Diabetes prevalence in India and its management through Indian system of medicines

Tabasum Fatima, Beenish and Bazila Naseer

Abstract
Diabetes describes a group of metabolic diseases in which either the person has inadequate insulin production or body is not properly responding to insulin, or both. This results in high blood sugar levels. Over-weight people have a much higher risk of developing diabetes compared with those having a healthy body weight. Being over-weight can destabilize metabolic systems. The diabetes capital of the world with as many as 50 million people suffering from diabetes (type 2), India has a challenge to face. India has been witnessing an alarming rise in the incidence of diabetes. According to WHO, 80% of diabetes deaths are occurring in low and middle income countries. This disease is triggered by persistent hyperglycemia which should not be underestimated, because the progress of the disease may lead to foot ulcers, followed by gangrene that may require amputation. In Unani system of medicine, various formulations have been proven to be useful in this condition but its efficacy has not been evaluated so far, on scientific parameters, particularly for the management of diabetic peripheral neuropathy. In this comprehensive review, focus is laid on various such drugs.

Keywords: Diabetes, status, unani medicine, control measures

Introduction
Like climate change, the relentless worldwide spread of non-communicable diseases offers an opportunity for low-middle-and high-income countries to join forces in addressing a major global challenge that threatens health and economies alike. A recent report from the World Health Organization identified six risk factors associated with non-communicable diseases as the leading global risk. Factors for death: high blood pressure, tobacco use, high blood glucose levels, physical inactivity, overweight or obesity, and high cholesterol levels. Non-communicable diseases are intricately linked to globalization, urbanization, and demographic and lifestyle transitions-all ubiquitous forces. Increasingly, such diseases are also linked to poverty and socioeconomic disparity and are no longer “diseases of affluence.” There are also complex but measurable associations between early life circumstances (e. g. maternal and childhood nutrition) and the risk of non-communicable disease in adulthood; hence, many developing countries now find themselves at a stage of epidemiologic and behavioral transition in which they face a growing burden of non-communicable disease on top of the ongoing hazards of under nutrition and communicable disease. Persons with a non-communicable disease are also vulnerable to common infectious diseases, such as tuberculosis and community-acquired pneumonias-and therefore to the poorer outcomes associated with these complications (Narayan et al. 2010) [28]. In the U. S. certain health conditions are readily accepted as “public-health disorders,” and others continue to be primarily viewed as “clinical diseases.” Reflecting on infectious conditions, it appears that disease burden, rapid change in disease incidence (suggesting preventability), and public concern about risk are three essential characteristics that define a public-health disorder. By any one of several criteria, diabetes is associated with a very high burden to individuals with the disease, as well as to society in general. Further, there is convincing and increasing evidence that primary, secondary, and tertiary prevention strategies are effective in reducing the disease burden associated with diabetes. Yet most would still consider diabetes primarily to be a clinical disease. In part, this perception is based on the fact that, in association with aging and a possible strong family history, diabetes and its complications may appear inevitable to many. Further, much of the burden associated with diabetes is insidious, coming on gradually only after a considerable number of years. Thus, the burden associated with diabetes has not dramatically increased in the past few months or years; it has been here for some time and is increasing steadily. Finally, our understanding of public concern is only now being systematically investigated (Vinicor et al. 1994) [46].
According to recent estimates, approximately 285 million people worldwide (6.6%) in the 20-79 year age group will have diabetes in 2010 and by 2030, 438 million people (7.8%) of the adult population, is expected to have diabetes. (IDF Diabetes Atlas, 4th edition International Diabetes Federation, 2009) [17]. The largest increase will take place in the regions dominated by developing economies. The global increase in the prevalence of diabetes is due to population growth, aging, urbanization and an increase of obesity and physical inactivity. The primary determinants of the epidemic are the rapid epidemiological transition associated with changes in dietary patterns and decreased physical activity. Unlike in the West, where older populations are most affected, the burden of diabetes in Asian countries is disproportionately high in young to middle-aged adults (Ramachandran et al. 2010) [16]. This could have long-lasting adverse effects on a nation’s health and economy, especially for developing countries. Estimated global healthcare expenditures to treat and prevent diabetes and its complications are expected to total at least 376 billion U. S. Dollars (USD) in 2010. By 2030, global healthcare expenditures to treat and prevent diabetes is projected to exceed some USD 490 billion (IDF Diabetes Atlas, 4th edition. International Diabetes Federation, 2009) [17].

