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### Original Article

## Diabetes Mellitus and its Herbal Treatment

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#### ABSTRACT

Diabetes mellitus is the most prevalent metabolic syndrome world- wide and is characterized by hyperglycemia resulting in various short- term metabolic changes in lipid and protein metabolism and long- term irreversible vascular changes which include diabetic- specific complications viz., retinopathy, nephropathy and neuropathy. In the present study eleven patients of Type- 2 diabetes mellitus were surveyed who were consumed a daily dose of Metformin hydrochloride 500mg(SR) as glycemic control. All patients were fed with one tea spoon full (about 5gm.) of dried seeds of *Trigonella foenum-graecum* before morning breakfast. An aqueous extract from dried flowers of *Costus igneus* was also given to each patient after seed consumption. The fasting and post prandial plasma glucose level of all the eleven Type-2 diabetic subjects were elevated even after oral consumption of daily dose of Metformin hydrochloride 500mg (SR). All the eleven subjects were suggested to consume herbal preparation in the combination: 5gm ( one tea spoonful) of Methi ( *Trigonella*) plus one glass aqueous extract of flowers of *Costus igneus*( *Insulin plant*). One month after receiving herbal treatments, their lipid profile and plasma glucose level ( both fasting and PP) were assayed by pathologists of SRL Ranbaxy and the results obtained clearly indicated that all the subjects showed a progressive decline in the level of Chol-LDL, Total-Chol and Triglyceride after 30 days consumption of formulated herbal medicine. In the present investigation it has been found that the daily Fenugreek consumption along with aqueous extract of *Costus igneus*, in addition to Metformin caused the lowering of both fasting and post prandial plasma glucose level as well as to lower the cholesterol level.

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### 1. Introduction

Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycemia due to either a deficiency of insulin secretion or to a combination of insulin resistance and inadequate insulin secretion to compensate. There are two classes of diabetes mellitus, Type- 1 and Type- 2. Type- 1 diabetes is due to pancreatic islet B cell destruction predominantly by an autoimmune process, and these patients are prone to ketoacidosis. Type- 2 diabetes is the more prevalent form and results from insulin resistance with a defect in compensatory insulin secretion.

In over 90%of cases Type- 1 diabetes is immune- mediated and in less than 10% cases it is idiopathic. The rate of pancreatic B cell destruction is quite variable. Type- 1 diabetes is usually associated with ketosis in its untreated state. It occurs most commonly in

juveniles, with highest incidence among the 10 to 14- year- old group, but occasionally occurs in adults, especially the nonobese and those who are elderly when hyperglycemia first appears. It is a catabolic disorder in which circulating insulin is virtually absent, plasma glucagon is elevated, and the pancreatic B cell fail to respond to all insulinogenic stimuli. Exogenous insulin is therefore required to reverse the catabolic state, prevent ketosis, reduce the hyperglucagonemia, and reduce blood glucose.

Certain human leukocyte antigens (HLA) are strongly associated with the development of Type- 1diabetes [1]. About 95% of Type- 1 patients possess either HLA- DR3 or HLA- DR4, compared with 45%- 50% of Caucasian controls. HLA- DQ genes are even more specific markers of Type- 1 susceptibility, since a particular variety (HLA- DQB1\*0302) is found in the DR4 patients with Type- 1, while a“protective” gene (HLA- DQB1\*0602) is often present in the DR4 controls. In addition, circulating islet cell antibodies have been detected in as many as 85% of patients, and

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the majority of these patients also have detectable anti- insulin antibodies prior to receiving insulin therapy[1]. Most islet cell antibodies are directed against glutamic acid decarboxylase, an enzyme localized within pancreatic B cells.

Immune- mediated Type- 1 diabetes is felt to result from an infectious or toxic insult to persons whose immune system is genetically predisposed to develop a vigorous autoimmune response either against altered pancreatic B cell antigens or against molecules of the B cell resembling the viral protein (molecular mimicry). Extrinsic factors that affect B cell function include damage caused by viruses such as mumps or coxsackie B4 virus, by toxic chemical agents, or by destructive cytotoxins and antibodies released from sensitized immunocytes. Specific HLA immune response genes are believed to predispose patients to a destructive autoimmune response against their own islet cells (auto aggression) which is mediated primarily by cytotoxic T cells. In such patients immunosuppressive agent (e.g. cyclosporine) is given to ameliorate hyperglycemia.

