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Original Research Article

EFFICACY OF MALAYSIAN HERBAL PRODUCT IN TREATING DIABETES MELLITUS

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ABSTARCT

Aim of the study was to examine the efficacy of a combination herbal product from Malaysian market. This herbal product is traditionally being used for managing diabetes mellitus. The herbal combination is a mixture of *Momordica charantia, Punica granatum, Lawsonia inermis* and *Tamarindus indica.* The drug was administered orally at the dose of 620mg/70kg once daily for the duration of 42 days to alloxan induced diabetic rats. The effects of this herbal combination were compared with standard drug, sulphonylurea (Glibenclamide). Efficacy of the drug was monitored at intervals with respect to fasting and random glucose levels and glycosylated hemoglobin. Results revealed that the combination of four herbs reduced fasting glucose levels and random glucose levels. HbA1C was observed to be less than 7% by this herbal combination. However, the herbal combination failed to produce the efficacy comparable to the standard drug, Glibenclamide.

Keywords: Alloxan, *Momordica charantia, Punica granatum, Lawsonia inermis* and *Tamarindus indica.*

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INTRODUCTION

Diabetes mellitus is a metabolic disorder that has occurred as a most prevalent disease around the globe. This disorder has no absolute cure (Malvia et.al 2010). According to estimate by WHO, in 2004, globally there were 346 million individuals who suffered from this disorder. Also, millions of individuals lost their lives due to this disease. WHO predicts that there is a possibility that deaths due to diabetes mellitus will double between the years 2005-2030 (WHO, 2011). There is a list of drugs that are available for treating diabetes mellitus. However, the requirement for new anti-diabetic agents is still open due to the adverse effects and limitations of the available anti-diabetic agents (Azza, 2012). Therefore, new agents that can be employed in managing diabetes mellitus are in great demand. Since traditional medicines are long been used by the people, they provide the researchers with a rich source for the discovery of new anti-diabetic agents (Hung et al 2012; Bailey et al 1989). Main feature which is observed in the case of diabetes mellitus is high blood glucose levels. In the long term, this high blood glucose level can result in affecting different organs of the body. Hyperglycemia may be due to deficiency or insufficiency of insulin release from the beta cells of pancreas. This insufficiency or deficiency of insulin release may be with or without concurrent alteration in the action of insulin (CDC, 2011). According to American Diabetes Association, 70-100mg/dl of fasting blood glucose and 135-140mg/dl of random glucose levels are considered as normal glucose levels. Diabetes mellitus is mainly of three different types, Type 1, Type 2 and gestational diabetes (Hung et.al 2012). Among all the three type of diabetes, type 2 is the most frequent type. It is present with the incidence rate of 80% around the globe (Peggy Yarborough, n.d). Treatment of diabetes mellitus has its basis on diet, oral anti-diabetics and insulin (CDC, 2011). In addition to these drugs, there is a variety of herbs which are used due to their anti-diabetic potential.
Traditional medicines are employed for a variety of reasons in the current era. It is used in treating, diagnosing, preventing and maintaining the health status (WHO, 2000). Eighty percent of African

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and Asian countries depend on the use of these traditional medicines for attaining primary health care (WHO, 2008). It clearly depicts the interest and trust of the people on traditional medicines. These medicines that are employed by the people in maintaining the status of health, provides hints for the development of novel drugs that can be used in managing diabetes mellitus (Bailey et.al 1989).

Drug which was selected in this research study was a combination of *Momordica charantia, Punica granatum, Lawsonia inermis* and *Tamarindus indica. Punica granatum* is also termed as pomegranate and belongs to the family Punicacea (Julie, 2008). Peel of pomegranate consists of flavanoids, tannins, polysaccahrides (Maria et al 2010).It has phenolic punicalagins; gallic acid and other fatty acids, catechin, quercetin, rutin, flavonols, flavones, flavonones and anthocyanidins (Julie 2008). *Lawsonia inermis* is termed as henna and belongs to the family Lythracea (Gagandeep et.al 2010). It consists of gallic acid, glucose, mannitol, fats, resin (2 %), mucilage and traces of an alkaloid (Gangadeep et al 2010). *Tamarindus indica* is also called as Tamarind. Tamarind belongs to the family of Fabaea (Emmy at.al 2009). It contains saponins, tannins, alkaloids, sesquiterpenes and phlobatamin (Doughari 2006). All the mentioned herbs have reported anti-diabetic efficacy.