**Status of diabetes in India**

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease (Joshi et al. 2007; Kumar et al. 2013) [19, 21]. In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) and United States (17.7 million) in second and third place respectively. According to Wild et al. (2013) [46], the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease (Wild et al. 2013) [46]. India currently faces an uncertain future in relation to the potential burden that diabetes may impose upon the country (Kaveeswar et al. 2014) [20]. Table 1 is showing recent reports of prevalence of diabetes country wise (Ramachandran et al. 2009) [34].

**Table 1:** Top 10 countries for estimated numbers of adults with diabetes, 2010 and 2030

<table>
<thead>
<tr>
<th>Country / Territory</th>
<th>2010 (millions)</th>
<th>2030 (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rank</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. India</td>
<td>50.8</td>
<td>67.0</td>
</tr>
<tr>
<td>2. China</td>
<td>43.2</td>
<td>62.6</td>
</tr>
<tr>
<td>3. U.S.</td>
<td>26.8</td>
<td>36.0</td>
</tr>
<tr>
<td>4. Russian</td>
<td>9.6</td>
<td>13.8</td>
</tr>
<tr>
<td>5. Federation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Brazil</td>
<td>7.6</td>
<td>12.7</td>
</tr>
<tr>
<td>2. Germany</td>
<td>7.5</td>
<td>12.0</td>
</tr>
<tr>
<td>3. Pakistan</td>
<td>7.1</td>
<td>11.9</td>
</tr>
<tr>
<td>4. Japan</td>
<td>7.1</td>
<td>10.4</td>
</tr>
<tr>
<td>5. Indonesia</td>
<td>7.0</td>
<td>10.3</td>
</tr>
<tr>
<td>Mexico</td>
<td>6.8</td>
<td>8.6</td>
</tr>
</tbody>
</table>

Source: Ramachandran et al. (2009) [34].

There are, however, patterns of diabetes incidence that are related to the geographical distribution of diabetes in India. Rough estimates show that the prevalence of diabetes in rural populations is one-quarter that of urban population for India and other Indian sub-continent countries such as Bangladesh, Nepal, Bhutan, and Sri Lanka (Anjana et al. 2011) [3]. Preliminary results from a large community study conducted by the Indian Council of Medical research (ICMR) revealed that a lower proportion of the population is affected in states of Northern India (Chandigarh 0.12 million, Jharkhand 0.96 million) as compared to Maharashtra (9.2 million) and Tamil Nadu (4.8 million), (Anjana et al. 2011) [3]. The National Urban Survey conducted across the metropolitan cities of India reported similar trend: 11.7 per cent in Kolkata (Eastern India), 6.1 per cent in Kashmir Valley (Northern India) (Zargar et al. 2004) [47]. 11.6 per cent in New Delhi (Northern India), and 9.3 per cent in West India (Mumbai) compared with (13.5 per cent in Chennai (South India), 16.6 per cent in Hyderabad (south India), and 12.4 per cent Bangalore (South India) (Ramachandran et al. 2001) [30]. A suggested explanation for this difference is that the north Indians are migrant Asian populations and south Indians are the host populations (Arora et al. 2010) [14], however this possible cause-and-effect has not been corroborated through further research. Similar ethnographic disparities have been observed in indigenous and non-indigenous populations in countries colonised by the Great Britain: indigenous people from New Zealand and Australia have been shown to suffer from diabetes and cardio-metabolic disorders more than the non-indigenous people (Bramley et al. 2004) [9]. Further studies are required in India to highlight cultural and ethnic trends and provide a more complete understanding of the differences in diabetes aetiology between Indian and other ethnic groups within India (Kaveeswar et al. 2014) [20]. Aged care facilities in rural areas report disparity in the diabetes management compared with their urban counterparts, with these populations more likely to suffer from diabetic complications compared to their urban counterparts (Khalil et al. 2012) [21]. More needs to be done to address the rural-urban inequality in diabetes intervention. Prevalence of diabetes in urban areas is shown as under in Table 2.

