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Anti-hyperglycemic activity of the herbo-mineral siddha preparation in alloxan induced diabetic rats

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ABSTRACT

To evaluate the anti hyperglycemic effect of this new Herbo -Mineral preparation in alloxan induced albino diabetic rats and Acute toxicity studies for this new Herbo -Mineral preparation. Experimental Rats were allowed to fast 24 hrs prior to diabetes ,induced by administration of a single dose of(120 mg/kg body weight) Alloxan mono hydrate intraperitoneally ,after 24 hours blood was collected from the tail vein and blood glucose was determined using electronic Glucometer. This was done in three groups, Gr-1 were fed only Carboxy Methyl Celluose (CMC) sodium orally,0.5 ml for 15 days Gr-II were given alloxan Intra Peritonally and Gr-III: After overnight fasting, the new product (10 mg/daily) orally,0.5 ml in Carboxy Methyl Celluose (CMC) sodium for 15 days. The animals were tested after 48 hours and other biochemical parameters were done to assess for toxicity profile by using standard kit methods .Chi-square,mean and SD was calculated using SPSS software. Alloxan has been shown to produce hyperglycemia .Restoration of normal levels of blood glucose by the product was 75% in group III which categorically an excellent figure in small animals. This reversion of the blood Glucose levels to normalcy due to reversion of the damaged pancreatic beta cells activity and the alloxan induced diabetes may be due to complete destruction of beta cells in the animals. No mortality with in a period of 48 hours and the bio chemical parameters were totally normal. The new Herbo -mineral combinations have effects to regulate blood glucose level and other parameters.

Key words: Alloxan, Carboxy Methyl Celluose, diabetes

INTRODUCTION

Diabetes mellitus (DM) is a serious health problem being the third greatest cause of death all over the world, and if not treated, it is responsible for many complications affecting various organs in the body. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of various organs. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world[1]. The current study focuses on herbal drug preparations and plant used in the treatment of diabetes mellitus, a major crippling disease in the world leading to huge economic losses. Recently, some medicinal plants have been reported to be useful in diabetes worldwide and have been used empirically as antidiabetic and antihyperlipidemic remedies. There

are many herbal remedies suggested for diabetes and diabetic complications. Medicinal plants form the main ingredients of these formulations. The following drugs are used for as a antidiabetic treatment.

Table 1 Indian medicinal plants with antidiabetic and related beneficial properties [2-16]

