ABSTRACT

Cancer is the uncontrolled growth of abnormal cells in the body. Cancer being multifactorial in its origin possess heterogeneous nature and is characterized by accelerated and uncontrolled growth, dysregulation of apoptosis, invasion, angiogenesis and metastasis. Literature provides evidence for the application of various plants and plant derived products for successful cancer treatment. In our study, we have investigated on the immunomodulatory efficacy of Rhizophora apiculata (R.apiculata) and its application in inhibiting inflammation, tumor and ulcerative colitis.

Initially, we studied the anti-inflammatory activity of R.apiculata extract. R.apiculata prevented carrageenam and formalin induced paw edema showing significant anti-inflammatory effect. R.apiculata showed significant inhibitory effect on the edema formation and also reduced serum inducible nitric oxide synthase (iNOS), cyclooxygenase (COX-2) and prostaglandin E-2 levels suggesting that the main mechanism of action of the tested plant extract may involve interfering in the histamine and prostaglandin biosynthesis pathway and may influence inflammatory mediators. It is then be known that R.apiculata prevented carrageenan and formalin induced paw edema showing significant anti-inflammatory effect preventing chronic inflammation and thus preventing tumor progression.
Administration of *R. apiculata* has shown significant (*p* < 0.05) increase in total White blood cells (WBC) count, haemoglobin content, relative organ weight, bone marrow cellularity, *α*-esterase positive cells and phagocytic index of the host determining its strong immunostimulant potential. *R. apiculata* shown convincing anti-tumor activity by inhibiting solid tumor development *in vivo*. In this study the *R. apiculata* significantly (*p*<0.05) reduced tumor volume, body weight, serum gamma-glutamyl transferase (GGT), nitric oxide (NO), glutathione level and tumor necrosis factor-α (TNF-α). Also *R. apiculata* significantly increased the total WBC count, haemoglobin content, relative organ weight, bone marrow cellularity, *α*-esterase positive cells and survival rate of the mice. Tumor histopathology further supported these protective findings which confirm the anti-tumour efficacy of *R. apiculata*.

The process by which cancer cells spread to other parts of the body called as metastasis. Tumor formed by metastatic cancer cells is called a metastatic tumor or a metastasis. WHO report reveals that metastasis is the major cause of death from cancer. In the current study, anti-metastatic activity of *R. apiculata* was analyzed using *in vivo* models. Administration of *R. apiculata* significantly inhibited the lung tumor nodule formation and enhanced the life span of the metastasis induced animals. The higher level of lung hydroxyproline, uronic acid and hexosamine, markers during the onset of metastasis was significantly reduced after *R. apiculata* treatment. Similarly serum GGT, serum NO and serum sialic acid levels were also decreased after the treatment with
R. apiculata. Therefore these investigations provide a valid claim that R. apiculata could serve as a potential anti-metastasis agent.

The chemoprotective effect of R. apiculata was evaluated. R. apiculata inhibited the experimental mice from the adverse effect of cyclophosphamide (CTX) as evidenced by increased total WBC count, differential count, haemoglobin content, organ weight, bone marrow cellularity and α-esterase positive cells and significantly reduced the serum NO and glutathione levels. Further, R. apiculata significantly decreased the CTX induced urotoxicity and intestinal toxicity as evidenced from histopathological analysis. The above evidences clearly underline R. apiculata as an effective chemoprotective agent during cancer chemotherapy.

Since R. apiculata exhibited anti-inflammatory activity we had also studied its protective effect during ulcerative colitis, an inflammatory bowel disease. R. apiculata could significantly inhibit the ulceration and macroscopic scoring. Biochemical analysis showed that the R. apiculata could significantly alter lipid peroxidation, myeloperoxidase, superoxide dismutase and glutathione levels compared to ulcerative colitis control group. The increased NO, iNOS, COX-2, TNF-α and lactate dehydrogenase (LDH) during ulcerative colitis was significantly (p<0.01) reduced by R. apiculata treatment. These reports were further supported by histopathological analysis showing minimal damage to the mucosa with slight sub-mucosal edema and
mild inflammatory cell infiltration of colon in *R.apiculata* treated group compared with the ulcerative colitis control group.

In conclusion, the results obtained from our study indicate the effectiveness of *R.apiculata* in the inhibition of inflammation, tumor and metastasis. *R.apiculata* also exhibited a protective role over ulcerative colitis. Therefore the overall efficacy of *R.apiculata* might be due to its immunomodulatory effect or due to the presence of pharmacologically active ingredients. The present study will shed light in the future to attract new investigations related with drug discovery to cure cancer, colitis and other inflammatory disorders.