**Table 2:** Prevalence of diabetes in urban India since 2000

<table>
<thead>
<tr>
<th>Region</th>
<th>Year</th>
<th>Age of subjects (years)</th>
<th>Diabetes</th>
<th>IGT</th>
<th>IFG</th>
</tr>
</thead>
<tbody>
<tr>
<td>National</td>
<td>2000</td>
<td>&gt; 20</td>
<td>12.1</td>
<td>14.0</td>
<td>14.0</td>
</tr>
<tr>
<td>Reddy et al.</td>
<td>2003</td>
<td>20-69</td>
<td>8.4</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Sodhi et al.</td>
<td>2004</td>
<td>20-69</td>
<td>5.9</td>
<td>6.3</td>
<td>4.8</td>
</tr>
<tr>
<td>Northern India</td>
<td>2000</td>
<td>&gt; 20</td>
<td>11.6</td>
<td>8.6</td>
<td>--</td>
</tr>
<tr>
<td>Ramachandran et al.</td>
<td>2002</td>
<td>&gt; 20</td>
<td>13.5</td>
<td>16.8</td>
<td>--</td>
</tr>
<tr>
<td>Gupta et al.</td>
<td>2005</td>
<td>20-59</td>
<td>15</td>
<td>37</td>
<td>--</td>
</tr>
<tr>
<td>Prabhakaran et al.</td>
<td>2006</td>
<td>&gt; 20</td>
<td>14.3</td>
<td>10.2</td>
<td>--</td>
</tr>
<tr>
<td>Mohan et al.</td>
<td>2004</td>
<td>&gt; 20</td>
<td>19.5</td>
<td>4.1</td>
<td>7.0</td>
</tr>
<tr>
<td>Meenakshi et al.</td>
<td>2005</td>
<td>19-60</td>
<td>14.5</td>
<td>5.1</td>
<td>7.0</td>
</tr>
<tr>
<td>Ramachandran et al.</td>
<td>2005</td>
<td>&gt; 20</td>
<td>15.6</td>
<td>7.4</td>
<td>--</td>
</tr>
</tbody>
</table>

Other study was conducted in industrial workers (men only).
Source: Ramachandran et al. (2009) [34].

Obesity is one of the major risk factors for diabetes, yet there has been little research focusing on this risk factor across India (Zimmet et al. 2003) [48]. Despite having lower overweight and obesity rates, India has a higher prevalence of diabetes compared to western countries suggesting that diabetes may occur at a much lower body mass index (BMI)
in Indians compared with Europeans (Rao et al. 2011) [38]. Therefore, relatively lean Indian adults with a lower BMI may be at equal risk as those who are obese (Zargar et al. 2004) [47]. Diabetes mellitus is reaching potentially epidemic proportions in India. The level of morbidity and mortality due to diabetes and its potential complications are enormous, and pose significant healthcare burdens on both families and society. Worryingly, diabetes is now being shown to be associated with a spectrum of complications and to be occurring at a relatively younger age within the country. In India, the steady migration of people from rural to urban areas, the economic boom, and corresponding change in life-style are all affecting the level of diabetes. Yet despite the increase in diabetes there remains a paucity of studies investigating the precise status of the disease because of the geographical, socio-economic, and ethnic nature of such a large and diverse country. The disease is now highly visible across all sections of society within India; there is now the demand for urgent research and intervention-at regional and national levels-to try to mitigate the potentially catastrophic increase in diabetes that is predicted for the upcoming years (Kaveeshwar et al. 2014) [29].

**Diabetes Control Measures**

To reduce the disease burden that diabetes creates in India, appropriate government interventions and combined efforts from all the stakeholders of the society are required (Kumar et al. 2013) [23]. Clinicians may be targeted to facilitate the implementation of screening and early detection programmes, diabetes prevention, self-management counseling, and therapeutic management of diabetes in accordance with the appropriate local guidelines form the backbone of controlling the predicted diabetes epidemic. Early screening and detection of pre-diabetes (especially in pregnant women, (Sui et al. 2013) [41] children and adults with BMI ≥25) may yield positive health outcomes in society (Minnie et al. 2012) [25].

