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ANTI-HYPERGLYCEMIC AND ANTI-HYPERLIPIDEMIC POTENTIAL OF A POLYHERBAL PREPARATION "DIABEGON" IN METABOLIC SYNDROME SUBJECT WITH TYPE 2 DIABETES

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Abstract

Background: In the present study, "Diabegon" a poly-herbal preparation, with hypoglycemic activity, was evaluated for its preventive effect in metabolic syndrome subjects with type 2 diabetes and also to reveal its side effects, on liver and kidney.
Materials and Methods: Type 2 diabetic subjects with metabolic syndrome (N=58) were categorized on the basis of age and fasting blood glucose. The grouping was as follows: Group I (35-50 yrs), Group II (51-65 yrs), Group III >65 yrs, Group IV FBS<145.9, Group V FBS>145. Each group was administered 4 gm of diabegon daily. Blood glucose levels, lipid profile, liver and kidney function of the subjects were regularly monitored within 3 months of interval to 18 months.
Results: The reduction in fasting blood glucose level ranged from 12.3% ($P<0.05$) to 42% ($P<0.001$) after 18 month of therapy whereas in postprandial blood glucose, the decrease ranged from 28% ($P<0.05$) to 32% ($P<0.05$) after 18 month of therapy. Overall reductions in the individual parameters of the metabolic syndrome subjects were significantly higher in Group I. Cholesterol level decreased from 11% to 27.2% ($P<0.001$), triglyceride levels decreased from 24% to 55%, VLDL and LDL levels reduced by 60% & 54% respectively after 18 months of therapy. The HDL-C level increased in all groups. Moreover, diabegon administration for 1.5 years exhibited no alteration in liver and kidney function tests, which indicate its non-toxicity.
Conclusion: Our study suggests that diabegon could be included as a preventive treatment in metabolic syndrome subjects with type 2 diabetes especially for long term treatment as it efficiently shows anti-hyperglycemic and anti-lipidemic effects with no adverse impacts on the liver and kidney.

Key words: Metabolic syndrome, Type 2 diabetes, Diabegon, Polyherbal preparation.

Introduction

Metabolic syndrome combines a group of several risk factors like insulin resistance, hypertension, dyslipidemia and obesity. T2 diabetes and CVD play an important role in the increasing the burden of death because of the severity and complication of the disease. Studies reveal that metabolic syndrome with type 2 diabetes leads to more cardiovascular events than only metabolic syndrome (Sone et al., 2009; Wilson et al., 2005). So these subjects require more attention on health and also needed a follow-up or intervention study.

There are many studies that focus on the prevalence of metabolic syndrome in different populations. Some of those observed in respect of prevalence that ranges from 13-30% and 70-80% among the Caucasian non-diabetic (Ford et al., 2002; Novakovic et al., 2001) and diabetic (Balkau et al., 2002) populations, respectively. According to Reaven et al genetically determined insulin resistance in a setting of suitable environmental factors is the pivotal pathogenic mechanism underlying the metabolic syndrome.

The clinical management of T 2 diabetic patients with the metabolic syndrome is to reduce the risk of further cardiovascular disease. It is associated with the drug therapy for the metabolic syndrome imply on amendment of the individual risk factors i.e. hypertension, dyslipidemia, adiposity and hyperglycemia (Eckel et al., 2005; Grundy, 2006). Hyperglycemia associated with lipid disorder leads to dysfunction of liver, skeletal muscle and adipose tissue later it passes to vital organ of the body like kidney, eyes and nervous system. Hence metabolic syndrome could be a prognostic marker for the severity of complication in T2 diabetes. Therefore our study focuses on metabolic syndrome subjects with T2 diabetes. A lot of pharmaceutical drug has been available for the treatment of metabolic syndrome and T2 diabetes but none of them are well suited in every respect of side effects. Sulfonylurea and biguanides used for treatment of diabetes are highly expensive or have undesirable side effects or contraindication (Halim and Hussain, 2002; Chen et al., 2003). Drugs like sulfonylurea shows some toxic effect like heartburn, vomiting, skin rashes etc (Seshiah, 2004). Biguanides (metformin) on long-term consumption may generate gastrointestinal effects, anorexia, vomiting, and B_{12} malabsorbtion.
Hence there arises an urgent need to identify natural resources and study their potential on different identified targets in order to develop them as new anti-diabetic therapeutics (oral hypoglycemic agents and insulin) for the treatment of diabetes mellitus. Many experimental and clinical trials have been carried out for anti-diabetic property of herbal preparation in diabetes (Babu et al., 2004; Bhandari et al., 2005; Tongia et al., 2004). Even WHO suggested the evaluation of the potential of plants as effective therapeutic agents, especially in areas where we lack safe modern drugs WHO (World Health Organization Geneva 1994).