Plant Name	Ayurvedic/common name/herbal formulation	Antidiabetic and other beneficial effects in traditional medicine
Annona squamosa	Sugar apple	Hypoglycemic and antihyperglycemic activities of ethanolic leaf-extract, Increased plasma insulin level
Artemisia pallens	Davana	Hypoglycemic, increases peripheral glucose utilization or inhibits glucose reabsorption
Areca catechu	Supari	Hypoglycemic
Beta vulgaris	Chukkander	Increases glucose tolerance in OGTT
Boerhavia diffusa	punarnava	Increase in hexokinase activity,decrease in glucose-6-phosphatase and fructose bis-phosphatase activity, increase plasma insulin level, antioxidant
Bombax ceiba	Semul	Hypoglycemic
Butea monosperma	palasa	Antihyperglycemic
Camellia sinensis	Tea	Anti-hyperglycemic activity, antioxidant
Capparis decidua	Karir or Pinju	Hypoglycemic, antioxidant, hypolipidaemic
Caesalpinia bonducella	Sagarghota, Fevernut	Hypoglycemic, insulin secretagogue, hypolipidemic
Coccinia indica	Bimb or Kanturi	Hypoglycemic
Emblica officinalis	Amla, Dhatriphala, a constituent of herbal formulation, “Triphala”	Decreases lipid peroxidation, antioxidant, hypoglycemic
Eugenia uniflora	Pitanga	Hypoglycemic, inhibits lipase activity
Enicostema littorale	krimihrita	Increase hexokinase activity, Decrease glucose 6-phosphatase and fructose 1,6 bisphosphatase activity. Dose dependent hypoglycemic activity
Ficus bengalenesis	Bur	Hypoglycemic, antioxidant
Gymnema sylvestre	Gudmar or Merasingi	Anti-hyperglycemic effect, hypolipidemic
Hemidesmus indicus	Anantamul	Anti snake venom activity, anti-inflammatory
Hibiscus rosa-sinesis	Gudhal or Jasson	Initiates insulin release from pancreatic beta cells
Ipomoea batatas	Sakkargand	Reduces insulin resistance
Momordica cymbalaria	Kadavanchi	Hypoglycemic, hypolipidemic
Murraya koenigii	Curry patta	Hypoglycemic, increases glycogenesis and decreases gluconeogenesis and glycogenolysis
Musa sapientum	Banana	Antihyperglycemic, antioxidant
Phaseolus vulgaris	Hulga, white kidney bean	Hypoglycemic, hypolipidemic, inhibit alpha amylase activity, antioxidant. Altered level of insulin receptor and GLUT-4 mRNA in skeletal muscle
Punica granatum	Anar	Antioxidant, anti-hyperglycemic effect
Salacia reticulata	Vairi	inhibitotory activity against sucrase, α-glucosidase inhibitor
Scoparia dulcis	*Sweet broomweed*	Insulin-secretagogue activity, antihyperlipidemic, hypoglycemic, antioxidant
Swertia chirayita	Chirata	Stimulates insulin release from islets
Syzygium alternifolium	Shahajire	Hypoglycemic and antihyperglycemic
Terminalia belerica	Behada, a constituent of “Triphala”	Antibacterial, hypoglycemic
Terminalia chebula	Hirda	Antibacterial, hypoglycemic
Tinospora crispa		Anti-hyperglycemic, stimulates insulin release from islets
Vinca rosea	Sadabahar	Anti-hyperglycemic
Withania somnifera	Ashvagandha, winter cherry	Hypoglycemic, diuretic and hypocholesterolemic

Table 2Formulated Herbal Drugs with antidiabetic properties

Drug	Company	Ingredients
Diabecon	Himalaya	*Gymnema sylvestre, Pterocarpus marsupium, Glycyrrhiza glabra, Casearia esculenta, Syzygium cumini, Asparagus racemosus, Boerhavia diffusa, Sphaeranthus indicus, Tinospora cordifolia, Swertia chirata, Tribulus terrestris, Phyllanthus amarus, Gmelina arborea, Gossypium herbaceum, Berberis aristata, Aloe vera*, Triphala, *Commiphora wightii*, shilajeet, *Momordica charantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumex maritimus*
Diasulin		Cassia auriculata, Coccinia indica, Curcuma longa, Emblica officinalis, Gymnema sylvestre, Momordica charantia, Scoparia dulcis, Syzygium cumini, Tinospora cordifolia, Trigonella foenum graecum
Pancreatic tonic 180 cp	ayurvedic herbal supplement	Pterocarpus marsupium, Gymnema sylvestre, Momordica charantia, Syzygium cumini, Trigonella foenum graceum, Azadirachta indica, Ficus racemosa, Aegle marmelos, Cinnamomum tamala
Ayurveda alternative herbal formula to Diabetes:	Chakrapani Ayurveda	Gurmar (*Gymnema sylvestre*) Karela (*Momordica charantia*) Pushkarmool (*Inula racemosa*) Jamun Gutli (*Syzygium cumini*) Neem (*Azadirachta indica*) Methika (*Trigonella foenum gracecum*) Guduchi (*Tinospora cordifolia*)
Bitter gourd Powder	Garry and Sun natural Remedies	Bitter gourd (*Momordica charantia*)
Dia-care	Admark Herbals Limited	Sanjeevan Mool; Himej, Jambu beej, Kadu, Namejav, Neem chal.
Diabetes-Daily Care	Nature's Health Supply	Alpha Lipoic Acid, Cinnamon 4% Extract, Chromax, Vanadium, Fenugreek 50% extract, *Gymnema sylvestre* 25% extract Momordica 7% extract, Licorice Root 20% extract
Gurmar powder	Garry and Sun natural Remedies	Gurmar (*Gymnema sylvestre*)
Epinsulin	Swastik Formulations	vijaysar (*Pterocarpus marsupium*)
Diabecure	Nature beaute sante	*Juglans regia, Berberis vulgaris, Erytherea centaurium*, Millefolium, Taraxacum
Diabeta	Ayurvedic cure Ayurvedic Herbal Health Products	*Gymnema sylvestre, Vinca rosea* (Periwinkle), *Curcuma longa* (Turmeric), *Azadirachta indica* (Neem), *Pterocarpus marsupium* (Kino Tree), *Momordica charan*tia (Bitter Gourd), *Syzygiumcumini* (Black Plum), *Acacia arabica* (Black Babhul), *Tinospora cordifolia , Zingiber officinale* (Ginger)
Syndrex	Plethico Laboretaries	Germinated Fenugreek seed extract