MATERIAL AND METHODS

Selection of Animal and Treatment

The study was conducted on Wister albino rats. 30 male rats were selected for the study. The weight of animals ranged from 150-250 grams. Rats were bred locally in the Department of Pharmacology in the University of Karachi. Animals were housed locally in 12:12 light/dark cycle, 25±1 °C temperature. Rats were kept on standard rat diet ad libitum. Handling of animals was conducted according to the specifications present in Helsinki resolution. This study was approved by "University Board of Advanced Studies and Research".

Induction of Diabetes

Alloxan is used to induce diabetes in rats. An aqueous solution of the agent (alloxan) is administered intraperitoneally at the dose of 120mg/kg to rats (Govindarajulu et al, 2011). 15-20ml of 20% glucose was administered to the rats after six hours of alloxan administration. This was solely done to prevent fatal hypoglycemia after the administration of alloxan. Animals were then kept on 5% oral glucose for coming twenty-four hours (Kiran et al, 2012). Group of animals which was considered as diabetic control was treated in the same manner. After 48 hours of alloxan intraperitoneal administration, blood samples were drawn to check the glucose levels in animals. Glucometer ("Abbott Medisense Optium Blood Glucose Analyzer") was used to check blood glucose levels. Animals with glucose levels of 200mg/dl or more were considered diabetic and were selected for the study (Baldi et al 2011).

Protocol of the Study

Three groups of animals were selected for the study:

- Group I was termed as Alloxan treated (Diabetic control)
- Group II was termed as treated group (treated with Malaysian herbal product). Dose of herbal product was 620mg/70kg once daily. The dose is as per drug information provided with the Malaysian herbal product.
- Group III was termed as standard group, treated with Glibenclamide. Dose of Glibencalmide was 20mg/70kg (Micromedix, 2012)

Group II and III were administered drugs orally for duration of 42 days. Group I was orally administered distilled water only. Results on blood glucose levels were assessed and monitored at intervals. Glycosylated hemoglobin was monitored at the end of 42 days.

Blood Glucose Levels

All the samples were subjected to glucose levels testing within three hours of collection on

Humalyzer, 3000 (Semi-automatic chemistry analyzer model-16700 by Human, Germany) by GOD PAP Enzymatic Colorimetric Test Method (Trinder 1969, Barham and Trinder 1972) by using standard kits.

Estimation of Glycosylated Hemoglobin (HbA1C)

Samples were also sent to Dr. Panjwani Centre for Molecular and Drug Research (PCMD) within one hour of collection for the analysis of glycosylated hemoglobin. PCMD is situated in Hussain Ebrahim Jamal (HEJ) Research Institute in University of Karachi.

Statistical Analysis

The results are presented as mean value ± S.D. Results were statistically analyzed using student t-test. P-values < 0.001 were considered significant.

RESULTS AND DISCUSSION

Fasting glucose levels of Group II were significantly decreased at different intervals. Moreover, these effects were observed comparable with Glibenclamide (Group III) (Table #1). Random glucose levels were also checked for the treated group of animals. Results revealed that herbal product significantly controlled random blood glucose in comparison to diabetic control. However, when the results of random blood glucose levels of herbal product were compared to standard drug, Glibenclamide, the drug failed to show better results than standard. It did not even show results comparable to standard. Glycosylated hemoglobin was decreased significantly in comparison to diabetic control. On the contrary, herbal product failed to show a better control on glycosylated hemoglobin in comparison to standard, at the end of 42 days of study (Table #2).