Based on the ancient Indian Ayurvedic text that describes the cure for diabetes, a polyherbal mixure is prepared by Dindayal Aushdhi Ltd. Gwalior namely Diabegon® . The diabegon, a polyherbal formulation of containing 18 plant extracts with known hypoglycemic activity is shown in our previous study in animal by Hariom et al., 2007. Hariom et al. evaluated the hypoglycemic effect of diabegon in animal model but the long term follow-up treatment has not been evaluated with special reference to metabolic syndrome. Hence the present study assessed therapeutic potential of polyherbal preparation "Diabegon" in metabolic syndrome subjects with type 2 diabetes and also study revealed its side effect, on liver, kidney.

Material and methods

Selection of subjects

Type 2 diabetes with metabolic syndrome subjects was randomly selected from different age groups from our weekend diabetic clinic run in the school of studies in Biotechnology at Jiwaji University Gwalior. The time period was in between (2007-2009). All the recruited subjects expressed

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their willingness to participate in the study. The study group consisted of 58 T2 diabetic subjects with metabolic sydrome on the basis of age and fasting blood sugar (FBS). First three groups divided accordingly to age and other two groups were based on lower (FBS<145.9 mg/dl) and higher blood group (FBS>145.9 mg/dl).
Group I NIDDM age group (35-50) N=10, Group II NIDDM age group (51-65) N=34, Group III NIDDM age group >65 N=14,
Group IV NIDDM FBS<145.9 (N=43), Group V NIDDM FBS>145.9 (N=15).
A baseline questionnaire requested information on diet pattern, lifestyle, known risk factors for diabetes and socioeconomic background etc. The study design and experimental protocols were approved by the Institutional Human Ethics Committee. The drug was prescribed by Ayurvedic physician personally to every subject at a dose of 4 Gms. (twice a day) with water as prescribe in Ayurvedic Pharmacopoeia of India. The treatment was monitored at about one and half year and followed by monthly checkup. The subjects were kept away from any other type of anti-diabetic medication.

Anthropometrical and biochemical parameters

Selected anthropometric variables like Height, weight and waist circumferences were measured with the subject barefooted and lightly dressed. Table 1 showed the different groups characterized on the age group and fasting blood glucose level

Sample collection and biochemical estimations

Fasting blood glucose and lipid profile were measured at baseline and followed up every month till 18 month of therapy. The fasting blood glucose level was represented at 3 month intervals and lipid profile was represented in 6 months interval. The blood glucose level was determined by glucose oxidase-peroxidase method using a kit Monozyme India limited, Ahmadabad (Trinder, 1969). Total cholesterol, triglyceride and HDL-cholesterol were estimated by CHOD-PAP (Stockbridge et al., 1989), triglycerides (Fossati and Prencipe, 1982) and HDL- Cholesterol (Lopes-virella et al., 1977) was estimated by spectrophotometric assays employing commercially available kits. LDL and VLDL were calculated from Freidewald's formula. Kidney function was monitored by studying the changes in urea using the (Fawcett, 1960) uric acid (Fossati, 1980)) and creatinine (Bowers, 1980). Liver function was assessed by monitoring bilirubin (modified Jendrassik and Grof's method, 1938), serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) (modified International Federation of Clinical Chemistry [IFCC] method, Burtis and Ashwood, 1999).

Diagnostic criteria of the metabolic syndrome

NCEP-ATP III criteria were used for the diagnosis of metabolic syndrome (NCEP JAMA, 2001).

Statistical Analysis

The results were expressed as mean ± standard deviation. The data obtained from the experiments were analyzed using one-way ANOVA (Bonferroni t-test) employing Sigma Stat, statistical software, version 1.0 (Jandal corporation, USA). For computation of data, software application programmes like Microsoft Excel, Sigma Direct. The values were tested for significance at $P<0.001$, $P<0.05$.

