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Pharmacological Investigations on *Aglaia roxburghiana* (W & A) Miq. Var. *Beddomei* Leaves

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***Aglaia roxburghiana* is a traditional remedy for a variety of diseases in Ayurveda. The ethanolic extract of the leaves was screened for related activities whereupon it exhibited significant antiinflammatory activity in rats in acute and chronic models. The LD_{50} value was 2 g/kg. The extract protected mast cell degranulation by compound 48/80 and inhibited histamine-induced contractions in guinea pig ileum. The data obtained in this study suggest that the extract may act by stabilizing mast cells and blocking histamine receptors.**

Aglaia roxburghiana (W&A) Miq. Var. *Beddomei* (Meliaceae) is a source drug for Priyangu, used in Ayurveda[1]. The plant is considered as a remedy for dysentery, skin diseases; leprosy, inflammation, leucoderma and abdominal pain[2,3]. It is said to be cooling and useful in burning sensation of the body and painful micturition[4]. There is no detailed literature pertaining to the pharmacological activity of the leaves of this plant. Hence the ethanolic extract of the leaves, which has been found to contain alkaloids, steroids and triterpenoids[5,6] has been considered for the present study to evaluate specific pharmacological activities, if any, before initiating work to isolate chemical constituents.

MATERIALS AND METHODS

The leaves of *Aglaia roxburghiana* were freshly collected from Tirupathi hills in Andhra Pradesh and authenticated by the botanist, Captain Srinivasa Murti Drug Research Institute for Ayurveda, where a voucher specimen has been deposited.

Shade dried and coarsely powdered leaves (2 kg) were extracted with 90% alcohol by cold percolation method. The solvent was removed by distillation over water bath and traces under vacuum. This extract, designated as LF (yield 72.7 g) was suspended in carboxymethyl cellulose (CMC) and used for animal experiments. Swiss albino mice (20-25 g), Wistar albino rats (150-200 g), guinea pigs (400-500 g) were used for various experiments.

Preliminary screening and acute toxicity testing:

Mice were tested with different doses of LF extract (500-4000 mg/kg, s.c) and continuously observed for 6 h. The changes in various autonomic and behavioural responses were noted. The animals were kept under observation for a further period of 24 h and mortality, if any, was noted. Based on the results of preliminary screening[7] three doses (100, 200 and 400 mg/kg, s.c.) was selected for further experiments.

Analgesic activity:

This was investigated in mice using acetic acid-induced writhing[8]. Morphine sulphate (0.25 mg/kg, s.c) was used as a standard analgesic for comparison.

Antiinflammatory activity:

Carrageenan-induced hind-paw oedema in rats[9] was

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used to determine acute antiinflammatory effect. Different groups of rats were tested with three doses of LF extract. Carrageenan (0.1 ml 1% solution) was injected into the right hind paw 30 min after LF extract administration. The paw volume was measured plethysmographically 5 h after carrageenan injection.

Cotton pellet granuloma in the rat was used to evaluate chronic antiinflammatory potential of the extract[10]. Sterile cotton-pellets (10 mg) were implanted s.c in the arm-pits and groins of albino rats. The animals were treated with LF extract for 7 days. All the animals were sacrificed on day 8 and cotton-pellets were removed, dried at 50° for 24 h and weighed. In the acute and chronic models of inflammation, the activity of LF extract was compared with ibuprofen (100 mg/kg, s.c) treated animals.

Mast Cell degranulation (*in vitro* study):

This was carried out using the modified method of Kaley and Weiner[11]. LF extract was added to the incubates to produce a concentration of 1, 10 or 100 µg/ml. After 10 min the mast cell degranulator compound 48/80 (10 µg/ml) was added and incubated for further 10 min. The percentage degranulation was calculated. The effect of LF extract *per se* was studied in separate mesenteric bits and percentage degranulation was calculated. Disodium cromoglycate (DSCG) 1 µg/ml was included in the study for comparison.

Antiulcerogenic potential:

Adult male albino rats (130-150 g) were selected and ulcers were induced as described by Shay *et al*[12]. The animals were treated with LF extract 30 min prior to pyloric ligation. A separate group of animals received ranitidine 100 mg/kg orally 60 min prior to pyloric ligation.

The animals were sacrificed 18 h later, the volume, free and total acidity of gastric contents were examined. The gastric ulcers were scored visually according to severity in arbitary units raging from 0.5 and subjected to histopathological examination.

