Chapter 1

Introduction
Diabetes mellitus, long considered a disease of minor significance to world health, is now taking its place as one of the main threats to human health in the 21st century (Zimmet, 2000). The emergence of diabetes as the new-age killer is possibly one of the direct and visible outcome of our preoccupation with sedentary lifestyle and fast food culture. About 6% of Indians are estimated to have diabetes mellitus. According to WHO the number of persons affected by diabetes will get doubled by 2030 A.D. Diabetes mellitus is an endocrine disorder, characterized with hyperglycaemia. The disease is associated with three times higher mortality rate, three times higher incidence of heart disease and ten times higher incidence of blindness and gangrene. In modern medicine, no satisfactory effective therapy is still available to cure diabetes mellitus. It can be managed by exercise, diet and drug therapy. However, the pharmaceutical drugs are either too expensive or have undesirable side effects or contraindications. Therefore, the search for more effective and safer hypoglycaemic agents has continued to be an area of active research.

The past two decades have seen an explosive increase in the number of people diagnosed with diabetes worldwide (Amos et al., 1997). Pronounced changes in the human environment, and in human behaviour and lifestyle, have accompanied globalization, and these have resulted in escalating rates of both obesity and diabetes. Non-communicable diseases (NCD) such as diabetes and cardiovascular disease (CVD) have now become the main public health challenge for the 21st century, as a result of their impact on personal and national health and the premature morbidity and mortality associated with the NCDs (Zimmet, 2000). After taking so long to gain recognition, interest in diabetes is now mounting rapidly (Zimmet, 1999) and it is an exciting time for researchers and clinicians involved in the study and treatment of the disease. The problem has crept up on an unsuspecting public health community
The global figure of people with diabetes is set to rise from the current estimate of 150 million to 220 million in 2010, and 300 million in 2025 (Amos et al., 1997). This trend of increasing prevalence of diabetes and obesity has already imposed a huge burden on health-care systems and this will continue to increase in the future (Zimmet, 2000).

The diabetes epidemic, although apparent right around the world has been most pronounced in non-European populations, as evidenced by studies from Native American and Canadian communities, Pacific and Indian Ocean island populations (de Courten et al., 1997), groups in India (Ramachandran et al., 1997) and Australian Aboriginal communities (O’dea, 1991). WHO predicted India will have 79 million diabetics by 2030, an increase of 250% from 31 million in 2000 (WHO, 2005).

The potential for increase in the number of cases of diabetes is greatest in Asia (Amos et al., 1997). Data from Mauritius shows the highest yet reported prevalence in people of Chinese origin, in addition to demonstrating high diabetes prevalence and a notable secular increase between 1987 and 1998 in Asian Indians and Creoles (Zimmet, 1999). There is a need for developing safe and effective drugs for long-term management of diabetes.

A multidisciplinary ethnomedical approach by combining aspects of ethnobotany, traditional medicine and modern techniques of natural products chemistry to identify compounds from plant products as potential new therapeutic agents has become necessary. Potential plant leads are derived from ethnobotanical and ethnomedical field research by a team of botanists and Western-trained physicians in collaboration with traditional healers. We recently described this approach as an alternative pathway to discover potentially new drugs for the treatment of Type 2 diabetes mellitus.

Plants have always been an exemplary source of drugs and many of the currently available drugs have been derived directly or indirectly from them. The ethnobotanical information reports about 800 plants that may possess anti-diabetic potential (Alarcon-Aguilera et al., 1998). Several such herbs have shown anti-diabetic activity when assessed using presently available experimental techniques (Coimbra et al., 1992; Ajit Kar et al., 1999; Jafri et al., 2000). Wide arrays of plant derived active
principles representing numerous chemical compounds have demonstrated activity consistent with their possible use in the treatment of non insulin-dependent diabetes mellitus (NIDDM) (Ivorra et al., 1988; Marles and Farnsworth, 1995).

Diabetes often leads to disability from the vascular complications of coronary artery disease and cerebrovascular disease, renal failure, blindness, and limb amputation in addition to neurological complications and premature death (Weidmann et al., 1993). Commonly practiced pharmacological treatments of diabetes mellitus include oral hypoglycaemic agents and/or insulin injections (Lebovitz and Pasmanter, 1990). However, for many years people in Mexico have used plants to empirically treat diabetes. World ethnobotanical information about medicinal plants reports almost 800 plants used in the control of diabetes mellitus. In traditional practice, medicinal plants are used to control diabetes mellitus in many countries. This has caused an increase in the number of experimental and clinical investigations directed towards the validation of the anti-diabetic properties, which are empirically attributed to these remedies. Chemical studies directed to the isolation, purification and identification of the substances responsible for the hypoglycaemic activity were also reported (Ivorra et al., 1989; Alarcon-Aguilar et al., 1993).

Though development of modern medicine resulted in the advent of modern pharmacotherapeutics including insulin, biguanides, sulfonylureas and thiazolidinediones, there is still a need to look for new drugs as no drug (except strict glycemic control with insulin) has been shown to modify the course of diabetic complications.

The present study aims to evaluate the antidiabetic activity of flowers of two Unani medicinal plants Nelumbo nucifera and Punica granatum and to identify the possible mechanisms of action. A preliminary study on normal animals as well as on streptozotocin-induced diabetic animals was carried out. Based on the results of preliminary studies, chronic studies on streptozotocin-induced diabetic rats, streptozotocin-nicotinamide induced diabetic rats and high fat fed rats were also carried out.