In modern medical system, managing diabetes without side effects is still a challenge. Plant materials, which are being used as traditional medicine for the treatment of diabetes, are considered one of the good sources for a new drug or a lead to make a new drug. Plant extract or different folk plant preparations are being prescribed by the traditional practitioners and also accepted by the users for diabetes in many countries especially in third world countries. Now-a-days, more than 400 plants are being used in different forms for hypoglycemic effects. Therefore, a proper scientific evaluation and screening of plants by pharmacological tests followed by chemical investigations is necessary (Nahar et al. 1993)) [27]. Now a days, scientists and researchers are very much interested on research of natural plant products all over the world and a large amount of substantiation have shown the immense potential of medicinal plants used traditionally (Ali et al. 2009) [1]. In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects (Modak et al. 2007) [26].

**Cucurbitaceae (Cucurbits)**

Cucurbit family, which are established for their antidiabetic properties such as Momordica charantia (Hossain et al. 2011), and Coccinia indica. Preliminary screening results suggested that Cucumis sativus (cucumber) had well anti-diabetic effects. Cucumber (Cucumis sativus) originated in India but soon cultivated in different parts of the world. In Mexico, cucumber is one of the edible plants with hypoglycemic activity. Antihyperglycemic effect of this plant was studied in healthy rabbits, which significantly decreased the area under the glucose tolerance curve and the hyperglycemic peak (Stano et al. 2002) [40]. After single intraperitoneal injection of cucumber, white pumpkin, and ridge gourd extracts (200 mg/kg body weight), their fasting blood glucose (FBG) levels were measured at 0, 4, 8, and 12 hrs, respectively. The cucumber extracts reduced FBG level to 81.02, 58.65 and 32.61% at 4, 8 and 12 hrs, respectively. Whereas, white pumpkin reduced FBG level to 85.12, 58.82 and 34.60%; ridge gourd 85.73, 67.75 and 48.89% and metformin HCl to 69.20, 44.95 and 25.44% at 4, 8 and 12 hrs, respectively. In each case the effects were significantly different (P<0.05) at 8 and 12 hrs from the diabetic control group and maximum reduction of FBG level was achieved at 12 hr by 67.38, 65.39, 51.10 and 69.20% for cucumber, white pumpkin, ridge gourd and metformin HCl, respectively.

The possible mechanism by which these fruits extracts bring about their antidiabetic action may be by potentiation of the insulin effect of plasma by stimulating insulin release from the remnant pancreatic β-cells or its release from the bound form (Mahomed et al. 2003). Beside this, it might involve an extra-pancreatic action in these alloxan-diabetic rats, which might include the stimulation of peripheral glucose utilization or enhancing glycolytic and glycogenic processes with concomitant decrease in glycogenolysis and gluconeogenesis (Andrade-Cetto et al. 2001) [2]. The antihyperglycemic activity of cucumber, white pumpkin and ridge gourd may also be due to the presence of hypoglycemic saponins, tannins, triterpenes, alkaloids, flavonoids etc. (Ojewole et al. 2005) [30].

**Eugenia jambolana (Indian Black berry)**

In spite of the introduction of many hypoglycemic agents, diabetes and its related complications continue to be a major medical problem. Herbal remedies have become a major component of human health care as they may have fewer side effects. The Eugenia jambolana Lam (EJ) tree belongs to the Myrtaceae family and consists of about 90 genera and 2,800 species (Noomrio et al. 1996) [29]. It is commonly called Jamun, Black plum, or Indian Black berry. The barks, leaves, and seeds have been used by the natives in the treatment of diabetes (Chopra et al. 1958) [12] and have anti-inflammatory (Chaudhuri et al. 1990) [11] and neuro psychopharmacological (Chakraborty et al. 1985) [10] actions, antibacterial (Bhuiyan et al. 1996) [8] and anti-human immunodeficiency virus activities (Kusimoto et al. 1997), and anti-diarrheal effects (Indira et al. 1993) [18]. The present study was designed to evaluate the hypoglycemic activity of ethanolic extracts of whole seed, kernel, and seed coat of EJ seeds on streptozocin (STZ)-induced diabetic rats, and the efficacy was compared with that of glibenclamide, a standard hypoglycemic drug. The possible mechanism by which kernel brings about a decrease in blood glucose may be by potentiation of the insulin effect of plasma by increasing either the pancreatic secretion of.
Coriandrum sativum (coriander)