Results

Anthropometric parameters of Non Insulin Dependent Diabetes Mellitus subjects with metabolic sydrome having different age group selected for diabegon Study

The Subject of either sex was selected for studies which were grouped into five groups as shown in Table 1. The groups were studied with respect to anthropometric parameters; age, duration of disease, waist circumference, BMI, systolic blood pressure, diastolic blood and pulse rate. On comparing the age of Group II with Group I significance was observed. The age Group was found to be significant ($P\leq0.001$) when comparisons were made between Group I&III Group II& IIIGroup, V&III Group and IV&III Groups. In age group significance ($P\leq0.001$) was observed when comparisons were made between II &I IV&I Groups. Systolic blood pressure was significant ($P\leq.05$) when group I compared with III, V.

Table 1:. Anthropometric parameters of Non Insulin Dependent Diabetes Mellitus subjects with MetS having different age group selected for Diabegon Study

Groups	Age (Year)	Duration of dis. (Year)	Waist Circ. (Inches)	BMI (Kg/m2)	Systolic (mmHg)	Diastolic (mmHg)	Pulse
Group I (35-50) N=10 (a)	46±4.3	5.5±4.6	37.17±3	27.0±4.1	127±9.9	76.9±6.2	89.37±8.9
Group II (51-65) N=34 (b)	58.3±3.6 a**	4.3±2	36.6±3.9	25.9±3.6	134.29±17	74.2±7.2	85.71±8.6
Group III >65 N=14 (c)	70±5 (a**,b**d**,e**)	9.1±6.3	38.0±7.3	23.8±4.5	140.7±18.9 a*	72.8±8.6	82.99±8.9
CG- IV FBS<145.9 (d) N=43	59.4±7.4 a**	5.3±4	37.9±5.2	26.0±3.9	136.0±17.1	74.4±7	84.5±9.1
CG-V FBS>145.9 (e) N=15	57.7±12.1 a*	6.53±5.2	35.3±3.3	24.2±4.3	138.9±13.3a*	77.1±8.3	88.9±7.7

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Tables 2: Effect of Diabegon® on blood glucose level in MetS with Non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

(Groups)	Fasting blood glucose (mg/dl)							Post-prandial blood glucose (mg/dl)						
	Initial (a)	3 month of therapy (b)	6 month of therapy (c)	9 month of therapy (d)	12 month of therapy (e)	15 month of therapy (f)	18 month of therapy (g)	Initial(a)	3 month of therapy (b)	6 month of therapy (c)	9 month of therapy (d)	12 month of therapy (e)	15 month of therapy (f)	18 month of therapy (g)
Group I (35-50), N=10	160.3±33.9	150±50.1	142.7±55.8	120.5±38.2 a*	117.8±38.1 a*	118.6±41.6 a*	122.1±27.3 a*	238.6±50.4	218.8±82.3	210.6±80.5	193.2±75.2 a*	161.2±67.2 a*	173.7±50.2 a*	185.3±30.3 a*
Group II (51-65), N=34	139.7±35.2	134.1±48	116.4±5.5 a**b*	111.8±19 a**b*	110±23.2 a**b*	114.2±25.4 a**b*	102.5±34.3 a**b*c*d*	209.1±53.1	183.2±70.7	185.6±20.1 a*	157±44.8 a**c*	168.6±84.2 a*	164.2±34.6 a**c*	171.9±69.5 a*
Group III >65, N=14	130.5±34	127.8±43.2	131.8±12.8	123±50.8	133.4±29.7	124.9±30.7	114.4±26.7 c*	219.3±74	185.8±79	197.4±20.8	193.6±77.5	171.5±25.4 a*c*	181.4±34.8	162.1±40.3 a*c*
CB-IV, N=43 FBS<145.9	116±19.5	119.6±37.8	120.1±18.8	110.5±43.8	110.4±39.3	110.7±21.5	106.6±27 c*	189.8±28.6	161.5±39.3 a**	177.2±30.8 b*	163.9±67 a*	174.6±88	170.3±61.2	164.4±52.3 a*
CB-V, N=15 FBS>145.9	189.2±19.2	174±77.3	139.8±25.4 a**b*	118.2±24.7 a**b*c*	130.6±34.1 a**c*	162.9±45.6 a*d*e*	110.2±36.1 a**b**c*f*	249.6±46.1	224±80.5	234.3±53	218.6±76.5	211.1±50.9 a*	192.5±8.84 a**c*	196±69.8 a*