Type- 2 diabetes represents a heterogeneous group comprising milder forms of diabetes that occur predominantly in adults but occasionally in juveniles. More than 90% of all diabetics are included under this classification. Circulating endogenous insulin is sufficient to prevent ketoacidosis but is inadequate to prevent hyperglycemia in the face of increased needs owing to tissue insensitivity. In most cases of this type of diabetes, the cause is unknown.

Tissue insensitivity to insulin has been noted in most Type- 2 patients irrespective of weight and has been attributed to several interrelated factors. These include a putative genetic factor, which is aggravated in time by additional enhancers of insulin resistance such as aging, a sedentary lifestyle, and abdominal- visceral obesity. In addition, there is an accompanying deficiency in the response of pancreatic B cells to glucose. Both the tissue resistance to insulin and the impaired B cell response to glucose appear to be further aggravated by increased hyperglycemia, and both defects are ameliorated by treatment that reduces the hyperglycemia towards normal. Most epidemiologic data indicate strong genetic influences in Type- 2 diabetes. The genetic factors responsible for Type- 2 diabetes have not yet been identified, though linkage to a gene on chromosome 2 encoding a cysteine protease, calpain- 10 has been reported in a Mexican- American population.

Diabetes mellitus has been classified into some other specific types:

1. Maturity- onset diabetes of the young (MODY): This subgroup is a relatively rare monogenic disorder characterized by non- insulin- dependent diabetes with autosomal dominant inheritance and an age at onset of 25 years or younger. Patients are nonobese, and their hyperglycemia is due to impaired glucose-induced secretion of insulin.

2. Diabetes due to mutant insulin: This is a very rare subtype of nonobese Type- 2 diabetes. Since affected individuals were heterozygous and possessed one normal insulin gene, diabetes was mild, and showed autosomal dominant genetic transmission.

3. Diabetes due to mutant insulin receptors: In more than 40 people with diabetes, defects in one of their insulin receptor gene have been observed.

4. Diabetes mellitus associated with a mutation of mitochondrial DNA: Diabetes due to a mutation of mitochondrial DNA that impairs the transfer of leucine or lysine into mitochondrial proteins has been described. Most patients have a mild form of diabetes that responds to oral hypoglycemic agents. Two- thirds of patients with this subtype of diabetes have a hearing loss, and a smaller proportion had a syndrome of myopathy, encephalopathy, lactic acidosis, and stroke- like episodes (MELAS).

5. Obese Type- 2 patients: The most common form of diabetes is secondary to extra pancreatic factors that produce insensitivity to endogenous insulin. When an associated defect of insulin production prevents adequate compensation for this insulin resistance, nonketotic mild diabetes occurs. The primary problem is a "target organ" disorder resulting in ineffective insulin action that can secondarily influence pancreatic B cell function.

#### Chronic Complications of Diabetes:

Diabetes mellitus is associated with late clinical manifestations that include a number of pathologic changes that involve small and large blood vessels, cranial and peripheral nerves, and the lenses of eye. These lesions lead to hypertension, renal failure (nephropathy), blindness (retinopathy), autonomic and peripheral neuropathy, amputations of the lower extremities, myocardial infarction, and cerebrovascular accidents.

Type- 2 diabetes is the commonest form of diabetes constituting 90% of the diabetic population. The global prevalence of diabetes is estimated to increase to 5.4% by the year 2025 [2]. The World Health Organization has predicted that the major burden will occur in the developing countries. The countries with the largest number of diabetic people are, and will be India, China and United States in 2025 [2]. Epidemiological studies among migrant Asian Indians showed higher prevalence of Type- 2 diabetes compared with the host populations and other migrant ethnic groups [3]. Studies conducted in India have highlighted that not only is the prevalence of Type- 2 diabetes high, but also that it is increasing rapidly in the urban population [4, 5, 6, 7, and 8]. The burden of Type- 2 diabetes and its complications related to Indian scenario has been illustrated by Ramachandran et al., [9].

The genetics of Type- 2 diabetes has been reviewed by Torben Hansen [10]. Beck- Nielson and Groop [11] have suggested that the diabetic phenotype is the result of interaction of both genetic component and an important non- genetic component.

