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Comparative Evaluation of Anti-Ulcer Activity of Root Stem and Leave of *Murrya koenigii* (Linn.) Spreng in Rats

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Anti ulcer activity of root, stem and leave of *Murrya koenigii* (Linn.) Spreng was studied against ethanol, hydrochloric acid, indomethacin, stress and pyloric ligation induced gastric ulceration in albino rats. Significant antiulcer activity was observed in root, stem as well as leave of *Murrya*Koenigii (Linn.) Spreng in all the gastric ulcer models studied. Maximum anti ulcer activity was found in root followed by leave and stem of *Murrya koenigii* (Linn.)Spreng.

Keyword: Anti ulcer activity, *Murrya koenigii* (Linn.) Spreng

1. Introduction

Murrya koenigii (Linn.) Spreng has been described as a medicinal plant of the family 'Rutaceae'. It has several names. In Nepali it is called 'meehi saag', in Hindi 'bursunga' and in English it is known as 'curry leaf tree'. *Murrya koenigii* (Linn.) Spreng is widely distributed at foothills of Himalayas from Kumaon to Sikkim, Bengal, Assam, middle and lower hill forests up to the height of 5000 ft. It is a small tree with dark green bark, often cultivated. February to May is the flowering time of the plant. *Murrya koenigii* (Linn.) Spreng has several medicinal uses. Leaves and roots are bitter, acrid, cooling, alexeteric, antihelmintic, analgesic, cure piles, useful in leucoderma and blood disorders. Burk is used to cure eruptions, poisonous animal bites etc. The plant has also stomachic and tonic properties[1,2].

Recently we observed anti ulcer activity of *Murrya koenigii* (Linn.) Spreng leaf against ethanol
induced gastric ulcer in albino rats[3]. We also isolated active compound from *Murrya koenigii* (Linn.) Spreng leaf and confirmed its anti ulcer activity in various experimental ulcer models[4]. However, we took interest to note anti ulcer activity of root and stem of *Murrya koenigii* (Linn.) Spreng to make a comparison with the anti ulcer activity of leaves. In this communication results of the comparative study of anti ulcer activity of root, stem and leave of *Murrya koenigii* (Linn.) Spreng against ethanol, hydrochloric acid, indomethacin, stress and pyloric ligation induced gastric ulceration in albino rats are being reported

2. Materials and Methods

2.1 Plant Material:

Murrya koenigii (Linn.) Spreng was collected from the garden of medicinal plants of the University of North Bengal during September, 2012 and identified by the expert of the department of Botany of the said University. A voucher specimen was kept in the department for future use.

2.2 Test Drugs:

Root, leave and stem were separated from *Murrya koenigii* (Linn.) Spreng. They were then sundried and powdered. Powdered root, leave and stem were used as test drugs.

2.3 Experimental animals:

Wistar strain albino rats of both sex were used for the study. The animals were housed in colony cages (5 rats/cage) and were kept for at least a week in the experimental wing of the animal house (room temperature 25–28^{0}C and humidity 60–65% with 12 h light and dark cycle) before experimentation. Animals were fed on laboratory diet with water *ad libitum*. For each set of experiment 8 animals were used. The animal experiment was approved by the ethics committee of the Institute.

2.4 Chemicals:

Chemicals and drug were procured from the following centres.

Indomethacin (Torrent Research Centre, Gandhinagar), ethanol (Baroda Chemical industries Ltd., Dabhoi), HCl LR (Thomas baker, Mumbai), omeprazole (Kopran Pharma Ltd. Mumbai).

2.5 Production of gastric ulcers:

2.5.1 Ethanol induced gastric ulcer

Ethanol induced gastric ulcer was produced by the method of Sairam *et al.*[5]

Rats were fasted for 18 h when no food but water was supplied *ad libitum*. Gastric ulcers were induced by administering ethanol (95%, 1 mL/200 g body weight) orally through a feeding tube. 1h after administration of ethanol, animals were sacrificed by cervical dislocation and the stomach was taken out and incised along the greater curvature. Stomach was then examined for the presence of ulcers.

2.5.2. HCl induced gastric ulcer

This was produced by the method of Parmar and Desai[6] 0.6M HCl (1 mL/200 g body weight) was orally administered to all rats. Rest part is same to that of ethanol induced gastric ulcer group.

2.5.3 Indomethacin induced gastric ulcer

This was produced by the method of Parmar and Desai[6] Indomethacin (10 mg/kg) was given orally to rats in two doses at an interval of 15 hour. Rest part is same to that of ethanol induced gastric ulcer group.