The observations in the present study revealed that the herbal combination of *Momordica charantia, Punica granatum, Lawsonia inermis* and *Tamarindus indica* has a good efficacy in controlling fasting and random glucose levels. Glycosylated hemoglobin was also found under control with the use of herbal combination. However, the herbal product did not show results comparable to standard, Glibenclamide. The efficacy of this herbal combination in controlling blood glucose levels may be attributed to multiple actions of *Momordica charantia* in controlling blood glucose levels. It is presented in the literature that *Momordica charantia* stimulates glycogen storage by liver and increases uptake of glucose by cells (Fernandes et.al 2007).

Table 1: Effects on Blood Glucose Levels

Groups	Fasting Blood Glucose Level (mg/dl)								
	1st Week			3rd Week			6th Week		
	Mean±S.D	P (DC)	P (Std)	Mean±S.D	P (DC)	P (Std)	Mean ±S.D	P (DC)	P (Std)
Group I (DC)	276.1±22.7	-	-	264.2±24.8	-	-	289.6 ±11.7	-	-
Group II (Tr)	87.5±3.03	0.000***	0.357+	98.0±25.3	0.000***	0.359+	72.0± 6.5	0.000***	0.929+
Group III (Std)	95.5±25.9	0.000***	-	90.2±2.94	0.000***	-	72.2± 2.3	0.000***	
Groups	Random Blood Glucose Level (mg/dl)								
	1st Week			3rd Week			6th Week		
	Mean±S.D	P (DC)	P (Std)	Mean±S.D	P (DC)	P (Std)	Mean±S.D	P (DC)	P (Std)
Group I (DC)	349.9±18.0	-	-	367.0±8.26	-	-	338.3±5.	-	-

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Group II (Tr)	282.0±4.11	0.000***	0.000^{+++}	179.8±8.2	0.000***	0.391^{+}	186.0±13.8	0.000***	0.000^{+++}
Group III (Std)	173.9±3.11	0.000***	-	156.4±3.86	0.000***	-	158.9±5.72	0.000***	0.000^{+++}

N=10, Values are mean ± S.D, Significant differences by Student t-test ***<p0.001; $^{+++}$<p0.001, $^{+}$<p0.05 as compared to diabetic control rats* and standard group of rats^{+}
(DC= Diabetic Control, Tr = Treated, Std= Standard)

Table 2: Effects on HbA1C

Groups	**Glycosylated Hemoglobin (HbA1C) %**		
	Mean ± S.D	P (DC)	P (Std)
Group I (DC)	8.87±0.461	-	-
Group II (Tr)	6.06±0.061	0.000***	0.000^{+++}
Group III (Std)	3.62±0.033	0.000***	-

N=10, Values are mean ± S.D, Significant differences by Student t-test ***<p0.001; $^{+++}$<p0.001 as compared to diabetic control rats* and standard group of rats^{+}
(DC= Diabetic Control, Tr = Treated, Std= Standard)

Moreover, *Momordica charantia* increases the recovery of damaged pancreatic beta cells and hence improves the secretion of insulin (Ahmed et.al 1998). *Punica granatum* enhances level of insulin with increased insulin sensitivity of insulin receptor (Huang et.al, 2005). It is also believed to inhibit alpha glucosidase enzyme which further controls blood glucose levels (Li et.al 2005). *Lawsonia inermis* (Arati et.al, 2012) and *Tamarindus indica* (Maiti et.al 2012) are also observed to increase the levels of insulin and increase effects of insulin in controlling blood glucose levels.

CONCLUSION

It is concluded that the herbal combination of drugs obtained from the markets of Malaysia has a good efficacy in controlling fasting and random blood glucose levels. However, long term control is not evident by the study as the glycosylated hemoglobin was not observed to be within normal limits. Also, the herbal combination failed to show results comparable to our standard drug Glibencalimde.

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