MATERIALS AND METHODS

Preparation of Drug

The drug madhu mega karpam (new herbo minaral combination)was prepared in the GMP certified Siddha drug manufacturing Company at Chennai. The drug was purchased from same Company for the studies.

Experimental design

Healthy Albino rats of male sex weighing 150 g were used and grouped into three with 15 animals in each.

Group I: Control animals--all animals were given Carboxy Methyl Celluose(CMC) orally, 0.5 ml for 15 days
Group II: Experimental animals: All animals were given alloxan Intra Peritonally.
Group III: experimental animals: All animals were given alloxan and the new product (10 mg/daily) orally,0.5 ml in CMC sodium for 15 days.

Experimental animal

Experimental Rats were allowed to fast 24 hrs prior to diabetes, induced by injecting Alloxan mono hydrate intraperitoneally at a dose of 120 mg/kg body weight in ice cold citrate buffer pH 4.5.After 24 hours blood was collected from the tail vein under ether anesthesia of all surviving rats and blood glucose was determined using electronic Glucometer (Roche Diagnostic,Germany). On days 3,5,7,9,11,13 &15 blood samples were taken for the estimation of blood glucose. Rats with blood glucose levels of 200 -350 mg/dl was considered as diabetic and were employed in the study. The mortality rate of the rats after alloxan treatment was found to be approximately 25%.

Acute Toxicity Studies

Albino rats were used and they housed in polypropylene cages, 5 animals in each cage, given adequate ventilation and fed with Hindustan Lever feed (Bangalore) and water ,and libitum. The animals had 12 hours day and night cycle. The husk for the purpose of keeping as a bed to the animals was cleaned and autoclave .Before the animals were kept the cages were sterilized along with water feeding bottles. Albino rats of male sex weighing 150g on an average were used to determine the acute toxicity evaluation at a single dose of 10gms / animal / 0.5ml in CMC sodium orally ,The animals were divided into :Group I : 30 animals : Carboxy Methyl Celluose (CMC) sodium orally,0.5 ml as single dose per animal. Group II : 30 animals :the new product (10 mg/daily) orally,0.5 ml in Carboxy Methyl Celluose (CMC) sodium as single dose per animal .The animals were tested for any mortality for 48 hours and other parameters tested were SGOT,SGPT,ALP,WBC,RBC,Hb,Urea,Creatinine, Cholesterol, Triglycerides and Total protein to assess for toxicity profile. All the Bio Chemical parameters were carried out by using standard kit methods. The body weight was noted for any change.

