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Effect of Polyherbal Formulation in Patients with Type 2 Diabetes Mellitus

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Abstract

A study was undertaken for evaluating the biochemical effects of an ayurvedic Poly Herbal formulation (PHF) (containing Glycine max, Cicer arietin, Trigonella foenum graecum, Murraya koenigii, Garcinia cambogia and Sodium chloride) in type II diabetic patients over a period of 3 months. A total of 30 patients diagnosed with diabetes mellitus by the clinical features and FBS values, when appeared for the medical camp. The basic data like life style, diet habits, etc and anthropometric measurements like weight, height, BMI, etc were collected using a questionnaire. The patients were asked to stop taking hypoglycemic drugs and were given PHF. The dosage of PHF was fixed by the medical practitioner on a case to case basis. Of the five medical camps conducted consequently within three months to monitor the patients, but the parameters of first (i.e. prior to the PHF administration) and the final camp were only recorded for statistical analysis. The patients were divided into 5 groups based on their age; Group I -Normal healthy Subjects (40–75 yrs), Group II - 40-48 yrs, Group III - 49-57 yrs, Group IV–58-66 yrs, and Group V – 67-75 yrs. The biochemical parameters like FBS, HbA1C, Lipid profile, AST, ALT, Urea, Blood urea nitrogen (BUN) and Creatinine were analyzed by using kit methods. P value < 0.05 is considered significant. Study was approved by institutional ethical committee. In the present study, we found that PHF have beneficial when given to Type 2 Diabetes Mellitus patients by showing significant hypoglycemic and hypolipidemic effects when serum Glucose, TC, TG, LDL-C and HDL-C were observed and no after effects were noticed.

Key words: Diabetes mellitus, Garcinia cambogia, Glycine max, Murraya koenigii, Trigonella foenum, Polyherbal formulation.

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Introduction:

Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both. A consequence of this is chronic hyperglycaemia (that is elevated levels of plasma glucose) with disturbances of carbohydrate, fat and protein metabolism. Long-term complications of DM include retinopathy, nephropathy and neuropathy. There is a constant need for better treatments for DM. [1] In last few years, the herbal medicine and drugs are gaining popularity, because of their natural origin and lesser side effects compared to modern synthetic chemical drugs. The hypoglycemic effects of plants may be due to various reasons like their ability to restore the function of pancreatic tissues by causing an increase in insulin output, inhibition of the intestinal absorption of glucose, the facilitation of metabolites in insulin dependent processes and

presence of antioxidants.[2] Traditional antidiabetic plants might provide a useful source for developing new oral hypoglycemic compounds as therapeutic entities or simple dietary adjuncts to the existing therapies. Studying such traditional medicine might offer an alternative and natural way to treat diabetes.

Patients with diabetes and other common chronic medical conditions are more likely to use complementary and alternative medications than individuals in the general population. [1] In Indian traditional medicine system, the herbal formulations and combined extracts of plants are commonly used than individual one.[3] Here, we tried to study the effects of a polyherbal formulation (PHF) (already available in market) in patients with Type 2 Diabetes mellitus.

Materials and Methods

The study was carried out with 30-diabetic patients (17 males, 13 females) with the age range of 40-75 years. Written consent forms were taken from the patients who were willing to participate in the study. The basic data like life style, diet, habits, etc and anthropometric measurements like weight, height, BMI, etc were collected using a questionnaire. The patients were asked to stop taking hypoglycemic drugs (under supervision of medical practitioner) and were given the PHF (Table1) for three months. The dosage of PHF was fixed by the medical practitioner on a case to case basis. Insulin treated patients were excluded from this study and also, other medications used by the subjects were ignored. Of the five medical camps conducted consequently within three months to monitor the patients, but the parameters of first (i.e. prior to the PHF administration) and the final camp were only considered for statistical analysis. Study was in compliance to patients. The present study was approved by institutional ethical committee.