Coriander has been documented as a traditional treatment of diabetes. In a study, coriander incorporated into the diet (62.5 g/kg) and drinking water (2.5 g/l, prepared by 15 min decoction) reduced hyperglycaemia of streptozotocin-diabetic mice. An aqueous extract of coriander (1 mg/ml) increased 2-deoxylucose transport (1.6-fold), glucose oxidation (1.4-fold) and incorporation of glucose into glycogen (1.7-fold) of isolated murine abdominal muscle comparable with M-insulin. In acute 20 min tests, 0.25-10 mg/ml aqueous extract of coriander evoked a stepwise 1.3-5.7-fold stimulation of insulin secretion from a clonal B-cell line. This effect was abolished by 0.5 mM-diazoxyde and prior exposure to extract did not alter subsequent stimulation of insulin secretion by 10 mM-L-alanine, thereby negating an effect due to detrimental cell damage. The effect of extract was potentiated by 16.7 mM-glucose and 10 mM-L-alanine but not by 1 mM-3-isobutyl-1-methylxanthise. Insulin secretion by hyperpolarized B-cells (16.7 mM-glucose, 25 mM-KCl) was further enhanced by the presence of extract. Activity of the extract was found to be heat stable, acetone soluble and unaltered by overnight exposure to acid (0.1 M-HCl) or dialysis to remove components with molecular mass <2000 Da. Activity was reduced by overnight exposure to alkalai (0.1 M-NaOH). Sequential extraction with solvents revealed insulin-releasing activity in hexane and water fractions indicating a possible cumulative effect of more than one extract constituent. These results demonstrate the presence of antihyperglycaemic, insulin-releasing and insulin-like activity in Coriandrum sativum (Gray et al. 1999) (15).

Trigonella foenum-graecum (Fenugreek)

Due to the etiopathogenesis of diabetes mellitus, harmful side effects of synthetic drugs, the inability of existing modern therapies to control all the pathological aspects of the diabetic disorder, enormous cost of modern drugs as well as the poor availability of the advanced therapies for many rural populations in developing countries (Tanaka et al. 1992), alternative strategies to current pharmacotherapy of diabetes mellitus are urgently. Trigonella foenum-graecum (also known as fenugreek, locally as methi), is a well-known traditional medicinal herb in Bangladesh, possesses diverse biological activities and pharmacological functions. T. foenum-graecum seeds have been used as traditional medicines not only in diabetes but also in high cholesterol, inflammation and gastrointestinal ailments (Sharma et al. 1990). Preliminary animal (Hannan et al. 2003) and human (Sharma et al. 1990) trials suggested possible hypoglycemic effect and antihyperlipidemic properties of oral fenugreek seed powder. T. foenum-graecum seeds have also previously been shown to have hypoglycemic and hypcholesterolemic effects on type 1 and type 2 diabetes mellitus patients and experimental diabetic animals. However, the report published so far on the hypoglycemic effect of T. foenum-graecum could not establish the optimum dose-level for experimental subjects. In view of the above considerations, the present study has administered ethanol extract of T. foenum-graecum at different doses to the alloxan induced diabetic rat and the hypoglycemic effect of respective doses was compared with those of standard antidiabetic drug (glimepiride) to the induced diabetic rat. The study was also undertaken to evaluate some preliminary qualitative phytochemical analysis of crude extract of seeds as well as to examine the level of toxicity of crude extracts.

The possible mechanism of action of extracts could be correlated with the reminiscent effect of the reference antidiabetic drug glimepiride that promotes insulin secretion by closure of K⁺-ATP channels, membrane depolarization and stimulation of Ca²⁺ influx, an initial key step in insulin secretion. Since alloxan is known to destroy pancreatic cells, the present findings appeared to be in consonance with the earlier suggestion (Jackson and Bressler, 1981) that sulphonylureas (e. g. glimepiride) have extra-pancreatic antihyperglycemic mechanism of action secondary to their insulin secreting effect and the attendant glucose uptake into, and utilization by, the tissues (Jackson and Bressler, 1981). Other probable mechanisms by which the plant extracts lowered blood glucose may be by increasing glycogenesis, inhibiting gluconeogenesis in the liver, or inhibiting the absorption glucose from the intestine.