The coexistence of obesity, glucose intolerance, dyslipidemia, and hypertension, is termed as insulin resistance syndrome (IRS). Gerald Reaven [12] initially proposed that resistance to insulin-mediated glucose disposal is the pathophysiological interface for several complex metabolic alterations and disease. Insulin resistance syndrome in Asian Indians has been reviewed by AnoopMisra and Naval k. Bikram [13]. Regarding chromosomal abnormalities deletion syndrome due to chromosome 22q11.2 has been investigated by Elder et al., [14].

Transient neonatal diabetes mellitus (TNDM) is a rare condition which represents with intrauterine growth retardation, dehydration, and failure to thrive. The condition spontaneously resolves before 1 year of age but predisposes patients to Type- 2 diabetes later in life. Rebecca J Gardner et al., [15] have previously shown that, in some cases, TNDM is associated with paternal uniparental disomy (UPD) of chromosome 6 and suggested that an imprinted gene responsible for TNDM lies within a region of chromosome 6q. By analyzing three families, two with duplications (family A and patient C) and one with several affected subjects with normal karyotypes (family B), Elder et al., [14] have further defined the TNDM critical region. In patient A, polymorphic microsatellite repeat analysis identified a duplicated region of chromosome 6, flanked by markers D6S472 and D6S311. This region was identified on the Sanger Centre's chromosome 6 radiation hybrid map (<http://www.sanger.ac.uk/HGP/Chr6>) and spanned approximately 60 cR3000. Using markers within the region, 418 unique P1 derived artificial chromosomes (PACs) have been isolated and used to localize the distal breakpoints of the two duplications. Linkage analysis of the familial case with abnormal karyotype identified a recombination within the critical region. This recombination has been identified on the radiation hybrid map and defines the proximal end of the region of interest. They therefore propose that an imprinted gene for TNDM lies within an 18.72 cR3000 (~5.4Mb) interval on chromosome 6q24.1-q24.3 between markers D6S1699 and D6S1010.

Vladimir K. Bakalov et al., [16] have investigated that Turner syndrome (TS) is caused by the absence or fragmentation of the second sex chromosome, which is associated with increased risk of diabetes mellitus (DM), but the specific phenotype and genetic etiology of this trait are unknown.

Cytogenetic factors related with diabetes have been largely reviewed by [17, 18, 19, 20, 21, 22, 23 etc]. Suheir Assady [24] has suggested the stem cell based therapy of diabetes mellitus.

Pallab Das Gupta and Amartya De [25] have compiled some herbal plants and their active ingredients which play an important role in the management of diabetes mellitus. The antidiabetic properties of Bitter melon (*Momordica charantia*), Fiery costus (*Costus igneus*), Dandelium (*Taraxacum officinale*), French Lilac (*Golega officinalis*), Turmeric (*Curcuma longa*), Bael (*Aegle marmelos*), Amla (*Emblica officinalis*), Fenugreek (*Trigonella foenum-gracum*), Ginseng (*Panax ginseng*), Noyantara (*Catharanthus roseus*), Neem (*Azadirachta indica*), Cinnamon (*Cinnamomum zeylanicum*), black berry (*Rubus fruticosus*) etc. have been greatly illustrated [26, 27, 28, 29, 30, 31, 32, 33, 34] etc.

In the present investigation the efficacy of dried seeds of METHI (*Trigonella foenum-graecum*) of family Papilionaceae and Fiery Costus (*Costus igneus*) of family Costaceae was evaluated against eleven subjects of Type-2 diabetes mellitus.

### Materials and Methods

Eleven patients of Type-2 diabetes mellitus of different age groups in urban area of Patna who have been taken daily dose of insulin sensitizing antidiabetic drug, the Metformin Hydrochloride 500mg sustained release (SR) were surveyed. Their lipid profiles and plasma glucose level, both fasting and postprandial (pp) i.e. post glucose load were analyzed by SRL Ranbaxy, Patna before starting herbal therapy. All patients were fed with one tea spoon full (about 5gm.) of dried seeds of *Trigonella foenum-graecum* before morning breakfast. An aqueous extract from dried flowers of *Costus igneus* was also given to each patient after seed consumption. The aqueous extract was prepared by placing five dried flowers of *Costus igneus* in one glass of water (250ml) overnight and after rubbing the turgid flowers with glass wall the mixture was filtered and the filtrate was used as herbal medicine. After 30 days the lipid profile and plasma glucose level were again analyzed by SRL Ranbaxy, and the results obtained have been presented in Table-1, 2, 3 and 4.