Table 3: Effect of Diabegon® on blood cholesterol, triglyceride & HDL-C in MetS with Non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

(Group)	Total Cholesterol (mg/dl)				Triglyceride (mg/dl)				HDL-C (mg/dl)			
	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)
Group I (35-50) ,N=10	197.9±19.2	161.7±47.8 a*	139.9±31.4 a**	147.1±17.6 a**	281.4±93.9	192.5±31 a*	110.06±8.8 a**b**	126.3±37.8 a**b**	27.9±1.43	36.7±5.3 a**	39.5±16.7	54.5±23 a*b*
Group II (51-65) ,N=34	167.4±20.1	183.5±42.1 a*	153.5±23.2 a*b**	148.9±44.8 a*b*	169.3±29.4	120.3±56.7 a**	121±16 a**	111.7±47.6 a**	44±10.4	32.2±5.8 a**	42.2±21.5 b*	51.9±15 a*b**
Group III >65, N=14	176.7±10.6	163.3±65.8	163.1±17.8	151±43 \a*	133.5±33.4	157.4±14.4 a*	136.8±43.4	101.2±30 a*b**c*	40.7±11.6	41.7±8.1	40.95±5.9	51.2±25
CB-IV, N=43 FBS<145.9	158.9±18.3	166.7±50.4	156±57.7	144.7±39.4 a*b*	158±80.6	131.8±49.6	114.6±50.9 a*	114±59 a*	41.4±13.3	35.2±6.2 a*	40.5±16.9	52.7±19.3 a**b**c**
CB-V, N=15 FBS>145.9	204.3±16.3	168.2±19.9 a**	145.7±35.2 a**b*	148.6±11.8 a**b*	195.2±41.2	131.7±16.6 a**	118.2±27.1 a**	123.1±28.9 a**	33.5±4.1	42.8±10.3 a*	41.9±19.5	52±30 a*

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Table 4: Effect of Diabegon® on VLDL & LDL level in MetS with Non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

(Group)	VLDL (mg/dl)				LDL (mg/dl)			
	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)
Group I (35-50) ,N=10	56.2±18.7	38.4±6.3 a*	22±1.76 a**b**	25.2±7.57 a**b**	113.7±30.2	87±55.9	71.9±15 a**	51.7±19 a**c*
Group II (51-65) ,N=34	33.8±5.8	24±11.3 a**	24.2±3.2 a**	25.1±9.4 a**	89.5±23	127.1±24.9 a**	106.2±42.3 a*b*	64±41.7 a*b**c**
Group III >65, N=14	26.7±6.6	31.4±2.8 a*	27.3±8.6	20.2±9.3 a*b**c*	109.2±20.1	100.5±56.8	96±7.1 a*	75±15.4 a**c**
CB-IV, N=43 FBS<145.9	27±18.5	26.3±9.9	22.9±10.1	21.7±13b*	90.3±22.6	110.9±41.1 a*	108.7±51.3 a*	70±40 a*b*c**
CB-V, N=15 FBS>145.9	39.04±8.24	26.3±3.3 a**	22±4.4 a**b*	28.7±5.3 a**c**	131.77±12.1	98.9±6.28 a**	96.07±11.2 a**	61±8.2 a**b**c**

FBS, fasting blood sugar; CB, Combination, data were analyzed by ANOVA Bonferroni t-test. Levels of significance were represented in the form of $^{bcdefgh}P<0.001(**)$, $^{bcdefgh}P<0.05(*)$ when compared with initial (a) group.

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Table 5: Effect of Diabegon® on kidney functions in MetS with Non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

