Antiinflammatory Activity of Bark of *Machilus macrantha* Nees. (Lauraceae)

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In the present study, the bark of *Machilus macrantha* Nees. (Lauraceae) was investigated for anti-inflammatory activity in carrageenan-induced rat paw oedema. The alcoholic and aqueous extract showed dose-dependent inhibition of rat paw oedema, at per oral doses of 100 and 200 mg/kg, when compared to control group. The activity was compared with that of the standard drug, diclofenac sodium (15 mg/kg, p. o.)

Inflammatory diseases including different types of rheumatic disease are very common throughout the world. The greatest disadvantage in the presently available potent synthetic drug lies in their side effects, toxicity and reappearance of symptoms after discontinuation. Hence, search for new antiinflammatory agents that retain therapeutic efficacy and yet devoid of adverse effects are justified. There is much hope for finding active antirheumatic compounds from indigenous plants as these are still used in therapy despite the progress in conventional chemistry and pharmacology in producing effective drugs[1].

Machilus macrantha Nees. (Lauraceae), commonly known as *Gulmavu* (in Kannada), is a large tree grows up to 27 m in height, found in Bihar, Deccan peninsula and Western Ghats. The bark is pale brown with darker spots and rough[2]. It is used in asthma and rheumatism[3]. The bark is traditionally used in rheumatism by local practitioners (personal communication). A literature survey revealed that no scientific investigation regarding antiinflammatory activity of the bark of plant. In the present investigation, an attempt was made to test the bark for antiinflammatory activity based on its use.

For the present study, the bark was collected from Jamboti area of Belgaum district and the identity of the drug was established by microscopic study at the Department of Botany. R. L. Science Institute, Belgaum. The freshly collected bark was shade dried and then powdered to particle size No. 40. A powder (100 g) was subjected to cold maceration with distilled water (250 ml) for 7 d and the remaining powder (150 g) was exhaustively extracted with 95% alcohol (450 ml) in a Soxhlet extractor. Aqueous extract was dried at room temperature while alcohol extract was concentrated on rotary vacuum flash evaporator at 50° and finally to dry residue. The yield of aqueous and alcohol extract was found to be 4.0 g (4% w/w) and 15.0 g (10% w/w), respectively. The preliminary phytochemical screening of aqueous and alcohol extracts were performed using standard qualitative chemical tests[4-6]. Both the extracts were kept in a desiccator till experimentation. The test and standard drugs were suspended in distilled water to get concentration of 10 mg/ml each.

Antiinflammatory activity was assessed using the carrageenan-induced rat paw oedema method[7]. The ethical clearance was obtained by the Institutional Animal Ethics committee (Registration no. 221/CPCSEA) before the experiment. Male Wistar rats, weighing between 100-150 g, were procured from the animal house of J. N. Medical College, Belgaum. Rats were kept in polypropylene cages and fed on standard laboratory diet with water *ad libitum*. The animals were exposed to alternate cycle of 12 h of darkness and light each. Animals were divided into six groups of 6 animals each and were given the following treatments.

Group 1 (control) received 1 ml distilled water orally. Group 2 received 15 mg/kg of diclofenac sodium orally. Groups 3 and 4 received alcoholic extract 100 mg/kg and

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TABLE 1: MEAN INCREASE IN PAW VOLUME AND PERCENT INHIBITION AFTER TREATMENT WITH TEST MATERIAL.

Group	Test material (dose)	Mean increase in paw volume± SE. (ml)					
		1 h	2 h	3 h	4 h	5 h	6 h
1	Control	0.33±0.04	0.47±0.01	0.81±0.01	1.00±0.04	1.05±0.02	1.00±0.02
2	Diclofenac (15 mg/kg)	0.16±0.02 (51.5)*	0.28±0.03 (40.4)*	0.52±0.02 (35.8)*	0.57±0.01 (43.0)*	0.42±0.01 (60.0)*	0.25±0.01 (75.0)*
3	Alcohol extract (100 mg/kg)	0.25±0.03 (24.2)	0.39±0.02 (17.0)	0.55±0.02 (32.0)*	0.60±0.02 (40.0)*	0.55±0.02 (47.6)*	0.39±0.02 (61.0)*
4	Alcohol extract (200 mg/kg)	0.19±0.01 (42.4)	0.33±0.05 (29.8)	0.37±0.08 (54.3)*	0.21±0.06 (79. 0)*	0.09±0.02 (91.4)*	0.05±0.02 (95.0)*
5	Aqueous extract (100 mg/kg)	0.27±0.02 (15.2)	0.34±0.05 (23.4)	0.60±0.03 (25.9)*	0.55±0.03 (45.0)*	0.48±0.04 (54.3)*	0.40±0.04 (60.0)*
6	Aqueous extract (200 mg/kg)	0.17±0.04 (48.5)	0.25±0.05 (46.7)	0.50±0.02 (38.3)*	0.33±0.06 (67.0)*	0.40±0.06 (61.9)*	0.08±0.03 (92.0)*

*Indicates significant anti-inflammatory activity at P<0.001 compared to control. All values are mean±SE of sample size of 6. All treatment are given orally. Values in parenthesis are percent inhibition of increase in paw volume.