**Table-1: Showing lipid profile of eleven patients of Type-2 diabetes mellitus receiving daily dose of Metformin hydrochloride 500mg before start of herbal treatment**

Patient's code	Age yrs./sex	Cholesterol-LDL mg/dL	Total Cholesterol mg/dL	Cholesterol-HDL mg/dL	Cholesterol-VLDL mg/dL	Triglyceride mg/dL
001	63/M	54.5	120.90	57.40	9.00	45.50
002	70/M	55.6	121.6	46.00	20.00	100.00
003	70/F	58.50	118.90	45.40	15.00	75.00
004	50/M	66.80	127.10	39.30	21.00	103.9.
005 <sup>a</sup>	51/F	178.40	297.00	42.60	76	381.00
006	32/M	121.80	191.00	42.20	27.00	132.70
007 <sup>a</sup>	36/F	137.30	219.00	49.70	32.00	162.40
008	53/M	93.50	160.10	44.60	22.00	108.40
009 <sup>a</sup>	38/F	140.7	219.20	39.50	39.00	192.50
010	54/M	124.00	199.00	44.00	31.00	156.90
011	58/M	49.90	90.90	42.00	19.00	95.40

### Reference Range

Cholesterol-LDL: 0 to 130mg/dL; 131-155 border line; >155 High

Total Cholesterol: 0 to 200mg/dL; 200 to 239 border line; >240 High

Cholesterol- HDL: 40to60mg/dL

VLDL-Cholesterol: 0 to 30.0mg/dL

Triglyceride: 0 to 150mg/dL; 150 to 199mg/dL border line; 200 to 499mg/dL high; >500mg/dL very high.

a: diagnosed as hypercholesterolemic

**Table- 2: Showing fasting and post prandial plasma sugar level of eleven patients of Type-2 diabetes mellitus receiving daily dose of Metformin hydrochloride 500mg (SR) before start of herbal treatment**

Patient's code	Age yrs./ sex	Fasting plasma glucose in mg/dL	Post prandial plasma glucose in mg/dL	Reference range in Fasting	Reference range 2hrs. after glucose load
001	63/M	130	170	60 to 110 mg/dL	110 to 140mg/dL
002	70/M	134	168		
003	70/F	132	165		
004	50/M	131	172		
005	51/F	128	167		
006	32/M	140	210		
007	36/F	142	220		
008	53/M	133	200		
009	38/F	123	160		
010	54/M	120	145		
011	58/M	124	198		

**Table- 3: Showing lipid profile of eleven patients of Type-2 diabetes mellitus receiving daily dose of Metformin hydrochloride 500mg (SR) one month after herbal treatment**

Patient's	Age yrs./ sex	Cholesterol -LDL mg/dL	Total Cholesterol mg/dL	Cholesterol -HDL mg/dL	Cholesterol -VLDL mg/dL	Triglyceride mg/dL
001	63/M	60.5	115.5	50.40	10.00	55.50
002	70/M	65.6	120.6	43.00	16.00	85.00
003	70/F	60.50	115.60	45.40	15.00	65.00
004	50/M	62.80	122.10	41.50	18.00	92.12
005	51/F	155.40	285.00	44.60	71.60	352.00
006	32/M	116.50	187.00	45.20	25.00	127.70
007	36/F	130.30	212.00	45.70	30.00	155.40
008	53/M	75.50	142.10	40.00	21.00	97.50
009	38/F	134.7	212.20	32.50	34.00	172.50
010	54/M	115.00	180.00	41.00	30.00	150.60
011	58/M	42.90	85.70	40.00	20.00	90.50

Reference Range

Cholesterol-LDL: 0 to 130mg/dL; 131-155 border line; >155 High

Total Cholesterol: 0 to 200mg/dL; 200 to 239 border line; >240 High

Cholesterol- HDL: 40 to 60mg/dL

VLDL-Cholesterol: 0 to 30.0mg/dL

Triglyceride: 0 to 150mg/dL; 150 to 199mg/dL border line; 200 to 499mg/dL high; >500mg/dL very high.