It is noted that the induction with alloxan of same dose to different groups of rat is also varied. It could be explained by the fact that the metabolic rate could be different with the age, sex and weight of animals. The same artifact may be implied to the administration and effect of extracts and glimepiride. Table 1 showed that the effect of all the doses of T. foenum-graecum is still lower than that of reference drug glimepiride. T. foenum-graecum can be a remedy of diabetic mellitus in the manner that the synthetic drugs (glimepiride) possess some side effects, contraindication and adverse reactions which the natural drugs don’t have. Rather the T. foenum-graecum helps improve diabetic mellitus by the ways detailed henceforth. First, antioxidant circulating activity of T. foenum-graecum through significant lipid peroxide level decrease (Devasena and Menon, 2002) exerts beneficial effects (Maxwell, 1995) in oxidative stress increased in patients with diabetes mellitus (Baynes, 1991) (16). Second, our preliminary phytochemical screening of T. foenum-graecum suggests that it contains carbohydrate, steroids and alkaloids. These findings validate previous report on the presence of trigonelline, trigocoumarin, and trimecoumarine alkaloids (Al-Habri and Raman, 1998) in the studied plant and they have antihyperglycemic action. Therefore, it is not unreasonable to speculate that some of these compounds present in the plant extracts are probably responsible for hypoglycemic activities. Third, the seed fibres of T. foenum-graecum reduces the rate of glucose absorption and may also delay gastric emptying, thereby preventing the rise in blood sugar levels following a meal (Gupta et al. 2001). Amino acid, 4-hydroxyisoleucine of seed fibre also powerfully stimulates insulin secretion at all levels of cellular organization since the cells are more sensitive to insulin and increase in the number of insulin receptor sites to burn cellular glucose at high fiber diet. Fourth, guar gum of T. foenum-graecum prevents the rapid uptake of glucose in the small intestine, aids in blood sugar retention in diabetic patients and may also be effective in the treatment of hypercholesterolemia (Sharma et al. 1996).

Asphaltum (Shilajit)

Shilajit is a herbo-mineral drug, which oozes out from a special type of mountain rocks in the peak summer months. It is found at high altitudes ranging from 1000 to 5000 meters. The active constituent of shilajit consists of dibenzo-alpha-pyrones and related metabolites, small peptides (constituting non-protein amino acids), some lipids and carrier molecules (fulvic acids). Standard shilajit contains at least 5-7% dibenzo-alpha-pyrones (Trivedi et al 2004) [143]. In alloxan-treated rats, the rise in blood glucose level reached its peak value on the 5th day and then remained stable throughout the study period. Treatment with all the three doses of shilajit (50, 100 and 200 mg/kg) produced significant reduction in the blood glucose level with maximum reduction being achieved with the dose 100 mg/kg (P<0.001). The peak reduction in blood glucose level with all the three doses was observed at the end of the 2nd week of treatment, which remained stable up to the 4th week. Similar effects were also observed in the lipid profile. Treatment with 50, 100 and 200 mg/kg of shilajit produced significant reduction in TCh level, with maximum reduction caused by 100 mg/kg (P<0.001). There was dose-dependent reduction in the TG level. All the three doses of shilajit also produced significant increase in the HDL level with the maximum elevation being produced with the dose of 100 mg/kg (P<0.001). Although the precise mechanism of alloxan-induced diabetes remains unclear, there is increasing evidence that it involves the degeneration of islet β-cells by accumulation of cytotoxic free radicals (Halliwell et al. 1989) following its administration, alloxan is concentrated in the islets and in the liver, where it is reduced to dialuric acid. This acid is unstable in aqueous solutions and undergoes oxidation back to alloxan, accompanied by generation of reactive oxygen species, hydrogen peroxide and hydroxyl radicals by Fenton type reaction. The liver contains high super oxide dismutase (SOD), catalase and glutathione peroxidase activities, which can scavenge these free radicals. On the contrary, the islet cells have low concentrations of these enzymes and are vulnerable to the cytotoxic effects of the free radicals. It is reported that increase in islet cell SOD activity can prevent or decrease alloxan toxicity. Experimental diabetes is suggested to result from initial islet inflammation, followed by infiltration of activated macrophages and lymphocytes in the inflammatory focus. These cells might be the source of the cytotoxic oxygen radicals. Shilajit has been reported to reduce macrophage and lymphocyte activation and migration, as a part of its immunomodulatory activity (Bhattacharya et al. 1995) [17]. Moreover, being an antioxidant it will prevent damage to the pancreatic islet cell induced by the cytotoxic oxygen radicals (Bhattacharya et al. 1995; Ghosal et al. 1995) [7, 14]. In the present study, treatment with shilajit (100 mg/kg) in euglycemic rats produced significant hypoglycemia. Gupta (1966) [16] suggested that long-term treatment with shilajit increases the number of β -cells of pancreas, i.e. pancreatotrophic action, which may result in better sensitivity of pancreatic β-cells with prompt secretion of a large quantity of insulin in response to hyperglycemia. Combination of shilajit with glibenclamide produced a significant decrease in the blood glucose level which is higher than that produced by either drug alone. Thus, it seems likely that, apart from its pancreatic action, shilajit may also possess extrapancreatic action, which could have contributed to its hypoglycemic action. The hypoglycemic effect of shilajit (100 mg/kg) is significantly higher than that of metformin (500 mg/kg). But the combination of shilajit with metformin produced no further significant reduction in the blood glucose level compared to that produced by shilajit (100 mg/kg).