Intestinal Smooth muscle (*in vitro*):

Healthy adult guniea pig starved overnight was sacrificed, the terminal ileum was cut, washed, mounted in an organbath. The contractions were recorded with histamine according to the method of Ghosh[13]. Following this the LF extract was added and contractions were recorded. The effect of LF extract on histamine-induced contractions was also investigated.

Statistical analysis:

The results were analysed by Analysis of variance followed by Dunett's test. Statistical significance was considered at $p \leq 0.05$ level.

RESULTS

Preliminary screening and acute toxicity:

There was no significant change in the various autonomic and behavioural responses in mice after LF extract administration compared to the control animals. The LD_{50} value was found to be 2.0 g/kg.

Analgesic activity:

Treatment with LF extract did not alter the number of acetic acid induced writhings in mice compared to vehicle treated animals. But, morphine treatment significantly reduced the number of writhings in mice.

Antiinflammatory activity:

In carrageenan-induced paw oedema, ibuprofen produced a significant reduction in paw oedema. Similarly a significant reduction was observed with different doses of LF extract (Table-1). In the cotton pellet granuloma test, dose-dependent reduction in the weight of the cotton-pellets was observed after LF extract administration. The reduction was significant at all the doses tested (Table-2) and comparable with ibuprofen.

TABLE 1 : EFFECT OF *AGLAIA ROXBURGHIANA* ON ACUTE INFLAMMATION

Treatment (mg/kg; s.c)	Paw oedema (ml)
Vehicle	0.73±0.04
Ibuprofen 100	0.43±0.04*
LF extract	
100	0.37±0.06*
200	0.38±0.06*
400	0.33±0.04*

Each value represents the mean±SEM of (n=6) observations. Asterisks denote Statistical significance at $p \leq 0.05$ (Dunett's test)

TABLE 2 : EFFECT OF *AGLAIA ROXBURGHIANA* ON CHRONIC INFLAMMATION

Treatment (mg/kg; s.c)	Cotton pellets (mg)
Vehicle	48.73±7.05
Ibuprofen 100	23.25±1.36*
LF extract	
100	37.40±1.8*
200	32.60±1.0*
400	22.65±0.9*

Each value represents the mean±SEM of (n=6) observations. Asterisks denote Statistical Significance at $p \leq 0.05$.

Effect on mast cells:

Compound 48/80 *per se* produced extensive degranulation of mast cells. Pretreatment with LF extract reduced this degranulation significantly at 10 and 100 µg/ml (Table-3). However, it was less compared to disodium cromoglycate.

Effect on gastric secretion and ulceration:

Treatment with a potent histamine (H_2) antagonist, ranitidine significantly reduced the volume of gastric secretion, free acidity, total acidity and also the ulcer score compared to vehicle treatment in pyloric ligated rats. Treatment with LF extract reduced the volume significantly which was dose-dependent. But free acidity was reduced only at 100 mg/kg and total acidity was not reduced by all the doses tested. The ulcer score did not reveal any protection with the different doses of the extract (Table-4). Severity of the ulcer was represented by ulcer score and not by ulcer index. Histopathological examination revealed extensive ulceration after LF extract treatment and confirmed the ulcerogenic potential.

Effect on isolated guinea pig ileum:

LF extract *per se* did not produce any significant effect on the intestinal smooth muscle (results not shown). However, a dose-dependent reduction in histamine response was observed after treatment with LF extract.

DISCUSSION

The experiments designed in the present study were based on traditional claims. In acute toxicity experiments, the LD_{50} values were found to be 2 g/kg. Hence the doses of 100, 200 and 400 mg/kg (5%, 10% and 20% LD_{50}) were selected for experiments. The results of the present study indicates a potent antiinflammatory effects of the leaf extract of *Aglaia roxburghiana* as evidenced by a significant reduction in carrageenan-induced paw oedema and cotton pellet granuloma. The strong antiinflammatory activity of *Aglaia roxburghiana* leaf extract may probably be due to stabilization of mast cells and histamine receptor antagonism. Histamine is liberated in acute inflammation and is important during the early phase in initiating axon reflex and in allergic responses. Platelet activating factor (PAF), another mast cell constituent

TABLE 3 : EFFECT OF *AGLAIA ROXBURGHIANA* ON COMPOUND 48/80 INDUCED DEGRANULATION OF MAST CELLS

Pre-treatment (µg/ml)	Treatment (µg/ml)	% degranulation
Vehicle	Vehicle	21.8±1.51
Vehicle	48/80-10	66.0±1.15
LF extract		
1	48/80-10	66.0±1.7
10	48/80-10	55.0±2.31*
100	48/80-10	43.6±1.45*
DSCG I	48/80-10	20.0±1.9*

