CHAPTER-5
5.0 SUMMARY AND CONCLUSION

*Calotropis gigantea* is used as a traditional medicinal plant with unique properties. Traditionally *Calotropis* is used alone or with other medicinals to treat common disease such as fevers, rheumatism, indigestion, cough, cold, eczema, asthma, elephantiasis, nausea, vomiting, diarrhoea. According to Ayurveda, dried whole plant is a good tonic, expectorant, depurative, and anthelmintic. The dried root bark is a substitute for ipecacuanha, febrifuge, anthelmintic, depurative, expectorant, laxative, asthma, bronchitis, and dyspepsia. The leaves are useful in the treatment of paralysis, arthralgia, swellings, and intermittent fevers. The flowers are bitter, digestive, astringent, stomachic, anthelmintic, and tonic. *Calotropis* is also used as a reputed homeopathic drug.

The purpose of the present study was to evaluate scientifically *Calotropis gigantea* using various animal models in our laboratory. In the present study, the hydroalcoholic (50:50) extract of the aerial part of *Calotropis gigantea* was studied for its anti-inflammatory, analgesic, antipyretic, antiulcer, antidiarrheal and toxicological properties. Anti-inflammatory activity was evaluated on the basis of inhibitory effect of the extract on topical, acute and chronic methods by using xylene-induced ear oedema in mice, carrageenan-induced hind paw oedema and cotton-pellet induced granuloma in the rats. The extract dose-dependently produced significant (P<0.001) inhibition of xylene-induced ear oedema in mice. The extract showed a maximum inhibition (84.62%) at a dose of 400 mg/kg against ear oedema and its effect was higher than diclofenac sod. (73.06%). It also demonstrated significant (P<0.001) inhibition of carrageenan-induced paw oedema in rats. Extract at a dose of 200 and 400 mg/kg produced significant inhibition of the oedema at 3rd and 4th h (P<0.05 and P<0.001 respectively) after administration of the phlogistic agent. On the cotton pellet induced granulomatous tissue formation in rats, the extract at a dose of 400 mg/kg significantly reduced the weight of
cotton granuloma in rats compared to the vehicle treated rats (P<0.05). These findings suggest that extracts of the aerial part of *Calotropis gigantea* possess potent anti-inflammatory effects indicating the possibility of developing *Calotropis gigantea* as the cheaper and potent anti-inflammatory agent.

Analgesic activity was evaluated by using hot-plate test in mice, tail-flick latent period in rats and acetic acid-induced writhing response in mice. Hydroalcoholic extract of *Calotropis gigantea* produced a significant increase in the latency to response of mice to hot plate thermal stimulation dose dependently. Maximum dose of the extract produced significant effect from 1h to 2 h of the study (P<0.01), highly significant increase in the latency to response was observed from 3 h to 5 h. All the doses considered for the present study (100, 200 and 400 mg/kg, ip) produced a significant increase in the tail-flick latency, throughout the 5 h study. The extract at 100 and 200 mg/kg exerted a moderate activity inducing a protection of 37.23% and 48.92% respectively, for acetic acid-induced writhing. However, extract at a dose of 400 mg/kg exhibited about 69.15% inhibition. These findings suggest that extracts of the aerial part of *Calotropis gigantea* possess potent analgesic effects indicating the possibility of developing *Calotropis gigantea* as potent therapeutic agent for the treatment of pain.

Pharmacologically it was evaluated for its antipyretic activity by using yeast-induced and TAB vaccine-induced pyrexia in rats and rabbits. In both yeast-induced and TAB vaccine-induced fever, the fever was significantly (P<0.001) reduced and body temperature was normalized by administration of 200 and 400 mg/kg dose intraperitoneally. Based on the results of the present study it can be concluded that the extract of *Calotropis gigantea* has potent antipyretic activity against both yeast-induced and TAB vaccine-induced fever.
The anti-ulcer activity of 50% ethanolic extract of *Calotropis gigantea* aerial part in pyloric ligation and stress models of ulcer was assessed in rats. Intraperitoneal administration of extract (100, 200 and 400 mg/kg) exhibited significant anti-ulcer activity in both models. The extract of *Calotropis gigantea* at doses of 100 (P<0.01), 200 and 400 mg/kg, ip significantly (P<0.001) attenuated the gastric mucosal damage induced by pyloric ligation dose dependently when compared with control group. The percent inhibition of acid secretion at 400 mg/kg, ip was more than the effect of ranitidine (77.75 V/s 60.32). Pretreatment with extract caused a dose-related reduction in stress-induced ulceration (P<0.001) and the results are comparable to ranitidine. The present study provides strong evidence of antiulcer activity of *Calotropis gigantea* against the models selected for the present study. The antiulcer action is mediated partially by a decrease in gastric acid secretion and an enhancement of defensive agents.

