± S.E.M. n= number of animals in each group. Significant differences with respect to solvent control group were evaluated by student's-test. ([a]p<0.001)

index were 2.45±0.15, 1.96±0.35 respectively which was compared with the solvent control. The percentage protection for the extract and ranitidine were 56.41%, 65.12% respectively against ethanol damage.

Effect of aspirin induced gastric ulcer

In MTE treated group (300mg/kg) the ulcer index value is 0.67±0.41 were significantly reduced ($p<0.001$) when compared to solvent control (2.0±0.89) while the ulcer index for Ranitidine treated group was 0.26±0.26 ($p<0.001$) the percentage inhibition of ulcer showed by extract and Ranitidine were 66.5% and 87% respectively (TABLE 3).

DISCUSSION

Although in most of the cases the aetiology of ulcer is unknown, it is generally accepted that it results from an imbalance between aggressive factors and the maintanance of mucosal integrity through the endogenous defense mechanism[11]. To regain the balance different therapeutic agents including plant extracts are used to inhibit the gastric acid secretion and to boost the mucosal defense mechanism by increasing mucus production.

The anti ulcer activity of MTE was tested against gastric lesions induced by pylorus ligation, ethanol and aspirin. MTE reduced the mucosal lesion induced by pylorus ligation, ethano and aspirin. It also decreased the total acidity, free acidity and volume of gastric secretions. Theses effects of MTE treatment on the parameters that influence the initiation and induction of ulceration may consider as highly desirable property of antiulcerogenic agent.

In pyloric ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for induction of ulceration[12]. The antiulcer activity of MTE in pylorus ligation model is evident from its significant reduction in gastric volume, free acidity, total acidity and ulcer index. MTE treated animals significantly inhibited the formations of pylorus ligated ulcer in the stomach and also decreased both acid concentration and gastric volume, it is suggested that MTE can suppress gastric damage induce by aggressive factors.

Ethanol serves as a most common ulcerogenic agent and when given intragastrically to rats it produces severe gastric hemorrhagic erosions[13]. The ethanol induced gastric lesions is multifactorial with the depletion of gastric wall mucus content as one of the involved factors[14] and this damage induced by ethanol may be due to mucosal leukotriene release. Ethanol induced damage to thw gastric mucosa is associated with a significant production of free radicals leading to an increased lipid peroxidation and damage to the cell and cell membranes. Accumulation of activated neutrophils in the gastric mucosa may be the source of free radicals[15]. The effective scavenging of free radicals by MTE may have reduced progressive ulceration. It also contains flavanoid[16], which reduces gastric tissue histamine content that in turn cause the reduction in the ulcer index.

NSAID'S like aspirin, indomethacin are known to induce peptic ulcer by denaturing mucous glycoprotein[17] and also by decreasing prostaglandin levels through inhibition of PG synthesis. MTE was significantly effective in protecting gastric mucosa against aspirin induced ulcer in rats.

On the basis of present results it can be concluded that antiulcer activity of *Morinda tinctoria* Roxb could be mainly due to the modulation of defensive factors through an improvement of gastric cytoprotection, anti secretory and partly due to acid inhibition and free radical scavenging activity.

Full Paper

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