1. INTRODUCTION

Diabetes mellitus is one of the most common endocrine diseases in all populations and all age groups. It is a syndrome of disturbed intermediary metabolism caused by inadequate insulin secretion or impaired insulin action, or both. Diabetes mellitus comprises of heterogeneous group of disorders characterized by hyperglycemia, altered metabolism of carbohydrates, lipids and proteins. Along with this diabetes mellitus is associated with complications such as nephropathy, retinopathy, neuropathy and cardiovascular disease (Expert committee, 1997; Alberti and Zimmette, 1998).

Diabetes is mainly classified into two types as: Type-I (Insulin-Dependent Diabetes Mellitus, IDDM) and Type-II (Non-Insulin-Dependent Diabetes Mellitus, NIDDM). Both types are associated with excessive morbidity and mortality. Type I diabetes accounts for 5% to 10% of diabetes, usually occurs in children or young adults. This disease is caused by autoimmune destruction of the pancreatic β-cells that secrete insulin. The process involves a smoldering destructive process that can persist for several years and ultimately leading to failure of insulin secretion. Patients with type I diabetes require insulin therapy for survival and most patients ultimately develop devastating complications of this disease. The present need is for improved means of treating type I diabetes (strict glycemic control) until it is practical to prevent its development (Alberti and Zimmette, 1998).

Type II diabetes accounts for 90% to 95% of all patients with diabetes and is increasing in prevalence. Some of the known environmental factors that contribute to development of type–II diabetes are obesity, a sedentary lifestyle, and aging. Insulin resistance is a characteristic metabolic defect in the great majority of patients with
type II diabetes. As a consequence of insulin resistance, the \( \beta \)-cell produces increased amounts of insulin, and, if sufficient, the compensatory hyperinsulinemia maintains glucose levels within the normal range. In those individuals destined to develop diabetes, \( \beta \)-cell function eventually declines, and relative insulin insufficiency occurs. Thus, insulin resistance combined with \( \beta \)-cell failure leads to the decompensated hyperglycemic diabetic state.

In animals, particularly in canine and feline species incidence of diabetes mellitus is increasing. It is estimated that 2-3% of dog and cat population suffer from diabetes mellitus. Spontaneous diabetes is reported in many species of the animals. Rare cases of diabetes are reported in horses, cattle and sheep. Isolated cases of diabetes are reported in monkeys, mules, ferrets, pigs, buffaloes and pigs. Diabetes also has been reported in many breeds of birds (Anderson and Low, 1990).

Whereas in human beings diabetes is emerging as major threat to human health. It is the fifth leading cause of death in most developed countries. The world health organization estimated that there were 135 million diabetics in 1995 and this number would increase to 235 millions by the year 2010. An expected incidence of diabetes mellitus is 300 million by the year 2025.

India stands first with largest number of diabetics with 33 million diabetic populations at present and epidemiological studies indicate that the number will rise to 57 million by the year 2025. It is estimated that the annual cost of diabetes health care in India would be Rs.90 billion in an ideal situation of all patients receiving appropriate care. The estimated cost of diabetes in the United States is between $85bn and $92bn (Haffner, 1999)

Studies have shown that Indians are likely to get type II diabetes about a decade earlier than white people. Public health experts have cautioned that the early
onset of diabetes, coupled with an increasing life span, could burden India with a large number of patients with secondary health complications. Attempts to control diabetes have increased significantly over the last decade with the aim of extending life duration and simultaneously improving its quality by preventing the development of diabetes induced complications (Haffner, 1999).

The high costs of modern treatment of diabetes indicate an urgent need for the development of alternate strategies for the prevention and treatment of diabetes. In this regard current importance is on the higher plants as drugs per se and as sources of useful drugs on global basis. According to WHO, over 70% population in rural areas of developing countries still relies on traditional medicines for their primary health care. Since about 80% of the world’s population resides in the developing countries, about 64% of the total population of the world utilizes the plants as drugs, i.e. more than 3.2 billion people (Marles, 1995)

One approach in the discovery of new treatments is based on the reputed properties and uses of plants. This approach can find not only new remedies; but also new lead molecules may be obtained. Scientific investigations on such traditional medicines have led to the discovery of at least 119 plant derived chemical compounds of known structure are currently used as drugs or biodynamic agents that affect human and animal health.

In India, indigenous remedies have been used in the treatment of diabetes mellitus since 600 BC, the time of Charaka and Sushruta. Plants have always been an excellent source of drugs and many of the currently available antidiabetic drugs have been derived directly or indirectly from them. Even the discovery of widely used oral hypoglycemic drug, metformin came from the plant source *Galega officinalis*. The
traditional ethnobotanical literature reports about 800 plants that may possess anti-diabetic potential.

*Murraya koenigii* is one of the traditional medicinal plants mentioned in the ayurvedic literature for treatment of diabetes mellitus and other ailments. Today ayurvedic practitioners recommend the *Murraya koenigii* leaf decoction to diabetic patients to control hyperglycemia. There is an urgent need to systematically validate this traditional medicinal plant for antidiabetic activity using the scientific methodology. This study is conducted to evaluate the pharmacological and toxicological properties of different solvent extracts of *Murraya koenigii* leaves with following objectives:

1. To investigate antidiabetic activity of different extracts of *Murraya koenigii* leaves.
2. To investigate antioxidant activity of different extracts of *Murraya koenigii* leaves.
3. To investigate the hypolipidemic effect of different extracts of *Murraya koenigii* leaves.
4. To understand the possible mechanism of antidiabetic action of leaf extract(s) of *Murraya koenigii*.
5. To evaluate safety of the most promising leaf extract(s) of *Murraya koenigii*. 