*$p<0.05$ (Dunett's test) Compared with vehicle+48/80 treatment. Each value represents the mean±SEM of (n=5) observations

TABLE 4 : ANTI ULCER ACTIVITY OF *AGLAIA ROXBURGHIANA* LEAVES

No.	Treatment (mg/kg)	Volume (ml)	#Free acidity	#Total acidity	Ulcer score
1.	Vehicle	8.48±0.48	2.10±0.37	4.6±0.08	2.83±0.46
2.	Ranitidine 100	6.51±0.51*	1.0±0.0	0.6±0.0	0.33±0.20*
	LF extract				
3.	100	1.60±0.15*	0.63±0.1	5.56±0.3	1.8±0.64
4.	200	0.60±0.06*	1.9±0.4	5.0±0.44	2.0±0.62
5.	400	0.43±0.04*	3.8±0.58	3.8±0.58	2.3±0.54

Each value represents the mean±SEM of (n=6) observations. Asterisks denote significance at $p \leq 0.05$. # Free and Total acidity expressed as the volume of 0.01 N NaOH required to neutralise 1 ml of gastric juice.

causes vasodilatation, increased vascular permeability and is chemotactic to white cells[14]. These mediators from mast cells can be released by injury, various histamine releasing agents, interleukin-1, histamine releasing factors derived from neutrophils, macrophages and platelets[14]. The protective effect of *Aglaia roxburghiana* extracts against mast cells degranulation may be responsible for the observed antiinflammatory effect of this plant. However the effect of *Aglaia roxburghiana* on other inflammatory mediators cannot be excluded as mast cell degranulation is only one of the complex mechanisms in the pathogenesis of inflammation.

Similar to nonsteroidal antiinflammatory agents the leaf extract of this plant exhibits ulcerogenic potential eventhough it reduced the volume of gastric secretion. The extract does not possess any analgesic activity. As there is similarity in the antiinflammatory and ulcerogenic actions of nonsteroidal antiinflammatory drugs and *Aglaia roxburghiana* extract, it is logical to suggest that *Aglaia roxburghiana* may also inhibit prostaglandin synthesis while mediating its effect. However this suggestion needs to be verified.

The phytochemical analysis of the LF extract of *Aglaia roxburghiana* has revealed the presence of triterpenoids, steroids and alkaloids. The antiinflammatory activity may be attributed to one or more of the above mentioned substances found in the leaf extract of *Aglaia roxburghiana*.

REFERENCES

1. Chopra, R.N., Nayar, S.L and Chopra, I.C., In; Glossary of Indian Medicinal plants, C.S.I.R, New Delhi 1956, 9.
2. Kirtikar, K.R. and Basu, B.D. In; Indian Medicinal plants. Vol 1, International Book Distributors, Dehra Dun, India, 1975, 550.
3. Chunekar, K.C. In; Indian Materia Medica, Choukhamba Vidya Bhavan, Varanasi, 1969, 251.
4. Georgewatt, In; Dictionary of Economic products of India, Vol 1, Periodical experts, 42-D, Vivek Vihar, Delhi, 1972, 145.
5. Purushothaman, K.K., Sarada, A., Connolly, J.D., and Akinniji, J.A., **J. Chem. Soc Perkin.** 1979, 1, 3171.
6. Balakrishna, K., Kundu, A.B. and Patra, A., **J. Nat. Products.,** 1990, 53, 523.
7. Miller, L.C. and Tainter, M.L., **Proc. Soc. Exp. Biol. Med.** 1944, 57, 262.
8. Koster, R.M., Anderson, M. and De Beer, E.J., **Fed. Proc.** 1959, 18, 412.
9. Winter, C.A., Risley, E.A. and Nuss, G.W., **Proc. Soc. Exp. Biol. Med.** 1962, 111, 544.
10. Winter, C.A., Risley, E.A. and Nuss, G.W. **Proc. Soc. Exp. Biol. Med.** 1963, 141, 369.
11. Kaley, G. and Weiner, R., **Annals of New York Academy of Sciences.** 1971, 180, 347.
12. Shay, H., Homarnov, S.A., Fils S.S., Moranzul, D., Gruenstein, M., and Siplet, H., **Gastroenterology,** 1945, 5, 43.
13. Ghosh, M.N. In; Fundamentals of experimental Pharmacology, Scientific book agency, Calcutta 1984, 88.
14. Water, J.B. and Talbot, I.C., Eds In; Water and Israel General Pathology, Churchill Livingstone, New York, 1996, 117.