The patients were divided into 5 groups based on their age.[4] The Groups are as follows: Group I - Normal healthy Subjects (40-75 yrs), Group II - 40-48 yrs, Group III - 49-57 yrs, Group IV–58-66 yrs, and Group V – 67-75 yrs. The various parameters like FBS, HbA1C, Lipid profile, AST, ALT, Urea, Blood urea nitrogen (BUN) and Creatinine were analyzed by using kit methods in Stat fax semi-auto analyzer. P value < 0.05 is considered significant

S. No	Botanical name	Common name	Family	Part using
1	Glycine max	Soybean	Fabaceae	Seeds
2	Cicer arietin	Bengal gram	Fabaceae	Seeds
3	Trigonella foenum graecum	Fenugreek	Fabaceae	Seeds
4	Murraya koenigii	Curry leaf	Rutaceae	Leaves
5	Garcinia cambogia	Kudampuli	Clusiaceae	Fruits
6		Salt (NaCl)		

Table 1: Ingredients of the PHF

Results

There is a significant reduction in FBS, HbA1C, Total cholesterol, LDL and Atherogenic index level in all groups of patients after three months of PHF administration, compared to their levels before administration (Table 2&3). Similarly, there is a significant reduction in serum Triglycerides and VLDL level in Group III, IV & V (Table 3). Though there was a decrease in triglycerides and VLDL level in majority of patients (83.3%) belonging to group II, it was not statically significant (Table 3). All groups except group II showed a significant increase in HDL value. Anyway majority of the patients in group II (66.6%) showed an increased HDL level at the end of the study period (Table 3).

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		FBS (mg/dl)	HbA1c%
Group I		87.2±6.46	5.44±0.18
Group II	PRIOR	147.3±22.0	8.8±0.97
	AFTER	141.8±38.5	7.2±1.0
		p<0.02	p<0.05
Group III	PRIOR	170.7±19.1	10.7±2.0
	AFTER	146.7±22.3	9.0±1.9
		p<0.01	p<0.02
Group IV	PRIOR	134.8±36.7	9.8±2.28
	AFTER	129.1±31.8	8.9±1.9
		p<0.01	p<0.01
Group V	PRIOR	141.5±52.3	9.1±1.3
	AFTER	137.8±39.8	8.0±1.7
		p<0.05	p<0.05

Table 2: Blood/Serum levels of FBS, and HbA1c (Mean ± SD)

		Total Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	Atherogenic Index
Group I		153.2±17.86	81.2±14.57	52.1±10.12	81.8±23.53	16.2±2.91	3.0±0.72
Group II	PRIOR	209.3±41.1	146.3±36.5	49.2±1.2	131.0±39.5	29.2±7.3	4.3±0.85
	AFTER	201.2±22.3	134.2±50.8	50.3±3.1	123.9±18.2	26.8±10.1	3.99±0.62
		p<0.01	p<0.1*	p<0.50*	p<0.05	p<0.10*	p<0.01
Group III	PRIOR	169.2±35.6	135.1±28.0	50.7±1.6	91.9±33.6	26.7±5.8	3.3±0.7
	AFTER	156.5±27.5	125.1±34.0	51.6±2.0	79.2±23.8	25.2±6.6	3.0±0.5
		p<0.02	p<0.02	p<0.05	p<0.02	p<0.02	p<0.02
Group IV	PRIOR	188.8±34.7	142.9±33.4	49.9±1.1	110.2±31.9	28.7±6.6	3.8±0.6
	AFTER	185.9±31.1	141.0±21.2	50.4±2.5	106.5±30.5	29.0±5.0	3.7±0.7
		p<0.001	p<0.01	p<0.001	p<0.001	p<0.01	p<0.001
Group V	PRIOR	179.4±41.5	129.0±32.4	51.3±1.28	102.4±39.1	25.8±6.4	3.5±0.7
	AFTER	166.0±38.3	124.8±26.9	51.7±2.6	79.95±34.9	25.6±6.1	3.2±0.7
		p<0.01	p<0.05	p<0.001	p<0.01	p<0.01	p<0.01

