ABSTRACT

The untapped wealth of plant kingdom has become target for the search by multinational drug companies and research institutes for new drugs and lead molecules. There has been a global resurgence of interest in plant-based drugs probably due to the reasons like i) high cost (Upwards of $ 2000 million) of synthetic drugs, ii) non-renewable source of basic raw materials of synthetic drugs, iii) environmental pollution by the chemical industry iv) long history of use and better patient tolerance as well as public acceptance of plant based drugs, v) renewable sources of plant drugs, vi) cultivation and processing of plant drugs is environmental friendly, vii) plants constitute to be a major source of new lead molecules. Though herbal medicines are effective in the treatment of various ailments, very often these drugs are unscientifically exploited or improperly used. Therefore, these plant drugs deserve detailed studies in the light of modern science.

The modern system of medicine still lack in providing suitable medicament for a large number of disease conditions like peptic ulcer and diabetes mellitus and in spite of tremendous advances made in the discovery of new therapeutic compounds. Among these ailments, diabetes mellitus is one of the most prevalent health problems in the world, and is more alarming in the developing countries like India and china. The development of herbal drugs for peptic ulcer and diabetes mellitus is a major thrust area in natural product research and pharmacology and need through investigation.

There are no scientific reports on anti-oxidant activity, anti-ulcer activity and anti-diabetic activity of Ficus racemosa Linn. fruit extract and Aegle marmelos root
extract. Hence, the present research work has been undertaken with an objective to investigate selected herbal drugs, *Ficus racemosa* Linn. (Gular) and *Aegle marmelos* (Bael) to screen biological activities like anti-oxidant, anti-ulcer and anti-diabetic activities in various experimental animal models. Moreover, in the traditional system of Indian medicine, plant formulation and combined extracts of plants are used as drug of choice rather than single drug. In this context, the present studies have been designed to scientifically validate the traditional claims of *Ficus racemosa* Linn. (Gular) and *Aegle marmelos* (Bael) and formulate a potent anti-ulcer and anti-diabetic herbal formulation.

As a part of *in-vitro* anti-oxidant activity of *Ficus racemosa* and *Aegle marmelos*, total phenol content (TPC), DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity, hydroxyl radical scavenging activity, scavenging of H$_2$O$_2$, lipid peroxidation were estimated in the present study. *In vitro* antioxidant activity of *Ficus racemosa* (Fruit extract) and *Aegle marmelos* (root & leaf extract) was clearly evident from the DPPH radical scavenging activity, hydroxyl radical scavenging activity and H$_2$O$_2$ scavenging activity. This is also clearly reflected by decreased lipid peroxidation of free radicals. Antioxidant activity of *Ficus racemosa* (Fruit extract) and *Aegle marmelos* (root & leaf extract) probably owing to the presence of high amounts of observed total phenol content (TPC) in the present study.

The results proved the excellent antioxidant activity of *Ficus racemosa and Aegle marmelos* in cell-free (*in vitro*) ROS-generating systems. To further evaluate, *in-vivo* anti-oxidant effect of *Ficus racemosa* (Fruit extract) and *Aegle marmelos* (root & leaf extract) in CCl$_4$ induced rat liver by assessing the parameters, lipid peroxidation
(LPO), superoxide dismutase (SOD) and catalase (CAT) studied. *Ficus racemosa* (Fruit extract) and *Aegle marmelos* (root & leaf extract) at a dose of (100 mg/ kg & 200 mg/kg) treatment significantly decreases the LPO level but increases SOD and CAT enzyme activity. When the antioxidant activity of *Aegle Marmelos* leaf extract compared to the root extract clearly shows that root extract produces more potent anti-oxidant activity than the leaf extract.

Gastroprotective effect of *Ficus racemosa* fruit extract and *Aegle marmelos* root extract was evaluated using the different standard experimental models of ulcer like pylorus ligation-induced gastric ulcers, aspirin-induced gastric ulcers, ethanol (EtOH) -induced gastric ulcers, cold restraint stress -induced gastric ulcers. Both *Ficus racemosa* fruit extract and *Aegle marmelos* root extract have demonstrated the efficacy in different models of ulcer in the following order: Pylorus ligation-induced gastric ulcers > Aspirin-induced gastric ulcers > Ethanol (EtOH) -induced gastric ulcers > Cold restraint stress -induced gastric ulcers. *Ficus racemosa* fruit extract has shown much better efficacy than *Aegle marmelos* root extract in these models of ulcer. Both *Ficus racemosa* fruit extract and *Aegle marmelos* root extract have exhibited the dose dependent anti-ulcer activity with all the doses. The dose of 400mg/kg has produced maximal anti-ulcer efficacy. Hence, this dose of *Ficus racemosa* fruit extract and *Aegle marmelos* root extract was used for the assessment of parameters of gastric secretion or mucosal studies. Anti-ulcer activity was clearly evident from the reduced gastric secretion parameters and elevated mucoprotective parameters. The observed anti-ulcer activity of *Ficus racemosa* fruit extract and *Aegle marmelos* root extract are probably attributed to observed anti-oxidant activity of
Ficus racemosa fruit extract and Aegle marmelos root extract in the gastric tissue. This was clearly evident by the decreased levels of MDA, decreased activities of SOD and CAT.

The antidiabetic activity of Ficus racemosa and Aegle marmelos root extracts were studied at a dose level of 200 mg/kg. The drugs were administered daily for three weeks. After three weeks of treatment the blood samples was analyzed for blood glucose content. Results revealed that both the plant extracts significantly reduced the serum glucose levels in STZ induced diabetic rats. Hence, both the plant extracts clearly shows the antidiabetic activity. Particularly, Ficus racemosa has shown more degree of these effects than Aegle marmelos.

The effect of combinations of these two plant extracts with a dose ratio of (1:1), were demonstrated on experimental models of ulcer and diabetes. So the results clearly implied that the three combinations A1-50mg/kg (25mg of FRE + 25 mg of AME), A2-75mg/kg (37.5 mg of FRE + 37.5mg of AME) & A3-100mg/kg (50mg of FRE + 50mg of AME) show significant antiulcer in CRS induced ulcer model and anti-diabetic activity in STZ induced diabetic model. The FT-IR spectral studies were carried out to study the drug and excipient interactions. The spectral data clearly reveals that there was no interference of the drug with the excipients used.

The selected combinations of these two plant extracts were formulated into compressed tablets and evaluated for various physical parameters of the compressed tablets. The results show that all the physical parameters of the compressed tablets meet the USP specifications.