

# Efficacy of combination herbal product (*Curcuma longa* and *Eugenia jambolana*) used for diabetes mellitus

Sadia Saleem Rao\* and Rahila Najam

Department of Pharmacology, Faculty of Pharmacy & Pharmaceutical Sciences, University of Karachi, Karachi, Pakistan

**Abstract:** The purpose of this research was to evaluate the efficacy of a combination herbal product that is traditionally used for managing diabetes mellitus. Herbal drug contains *Curcuma longa* and *Eugenia jambolana* in the ratio of 1:1. It was orally administered at the dose of 1082 mg/70 kg twice a day for a period of 6 weeks to alloxan induced diabetic rats and compared with glibenclamide (standard). The effects of drug were observed at intervals, with respect to random and fasting glucose levels. HbA1C was also monitored after the drug treatment to monitor the overall diabetic effect. Results revealed that the combination of two herbs significantly reduced fasting and random glucose levels with HbA1C of less than 6% ( $p < 0.001$ ) in comparison to diabetic control. The control of fasting blood glucose levels by herbal combination is similar to the standard drug, glibenclamide ( $p < 0.05$ ). Random glucose levels by herbal combination is better than standard drug after one week and six weeks of treatment ( $p < 0.01$  and  $p < 0.001$  respectively) and similar after third week of treatment ( $p < 0.05$ ). Also, herbal drug combination showed HbA1C closer to the standard drug. It shows that this herbal combination can be of potential benefit in managing diabetes mellitus in future.

**Keywords:** *Curcuma longa*, *Eugenia jambolana*, Alloxan, Glibenclamide.

## INTRODUCTION

Traditional medicines are used in the treatment, diagnosis and prevention of different ailments. It is also used in maintaining the status of health (WHO Geneva guidelines 2000). For primary health care, 80% of Asian and African countries population depends on traditional medicines (WHO, 2002). This shows the interest of the population in herbs around the globe (Malviya *et al.*, 2010). Traditional medicines provide hints for the development of new agents that can be employed in the treatment of diabetes mellitus (DM) (Bailey and Day, 1989).

DM is a prevailing disease in the world and it has no absolute cure (Malviya *et al.*, 2010). World Health Organization presented that 346 million people from around the globe have diabetes and in 2004, more than 3 million people died from this disease. WHO projects by the year 2030, DM will become the seventh leading cause of death worldwide (WHO fact sheet 2011). The available drugs for the treatment of DM are playing their role but still the space is not filled due to their limitations and adverse effects. New anti-diabetics are in great demand and the herbal medicines that are being used traditionally for diabetes mellitus provide a rich source for new drug discovery and needs to be further investigated to get an ultimate therapeutic agent (Bailey and Day, 1989).

The characteristic feature of diabetes is elevated blood sugar levels (hyperglycemia). With the passage of time, the elevated blood glucose level damages systems of the body. The elevated blood sugar levels are due to absence or insufficiency of insulin release from beta cells with or

without concurrent impairment of insulin action. Post meal glucose levels of 135-140mg/dl and fasting blood glucose of 70-100mg/dl are considered normal levels as stated by American Diabetes Association. There are different types of diabetes mellitus. Most common among them are Type 1, Type 2, gestational DM. Type 2 is the most common type of diabetes among all of its types with incidence of 80%. Diet, insulin, and oral medication are basis of diabetes mellitus treatment (Centre for Disease Control and Prevention, 2011). Traditionally, different herbs are used due to their anti-diabetic potential. For this study, the herbal drug used was a combination of *Curcuma longa* and *Eugenia jambolana*.

*Curcuma longa* Linn is known as turmeric or haldi. It belongs to the family Zingiberaceae (Araujo and Leon, 2001). Curcumin is its major constituent (Hussain, 2002). It is observed to be effective in diabetes mellitus. *Curcuma longa* is also effective in diabetic wounds (Araujo and Leon, 2001). *Eugenia jambolana* Linn, (*Syzygium cumini* linn) is known as jamun in common language. It belongs to family Myrtaceae (Qadir and Malik, 2010). The seeds have flavonoids, alkaloid, glycoside, protein and calcium (Ayyanar and Subash-Babu, 2012). Seeds also contain saponins, tannins, triterpenoids (Trivedi *et al.*, 2010). Research shows that it has antihyperglycemic activity (Grover *et al.*, 2002).