(Group)	Urea (mg/dl)				Uric acid (mg/dl)				Creatinine (mg/dl)			
	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy(d)	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)
Group I (35-50) ,N=10	20.4±7.4	23.1±10.1	25.6±3.3	23.9±4.5	5.65±1.7	4.9±2.7	4.8±1.1	5.1±.2	1.6±.59	1.2±.38	0.5±.13 a**b**	0.74±.12 a**b*c*
Group II (51-65) ,N=34	30±5.9	17.6±2.9 a**	25.6±5.9 a*b**	21.1±4.3 a**b**c**	6.0±2.1	5.5±2.7	6.1±2	7.6±.66 a**b**c**	1.0±.106	0.91±.38	0.805±.27 a**	1±.13 c**
Group III >65, N=14	27.4±5.8	26.6±.2	21.9±1.5 a*b**	21.3±10.5	7.2±.47	6.2±1.2 a*	4.3±1.5 a**b**	5.7±1.9 a*c*	1.17±.86	1.1±.52	0.83±.2 b*	0.6±.4 a*b*
CB-IV, N=43 FBS<145.9	35.4±11.5	28±2 a**	24.2±5.2 a**b **	25.1±5.2 a**b**	4.9±1.1	6.9±1.7 a**	5.5±.90 a**b**	6.4±1.8 a**c*	1.4±.67	1.1±.37 a*	0.8±.29 a**b**	0.8±.5 a**b**
CB-V, N=15 FBS>145.9	23.3±7.3	27.6±1.2 a*	25.4±4.6	27±16	8.8±.98	6.7±.77 a**	5.9±.7 a**b**	5.7±1.7 a**b*	.96±.44	0.84±.32	0.97±.58	0.70±.26

Table 6: Effect of Diabegon® on liver functions in MetS with Non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

(Group)	SGOT (IU/L)				SGPT (IU/L)				Total Bilirubin (mg/dl)			
	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)	Initial (a)	6 month of therapy (b)	12 month of therapy(c)	18 month of therapy (d)
Group I (35-50) ,N=10	29.2±9.8	14.9±3.2 a**	23.9±2 b**	20.5±7 a*b*	31.5±12.1	19.5±9.1 a*	29.9±4 b*	28.2±18	0.6±.05	0.7±.10 a*	0.76±0.14 a*	0.65±.05 a*c*
Group II (51-65) ,N=34	24.6±2.3	30±8.7 a**	32.3±3.1 a**b*	26.4±10.2 b**c*	29.4±1.9	30.1±7	32.8±20.8 b*	16.3±3.2 a**b**c**	0.81±.34	0.72±.19	0.94±.45 b*	0.52±.26 a**b**c**
Group III >65, N=14	24.9±3.8	32.2±5.2 a**	30.9±2 a**	21.7±3.7 a*b**c**	29.9±5.7	32.9±2.3	30.7±6.3	20.8±8.5 a*b**c*	0.74±.06	0.83±.12 a*	0.9±.1 a**	0.66±.15 b*c**
CB-IV, N=43 FBS<145.9	29.2±7.8	18.1±3 a**	30.2±3.7	24.5±6.3 a*b**c**	33.9±9.8	16±4.4 a**	27.3±3.07 a**b**	17.6±3.3 a**b*c**	0.84±.08	0.71±.18 a**	0.91±.42 b*	0.67±.22 a**c*
CB-V, N=15 FBS>145.9	22.7±2.3	30.3±6 a**	23.8±6.8 b*	15.8±3.2 a**b**c**	25.5±5.9	32.8±4.3 a**	26.8±1.3 b**	22.1±16 b*	0.83±.03	0.54±.3 a*	0.71±.03 a**	0.85±.02 a*b*c**

FBS, fasting blood sugar; CB, Combination, data were analyzed by ANOVA Bonferroni t-test. Levels of significance were represented in the form of ^{bcdefgh}P<0.001(**), ^{bcdefgh}P<0.05(*) when compared with initial (a) group.

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Effect of diabegon® on blood glucose level in metabolic syndrome with type 2 diabetic subjects (N=58)

In Group I, when comparison was made between initial and to 18 of therapy, 23.9% reduction was observed in fasting blood glucose and the reduction was found to be significant (Table 2). When comparisons were made in group II from initial to 6, 9,12,15,18 months of therapies, reduction with 16.6%, 19.9%, 21.2%, 18.2%, 26.6% with significance (P≤.001) was seen in fasting blood glucose level. The percentage reduction was found to be 12.3% after 18 month of therapy in group III. For Group IV, Fasting blood group was significantly reduces when comparison was made between 6 & 18 months of therapy. 8.1% of decrease in fasting blood glucose level was seen after 18 month of therapy from its initial level. For Group V, significant (P≤.001) reduction was seen after therapy. In P.P blood glucose of group I, significant reduction was observed on 9, 12, 15, and 18 month of therapy at a level 19%, 32.4%, 27.2%, and 22.3% respectively. For group II, the comparisons made between initial to 6, 12, and 18 month of therapy showed significance (P≤.05) with 11.2%, 19.3% and 17.7% decrease respectively. The therapy showed a significant value in group III (P<0.05) while comparing initial with 12, 18 of therapy with a reduction of 21.7%, 26% respectively. For Group IV, significant reduction was observed in different time interval. Group V, When comparison was made between initial and 12, and 18 month of therapy significance (P<0.05) was found with 15.4%, 21.4% reduction in level respectively.

