

Clinical efficacy of *Withania coagulans* Dunal and *Trigonella foenum-graecum* Linn. in Type 2 Diabetes mellitus

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Received 15 May 2007; revised 6 July 2008

Type 2 *Diabetes mellitus* has become an epidemic. It is associated with several contributory factors including increased longevity, obesity, unsatisfactory diet, sedentary lifestyle and increasing urbanization. The medical and socioeconomic burden of the disease is caused by the associated complications, which impose enormous strains on healthcare system. Management includes not only diet and exercise but also anti-hyperglycaemic drugs. Several researches have been made to evaluate the hypoglycaemic effect of a lot of herbal drugs. In the trial, the combined effect of *Withania coagulans* Dunal and *Trigonella foenum-graecum* Linn. have been studied.

Keywords: *Withania coagulans*, *Trigonella foenum-graecum*, Diabetes, Unani medicine

IPC Int. Cl.⁸: A61K36/00, A61P5/00, A61P5/50

Diabetes is a mysterious illness, a statement made in antiquity by the physician Aerates of Cappadocia (81-138 AD) is still valid today. At first Galen suspected that this odd illness was caused by a kidney complaint. Avicenna alone has been credited with two additional discoveries, first, the mention of further symptoms—besides the triad (polydipsia, polyuria and marasmus) known to antiquity – namely physical, mental and sexual weakness and the occurrence of carbuncles and gangrene, and secondly the alleged discovery of the sweetness of diabetic urine¹. Type 2 Diabetes mellitus is a heterogeneous group of disorders usually characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Distinct genetic and metabolic defects in insulin action and/or secretion give rise to the common phenotype of hyperglycaemia in type 2 DM. The identification of distinct pathogenic processes in type 2 DM has important potential therapeutic applications, as pharmacologic agents that target specific metabolic derangement become available. It has a strong genetic component. Various genetic loci contribute to susceptibility, and environmental factors further modulate phenotype expression of the diseases. Even the genetic defect in insulin secretion or action may be present but unless an environmental factor is incorporated, disease does not

manifest. Genome-wide scanning for mutations or polymorphisms associated with type 2 DM is being used in an effort to identify genes associated with type 2 DM. Obesity particularly visceral or central is very common in type 2 DM. Insulin resistance associated with obesity augments the genetically determined insulin resistance of type 2 DM. Adipocytes secrete a number of biologic products like leptin, tumor necrosis factor, free fatty acids that modulate processes such as insulin secretion, insulin action and body weight and may contribute to insulin resistance in early stages despite insulin resistance glucose tolerance remains normal because beta cells compensate by increasing insulin output. As the disease progresses the beta cells become unable to sustain the hyperinsulinemia state. Thereby, there is an increase in postprandial glucose. A further decline in insulin secretion and increased in hepatic glucose production lead to overt diabetes with fasting hyperglycaemia. Ultimately, beta cell failure may ensue².

The number of people around the world suffering from diabetes has skyrocketed in the last two decades, from 30 to 230 million³. South East Asian countries have the highest burden of diabetes. India comprises 85% of the adult population of Southeast Asia and therefore the major contribution to diabetic population in Southeast Asia is from India⁴. It has been estimated that India, considered as the diabetic capital of the world with more than 32 million diabetes patients,

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would continue to lead even at 2030 with a whopping 80 million diabetics⁵. The incidence of both type 1 and type 2 is rising but this global pandemic principally involves type 2 diabetes, and is associated with several contributory factors including increased longevity, obesity, unsatisfactory diet, sedentary lifestyle and increasing urbanization⁶. Some 90% of diabetic individuals have type 2 diabetes mellitus⁷. It is usually asymptomatic for a considerable period of time. However if not diagnosed well in time, it may eventually lead to several acute and chronic micro and macrovascular complications, and even death. Optimistically, it can be diagnosed, controlled and managed easily. The drugs used in trial were *Withania coagulans* Dunal and *Trigonella foenum-graecum* Linn.

Withania coagulans Dunal. (*Tukhm-e-Hayat*), Solanaceae, Vernacular names: Vegetable Rennet⁸⁻¹⁰, *Panir*⁸, *Akri*, *Punir*⁹⁻¹¹, *Panir Dodi*⁸; Parts used: fruits; Temperament (*Mizaj*): Hot², dry^{2,8}; Medicinal properties: *Kasir-e-Riyah* (carminative)⁸⁻¹⁰, *Mudirr-e-Baul* (diuretic)⁹⁻¹¹, *Muqui* (emetic)⁹⁻¹¹, *Musaffi-e-dam* (blood purifier)¹¹, *Munjamid-e-Shir* (milk coagulant)^{8,10,11}, *Nafe Ziyabitus* (hypoglycemic)¹², and *Nafe Fart-e-Tadassum Fi dam* (hypolipidimic)¹³. Two esterase, fatty oil, an essential oil, amino acids such as proline, hydroxyproline, valine, tyrosine, aspartic acid, glycine, asparagines, cystine and glutamic acid and alkaloids are the phytoconstituents¹¹.