**Table- 4: Showing fasting and post prandial plasma sugar level of eleven patients of Type-2 diabetes mellitus receiving daily dose of Metformin hydrochloride 500mg (SR) one month after herbal treatment**

Patients	Age yrs./ sex	Fasting plasma glucose in mg/dL	Post prandial plasma glucose in mg/dL	Reference range in Fasting	Reference range 2hrs. after glucose load
001	63/M	107	150	60 to 110 mg/dL	110 to 140mg/dL
002	70/M	120	155		
003	70/F	123	141		
004	50/M	122	155		
005	51/F	119	152		
006	32/M	120	185		
007	36/F	121	162		
008	53/M	124	165		
009	38/F	116	140		
010	54/M	111	135		
011	58/M	118	150		

## Results and Discussion

The lipid profiles of eleven Type-2 diabetic subjects receiving oral antidiabetic drug, Metformin hydrochloride 500mg (SR)/day reveal that the Cholesterol-LDL, Total- Cholesterol, Cholesterol-HDL, Cholesterol-VLDL and Triglyceride were found to be within the normal range. However, the three subjects' viz., 005, 007 and 009 showed an elevated LDL-Cholesterol, Total Cholesterol and VLDL- Cholesterol and have been diagnosed by physicians as hypercholesterolemic (Table-1). Their HDL- Cholesterol were within the normal range. LDL-Cholesterol in 005, 007 and 009 were 178.40, 137.60 and 140.7mg/dL of blood respectively. Triglyceride of patient 005 was high about 381.00mg/dL of blood.

From the result (Table-2) it is evident that the fasting and post prandial plasma glucose level of all the eleven Type-2 diabetic subjects were elevated even after oral consumption of daily dose of Metformin hydrochloride 500mg (SR).

In addition to Metformin hydrochloride all the eleven subjects were requested to consume herbal preparation in the combination: 5gm (one tea spoonful) of Methi ( Trigonella) plus one glass aqueous extract of flowers of Costus igneus ( Insulin plant). One month after receiving herbal treatments, their lipid profile and plasma glucose level (both fasting and PP) were assayed by pathologists of SRL Ranbaxy and the results obtained clearly indicated that all the subjects showed a progressive decline in the level of Chol-LDL, Total-Chol and Triglyceride after 30 days consumption of formulated herbal medicine (Table-3 and 4). Cholesterol- HDL of all the eleven subjects was in the normal range. Cholesterol- VLDL and Triglyceride were also in the normal range in all the subjects, except in case of patient 005 whose VLDL and Triglyceride levels were 71.60mg/dL and 352.00mg/dL respectively. These subjects were diagnosed by physicians as hypercholesterolemic. All the eleven subjects of Type-2 diabetes mellitus showed normal fasting and post prandial plasma glucose level after 30 days of treatment with the present herbal formulation.



Metformin is a biguanide that has been used worldwide for the treatment of the Type-2 diabetes for last four decades. This oral glucose lowering agent was derived from *Galega officinalis*. It improves glycemic control by enhancing insulin sensitivity in liver and muscle. It is not associated with hypoglycemia. Improved metabolic control with Metformin does not cause weight gains and may lead to weight loss. Metformin has beneficial effects on several cardiovascular risk factors such as dyslipidemia, elevated plasma plasminogen activator inhibitor, other fibrinolytic abnormalities, and hyperinsulinaemia and insulin resistance [35]. Metformin is not metabolized by the liver and excreted intact in urine.

Fenugreek (*Trigonella foenum-graecum* .Linn.) belonging to the family Papilionaceae is a aromatic, 30-60 cm tall, annual herb, cultivated throughout the country. Phytochemical analysis by various workers revealed the presence of Alkaloides viz., Trimethylamine, Neurin, Trigonelline Choline, Genticanine, Carpaine and Betain, Amino acids viz., Isoleucine, 4-hydroxyisoleucine, Histidine, Leucine, lysine, L-tryptophan, Arginine. Saponins viz., Graecunins, fenugrin B, fenugreekine, trigofenosides A-G. Steroidal saponogens : Yamogenin, diosgenin, smilagenin, sarsasapogenin, tigogenin, neotigogenin, gitogenin, neogitogenin, yuccagenin, saponaretin. Flavonoids: Quercetin, rutin, vetixin isovetixin, Fibers, Gum, neutral detergent. Coumarin, lipids, vitamins, minerals. 28% mucilage, 22 % proteins,