The anti-diarrheal effect of hydroalcoholic (50:50) extract of aerial part of *Calotropis gigantea* was studied against castor oil-induced-diarrhea model in rats. The gastrointestinal transit rate was expressed as the percent of the longest distance traversed by the charcoal divided by the total length of the small intestine. The weight and volume of intestinal content induced by castor oil were studied by enteropooling method. Like atropine (3 mg/kg, ip) there were significant reductions in fecal output and frequency of droppings when the plant extracts of 200 and 400 mg/kg doses were administered intraperitoneally compared with castor-oil treated rats. All doses of the plant extracts also significantly retarded the castor-oil induced enteropooling and intestinal transit. The dose 100 (P<0.01), 200 and 400 mg/kg significantly inhibited (P<0.001) weight and volume of intestinal content. The remarkable anti-diarrheal effect of *Calotropis gigantea* extract against castor oil-induced diarrhea model attests to its utility in a wide range of diarrheal states.
The *Calotropis gigantea* has been studied extensively for its pharmacological activity in our laboratory. But a clear picture of its toxicokinetics is still obscure. In the present investigation the toxicity associated with crude hydroalcoholic (50:50) extract derived from aerial part of *Calotropis gigantea* have been evaluated in experimental animals. The acute toxicity was evaluated in mice and chronic toxicity was evaluated in rats. At the end of 30 days of treatment the histopathological and haematological study were done after sacrifice. The 50% mortality was noted at 4600 mg/kg dose of the extract, within 3 hours of drug administration. Therefore, the therapeutic index of the extract for antipyretic activity can be regarded as 30.6. In histopathological studies no abnormalities were detected in the organs of control or experimental animals, indicating that hydroalcoholic (50:50) extract of *Calotropis gigantea* had no severe adverse effects on cellular structures, at low doses selected for the present study indicating the possibility of developing *Calotropis gigantea* as the cheaper, safer and potent therapeutic agent for the treatment of various ailments. The changes in the blood vessels viz., dilation, periportal haemorrhage of pancreas and occluded lumen in lungs during chronic toxicity indicated the effect of *Calotropis gigantea* on endothelial cells of vascular system. The typical histopathological changes observed in this study should be regarded as diagnostic aid for toxicity of *Calotropis gigantea* in rats.

Although the extraction procedure adopted was intended to obtain an extraction similar in chemical composition to the one used in the traditional medicine, this may not hold true as far the proportion of individual components are concerned. Traditionally, the administration of the plant extract may also last from weeks to months. The extract was administered intraperitoneally, inspite of the fact this is not the route employed in folk medicine. This result seems to support the view that the plant has some influence on prostaglandin-biosynthesis because prostaglandin is believed to be a regulator of body
temperature. The exact nature of phytoconstituents present in this plant fraction is not clear, however, phytochemical analysis of the extract revealed the presence of terpenes, terpene derivatives, pentacyclic triterpenoids and triterpenoids and they have been isolated from the roots of the _Calotropis gigantea_ may also be responsible for its antiulcer activity. All the above arguments are in agreement with experiments undertaken for other species of the genus _Calotropis_ with similar chemical compounds, and it has been extensively studied for its anti-inflammatory, analgesic, antipyretic, antiulcer, antidiarrheal activity. Further studies on factors like histamine, serotonin, GABA, PGs, nitric oxide, cAMP, cGMP, ion channels and endogenous opioid peptides would throw more light on the precise mechanism of hydroalcoholic extract of _Calotropis gigantea_.

Apart from the medicinal and therapeutic uses of the drug, the safety of a drug is an important criterion. The present study shows that the hydroalcoholic (50:50) extract of _Calotropis gigantea_ has no severe toxic effects in rats at the dose and duration used in this study.

It can be concluded that the present results support the ethno-medical application and indicates that the hydroalcoholic extract (50%) of aerial part of _Calotropis gigantea_ contains biologically active components, which might be useful for the management of inflammatory, algesic, fever, gastric ulcer and diarrhea conditions. Further studies to isolate and characterize the active component, in order to understand the mechanism of action of the extract, which is on at our laboratory is therefore warranted.