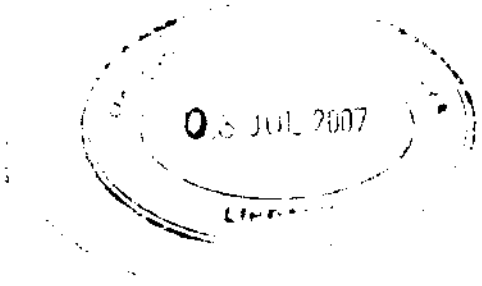
BIOACTIVITIES OF *Alpinia calcarata* Rosc. RHIZOME



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Rhizomes of *Alpinia calcarata* Rosc. (Zingiberaceae) are recommended as an aphrodisiac and used in traditional medicine of Sri Lanka to treat bronchitis, cough, respiratory ailments, diabetics, asthma and arthritis. However, validity of these claims has not been scientifically proved so far expect the antiinfalmmatory activity (using a single dose of the decoction). Further, it is reported to have antibacterial, antifungal, anthelmintic and insecticidal activities. The toxic effects of the rhizomes are not known and it may possess new bioactivities. Therefore, the objectives of this study were to (1) investigate the antioxidant, antinociceptive and gastroprotective activities and mode of actions which are not reported yet (2) scientifically validate the antidiabetic and antiinflammatory activities which are claimed by Aryuvedic physicians and investigate their mode of actions (3) standardization of *A. calcarata* extracts and (4) toxicological studies. These objectives were carried out using hot water extract (HWE) and hot ethanol extract (HEE) of *A. calcarata* rhizomes.

The results revealed that both HWE and HEE possess antioxidant, antinociceptive, gastroprotective, antiinflammatory and, hypoglycemic and antihyperglycemic activities in a dose dependent manner. In addition, there were no serious toxic effects within the doses that tested for bioactivities of the plant up to 42 days. *A. calcarata* extracts possess moderate antioxidant activities *in vitro* assays. Delaying the lipid peroxidation was more prominent by HWE and HEE than their ability to scavenge the free radicals. To investigate the antinocicpetive activity, different concentrations (100, 250, 500, 750, 1000 mg/kg) of *A. calcarata* extracts were orally administrated to rats and the reaction times were determined using three nociception models (hot plate, tail flick and formalin

tests). The antinociceptive activities of 500 mg/kg dose of both extracts were comparable with the effect of the reference drug, pethidine. The antinociceptive activity was supraspinally mediated via opioid receptors.

Three doses (500, 750, 1000 mg/kg) of HWE and HEE were evaluated for gastroprotective activity against ethanol induced gastric ulcers in rats. Oral administration of *A. calcarata* extracts provided dose dependent and significant protection against gastric damage caused by ethanol. The gastroprotective effect of HWE and HEE were superior to that of cimetidine, the reference drug. The HWE significantly inhibited gastric volume, acidity (total and free) and significantly increased the gastric pH. On the other hand, gastric mucosal secretion remained unaltered. Further, *A. calcarata* extracts had strong antihistamine and antioxidant activities, which could have played an active role in inducing gastroprotection.

The antidiabetic activity was tested in normoglycemic and streptozotocin (STZ) – induced diabetic rats by oral administration of three doses (250, 500, 750 mg/kg) of HWE and HEE. In normoglycemic rats both extracts significantly lowered the blood glucose level in a dose dependent manner. Hypoglycemic activity of tolbutamide, the reference drug, was comparable to that of HWE. However, hypoglycemia induced by 500 mg/kg and 750 mg/kg of HEE was superior to that of tolbutamide. Moreover, both extracts markedly improved the oral glucose tolerance test. Tolbutamide also improved the glucose tolerance test upto 3 h. This impairment was comparable to that of HWE but was inferior to HEE. Further, HEE significantly inhibited the glucose absorption from the small intestine and increased the glycogen accumulation in both liver and skeletal muscle.

The antiinflammatory activity of *A. calcarata* extracts was determined using four doses (250, 500, 750, 1000 mg/kg) in rats. All the tested doses of both extracts showed significant and dose dependent antiinflammatory activity compared to the respective controls. Among the tested doses, 500 mg/kg of HEE showed the best antiinflammatory activity during the early phase (1 – 2 h) by 54.9 - 68.3% and late phase (3 – 4 h) by 51.5

– 77.6%. Further, inhibitory activity elicited by 500 mg/kg dose of HEE during the late phase was comparable to that of the reference drug, Indomethacin. Furthermore, the results revealed that the antiinflammatory activity of *A. calcarata* possibly mediated via prostaglandin synthesis inhibition and antihistamine activity.

Physico-chemical parameters, phytochemical screening studies, TLC and densitometer fingerprints were used to standardize the rhizomes and their extracts of *A. calcarata* grown in Sri Lanka. Phytochemical screening revealed the presence of alkaloids, steroids, tannins, phenolic and flavonoids in both HWE and HEE. Although the classes of phytochemicals present are common to both extracts, chemical constituents belonging to HWE differ from that of HEE. *A. calcarata* extracts were devoid of unacceptable side effects even following sub chronic administration: The results showed that both extracts were well tolerated in terms of % weight gain, food and water intake, adverse behaviors, mortality, hepatotoxicity (in terms of AST, ALT), renotoxicity (as judged by serum urea and creatinine), haematotoxicity (in terms of WBC, RBC counts and Hb concentration) or organ weights expect the weight of the spleen. Both extracts increased the weight of the spleen, which possibly suggest lymphoproliferative activity.

In conclusion, this study scientifically revealed the multifaceted bioactivities of *A. calcarata* rhizomes and its potential to be developed as drugs in future.