In the present investigation it has been found that the daily Fenugreek consumption along with aqueous extract of *Costus igneus*, in addition to Metformin caused the lowering of both fasting and post prandial plasma glucose level as well as to lower the cholesterol level. The galactomannan-rich soluble fiber fraction of fenugreek might be responsible for the antidiabetic activity of the seeds. The present finding is in accordance with the work of Rashmi et al[36] who have suggested that the Insulinotrophic and antidiabetic properties have been associated with the amino acid 4-hydroxyisoleucine that occurs in fenugreek at a concentration of about 0.55%. In vitro studies have indicated that this amino acid caused direct pancreatic  $\beta$ -cell stimulation. Delayed gastric emptying and inhibition of glucose transport also have been postulated as possible mechanisms. A study of alloxan-induced diabetic mice has shown that the hypoglycemic activity of dialyzed fenugreek seed extract was comparable to that of insulin (1.5 U/ kg) Fenugreek seed extract also improved intraperitoneal glucose tolerance in normal mice.

It has been suggested that cholesterol lowering effects is due to Fecal bile acid and cholesterol excretion that are increased by fenugreek administration. This may be secondary to a reaction between the bile acids and fenugreek-derived saponins causing the formation of micelles too large for the digestive tract to absorb. The cholesterol lowering activities have also attributed to the fiber-rich gum portion of the seed that reduces the rate of hepatic synthesis of cholesterol. It is likely that both mechanisms contribute to the overall effect.

The phytochemicals of *Costus igneus* include Tannin, Phlobatannin, Saponin, Flavonoid, steroid, Terpenoids, Cardiac glycosides, and naturally occurring phenolic compound like quercetine. In the present investigation the aqueous extract of flowers of *Costus igneus* showed significant hypoglycemic and hypolipidemic activities. The present findings gain support from the work of Pazhanichamy Kalailingam et al[37] who have studied the efficacy of Methanolic Extract of *Costus Ignus* Rhizome on Hypoglycemic, Hypolipidemic activity in Streptozotocin (STZ) Diabetic Rats and HPTLC Analysis of its active Constituents. The present finding is also in accordance of Palanivel et al., [38]) who also studied the hypoglycemic activity of *Costus igneus* extract (whole plant) on alloxan induced diabetic rats.

## CONCLUSION

Diabetes mellitus is a serious chronic disease. Effective control of the blood glucose level is a key step in preventing or reversing diabetic complications and improving the quality of life in both types 1 and 2 diabetic patients [39, 40, 41].

In present study one tea spoon full of Fenugreek (Methi) along with one glass of aqueous extract of flowers of *Costus igneus* was found effective in controlling both hyperglycemia and hypercholesterolemia. The present study indicates that quercetine of *Costus igneus* and galactomannan rich soluble fibre and 4-hydroxyl leucine of Fenugreek may have beneficial effects as antidiabetic and antihyperglycemic agents and also warrants further studies to isolate and characterize potent molecules for the treatment of diabetes mellitus and its lipids associated complications.

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## REFERENCES

- [1]. Umesh Masharani and John H. Karam (2003): Diabetes Mellitus and Hypoglycemia, In Current Medical Diagnosis and Treatment, Edited by Lawrence M. Tierney, Jr. Stephen J. McPhee and Maxine A. Papadakis, Lange Medical Book/ McGraw- Hill, International Edition, pp. 1152-1198.
- [2]. King, H., Aubert, R. E. and Herman, W. H. (1998): Diab. Care, 21, 1414-1431.
- [3]. Zimmet, P. Z. (1999): Diabetologia, 42, 499-518.
- [4]. Mohan, V., Shanthirani, S., Deepa, R., Premalatha, G., Sastry, N. G. and Saroja, R. (2001): Diab. Med., 18, 280-287.
- [5]. Raman Kutty, Soman, C. R., Joseph, A., Pisharody, R. and Vijayakumar, K. (2000): Natl. Med. J. India, 13, 287-292.
- [6]. Misra, A., Pandey, R. M., Rama Devi, J., Sharma, R., Vikram, N. K. and Nidhi Khanna (2001): Int. J. Obesity, 25, 1-8.
- [7]. Verma, N. P. S. and Madhu, S. V. (2000): Diab. Res. Clin. Prac, 50, 615, Suppl. 1.

