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Summary & Conclusion
SUMMARY AND CONCLUSION

Management of diabetes is a challenging task in the current scenario of a fast moving life of human beings. Several methodologies have been followed or advised to control the blood sugar level. But, still the effective therapy has not yet evolved. An increase in the percentage of diabetes and its related consequences with organ damage alarm the people to look into the effective therapeutic options available. Management with allopathic molecules has long been accepted as one of the options, but, the requirement on the increased dosage levels upon usage suggested the incidence of resistance towards the molecules.

The involvement of herbal medicines in the management of diabetes has long been explored in the Indian system of traditional medicines. But the slow effect and the questions on availability of suitable herbs and the adulterations in the formulation make people to ignore these medicines at higher level. However, the recent realization on the efficacy of few herbal medicines and the advancement of delivery systems open up the new research inputs on herbal medicines and delivery systems.

Further, it has been realized that trace elements or the micronutrients play an important role in controlling the diabetes. Thus, most of the allopathic formulations carry the potential micronutrients like, Chromium, Copper, Zinc, Tin, Cobalt, etc. The essential role played by these micronutrients has not yet explored completely, but it has been said that these elements involved in the enzymatic system mediated insulin synthesis in the body system.
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Based on these information, in the present study, an approach was made on to evaluate the herbal active constituent and its representative micro-nutrient complexes in controlling the diabetes. The plant chosen for the study was Embelia ribes. The plant Embelia ribes has already been in reports for the various pharmacological efficacies including diabetes due to its active constituent embelin. However, the role of metal complexes of embelin in diabetes has not yet revealed or studied. Thus, the present has been taken up with the aim to extract the embelin from Embelia ribes and preparation of the metal complexes. Followed by preparation, the novel drug delivery system in the form of nanoparticles has been made and the efficacy of prepared nanoparticles studied under in vivo diabetes model.

The observations made in the present study have been framed in to Five Individual chapters. Chapter I summarizes the General Introduction on diabetes, treatment options, herbal medicines, importance of trace elements, etc in detail along with the aim and the major objectives of the study.

Chapter II describes the review of literatures available till date on the current scenario on diabetes, management, herbal medicines and its impact on diabetes, micronutrients and the related complexes in controlling diabetes, etc. in detail.

Chapter III summarizes the materials and methods followed in the present study on extraction of the active constituent, characterization of active constituent, preparation of representative copper and zinc complexes and the characterization studies on these prepared complexes in detail. It has been observed that the principle active constituent of Embelia ribes berries is embelin. About 1.9 ± 0.1 gram of pure
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Embelin was obtained from 100 gms of *Embelia ribes* berries by soxhlet extractor with n-hexane as a solvent for 6 hours. Characterization studies of embelin and its metal complexes revealed that the results obtained by UV-visible, XRD and NMR analyses were on par with the reported literatures.

Chapter IV describes the nanoparticles of embelin and its complexes to improve the efficacy of the drug. Optimization and preparation of nanoparticles were done by emulsification-cross linking method. Chemical cross linking was carried out with Glutaric acid as a cross linker and Span 80 was used as an emulgent. Characterization studies like SEM, TEM and related parameters suggested that spherical surfaced nanoparticles were obtained with a better encapsulation efficacy of the drug. The prepared nanospheres exhibited prolonged drug release i.e more than 8 hours by dialysis bag technique.

Chapter V has been subdivided into two sub-chapters, Chapter Va illustrates the *in silico* method of identifying the potency of the drugs prepared in the present study in controlling the diabetes using Discovery studio version 3.1. All the compounds tested were found to inhibit α-amylase and aldo reductase enzymes. Interestingly, copper-embelin complex fails to dock with both the enzymes, which might be due to poor binding property of the ligand.

Chapter Vb describes the *in vivo* studies carried out with animal models and revealed that treatment of diabetic animals with nanoparticles of embelin and its metal complexes significantly decrease the glucose levels compared to untreated diabetic animals. The results of histopathological studies suggested that damage was not at detectable level with the lower dose of the drugs, whereas, the severity of the
lesions were observed in the sections of pancreas, liver and kidney in all the high
dose groups. Moreover, Cu-embelin nanoparticles had shown antidiabetic activity
even though it failed to do in-silico analysis. All the above results confirm potent
antidiabetic activity for *Embelia ribes* and its metal complexes.

In conclusion, the results of the present study clearly demonstrated the
potential of nanoparticles of embelin and its metal complexes for the management
and treatment of diabetes and its complications.

The present thesis also encloses with the research papers published in
reputed Journals, presentation at both National and International conferences made
based on the results obtained from the study. Further, appreciation in the form of
best paper award and best poster award received for the presentation of the study
and a project grant from the University, were the credits of the present study.