2.5.4 Stress induced gastric ulcer

Stress induced gastric ulcer was induced by the method of Alder[7]. Rats were fasted for 24h when no food but water was supplied *ad libitum*. Stress ulcer was induced by forced swimming in the glass cylinder (height 45 cm, diameter 25 cm) containing water to the height of 35 cm maintained at 25 degree centigrade for 3h. Rats were then sacrificed. Rest part was same to that of ethanol induced gastric ulcer group.

2.5.5. Induction of gastric ulcer by pyloric ligation method

This was done as described by Parmar and Desai[6] Rats were fasted for 24h when no food but water was supplied *ad libitum*. Under light ether anesthesia, abdomen was opened and the pylorus was ligated. The abdomen was then sutured. After 4h the rats were sacrificed with excess of anesthetic ether and the stomach was dissected out. Rest part was same to that of ethanol induced gastric ulcer group.

2.6 Acute Oral Toxicity Study

Acute toxicity studies were carried out on Swiss albino mice as per the method of Ghosh [8] Separate experiment was done for root, leave and stem of *Murrya koenigii* (Linn.) Spreng. Test drug was given orally at doses of 100, 500, 1000 and 3000 mg/kg to five groups of mice, each group containing six animals. After administration of the compound, the animals were observed for the first three hours for any toxic symptoms followed by observation at regular intervals for 24 hours up to seven days. At the end of the study, the animals were also observed for general organ toxicity, morphological behavior and mortality.

2.7 Anti gastric ulcer study

Rats were divided into six groups,
Group 1 : Control
Group 2 : Ulcerogenic drug or Method (Ethanol / HCl / Indomethacin / Stress / Pyloric ligation)
Group 3 : Ulcerogenic drug or method + Root as test drug (1g/kg)
Group 4 : Ulcerogenic drug or method + Leave as test drug (1g/kg)
Group 5 : Ulcerogenic drug or method + Stem as test drug (1g/kg)

(Dose of the test drug was finalized based on our preliminary study. Test drug was given orally 30 minutes prior to administration of ulcerogenic drug or method Group 6 :Ulcerogenic drug or method + Omeprazole (8 mg/kg orally 30 minutes prior to administration of ulcerogenic drug or method). Omeprazole was used as per the method of Malairajan *et al*.[9]

2.8 Evaluation of ulcer index

This was done as described by Szelenyi and Thiemer[10]

Gastric lesions were counted and the mean ulcerative index was calculated as follows:

I - Presence of edema, hyperemia and single sub mucosal punctiform hemorrhage.
II – Presence of sub mucosal hemorrhagic lesions with small erosions.
III – Presence of deep ulcer with erosions and invasive lesions.
Ulcer index = (number of lesion I) x1 + (number of lesion II) x2 + (number of lesion III) x 3.

2.9 Statistical Analysis

The values were expressed as mean ± SEM and were analyzed using one-way analysis of variance (ANOVA) using Statistical Package for Social Sciences (SPSS). Differences between means were tested employing Duncan's multiple comparison test and significance was set at $p < 0.05$.

3. Results and Discussion

3.1 Acute toxicity studies

Acute toxicity studies revealed that test drugs viz. root, leave and stem of *Murrya koenigii* (Linn.) Spreng did not produce any toxic symptoms when administered orally to mice in doses of 100, 200, 500, 1000 and 3000 mg/kg. Animals were healthy, cheerful and behaved normal throughout the experimental period. No death of animal was recorded during seven days of experiment.

3.2 Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on ethanol induced gastric ulcer

Result is given inTable-1
Ethanol produced massive gastric ulcers in all the rats under study. Most of the ulcers were superficial in nature. There was bleeding in the stomach. Adhesion and dilatation were also noted in stomach. Ulcer index came 31.6 ± 1.79. Pretreatment of rats with root, leave or stem

of *Murrya koenigii* (Linn.) Spreng gave significant ($p<0.001$) protection of the animals from ethanol induced ulcers by 57.29%, 48.73% and 41.14% respectively. Omeprazole gave more protection (67.72%) to the rats from ethanol induced gastric ulcers.

Table-1. Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on ethanol induced gastric ulcer

Group	Ulcer index (mean ± SEM)	% Ulcer protection
Control	Nil	--
Ethanol	31.6 ± 1.79	--
Ethanol+ root of MK(1g/kg)	13.5 ± 1.42**	57.29
Ethanol+ leave of MK (1g/kg)	16.2 ± 1.51**	48.73
Ethanol+ stem of MK(1g/kg)	18.6 ± 1.12**	41.14
Ethanol+Omeprazole (8mg/kg)	10.2 ± 1.15**	67.72

Results were in mean ± SEM, Each group had ten rats, ** $p<0.001$
MK : *Murrya koenigii* (Linn.) Spreng.

