Introduction

Diabetes mellitus is a clinical syndrome, characterized by hyperglycemia due to an absolute or relative deficiency of insulin or non-responsiveness of tissues to insulin. The minimum defining characteristic feature to identify diabetes mellitus is chronic and sustained elevation of circulating glucose concentrations in the plasma. Diabetes is an endocrine disorder with long term metabolic derangement. It is frequently associated with permanent and irreversible structural and functional changes in the body\(^1\). Dysmetabolism leads to the development of complications of diabetes. Major complications include nephropathy, angiopathy, retinopathy, peripheral neuropathy and encephalopathy. Thus, diabetes causes substantial morbidity and disability, even contributing to the mortality, by causing renal failure and cerebrovascular diseases\(^2\). In 2011, around 4.6 million deaths occurred worldwide due to diabetes.

Latest figures from Diabetes Atlas (IDF, 2011) showed that presently 366.2 million people are living with diabetes. It is expected to rise up to 552.8 million by the year 2030 (Map 1). India is designated as diabetes capital of the world with 61.3 million diabetics in the year 2011 and estimated to rise up to 101.2 million by the year 2030. The global financial burden of the diabetes is increasing steadily at an exponential rate. Globally, healthcare expenditure for diabetes is expected to account for up to 11% of the total budget. In 2011, diabetes alone caused at least 465 billion USD in healthcare expenditures. An estimated average of USD 5,063 per diabetic patient was spent in high-income countries compared to USD 271 in low- and middle-income countries\(^3\).

Diabetes mellitus affects both the peripheral and central nervous system (CNS). However, central effects are less well documented and studied than peripheral deficits\(^4\). Behavioral and cognitive changes in Type 1 diabetes mellitus (T1DM) have
Introduction
gained attention since last two decades. Long-standing concern about the deleterious effects of diabetes on CNS has enhanced with the increasing incidence of T1DM in children\textsuperscript{5}. A recent meta-analysis (2005) showed mild cognitive impairment in diabetic patients, mainly reflecting in diminished mental speed and flexibility\textsuperscript{6}. Many studies have also reported behavioral changes such as elevated levels of anxiety, depression and fear complex in Type 1 diabetic rats and humans\textsuperscript{7-9}.

Children with onset of diabetes before the age of five years could be more prone to the effects of diabetic complications related to encephalopathy. Many researchers have shown the relationship between neuropsychological changes and T1DM of early onset\textsuperscript{8,10,11}. Children with T1DM have repeatedly shown mild to moderate deficits on a wide range of neuropsychological tests. Although the magnitude of the cognitive decrement is relatively modest, even moderate forms of behavioral and cognitive changes can potentially hamper day to day activities of the diabetic child. These may present problems in more demanding situations and can have a negative impact on the quality of life in particular. In a nutshell, diabetic encephalopathy, in the younger age group will have serious consequences on healthcare, education and their performance during the productive life span\textsuperscript{12}. Hence, it is imperative that diabetes in young children should be detected and treated at its earliest phase to prevent irreversible neuronal damage.

Diabetes induced behavioral and cognitive changes appear to be associated with several factors. Both chronic hyperglycemia\textsuperscript{13,14} and recurrent episodes of severe hypoglycemia\textsuperscript{15} are thought to be associated with cognitive dysfunction in patients with T1DM. However, the combined effects of juvenile onset and the occurrence of complications of diabetes may have an impact on cognition\textsuperscript{16,17}. The abnormalities
underlying diabetic encephalopathy are complex and not well understood. The questions that still remain unresolved are contribution of different disease variables such as duration of diabetes, levels of glycemic control and development of neuropsychological impairment. Although hypoglycemic effects on CNS are well understood, the acute effects of hyperglycemia have not been studied extensively. There is a need for resolving the issue of hyperglycemia induced diabetic encephalopathy.

Another major challenge posed to the health care system across the globe is the effective management of diabetes mellitus. Undoubtedly, the management of diabetes is to focus on the balanced modulation of several targets that can provide a superior therapeutic effect and a decrease in side effect profile. Currently, the only feasible treatment available for T1DM is insulin. Unfortunately, insulin has its own limitations such as cost, route of administration, undesirable side effects and development of resistance over a period of time. This has led to an increasing demand by patients for natural products with anti-diabetic activity\textsuperscript{18,19}. Between 70\% - 95\% of population in a majority of developing countries, especially those in Asia, Africa, Latin America and Middle East, use traditional and herbal medicines to address their health-care needs\textsuperscript{20}. Hence, a more easily ‘available, accessible and affordable’ alternative therapy, especially a newer herbal formulation is very much the need of the time.

The present study has been carried out to determine the effects of duration of diabetes in streptozotocin (STZ) induced young diabetic rat pups. The efficacy of \textit{Salacia reticulata} Wight, an anti-diabetic plant\textsuperscript{21} and \textit{Clitoria ternatea} Linn, a nootropic herb\textsuperscript{22} and enriched environment on various cognitive and behavioral parameters have been evaluated. The cognitive and behavioral changes were tested in
elevated plus maze (EPM), passive avoidance box (PA) and Morris water maze (MWM).

Map 1: IDF-2011, Global projections of the number of people with diabetes mellitus\(^3\)