Table 3: Serum Lipid profile level (Mean ± SD)

		ALT (IU/L)	AST (IU/L)	UREA (mg/dl)	BUN (mg/dl)	CREATININE (mg/dl)
Group I		18.9±5.08	20.7±5.77	27.7±4.47	12.9±2.10	0.93±0.14
Group II	PRIOR	32.0±19.3	32.5±15.2	19.3±5.8	9.0±2.7	0.86±0.13
	AFTER	29.0±16.3	23.3±8.0	20.3±5.4	9.5±2.5	0.83±0.13
		p<0.47*	P<0.12*	P<0.77*	P<0.10*	P<0.05
Group III	PRIOR	29.6±6.8	30.0±6.2	18.6±5.8	8.8±2.7	0.96±0.29
	AFTER	25.1±8.4	22.9±5.4	20.1±3.7	9.7±1.7	0.95±0.27
		P<0.05	P<0.02	P<0.02	P<0.02	P<0.02
Group IV	PRIOR	29.8±9.0	29.8±16.1	20.3±4.6	9.5±2.1	1.0±0.14
	AFTER	31.7±5.4	31.4±14.1	20.3±3.8	9.48±1.7	1.1±0.4
		P<0.10*	P<0.01	P<0.02	P<0.01	P<0.10*
Group V	PRIOR	29.1±18.7	29.6±16.7	29.5±14.2	13.8±6.6	1.0±0.16
	AFTER	29.1±16.6	25.4±9.4	29.6±13.7	13.9±6.4	1.2±0.3
		P<0.02	P<0.02	P<0.05	P <0.001	P <0.10*

Table 4: Blood/Serum levels of ALT, AST, Urea, Blood Urea Nitrogen (BUN) & Creatinine (Mean ± SD)
*** Not significant**

There is a significant reduction in serum AST levels in all groups (except group II), ALT (except group II & IV), Urea (except group II), BUN (except group II), and serum creatinine (except group IV & V) of patients at the end of the study, compared to their levels before administration of PHF. Anyway majority of the patients (62.5% in group V of creatinine and 66.6% in all other groups which are reported as not significant) showed decreasing levels of these parameters (Table 4).

Discussion

The hypoglycemic and hypolipidemic effects of all ingredients in this formulation were already reported. Soybeans **(***Glycine max***)** are considered as a source of complete protein for diabetes and are devoid of starch. Food and Drug Administration's (FDA) approved soy as official cholesterol lowering food, along with other health benefits. [5] Soy phytoestrogens (genistein and diadzein) adsorbed onto the soy protein were suggested as the agent reducing serum cholesterol levels. Recent studies shown that rats fed with a soy protein diet have reduced SREBP -1 expression which is indirectly required for cholesterol biosynthesis and for uptake and fatty acid biosynthesis. [6] It has also been reported that soy-based diet is effective in reducing total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C) and triacylglycerol (TG), and in increasing the high density lipoprotein-cholesterol (HDL-C), suggesting that soy products may be beneficial in the management of Type 2 Diabetes mellitus.[7]

Increased antioxidant and inhibitory potential of sprouted Bengal gram **(***Cicer arietin***)** against α-glucosidase and α-amylase (key enzymes linked to

type 2 diabetes) makes them desirable for dietary management/prevention of diabetes.[8] Methanolic extract of Bengal gram exhibited significant anti hyperglycemic activity along with antioxidant properties.[9] According to Mathur et al, the hypocholesterolemic action of Bengal gram has been confirmed in experimental rat studies.[10]