Table-2. Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on hydrochloric acid (HCl) induced gastric ulcer

Group	Ulcer index (mean ± SEM)	% Ulcer protection
Control	Nil	--
HCl	29.7 ± 1.49	--
HCl+ root of MK(1g/kg)	14.1 ± 1.32**	52.52
HCl+ leave of MK (1g/kg)	17.7 ± 1.41**	40.40
HCl+ stem of MK(1g/kg)	18.8 ± 1.52**	36.70
HCl+Omeprazole (8mg/kg)	10.7 ± 1.61**	63.97

Results were in mean ± SEM, Each group had ten rats, ** $p<0.001$
MK : *Murrya koenigii* (Linn.) Spreng.

Table-3. Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on indomethacin (INDO) induced gastric ulcer

Group	Ulcer index (mean ± SEM)	% Ulcer protection
Control	Nil	--
INDO	30.7 ± 1.89	--
INDO+ root of MK(1g/kg)	15.4 ± 1.41**	43.84
INDO+ leave of MK (1g/kg)	17.1 ± 1.52**	44.30
INDO+ stem of MK(1g/kg)	19.2 ± 1.72**	37.46
INDO+Omeprazole (8mg/kg)	10.4 ± 1.32**	66.12

Results were in mean ± SEM, Each group had ten rats, ** $p<0.001$
MK : *Murrya koenigii* (Linn.) Spreng.

Table-4. Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on Swimming Stress (SS) induced gastric ulcer

Group	Ulcer index (mean ± SEM)	% Ulcer protection
Control	Nil	--
SS	33.2 ± 1.71	--
SS+ root of MK(1g/kg)	16.7 ± 1.62**	49.70
SS+ leave of MK (1g/kg)	18.4 ± 1.93**	44.57
SS+ stem of MK(1g/kg)	20.1 ± 1.92**	39.46
SS+Omeprazole (8mg/kg)	9.9 ± 1.55**	70.18

Results were in mean ± SEM, Each group had ten rats, ** $p<0.001$
MK : *Murrya koenigii* (Linn.) Spreng.

Table-5. Effect of root, leave and stem of of *Murrya koenigii* (Linn.) Spreng on Pyloric Ligation(PL) induced gastric ulcer

Group	Ulcer index (mean ± SEM)	% Ulcer protection
Control	Nil	--
PL	28.9 ± 1.52	--
PL+ root of MK(1g/kg)	14.3 ± 1.09**	50.52
PL+ leave of MK (1g/kg)	15.3 ± 1.13**	47.06
PL+ stem of MK(1g/kg)	18.1 ± 1.12**	37.37
PL+Omeprazole (8mg/kg)	9.0 ± 1.12**	68.86

Results were in mean ± SEM, Each group had ten rats, ** $p<0.001$
MK : *Murrya koenigii* (Linn.) Spreng.

3.3 Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on hydrochloric acid induced gastric ulcer

Hydrochloric acid produced massive gastric ulcers in all rats. Ulcers were penetrating. Ulcer index came 29.7 ± 1.49. Adhesion and dilatation of the stomach were also seen. Bleeding was also seen in the stomach. Pretreatment with root, leave or stem of *Murrya koenigii* (Linn.) Spreng gave significant protection to the animals from formation of hydrochloric acid induced gastric ulcer. Ulcer index came 14.1 ± 1.32, 17.7 ± 1.41 and 18.8 ± 1.52 respectively with root, leave and stem of *Murrya koenigii* (Linn.) Spreng . Omeprazole gave further protection to the animals from formation of hydrochloric acid induced gastric ulcer. Ulcer index came 10.7 ± 1.61 that means 63.97% protection was achieved. Result is shown in Table – 2.

3.4 Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on indomethacin induced gastric ulcer

Result is given in Table-3
Indomethacin produced gastric ulcers in all albino rats. Ulcers were superficial in nature. There were adhesion, dilatation and bleeding in the stomach. Ulcer index came 30.7 ± 1.89. Pretreatment of rats with root, leave or stem of *Murrya koenigii* (Linn.) Spreng gave significant protection to the animals from formation of indomethacin induced gastric ulcers. Protections were 43.84%, 44.30% and 37.46% respectively with root, leave and stem of *Murrya koenigii* (Linn.) Spreng . Omeprazole produced more protection (66.12%) in course of production of gastric ulcer by indomethacin.