- [8]. Iyer, R., Upasani, S. and Baitule, M. N. (2000): *ibid*, 50, 519, Suppl. 1.
- [9]. Ramachandran A, C. Snehalata and Vijay Viswanathan (2002): Burden of type 2 diabetes and its complications- The Indian scenario, *CURRENT SCIENCE*, 83(12), 1471- 1476.
- [10]. Torben Hansen (2002): Genetics of Type 2 diabetes, *CURRENT SCIENCE*, 83(12), 1477- 1482.
- [11]. Beck- Nielsen, H. and Groop, L. C. (1994): *J. Clin. Invest.*, 94, 1714- 1721.
- [12]. Reaven, G. M. (1988): *Diabetes*, 37, 1595- 1607.
- [13]. Anoop Misra and Naval K. Vikram (2002): Insulin resistance syndrome (metabolic syndrome) and Asian Indians, *CURRENT SCIENCE*, 83 (12), 1483- 1496.
- [14]. Elder DA, Kaiser- Roger K, Aylsworth AS and Calikoglu (2001): Type I diabetes mellitus in a patient with chromosome 22q11.2 deletion syndrome. *Am J Med Genet*, 101 (1): 17- 19
- [15]. Rebecca J Gardner, Andrew J Mungall, Ian Dunham, John C K Barber, Julian P H Shield, I Karen Temple, David O Robinson (1999): Localization of a gene for transient neonatal diabetes mellitus to an 18.72 cR3000 (5.4 Mb) interval on chromosome 6q, *J Med Genet*; 36:192-196
- [16]. Vladimir K. Bakalov, Clara Cheng, Jian Zhou and Carolyn (2009): X-Chromosome Gene Dosage and the Risk of Diabetes in Turner Syndrome *J Clin Endocrinol Metab.*; 94(9): 3289-3296
- [17]. Bakalov VK, Cooley MM, Troendle J, Bondy CA (2004): The prevalence of diabetes mellitus in the parents of women with Turner's syndrome. *Clin Endocrinol (Oxf)* 60:272.
- [18]. Salgin B, Amin R, Yuen K, Williams RM, Murgatroyd P, Dunger DB (2006): Insulin resistance is an intrinsic defect independent of fat mass in women with Turner's syndrome. *Horm Res* 65:69-75.
- [19]. Song B, Scheuner D, Ron D, Pennathur S, Kaufman RJ (2008): Chop deletion reduces oxidative stress, improves  $\beta$  cell function, and promotes cell survival in multiple mouse models of diabetes. *J Clin Invest* 118:3378-3389
- [20]. Neve B, Fernandez-Zapico ME, Ashkenazi-Katalan V, Dina C, Hamid YH, Joly E, Vaillant E, Benmezroua Y, Durand E, Bakaher N, Delannoy V, Vaxillaire M, Cook T, Dallinga-Thie GM, Jansen H, Charles MA, Clément K, Galan P, Hercberg S, Helbecque N, Charpentier G, Prentki M, Hansen T, Pedersen O, Urrutia R, Melloul D, Froguel P (2005): Role of transcription factor KLF11 and its diabetes-associated gene variants in pancreatic  $\beta$  cell function. *Proc Natl Acad Sci USA* 102:4807-4812.
- [21]. Senée V, Chelala C, Duchatelet S, Feng D, Blanc H, Cossec JC, Charon C, Nicolino M, Boileau P, Cavener DR, Bougnères P, Taha D, Julier C (2006): Mutations in GLIS3 are responsible for a rare syndrome with neonatal diabetes mellitus and congenital hypothyroidism. *Nat Genet* 38:682-687.
- [22]. Zhao L, Guo M, Matsuoka TA, Hagman DK, Parazzoli SD, Poirout V, Stein R (2005): The islet  $\beta$  cell-enriched MafA activator is a key regulator of insulin gene transcription. *J Biol Chem* 280:11887-11894.
- [23]. Mokhtari D, Myers JW, Welsh N (2008): MAPK kinase kinase-1 is essential for cytokine-induced c-Jun NH2-terminal kinase and nuclear factor- $\kappa$ B activation in human pancreatic islet cells. *Diabetes* 57:1896-1904.
- [24]. Suheir Assady (2009): Challenges and Prospects for Stem Cell-Based Therapy in Diabetes Mellitus israel medical association world fellowship conference VOL11, 2009.
- [25]. Pallab Das Gupta and Amartya De\* (2012): Diabetes Mellitus and its Herbal Treatment *International Journal of Research in Pharmaceutical and Biomedical Sciences* Vol. 3 (2), 706- 721.