RESULTS

In this study, the mice were induced with Alloxan mono hydrate intraperitoneally, after 3days the blood glucose level was monitored till 15 days. The findings showed that, the blood glucose level was maintained from day 3 to day 15, in the Gr-2, blood glucose was increased and the mice died in the 9th day itself but in the Gr-3, blood glucose level was reduced from 3rd day to 15th day. Among three groups, the blood glucose level was significantly reduced in Gr-III and it shows that the new drug is playing major role in controlling blood glucose level. (p-value <0.05)

Table :3 Blood glucose level

Parameter	Groups	Days (blood glucose average and SD)						
		3	5	7	9	11	13	15
Blood glucose level at different days after treatment	Gr -I	78+_3.1	79+_1.5	81+_2.6	81+_0.9	78+_2.5	80+_1.3	83+_3.5
	Gr -II	271+_3.5	300+_2.5	415+_3.8	Died	-	-	-
	Gr -III	180+_3.6	175+_2.6	175+_3.1	117+_2.8	109+_3.0	98+_2.1	85+_3.6
p-value	<0.05							

Experimental drug was compared with control group; body weight was gained in the experimental group. WBC,RBC and Hb was also increased in experimental group. (p-<0.05)

Table:4 Comparison of biochemical parameters

Groups	Initial body wt (g) Average and SD	Final body wt (after 48 hrs)(g) Average and SD	WBC (Thousands /cumm) Average and SD	RBC (Millions/ cumm) Average and SD	Hb(%) Average and SD
I	150+_2.1	148+_2.5	7000+_15.1	7.9+_1.3	14.1+_0.6
II	152+_2.3	153+_3.5	7300+_4.5	8.1+_1.1	15.1+_0.5
p-value	<0.05	<0.05	<0.05	<0.05	<0.05

Kidney function test and Lipid profile was compared and it shows that urea and creatinine level was significantly reduced in experimental group but in contrast, total cholesterol and triglycerides level was significantly increased in experimental group.(p-value0.05)

Table: 5 Kidney function test and Lipid profile

Groups	Kidney function Test (Average and SD)		Lipid profile (Average and SD)	
	Urea(g/dl)	Creatinine (g/dl)	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)
I	36+_2.1	0.7+_0.02	67+_4.6	98.6+_2.3
II	35+_2.5	0.6+_0.03	68+_2.5	101+_2.4
p-value	<0.05	<0.05	<0.05	<0.05

The below table shows the level of SGOT,SGPT, ALP and total protein. While comparing Experimental group with control group, the results showed that SGPT and ALP was increased and SGOT and total protein was decreased in experimental group. (p-0.05)

Table 6: Biochemical parameters

Groups	SGPT(IU/L)	SGOT(IU/L)	ALP(IU/L)	Total protein(gm/dl)
I	63+_6.5	45+_4.2	168+_0.27	7.0+_0.5
II	65+_3.9	42+_5.5	170+_10.1	6.8+_0.3
p-value	<0.05	<0.05	<0.05	<0.05

DISCUSSION

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter[1]. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Though there are various approaches to reduce the ill effects of diabetes and its secondary complications, herbal formulations are preferred due to lesser side effects and low cost. To date, over 400 traditional plant treatments for diabetes have been reported, although only a small number of these have received scientific and medical evaluation to assess their efficacy. The hypoglycemic effect of some herbal extracts has been confirmed in human and animal models of type 2 diabetes. The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs be further investigated.

In the present study, glucose level was reduced by the experimental drug in albino mice from day 3 and the chi square test is also showing the significant difference while comparing with control and alloxan induced albino mice. This shows that this combination can be used as a antidiabetic drug. And also body weight, WBC,RBC and hb level was increased in experimental group. Urea and creatinine level was decreased in experimental group at the same time total cholesterol and triglyceride level was increased while comparing with control group. This shows that along with this drug combination some drug should be added to reduce total cholesterol and triglycerides. While comparing the biochemical parameters, SGPT and ALP was increased in experimental group but in contrast SGOT and total protein was decreased. Hence the drug combination is having antidiabetic effect than the antilipid activity and also this is a first study tried with the combination drug of MMK against diabetes.

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