ABSTRACT

PART -I

The fight against Cancer has been a major problem for many years. The formation of Cancer is a multistage process in which multiple genetic alternations occur usually over the span of years to derail sufficiently the control of cell growth, division and differentiation. Cancer arises from a step wise accumulation of genetic changes that liberates neoplastic cells from the homeostatic mechanism to normal cell poliferation.

In the present study we have dealt two plants, Holostemma adakodien and ophiorrhiza mungos as Part I and Part II. H. adakodien belongs to the family Asclepiadaceae, distributed mainly in tropical Himalayas, Deccan and Kerala. The root of this plant is an important ingredient of Rasayana drug, which is capable of maintaining youthful vigour and strength. The results of the present study revealed that root extract of H. adakodien possessed antioxidant activity. The 70% methanolic extract required for 50% inhibition of superoxide radical production, nitric oxide radical production, hydroxyl radical generation and lipid peroxide formation in vitro were 83.33 μg/MI, 250 μg/ml., and 80μg/ml respectively. The role of free radicals in the inflammatory process is well known and most of the antioxidants possess anti-inflammatory effect. The 70% methanolic extract of H. adakodien effectively inhibit the inflammation induced by formalin and carrageanen.

Oral administration of the extract (250mg/kg body weight and 500 mg/kg body wt.) inhibited the CCl₄ induced hepatotoxicity in male wistar rats. The levels of GOT, GPT, ALP, Total protein and Albumin were found coming closer to the normal level as compared to the control group in a dose dependent manner. The histopathological studies also confirmed the ability of the extract against induced hepatic damage.
Administration of 70% methanolic extract of H. adakodien (250 Kg/Body wt and 500 Kg/body wt) inhibited the toxic effects in mice treated with cyclophosphamide, a chemotoxic drug used against cancer. Administration of H adakodien enhanced the total count and hemoglobin level in a dose dependent manner. In treated groups the level of GSH, GPX and SOD were increased and came closer to normal level and the decrease in lipid peroxidation were also noticed. The results confirmed that H. adakodien root extract can be used as a chemoprotective agent.

The crude extract and the fractions obtained from column chromatographic separation were analysed for the preliminary cytotoxic test, and it was found that the acetone fraction (AF) of extract have maximum cytotoxicity (515µg/ml). The AF found to inhibit the proliferation of DLA and EAC cells at 5 hr. culture. It also effectively inhibits the cell proliferation of human breast cancer cells. (MDA MB 231 and MCF-7).

Administration of AF (100 mg/kg body wt and 250 mg/kg body wt) reduced the solid tumor volume in dose dependent manner. The AF showed synergistic effect along with radiation and cyclophosphamide in reducing solid tumor volume.

The results of experiments on the mechanism of cell death indicate that the inhibition of cell growth involves apoptotic cell death. The nuclear condensation in 300µg/ml H.adakodien AF treated cells were clearly evident in the inverted fluorescent microscopy by staining with ethidium bromide and acridine orange. Experiments with double labelling technique using annexin V flous/PI clearly showed the apoptotic changes on treatment with H.adakodien AF. So our results suggested that the induced cell death leads to antitumor effect by the induction of apoptosis.

The preliminary screening of crude as well as acetone fraction of H.adakodien root extract showed the presence of flavanoids. Further
investigations are necessary for the isolation and elucidation of active principle.

**PART II**

*Ophiorrhiza mungos* is a rich source of the potent antineoplastic therapeutic agent camptothecin, which is effective in the complete remission of lung, breast, uterine and cervical cancer. With increasing demand, most of the plants have been indiscriminately exploited from their natural habitat for the isolation of this valuable therapeutic agent. The biotechnological application such as plant tissue culture seems to be a viable option for the production of this high value therapeutic compound without destroying the natural flora. For this purpose various tissue culture techniques have been established to enhance the production of this compound from different parts of *O. Mungos*. The present study reveals that the biotic elicitors like chitin, chitosan and fungal extracts significantly enhance the production of camptothecin. Permeabilization with DMSO found to be enhancing the production of camptothecin. Hence the present study gives an alternative for large scale production of camptothecin without affecting the natural flora in a cost effective method.