- [26]. Shukla R, Sharma S. B., Buri D., Probhu K. M. (2000): Medicinal plants for the treatment of Diabetes Mellitus, *Indian J Clin Biochem*, 15 P: 169
- [27]. Wadkar K.A., Magdum C.S., Patil S.S. (2008): "Antidiabetic Potential and Indian Medicinal plants- A Review Article", *Journal of Herbal Medicine*
- [28]. Rakesh Kumar Singh, Dolly Jaiswal, Prashant Kumar Rai, (2009): Anti-diabetic activity of *Emblica officinalis* in animal models.
- [29]. ZHIJUN SONG, HELLE KROGH JOHANSEN, VIGGO FABER, CLAUS MOSER, ARSALAN KHARAZMI, JORGEN RYGAARD, AND NIELS HOIBY (1997): Ginseng Treatment Reduces Bacterial Load and Lung Pathology in Chronic *Pseudomonas aeruginosa* Pneumonia in Rats, *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*, 41 (5), 961- 964.
- [30]. MUSHTAQ AHMAD, RAHMATULLAH QURESHI, MUHAMMAD ARSHAD, MIR AJAB KHAN AND MUHAMMAD ZAFAR (2009) TRADITIONAL HERBAL REMEDIES USED FOR THE TREATMENT OF DIABETES FROM DISTRICT ATTOCK (PAKISTAN) *Pak. J. Bot.*, 41(6): 2777-2782, 2009.
- [31]. M. Upendra Rao, M. Sreenivasulu, B. Chengaiah, K. Jaganmohan Reddy, C. Madhusudhana Chetty (2010): Herbal Medicines for Diabetes Mellitus: A Review *International Journal of PharmTech Research* Vol. 2, No. 3, pp 1883-1892
- [32]. Kavishankar. G. B., N. Lakshmi Devi, S. Mahadeva Murthy, H. S. Prakash, S. R. Niranjana (2011): Diabetes and medicinal plants- A review *Int J Pharm Biomed Sci* 2011, 2(3), 65-80
- [33]. Suresh Kumar, Rajeshwar Singh, Neeru Vasudeva and Sunil Sharma (2012): Acute and chronic animal models for the evaluation of anti-diabetic agents, *Cardiovascular Diabetology* 2, 11:9
- [34]. Manisha Modak, Priyanjali Dixit, Jayant Londhe, Saroj Ghaskadbi, and Thomas Paul A. Devasagayam (2007): Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes *Clin Biochem Nutr*; 40(3): 163-173.
- [35]. Cusi, K. and DeFronzo, R. A. (1998): *Diab. Rev.*, 6, 89- 131
- [36]. Rashmi yadav, Rahul kaushik and Diptee Gupta (2011): THE HEALTH BENEFITS OF TRIGONELLA FOENUM- GRAECUM: A REVIEW, *International Journal of Engineering Research and Applications (IJERA)* www.ijera.com Vol. 1, Issue 1, pp. 032-035
- [37]. Pazhanichamy Kalailingam, Rajendran Kaliaperumal, Kumaran Shanmugam (2011): Efficacy of Methanolic Extract of *Costus igneus* Rhizome on Hypoglycemic, Hypolipidemic Activity in Streptozotocin (STZ) Diabetic Rats and HPTLC Analysis of Its Active Constituents, 2011 International Conference on Bioscience, Biochemistry and Bioinformatics IPCBEE vol. 5 (2011) © (2011) IACSIT Press, Singapore
- [38]. Palanivel. V, Mohamed Jihad EV, K. L. Senthil Kumar (2013): Evaluation of hypoglycemic activity of *Costus igneus* extract (whole plant) on alloxan induced diabetic rats, *International Journal of Advanced Pharmaceutical Genuine Research*, 1(2), 9-19
- [39]. Abaira. C, J. A. Colwell, F. Q. Nuttall, C. T. Sawin, N. J. Nagel and J. P. Comstock (1995): "Veterans Affairs Cooperative Study on glycemic control and complications in type II diabetes (VA CSDM). Results of the feasibility trial. Veterans Affairs Cooperative Study in Type II Diabetes," *Diabetes Care*, 18, 1113-1123.
- [40]. Ohkubo. Y, H. Kishikawa, E. Araki, T. Miyata, S. Isami, and S. Motoyoshi (1995): "Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with noninsulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res. Clin. Pract.*, 28, 103-117.
- [41]. DeFronzo. R. A. (1999): "Pharmacologic therapy for type 2 diabetes mellitus," *Ann. Intern. Med.*, 131, 281-303.