Effect of diabegon® on lipid profile (Total cholesterol, triglyceride, HDL-C, VLDL, LDL) level in metabolic syndrome with non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

Table 3 represents effect of diabegon therapy on lipid profile. A significant reduction in cholesterol after 6 to 18 month of therapy was seen. When comparison was made between initial to 12& 18 month of therapy for group II, a reduction with 8.3% and 11% were observed. Cholesterol level was reduced up to 8.9-14.5% after 18 month of therapy in group III&IV. For group V, Comparison between initial to 6, 12 and 18 month of therapy revealed reduction with 17.6%, 28.6% and 27.2%. Triglyceride level in group I showed a significant reduction of 50-60%. For group II, when comparisons were made between initial to 6, 12, 18 month of therapy reduction of 28.9%, 28.5% and 34% were observed. The triglyceride level in group III was within the normal range during the study. A reduction in triglyceride observed with 27.4% and 27.8% in group IV after the therapy. A remarkable reduction was observed in group V. HDL-C level in group I showed 95% increase after treatment for 18 month. In group II, when initial value was compared with 6 and 18 month of therapy, a slight increase of 17.9-26.8% were seen. When initial value of group III and IV in HDL-C level was compared, elevation of 6-25.7% had been observed in different intervals of therapy. An increase in group V for HDL-C was observed with 27.7% and 55.2% when compared with initial to 6 and 18 month of therap. For the VLDL in group I showed a reduction of 31.6% to 60.8% in different point of therapy. Reduction of 28.9%, 28.4% and 25.7% in VLDL after 6, 12 and 18 month of therapy in group II. After 6, 12 and 18 month of diabegon therapy yielded significance (P<0.001) with 32.5%, 43.5% and 26.4% reduction in group V. Subject in group I compared between initial to 12 & 18 month of therapy, 36.7% and 54.5% reduction were observed in LDL level. For group III, when initial value was compared with 12 and 18 month of therapy, a reduction was seen with 12% and 31.3%. The baseline value in Group II and IV was found to be normal and it maintained during the therapy. For group V, when initial value was compared with 6, 12 and 18 month of therapy, a reduction 24.9%, 27% and 53.6% observed.

Effect of diabegon® on kidney function (urea, uric acid, creatinine) level in metabolic syndrome with non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

Diabegon therapy on urea, uric acid, creatinine level in T2 diabetes with metabolic syndrome is shown in Table 5. The urea level of the study subjects were found to be normal at base line which was maintain during the therapy in all groups of the subjects. Uric acid level was found to be normal at initial therapy which was seems to be constant in group I, II and IV. For group III, when initial values were compared with 6 and 18 month of therapy, reduction of 13.8% and 20.8% was observed. Significant was also observed after 12 month of therapy. In group V, when subjects were compared between initial to 6, 12, and 18 month of therapy reduction of 23.4%, 32.9% and 35.2% were seen.
Creatinine in the studied subject was within the normal range except group I. For group I, when initial value was compared with 12 and 18 month of therapy, 68.7% and 53.7% reduction was observed which was found to be significant. Significant reduction was seen between the different duration of therapy.

Effect of diabegon® on liver function (SGOT, SGPT, Bilirubin) level in metabolic syndrome with non-insulin dependent diabetes mellitus subjects of different age groups (N=58)

Table 6. Showed the diabegon therapy on liver enzyme in human T2 diabetic subject. After observing the result in the table, we could find that the three enzymes that associated with diabetic complication of liver were at normal range that maintained during the all study follow-up. There was slight elevation and depression in the value but it was within the range of normal value.