## MATERIAL AND METHODS

### *Animal selection and treatment protocol*

The study was conducted on 30 male adult Wister albino rats. Their weights ranged from 150-250 grams. Animals bred locally in the animal house of the Pharmacology

\*Corresponding author: e-mail: dr.sadiasrao@yahoo.com

**Table 1:** Effects on blood glucose levels

Groups	Fasting Blood Glucose Level (mg/dl)								
	1 <sup>st</sup> Week			3 <sup>rd</sup> Week			6 <sup>th</sup> Week		
	Mean± S.D	p-value (DC)	p-value (Std)	Mean± S.D	p-value (DC)	p-value (Std)	Mean± S.D	p-value (DC)	p-value (Std)
Group I (DC)	276.1±22.7	-	-	264.2±24.8	-	-	289.6±11.7	-	-
Group II (T)	73.7±5.79	0.000***	0.029 <sup>+</sup>	86.6±4.43	0.000***	0.049 <sup>+</sup>	75.0±15	0.000***	0.574 <sup>+</sup>
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)								
	1 <sup>st</sup> Week			3 <sup>rd</sup> Week			6 <sup>th</sup> Week		
	Mean±S.D	p-value (DC)	p-value (Std)	Mean± S.D	p-value (DC)	p-value (Std)	Mean ±S.D	p-value (DC)	p-value (Std)
Group I (DC)	349.9±18.0	-	-	367.0±8.26	-	-	338.3±5.56	-	-
Group II (T)	143.6±2.66	0.000***	0.006 <sup>++</sup>	133.6±2.59	0.000***	0.022 <sup>+</sup>	90.6±22.5	0.000***	0.000 <sup>+++</sup>
Group III (Std)	173.9±3.11	0.000***	-	156.4±3.86	0.000***	-	158.9±5.72	0.000***	0.000 <sup>+++</sup>

N=10, Values are mean ± S.D, Significant differences by Student t-test \*\*\*<p0.001; +++<p0.001, ++<p0.01, +<p0.05 as compared to diabetic control rats\* and standard group of rats<sup>+</sup> (DC= Diabetic Control, T= Treated with Herbal Drug, Std= Standard)

**Table 2:** Effects on HbA1C

Groups	Glycosylated Hemoglobin (HbA1C) %		
	Mean ±S.D	p-value (DC)	p-value (Std)
Group I (DC)	8.87±0.461	-	-
Group II (T)	4.28±0.277	0.000***	0.000 <sup>+++</sup>
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<sup>+</sup> (DC= Diabetic Control, T= Treated with Herbal Drug, Std= Standard)

Department of University of Karachi. The rats were housed in specially designed cages, as groups of 3 rats per cage. They were kept at room temperature of 25±1°C and 12/12h, light and dark cycle. The animals were kept on water and standard diet ad libitum. Animals were handled according to the specifications provided in “Helsinki Resolution 1964.” The University “Board of Advanced Studies and Research” approved this study.

**Induction of diabetes**

Alloxan was procured from BDH chemicals through our supplier. Diabetes is induced in rats by intraperitoneal administration of Alloxan in a single dose. Alloxan (aqueous solution) at the dose of 120mg per kg body weight is administered to rats (Geetha *et al.*, 2011). To prevent fatal hypoglycemia from alloxan, 15-20ml of 20% glucose is administered intraperitoneally 6 h after alloxan administration. The rats were then kept on 5% oral glucose for next 24h (Pund *et al.*, 2012). Diabetic control was treated in the same manner. It takes 48h for induction of diabetes mellitus after the administration of alloxan (Qazi *et al.*, 2014). 48h after the administration of alloxan, blood samples were drawn to check the blood glucose level. Blood glucose levels were checked using portable glucometer. Levels of 50-135mg/dl are

considered normal glucose levels in rats (Tully, 2012). Rats with glucose level greater than 200mg/dl were taken as diabetic and chosen for this study (Ashish *et al.*, 2011).