Trigonella foenum-graecum Linn. (*Tukhm-e-Hulba*); Family: Papilionaceae; Vernacular names:

Fenugreek^{8,10,14}, *Methi*¹⁴, *Mothi*^{11,14,15}, *Medhika*, *Chandrika*, *Asumodhagam*¹¹, *Teelas*, *Shalin*, *Talas*, *Fariqa*¹⁶; Part used: seeds; Temperament (*Mizaj*): hot², dry^{2,8,10,14}; Medicinal properties: *Muhallil-e-Waram* (antiinflammatory)^{8,10,11,14,15}, *Mudirr-e-Baul wa Haiz* (diuretic & emmenagogue)^{8,10,14}, *Mulayyin* (laxative)^{8,14}, *Mulattif* (demulcent)¹⁴, *Nafe Ziyabitus* (hypoglycemic)^{17,18-20}, *Nafe Fart-e-Tadassum Fi dam* (hypolipidimic). Trigonelline, choline, diosgenin, gitogenin, togogenin, yamogenin, quercetin, luteolin, vitexin, Isovitexin, saponaretin, homoorientin and vicianin 1 & 2 are the phytoconstituents^{11,19-22}.

Methodology

The study was carried out at Ajmal Khan Tibbiya College Hospital, Aligarh Muslim University, Aligarh on 60 cases of type 2 DM of either sex, aged not more than 60 yrs during May 2004 to August 2006 (Table 1). Diagnosis was confirmed according to WHO criteria. Patients with known type 1 DM, thyrotoxicosis, chronic renal failure, peptic ulcer or pregnant women and patients with complications of diabetes were excluded from the study. Control group comprising 20 patients were advised to take 1,800 kcal diet/day, while in the test group comprising 40 patients, 1,800 kcal diet and test drugs were given as the decant 150 ml water of 10 seeds of *Withania coagulans* Dunal (*Tukhm-e-Hayat*) and 6 gm powder of *Trigonella foenum-graecum* Linn (*Tukhm-e-Hulba*) twice a day for the period of 90 days during which they were followed up 6 times, on

Table 1—Baseline demographics

	Control group		Test group	
	20	100%	40	100%
Number of subjects studied	20	100%	40	100%
Male: Female	11:9	55%: 45%	19:21	47.5%:52.5%
Age in years – 30 – 40	3	15.0%	9	22.5%
40 – 50	10	50.0%	16	40.0%
50 – 60	7	35.0%	15	37.5%
Occupation – Service	7	35.0%	9	22.5%
Business	5	25.0%	8	20.0%
Housewife	6	30.0%	19	47.5%
Other	2	10.0%	4	10.0%
Food habits – Vegetarian	8	40.0%	12	30.0%
Non-vegetarian	12	60.0%	28	70.0%
Temperament – Sanguineous	3	15.0%	8	20.0%
Phlegmatic	15	75.0%	27	67.5%
Bilious	2	10.0%	5	12.5%
Melancholic	0	0	0	0
Risk factors – Positive family history	9	45.0%	15	37.5%
Stress positive	2	10.0%	7	17.5%
No exercise	18	90.0%	35	87.5%
BMI \geq 23 kg/m ²	11	55.0%	29	72.5%

Table 2—Effect on classical symptoms in control group (n = 20)

Symptoms	0 Day	15 Days	30 Days	45 Days	60 Days	75 Days	90 Days
Polydipsia	6	5	4	4	2	2	2
No of improved patients	-	1	2	2	4	4	4
Improvement (%)	-	16.6%	33.3%	33.3%	66.6%	66.6%	66.6%
Polyphagia	2	2	2	2	1	1	1
No of improved patients	-	0	0	0	1	1	1
Improvement (%)	-	0%	0%	0%	50%	50%	50%
Polyuria	7	6	4	3	3	2	2
No of improved patients	-	1	3	4	4	5	5
Improvement (%)	-	14.2%	42.8%	57.1%	57.1%	71.4%	71.4%
Nocturia	12	10	8	7	7	5	4
No of improved patients	-	2	4	5	5	7	8
Improvement (%)	-	16.6%	33.3%	41.6%	41.6%	58.3%	66.6%
Weight Loss	5	5	3	3	3	3	3
No of improved patients	-	0	2	2	2	2	2
Improvement (%)	-	0%	40%	40%	40%	40%	40%
Chronic Fatigue	11	10	8	6	5	5	4
No of improved patients	-	1	3	5	6	6	7
Improvement (%)	-	9.09%	27.7%	45.4%	54.5%	54.5%	63.3%
Genital Candidiasis	0	0	0	0	0	0	0
No of improved patients	-	-	-	-	-	-	-
Improvement (%)	-	-	-	-	-	-	-
Erectile Dysfunction	0	0	0	0	0	0	0
No of improved patients	-	-	-	-	-	-	-
Improvement (%)	-	-	-	-	-	-	-
Paraesthesia	2	2	2	2	2	2	2
No of improved patients	-	0	0	0	0	0	0
Improvement (%)	-	0%	0%	0%	0%	0%	0%