200 mg/kg, p.o, respectively. Groups 5 and 6 received aqueous extract 100 mg/kg and 200 mg/kg, p.o, respectively. After 1 h, rats were challenged with a subcutaneous injection of 0.1 ml of 1% w/v solution of carrageenan into the subplanter side of the left hind paw. The paw was marked with ink at the level of lateral malleolus and immersed in mercury up to this mark. The paw volume was measured plethysmographically immediately after injection (0 h) and followed by every hour for 6 h after injection of carrageenan to each group. The difference between the initial and subsequent reading gave the actual oedema volume.

Percentage inhibition of inflammation was calculated using the formula, % inhibition=100 (1- vt/vc) where Vt represents oedema volume in test compounds and Vc represent oedema volume in control. The data was analyzed using student's t-test. Level of significance was set at p<0.001. The results obtained as mean increase in paw volume (ml) and % inhibition are represented in Table 1.

Carrageenan-induced inflammation is a biphasic phenomenon[8]. The first phase of oedema is attributed to release of histamine and 5-hydroxytryptamine. Plateau phase is maintained by kinin like substances and second accelerating phase of swelling is attributed to prostaglandin like substances[9].

The results obtained indicate that administration of alcoholic extract and aqueous extract resulted in dose-dependent decrease in the rat paw oedema at 1, 2, 3, 4, 5, 6 h. Both alcohol and aqueous extracts, in the doses administered, were found to have no antiinflammatory activity at 1st and 2nd h (P>0.001). However, both extracts showed significant activity at rest of the time periods studied (P<0.001) while standard drug, diclofenac sodium showed significant activity from all through out (P<0.001). These results suggest that the bark of *Machilus macrantha* show significant reduction in rat paw oedema in carrageenan induced inflammation. We are reporting the antiinflammatory activity of the bark for the first time. The preliminary phytochemical investigation on aqueous and alcohol extracts indicated presence of steroids, alkaloids, tannins. However, detailed phytochemical investigation of bark is worthwhile to pin point the activity.

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REFERENCES

1. Chawla, A.S., Handa, S.S., Sharma, A.K. and Kaith, B.S., **J. Sci. Ind. Res.**, 1987, 46, 214.

2. Kirtikar, K.R. and Basu, B.D., In; Indian Medicinal Plants , 2 nd Edn., Vol. III, India International Book Distributors, Dehradun, 1999, 2155.
3. Anonymous, In; The Wealth of India: A dictionary of Indian Raw Materials and Industrial Products, Vol. VI, Publications and Information Directorate, CSIR, New Delhi, 1988, 204.
4. Brain, K.R. and Turner, T.D., In; The Practical Evaluation of Phytopharmaceuticals., John Wright and Sons, London, 1975, 1.
5. Clarke, E.G.C., Eds., In; Isolation and Identification of Drugs, Vol. II, Pharmaceuticals Press, London, 1975, 905.
6. Farnsworth, N.R., **J. Pharm. Sci.**, 1966, 55, 225.
7. Winter, C.A., Risley, E.A. and Nuss, G.W., **Proc. Soc. Exp. Biol. Med.**, 1962, 111, 544.
8. Vinegar, R., Schreiber, W. and Hugo, R.J., **J. Pharmacol. Exp.Ther.**, 1969, 166, 95.
9. Rosa, M.D., Giroud, J.P. and Willoughby D.A., **J. Pathol.**, 1971, 104, 15.

Analgesic, Antiinflammatory and Antibacterial Activity of Some Novel 2-Phenyl-3-(substituted methyl amino) quinazolin-4(3*H*)-ones

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In view of the potent analgesic antiinflammatory and antimicrobial activities exhibited by quinazolin-4(3*H*)-ones, a series of novel 2-phenyl-3-(substitutedmethyl amino) quinazolin-4(3*H*)-ones have been synthesized. When these compounds were evaluated for analgesic, antiinflammatory and antibacterial activities, compounds I and II exhibited comparable analgesic activity, while the compounds II and III exhibited comparable antiinflammatory activity with the standard diclofenac sodium.

Bacterial infections often produce inflammation and pain. In normal practice, two groups of agents (chemotherapeutic, analgesic and antiinflammatory) are prescribed simultaneously. The compounds possessing all three activities are not common. Quinazolines and condensed quinazolines have received the attention of medicinal chemists due to their wide range of biological activities which include analgesic and antiinflammatory[1-3], antibacterial[4-7], antiviral[8-9], antihistaminic[10], antihypertensive[11] and anticancer[12] activities. Mannich bases of the above compounds were reported to possess potent antibacterial activity[13]. In the present study it was envisaged that a drug molecule possessing the above mentioned pharmacophore could be of advantage since it might possess analgesic, anti-inflammatory and antibacterial activities. The title compounds, 2-phenyl-3-(substitutedmethyl amino) quinazolin-4(3*H*)-ones [Mannich bases of 3-amino-2-phenylquinazolin-4(3*H*)-one] were synthesized by our earlier reported method[14], i.e. by condensing the active hydrogen atom of 3-amino of 3-amino-2-phenyl quinazolin-4-(3*H*)-one (3, Scheme I), with formaldehyde and the desired amines [Mannich reaction]. The starting material (3, Scheme I) was synthesized from anthranilic acid. The compounds were tested for analgesic, antiinflammatory and antibacterial activities.

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