3.5 Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on stress induced gastric ulcer

Compulsory swimming produces stress to yield massive ulcers in stomach of all rats. Adhesion and dilatation of the stomach were seen. In few stomach bleeding was noted. Ulcer index came 33.2 ± 1.71. Pretreatment with root, leave or stem of *Murrya koenigii* (Linn.) Spreng gave significant protection to the animals from formation of swimming stress induced gastric ulcers. Ulcer index came 16.7 ± 1.62, 18.4 ± 1.93 and 20.1 ± 1.92 respectively with root, leave and stem of *Murrya koenigii* (Linn.) Spreng . More protection was noted in omeprazole group. Ulcer index came 9.9 ± 1.55. Result is shown in Table -4.

3.6 Effect of root, leave and stem of *Murrya koenigii* (Linn.) Spreng on pyloric ligation induced gastric ulcer

Result is given in Table-5
Gastric ulcers were produced in all albino rats after pyloric ligation. There were adhesion, dilatation and bleeding in the stomach. Ulcers were superficial in nature. Ulcer index came 28.9 ± 1.52. Pretreatment of rats with root, leave or stem of *Murrya koenigii* (Linn.) Spreng produced significant ($p<0.001$) protection

to the animals from formation of pyloric ligation induced gastric ulceration. Protections were 50.52%, 47.06% and 37.37% respectively for root, leave and stem of *Murrya koenigii* (Linn.) Spreng. Omeprazole produced more protection (68.86 %) in course of formation of gastric ulcer by pyloric ligation method. Ulcer index in this group came 9.0 ± 1.12.

Gastric ulcer is a common disorder. In this disorder a discontinuity in the gastric mucosa is observed. There is medicine to treat ulcer[11]. These include drugs inhibiting proton pump, receptor blocking drugs, drugs affecting central nervous system and drugs that affect the mucosal barrier[12-15]. Many of these drugs, however, do not fulfill all requirements and

reports on clinical evaluation of these drugs show that there are incidences of relapses and adverse effects such as impotency, arrhythmias and haetopoietic changes occur[16] . Hence, the search for an ideal anti – ulcer drug continues and has also been extended to vegetables, medicinal plants, herbs etc. in search for new and novel molecules, which afford better protection and decrease the incidence of relapse.

Sanyal *et al.*[17] found that vegetable banana is efficacious not only for experimentally induced gastric ulcers in albino rats, mice, guinea pigs etc. but also for humans suffering from gastric ulcers. In 1999 Akah *et al.* demonstrated anti gastric ulcer activity of the herb *Cassampelos mucronata*[18]. Shetty *et al.*[19] , Sairam *et al.*[5] , Maity *et al* [20-21]. as well as Dharmani and Palit[22] confirmed anti gastric ulcer activity of *Ginkgo biloba*, *Convolvulus pluricaulis Chois,* tea root extract and *Vernonia lasiopus* respectively . We also reported anti gastric ulcer activity of few medicinal plants of this part of India in different experimental ulcer models [23-26]. During the work we have noted anti ulcer activity of *Murrya koenigii* (Linn.) Spreng leaf against ethanol induced gastric ulcer in albino rats[3].

In this context, we intended to see whether root and stem of *Murrya koenigii* (Linn.) Spreng also possess anti gastric ulcer activity or not. The present study was thus undertaken to know the anti gastric ulcer activity of root and stem of *Murrya koenigii* (Linn.) Spreng and, if so, to do a comparative evaluation of anti gastric ulcer activities of root, stem and leaves of *Murrya koenigii* (Linn.) Spreng against ethanol, hydrochloric acid, indomethacin, swimming stress and pyloric ligation induced gastric ulcer in albino rats.

Results showed that in all gastric ulcer models studied root, stem and leaves of *Murrya koenigii* (Linn.) Spreng exerted anti ulcer activity. Anti ulcer activities were statistically significant ($p<0.001$). Maximum activity was noted in roots followed by leave and stem.

It is known that numerous plants specially medicinal plants are going to extinct day by day. There are various reasons behind it but one important reason is the continuous use of root of medicinal plant in folk medicine[27,28]. In this context present study may convey the message that when root, leave or stem of *Murrya koenigii* (Linn.) Spreng showed anti gastric ulcer activity, root of the plants may be escaped in treatment of ulcer to save the plant from extinction.

4. Conclusion

Root, leave and stem of *Murrya koenigii* (Linn.) Spreng showed anti ulcer effect against ethanol, hydrochloric acid, indomethacin, swimming stress and pyloric ligation induced gastric ulcer in albino rats. Anti ulcer effect in all cases was found statistically significant though root of the plant had maximum anti gastric ulcer effect. The study thus gave a message that root of

Murrya koenigii(Linn.) Spreng should not be used to treat ulcer to save the plant from extinction.

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