Previous studies have shown that Fenugreek **(***Trigonella foenum graecum***)** seeds lowered blood glucose levels and partially restored the activities of key enzymes of carbohydrate and lipid metabolism, close to normal values in various animal model systems. Therefore, it is possible that active compounds of *Trigonella foenum-graecum* seed extract decrease the blood glucose levels by inhibiting the absorption of glucose from the alimentary tract.[7] Bioactive compounds isolated from fenugreek seeds are protodioscin, trigoneoside, diosgenin and yamogenin.[11,12] A study showed that a dialyzed aqueous extract of fenugreek seeds possess hypoglycaemic properties and stimulates insulin signaling pathways in adipocytes and liver cells.[13] The seeds and leaves of fenugreek are edible and are used as Ayurvedic medicine in the Indian subcontinent to treat diabetes, high cholesterol, wounds, inflammation, and gastrointestinal ailments. [7]

Garcinia cambogia acts in two ways, by suppressing appetite and by inhibiting lipid synthesis. It contains the principal organic acid (-) erythro-L-hydroxy - citric acid, an effective inhibitor of ATP-citrate lyase which cleaves citrate to produce acetyl CoA. [14] Acetyl CoA plays a major role in several biosynthetic pathways including lipogenesis. This herbal supplement promotes the oxidation of lipids and spares carbohydrates. This action will result in lowering levels of blood cholesterol and it also prevents the hepatic cells from hyperlipidemic cellular damage and becoming fibrotic. [15]

The important properties of ***Murraya Koenigii*** include much value as an antidiabetic, antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, anti-hypercholesterolemic etc. [16] Recent study shows that *M. koenigii* is a good glucosidase inhibitor to porcine pancreatic alfa-amylase as well as murine pancreatic and intestinal glucosidases.[17]

Sodium chloride promotes digestion, improve appetite, and relieve constipation and helps with the assimilation of the nutrients.

May be due to the combined effect of all the above ingredients of this polyherbal formulation, it showed effects in regulating diabetes by controlling blood glucose and lipid levels. Previous literatures showed that these compounds regulate diabetes individually and the effect was found similar even when these compounds were mixed together. It is postulated that ayurvedic formulations may act through potential pancreatic as well as extra-pancreatic effects. The probable mechanisms of action include: delaying gastric emptying, slowing carbohydrate absorption, inhibition of glucose transport, increasing the erythrocyte insulin receptors and peripheral glucose utilization, increasing glycogen synthesis, modulating insulin secretion, decreasing blood glucose synthesis through depression of the enzymes glucose-6-phosphatase, fructose-1, and 6-bisphosphatase, and enhanced glucose oxidation by the enzyme glucose-6-phosphatase-dehydrogenase pathway.[18] Individual components of the PHF has its own action in regulating the diabetes by different mechanism, as mentioned above. Similar effects were observed, when these compounds were administered in combination. Limitations of our work were that detailed study was not carried to find out the action of individual components, and the sample size was small. Further studies can also be done in this regards for more details on the effects.

Conclusion

In the present study, we found that intake of this PHF have beneficial effects on Type 2 Diabetes Mellitus patients when serum Glucose, TC, TG, LDL-C and HDL-C were observed and no after effects were noticed. Long term, in-depth toxicological and molecular level studies are needed to provide further information and confirmation of these findings.

References

1. Kalpana S, Roshni M, Sridharan R, Deepak P. Ayurvedic treatments for diabetes mellitus. *The Cochrane Collaboration* 2012:1-58

2. Neelesh M, Sanjay J, Sapna M. Antidaibetic potential of medicinal plants. *Acta Poloniae Pharmaceutica Drug Research 2010*;67(2):113-118.

3. Leela VP, Ramalingam S. Role of Diasulin - an herbal formulation on antioxidant status in Chemical induced diabetes. *International Journal of Pharmacology* 2006;2(1):110-115.

4. Faizal P, Suresh S, Satheesh K, Augusti KT. A study on the hypoglycemic and hypolipidemic effects of an ayurvedic drug rajanyamalakadi in diabetic patients. *Indian Journal of Clinical Biochemistry* 2009; 24(1):82-87.

