Conclusions

The present study was carried out to evaluate the efficacy of alcoholic extracts of roots of *Salacia reticulata*, *Clitoria ternatea*, combination of SR+CT, enriched environment, combination of SR+CT+ EE and insulin on diabetes induced behavioral and cognitive changes in young rats. Treatment was started from day one of diabetic state and given for 30 days. Efficacy of combination of SR+CT treatment, 20 days after the onset of diabetes was also studied. Before initiating different treatments, animals were tested for increased vulnerability of cognitive dysfunction with increasing duration of diabetes in young rats. The results of the present study suggest that the increasing duration of the diabetes not only induces learning and memory deficits, but also contributes to certain behavioral changes such as high levels of anxiety. However, the underlying mechanisms are yet to be established.

The present investigation demonstrated that treatment with combined extracts of SR+CT significantly decreased behavioral and cognitive deficits in young diabetic rats. The combination was found to be more effective, only when started from day one of confirmation of diabetes and given for 30 days. However, the same combined therapy of SR+CT failed to recover cognitive deficits when administered after 20 days of diabetic duration. Animals treated with combined herbal extracts and reared in enriched housing conditions (SR+CT+EE), showed improved behavioral and cognitive measures compared with other groups, which received single treatment. Effect of SR+CT+EE was found to be better than insulin, a conventional treatment for T1DM. After treatment with SR+CT+EE for 30 days, diabetic animals were able to attain not only the normoglycemic levels but also showed significantly improved measures in almost all three tests (EPM, PA and MWM), suggesting the recovery of deficits in cognition and behavioral changes.
A. CLINICAL IMPLICATIONS

Current study highlights the importance of early diagnosis of T1DM to prevent the deleterious effects of chronic diabetes on developing brain. The untreated hyperglycemia for longer durations may be one cause of diabetic encephalopathy. This may have an important implication for school performance of children with early EOD, in whom hyperglycemia induced impairment of complex cognitive function is seen.

Cognitive enhancers that are developed to treat cognitive disorders in diabetes may prove useful in other conditions, including neurological disorders in children or dementia in old age or for cognition enhancement in healthy younger population. However, the pattern of neuro degeneration in EOD may differ from that in other disease states.

Given the increasing young diabetic population, cognitive enhancement is likely to be increasingly required and desirable for therapeutic purposes. If potent cognitive enhancers are available in the future, they are likely to have substantial economic impact. However, the use of putative cognitive enhancers that span decades could lead to unanticipated long-term side effects, possibly necessitating long-term follow-up research of participants and post-marketing surveillance. Agents that enhance cognition are likely to have both beneficial and harmful effect and thus, more research is needed in the future to ensure that disease-modifying drugs are used to maximize benefits and minimize harms. In summary, the present study indicates the need of research into the area of integrative medicine, especially in understanding the efficacy of alternate cognitive enhancers such as herbal therapies and enriched environment.
B. SCOPE FOR FUTURE STUDIES

Diabetic encephalopathy is one of the thrust areas in neuroscience research. Although, results of the present study are in support of the above conclusion, further studies are clearly warranted to firmly establish the link between hyperglycemia and cognitive deficits. There is a need for advanced techniques to explore underlying mechanisms of diabetic encephalopathy in T1DM of early onset in particular. Molecular studies may bring more focus on pathogenicity and hence, the line of treatment for cognitive deficits in EOD.

Further studies are required to understand the mode of action of putative neurocognitive enhancers. The knowledge may improve the treatment strategies for cognitive deficits. The present study necessitates the in vitro studies of phytochemical constituents of SR and CT in diabetic encephalopathy. Further studies are needed to screen some more herbs with potent antidiabetic and nootropic properties.

C. LIMITATIONS OF THE STUDY

The results of the present study show the beneficial effect of herbal therapy in reducing the cognitive deficits in animals with EOD. The study can be improved but it has its own limitations. Newer diabetic animal models such as Non-obese diabetic (NOD), Knockout mice (KO) could be more relevant to study the cognitive deficits of T1DM. In the present study, data was collected manually. Hence, the possibility of human error cannot be ruled out. The precise data could have been collected by instruments installed with newer software and recorded through video camera. Analysis of neurochemicals in brain, in vitro models, image analysis and micronuclear assay would have improved the quality of the present study.