All the three doses of shilajit also produced a significant beneficial effect on the lipid profile in alloxan-induced diabetic rats. It is reported that the derangement of glucose, fat and protein metabolism during diabetes, results into the development of hyperlipidemia (Austin et al. 1994) [5]. The beneficial effects on the lipid profile by shilajit in alloxan-induced diabetic rats may be secondary to better glycemic control. Moreover, shilajit produced significant beneficial effects in the lipid profile in euglycemic rats also by reducing TCh and TG and increasing HDL significantly. Therefore, it is likely that shilajit-induced favorable changes in the lipid profile in diabetic rats may not only be due to better glycemic control (secondary), but could also be due to its direct action on lipid metabolic pathways.

Cinnamomum cassia (Cinnamon)

The first clinical trial to evaluate the effect of cinnamon in individuals with type 2 diabetes was conducted in Pakistan (Khan et al. 2003) [22]. It showed that cinnamon powder (Cinnamomum cassia), taken over a 40-day period, reduced mean fasting serum glucose (18-29%), triglyceride (23-30%), LDL cholesterol (7-27%), and total cholesterol (12-26%) levels. Three different doses of cinnamon were administered: 1, 3, and 6 g daily. All were equally effective. These findings led to widespread cinnamon use, although no study had yet evaluated the effects of cinnamon in Western diabetic populations with likely differences in diet, BMI, baseline glucose levels, and prescribed medication. It was shown that three different doses of cinnamon-1, 3, and 6 g daily—were equally effective at lowering fasting glucose, total cholesterol, LDL cholesterol, and triglyceride levels in subjects with type 2 diabetes. The study on population differed from theirs with respect to initial fasting glucose (139 vs. 232 mg/dl) and triglyceride (144 vs. 215 mg/dl) levels. Roughly three-fourths of our subjects were taking metformin, more than one-third were taking a thiazolinedione, and about one-half were taking a hydroxymethylglutar1-CoA reductase inhibitor-medicines not taken by subjects in their study. Khan et al. (2003) [22] did not provide data on diet, BMI, ethnic mix, or A1C, precluding further comparison of our studies. We conclude that the effects of cinnamon differ by population. Studies should be conducted to determine how specific variables (diet, ethnicity, BMI, glucose levels, cinnamon dose, and concurrent medication) affect cinnamon responsiveness. Until then, cinnamon cannot be generally recommended for treatment of type 2 diabetes in an American population. The hypoglycemic effect of cinnamon oil (CO) in a type 2 diabetic animal model (KK-A’ mice) was studied. The main component of CO was cinnamaldehyde, and other nineteen metabolites, small peptides (constituting non-protein amino acids), and carrier molecules (fulvic acids). Standard shilajit contains at least 5-7% dibenzo-alpha-pyrones (Trivedi et al. 2004) [143]. In alloxan-treated rats, the rise in blood glucose level reached its peak value on the 5th day and then remained stable throughout the study period. Treatment with all the three doses of shilajit (50, 100 and 200 mg/kg) produced significant reduction in the blood glucose level with maximum reduction being achieved with the dose 100 mg/kg (P<0.001). The peak reduction in blood glucose level with all the three doses was observed at the end of the 2nd week of treatment, which remained stable up to the 4th week. Similar effects were also observed in the lipid profile. Treatment with 50, 100 and 200 mg/kg of shilajit produced significant reduction in TCh level, with maximum reduction caused by 100 mg/kg (P<0.001). There was dose-dependent reduction in the TG level. All the three doses of shilajit also produced significant increase in the HDL level with the maximum elevation being produced with the dose of 100 mg/kg (P<0.001). Although the precise mechanism of alloxan-induced diabetes remains unclear, there is increasing evidence that it involves the degeneration of islet β-cells by accumulation of cytotoxic free radicals (Halliwell et al. 1989) following its administration, alloxan is concentrated in the islets and in the liver, where it is reduced to dialuric acid. This acid is unstable in aqueous solutions and undergoes oxidation back to alloxan, accompanied by generation of reactive oxygen species, hydrogen peroxide and hydroxyl radicals by Fenton type reaction. The liver contains high super oxide dismutase (SOD), catalase and glutathione peroxidase activities, which can scavenge these free radicals. On the contrary, the islet cells have low concentrations of these enzymes and are vulnerable to the cytotoxic effects of the free radicals. It is reported that increase in islet cell SOD activity can prevent or decrease alloxan toxicity. Experimental diabetes is suggested to result from initial islet inflammation, followed by infiltration of activated macrophages and lymphocytes in the inflammatory focus. These cells might be the source of the cytotoxic oxygen radicals. Shilajit has been reported to reduce macrophage and lymphocyte activation and migration, as a part of its immunomodulatory activity (Bhattacharya et al. 1995) [17]. Moreover, being an antioxidant it will prevent damage to the pancreatic islet cell induced by the cytotoxic oxygen radicals (Bhattacharya et al. 1995; Ghosal et al. 1995) [7, 14]. In the present study, treatment with shilajit (100 mg/kg) in euglycemic rats produced significant hypoglycemia. Gupta (1966) [16] suggested that long-term treatment with shilajit increases the number of β-cells of pancreas, i.e. pancreatotrophic action, which may result in better sensitivity of pancreatic β-cells with prompt secretion of a large quantity of insulin in response to hyperglycemia. Combination of shilajit with glibenclamide produced a significant decrease in the blood glucose level which is higher than that produced by either drug alone. Thus, it seems likely that, apart from its pancreatic action, shilajit may also possess extrapancreatic action, which could have contributed to its hypoglycemic action. The hypoglycemic effect of shilajit (100 mg/kg) is significantly higher than that of metformin (500 mg/kg). But the combination of shilajit with metformin produced no further significant reduction in the blood glucose level compared to that produced by shilajit (100 mg/kg).