5. Anderson JW, Smith BM, Washnock CS. Cardiovascular and renal benefits of dry bean and soybean intake. *Am J Clin Nutr* 1999;70:464-474.

6. Armando RT, Fernanda M, Cristino C, Rogelio HP, Carlose AAGS, Jose PC, Ricardo CR, Nimbe T. A Soy Protein Diet Alters Hepatic Lipid Metabolism Gene Expression and Reduces Serum Lipids and Renal Fibrogenic Cytokines in Rats with Chronic Nephrotic Syndrome. *J Nutr* 2002;132: 2562–2569.

7. Therasa SV, Sivaraj A, Sivakumar C, Elumalai EK, Thirumalai T, David E. Trigonella foenum gracum seed extract inhibit uptake of glucose across rat everted gut sacs in vitro. *International journal of pharmtech research* 2010;2(1):359-362.

8. Prathapan A, Fahad K, Thomas BK, Philip RM, Raghu KG. Effect of sprouting on antioxidant and inhibitory potential of two varieties of Bengal gram (Cicer arietinum) against key enzymes linked to type-2 diabetes. *International Journal of Food Sciences and Nutrition* 2011;62(3):234-238.

9. Tiwari AK, Swapna M, Ayesha SB, Zehra A, Agawane SB, Madhusudana K. Identification of proglycemic and anti hyperglycemic activity in antioxidant rich fraction of some common food grains. *International Food Research Journal* 2011;18(3): 915-923.

10. Mathur KS, Wahi PN, Sharma RD. Effect of dietary fats and proteins on serum cholesterol and lipid phosphorus in rats. *J Indian Med. A* 1963;41:379.

11. Murakami T, Kishi A, Matsuda H, Yoshikawa M. Medical food stuffs XVII. Fenugreek seed (3): structures of new furostanol-type steroid saponins, trigoneosides Xa, Xb, XIb, XIIa, XIIb and XIIIa from the seeds of Egyptian Trigonella foenum graecum. *L.Chem Pharm Bull* 2000;48:994-1000.

12. Yoshikawa M, Murakami T, Komatsu H, Murakami N, Yamahara J, Matsuda H. Medicinal food stuffs Fenugreek seed (1): structures of trigneosides Ia, Ib, IIa, IIb, IIIa, and IIIb, new furastanol saponins from the seeds of Indian Trigonella foenum graecum. *L.Chem Pharm Bull* 1997;45:81-7.

13. Vijayakumar MV. The hypoglycemic activity of fenugreek seed extract is mediated through the stimulation of an insulin signaling pathway. *Br J Pharamacol* 2005; 146(1):41-48.

14. Cheema D S, Halperin M L, Leznoff CC. Inhibition of enzymes which interact with citrate by (-) hydroxyl citrate and 1,2,3,Tricarboxybenzene. *Eur J Biochem* 1973;38:98-100.

15. Berkhout AT, Havekes ML, Pearce JN, Groot HEP. The effect of (-) hydroxyl citrate on the activity of the low density lipoprotein receptor and 3 – hydroxy -3- methylglutaryl-CoA reductase levels in the human hepatoma cell line. *HepG2 Biochem J* 1990;272:181-186.

16. Arulselvan P, Senthilkumar GP, Sathish kuamr D, Subramanyan S. Antidiabetic effect of Murraya Koenigii leaves on streptozotocin induced diabetic rats. *Pharmazie* 61; (10):874-7.

17. Menakshi B, Smita SZ, Shobha YB, Ameeta RK, Bimba NJ. Antidiabetic Indian Plants: A Good Source of Potent Amylase Inhibitors. *Evidence Based Complementary and Alternative Medicine* 2011;1:1-6.

18. Laura Shane-McWhorter. Biological Complementary Therapies: A Focus on Botanical Products in Diabetes. *Diabetes Spectrum* 2001;14:199-208