Table 3—Effect on classical symptoms in test group (n = 40)

Symptoms	0 Day	15 Days	30 Days	45 Days	60 Days	75Days	90 Days
Polydipsia	11	9	6	6	4	2	2
No of improved patients	-	2	5	5	7	9	9
Improvement (%)	-	18.18%	45.45%	45.45%	63.63%	81.81%	81.81%
Polyphagia	6	6	5	3	3	1	1
No of improved patients	-	0	1	3	3	5	5
Improvement (%)	-	0%	16.66%	50%	50%	83.33%	83.33%
Polyuria	19	17	13	6	5	5	4
No of improved patients	-	2	6	13	14	14	15
Improvement (%)	-	10.52%	31.57%	68.42%	73.68%	73.68%	78.94%
Nocturia	28	24	13	11	11	8	6
No of improved patients	-	4	15	17	17	20	22
Improvement (%)	-	14.28%	53.57%	60.71%	60.71%	71.42%	78.54%

(Contd)

Table 3—Effect on classical symptoms in test group (n = 40)—Contd

Symptoms	0 Day	15 Days	30 Days	45 Days	60 Days	75Days	90 Days
Weight Loss	11	11	10	10	8	6	5
No of improved patients	-	0	1	1	3	5	6
Improvement (%)	-	0%	9.09%	9.09%	27.27%	45.45%	54.54%
Chronic Fatigue	25	21	13	12	9	5	3
No of improved patients	-	4	12	13	16	20	22
Improvement (%)	-	16%	48%	52%	64%	80%	88%
Genital Candidiasis	5	5	3	2	2	1	1
No of improved patients	-	0	2	3	3	4	4
Improvement (%)	-	0%	40%	60%	60%	80%	80%
Erectile Dysfunction	4	4	4	3	3	2	2
No of improved patients	-	0	0	1	1	2	2
Improvement (%)	-	0%	0%	25%	25%	50%	50%
Paraesthesia	6	6	6	6	6	6	6
No of improved patients	-	0	0	0	0	0	0
Improvement (%)	-	0%	0%	0%	0%	0%	0%

Table 4—Effect on glycosuria

	0 Day	15 Days	30 Days	45 Days	60 Days	75 Days	90 Days
Control Group (n=20)							
No of patients	20	19	12	11	8	5	5
No of patients improved	-	1	8	9	12	15	15
% of improvement	-	5%	40%	45%	60%	75%	75%
Test Group (n=40)							
No of patients	40	36	25	14	9	8	8
No of patients improved	-	4	15	26	31	32	32
% of improvement	-	10%	37.5%	65%	77.5%	80%	80%

Table 5—Effect on Random Blood Sugar (mg %)

		0 Day	30 Days	60 Days	90 Days
Control Group (n=20)	Blood Sugar (Mean±SD)	222.8±26.8	189.2±30.9	171.9±28.0	168.6±23.6
	% of fall	-	15.08%	22.84%	24.32%
Test Group (n=40)	Blood Sugar (Mean±SD)	249.45±45.9*	186.15±49.4	167.0±95.9	157.2±38.7*
	% of fall	-	25.37%	33.05%	36.98%

* Indicates values are significant at $p < 0.05$ when compared to control

day 15, 30, 45, 60, 75 and day 90. The observations and results were obtained and statistical analysis was done.

Results and discussion

There was a significant improvement in symptoms (Tables 2-4) which may be due to good glycaemic control. The study also showed a significant ($p < 0.05$)

reduction in blood sugar in test group as compared to control group (Table 5). The reduction in control group is due to low caloric diet. It has been already been reported that about 50% of diabetic individuals can be controlled by diet alone⁶. But the better reduction in test group is due to low caloric diet and hypoglycaemic effect of *Trigonella foenum-graecum* (*Tukhm-e-Hulba*) and *Withania coagulans* (*Tukhm-e-*

Table 6—Effect on Glycated haemoglobin (%)

		Control Group (n=20)		Test Group (n=40)	
		0 Day	90 Days	0 Day	90 Days
HbA _{1c}	Sum	172.0	159.4	343.5	308.0
	Mean±SD	8.6±0.62	7.97±0.79	8.6±0.72	7.7±0.78

Hayat). The testa and endosperm of the seeds are thought to be the source of the hypoglycaemic effect of fenugreek, which have been attributed to various mechanisms. The amino acid, 4-hydroxyisoleucine in fenugreek seeds increased the glucose-induced release of insulin in the pancreatic islet cells of humans and rats²³. The hypoglycaemic effect of fenugreek seeds and *Withania coagulans* have been reported^{12,17,18,24-28}. The effect was not significant on glycated haemoglobin (Table 6) which may be due to short duration of trial.

Conclusion

The drugs, *Withania coagulans* Dunal and *Trigonella foenum graecum* Linn. exhibited hypoglycaemic activity. Significant improvement in symptoms and signs were observed and significant euglycemia was attained. But to observe the effect of drugs on the level of glycated haemoglobin, which was not significant, long-term studies are needed.

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