Discussion

Combination of metabolic syndrome variables with type 2 diabetes leads to more complex in term of the risk factor for mortality. Our study recruited these subjects with essentially required a multifactorial intervention including treatment of arterial hypertension and dyslipidaemia to prevent cardiovascular complications. In recent years the popularity of complementary medicine has increased. Much interest has been focused on exploring herbal preparations. Our study showed an Overall reduction in the individual parameter in metabolic syndrome subject and highly significant in the 35-50 years age group (Table 2). The reduction in fasting blood, triglyceride in the age group 35-50 years 21%, 49.1%. The HDL-cholesterol level was increased by 56%. The overall reduction in fasting blood, triglyceride in the age group 51-65 years 21.3%, 30.4%. The HDL-cholesterol level was increased by 17%. In the >65 years age group the reduction was 10%, 20%. The elevation in HDL-C levels was 12%. Generally, the reduction in fasting blood glucose range from 12.3% (P<0.05) to 42% (P<0.001) after 18 month of therapy while in post prandial blood glucose, the decrease ranged from 28% (P<0.05) to 32% (P<0.05) after 18 month of therapy (Table 2). Earlier study showed that the Oral administration of diabegon delayed the induction of glucose intolerance and euglycemia in high fructose diet fed rats. Diabegon treatment inhibits the disturbance in glucose metabolism in the liver by reducing the glycogen accumulation in liver, which might be due to induced glycogenolysis and/ or inhibited gluconeogenesis (Hariom et al., 2007).The *Momordica charantia* (bittermelon) fruits, seeds and seedlings have various compounds with antidiabetic properties (Basch et al., 2003). Administration of 230 g/day of *momordica* for 8-11 weeks to a group of nine diabetic patients, significantly improved

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the results of oral glucose tolerance (Leatherdale et al., 1981). New studies suggest bitter gourd has the ability to regenerate dormant pancreatic beta cells that stimulate insulin in the body (Saxena et al., 2004). *Gymnema sylvestrae* have a series of gemnemic acids that have antidiabetic properties.

The aqueous extract of *Gymnema sylvestrae* improved glucose control and insulin requirement in IDDM and NIDDM subjects (Shanmugasundaram et al., 1990). *Trigonella foenum graecum* (also known as fenugreek) has an alkaloid trigonelline which posses hypoglycemic properties (Grover et al., 2002). Fenugreek significantly lowered the fasting blood glucose and glucose intolerance (Sharma et al., 1990). The green and crude leaf extract of *Aegle marmelos* exhibited hypoglycemic potential in alloxan induced diabetes (Ponnachan et al., 1993). The ethanolic extract of *Eugenia jambolana* seed on hyperglycemia has been reported. *Curcuma longa* and *Emblica officinalis* contain various nutraceuticals such as terpenoids, curcuminoids and polyphenols/flavonoids respectively, they are all endowed with biological effects such as antioxidant, antidiabetic, immunomodulatory and hypolipidemic properties. The shilajit is reported to possess antihyperglycaemic and antilipidemic potentials when checked in alloxan induced diabetic rats (Trivedi et al., 2004). Liver and kidney functions were within the normal range at baseline in most groups. In the present investigation diabetic subjects with metabolic syndrome when administered with diabegon exhibited a significant decrease in lipid profile. In our study cholesterol level decreased from 11% to 27.2% ($P<0.001$) after 18 months of therapy. The percentage decrease in triglyceride level ranged from 24% to 55%. The HDL-C level increased in all groups of subjects (Table 3). The VLDL and LDL level reduced up to 60% & 54% respectively (Table 4). The level of HDL-cholesterol increased after diabegon therapy. This indicates that diabegon may help to increase transport of peripheral tissue cholesterol to liver and thereby decrease blood cholesterol level. The liver and kidney function tests were also significantly improved after the therapy. The urea, uric acid, creatinine decreases up to 30-60% in higher baseline values in groups and constantly maintained during the therapy (Table 5). The SGOT, SGPT & bilirubin levels showed 20 to 40% of reduction in group II and group IV. The liver functions of the recruited subject were normal at the baseline.

On the basis of results, it could be concluded that oral administration of diabegon, a polyherbal formulation has antihyperglycemic and antilipidemic potential for long term treatment with great promises for metabolic syndrome. The study also revealed that therapy does not show any toxic effect on liver and kidney. The herbal formulation considered as safe therapy for a long term and effective management of type II diabetes as well as metabolic syndrome.

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