All the three doses of shilajit also produced a significant beneficial effect on the lipid profile in alloxan-induced diabetic rats. It is reported that the derangement of glucose, fat and protein metabolism during diabetes, results into the development of hyperlipidemia (Austin et al. 1994) [5]. The beneficial effects on the lipid profile by shilajit in alloxan-induced diabetic rats may be secondary to better glycemic control. Moreover, shilajit produced significant beneficial effects in the lipid profile in euglycemic rats also by reducing TCh and TG and increasing HDL significantly. Therefore, it is likely that shilajit-induced favorable changes in the lipid profile in diabetic rats may not only be due to better glycemic control (secondary), but could also be due to its direct action on lipid metabolic pathways.
Meanwhile, glucose tolerance was improved, and the immunoreactive of pancreatic islets β-cells was promoted. These results suggest that CO had a regulative role in blood glucose level and lipids, and improved the function of pancreatic islets. Cinnamon oil may be useful in the treatment of type 2 diabetes mellitus (Ping et al. 2010) [32].

Conclusion
Diabetes is a chronic medical disorder but it won’t be wrong to say that it can be managed for a lifetime. Medical health experts assert that regular check up’s play an important role in managing this disease. However, patients tend to defer on detection and treatment that often leads to complications. India is by far the biggest consumer of sugar worldwide and diet consists of reduced amounts of fruits and veggies. People have poor glycemic control, therefore, there is an urgent need to develop novel therapeutic drugs to improve blood sugar control. The use of herbal medicines for the treatment of diabetes mellitus has gained importance throughout the world. Although, there are numerous traditional medicinal plants reported to have glucose lowering properties, many of them proved to be not very effective in lowering glucose levels in severe diabetes. Therefore, there is a need to search for effect through various biological parameters.

References