**Herbal combination product**

Herbal product is a combination of *curcuma longa* and *Eugenia jambolana*. These two herbs are in the ratio of 1:1 in the herbal product. *Curcuma longa* and *Eugenia jambolana* are present as 180.93mg/tab each herb. This herbal product was procured in tablet form from Qarshi industries (Pvt) Ltd through our supplier.

**Standard drug**

Glibenclamide was procured from Sanofi Aventis (Pakistan) Ltd as tablet through our supplier and is used as standard.

**Protocol of the study**

3 groups of 10 animals (rats) each were taken for this study:

- Group I was taken as diabetic control (Alloxan treated)
- Group II treated with herbal product at dose of 1082 mg/70kg twice a day (dose as per drug information provided with the herbal product).

- Group III treated with Glibenclamide (Standard) at dose of 20mg/70kg (Rambiritch *et al.*, 2014)

Group I was administered distilled water only orally while Group II and Group III were orally administered drugs for a period of 6 weeks. The herbal product was administered to the animals by means of weight. 1082mg (tablet weight)/70kg was the dose used for herbal product. Dose for animals was calculated by unitary method. Effects on blood glucose levels were observed at 1<sup>st</sup>, 3<sup>rd</sup> and 6<sup>th</sup> week of drugs treatment. HbA1C was checked after 6 weeks of treatment to observe the overall diabetic control of drugs.

#### **Blood glucose levels**

Fasting as well as random levels of glucose were estimated within three hours of sample collection by "GOD PAP Enzymatic Colorimetric Test Method" (Trinder, 1969) on Humalyzer, 3000 ("Semi-automatic chemistry analyzer by HUMAN, Germany, Model No. 16700") by the use of standard kits, which is supplied by HUMAN.

#### **Estimation of glycosylated hemoglobin (HbA1C)**

To estimate HbA1C, blood samples were sent to Dr. Panjwani Centre for Molecular and Drug Research (PCMD). This centre is situated at the HEJ Research Institute, University of Karachi. The samples were sent within 1 hour of collection.

#### **STATISTICAL ANALYSIS**

All observations are expressed as mean value  $\pm$ Std. Dev. Statistical analysis is done using student t-test. P-values < 0.001 were considered highly significant.

#### **RESULTS**

Fasting glucose levels of Group II (herbal product) were significantly decreased after one week, three weeks and six weeks of dosing in comparison to diabetic control. These effects were similar to the standard anti-diabetic drug, glibenclamide (Group III) as the difference in the fasting glucose levels between herbal product and glibenclamide is insignificant (table 1). Random glucose levels were significantly reduced in group II (herbal product) after 1 week of treatment in comparison to diabetic control. Also, group II showed a better control of random glucose levels in comparison with the standard drug, glibenclamide after 1 week of dosing. After 3 weeks of drug treatment, group II (herbal product) maintained its significant decrease in random glucose levels in comparison to diabetic control. The difference between the values of random glucose levels of standard and herbal product was insignificant after 3 weeks of dosing (table 1). After 6 weeks of treatment, herbal product showed significant decrease in random glucose level in comparison to diabetic control. Also, group II (herbal

product) showed better control than standard in controlling random glucose levels after 6 weeks of treatment (table 1). HbA1C levels, when compared with diabetic control, were found significantly decreased in-group II (herbal product) after 6 weeks of treatment. HbA1C level of group II (herbal product) was found closer to the standard drug (table 2).

#### **DISCUSSION**

The findings in our study indicates that combination of *Curcuma longa* and *Eugenia jambolana* has a good efficacy in controlling diabetes with an excellent control of glucose levels right from the first week of treatment with decreased fasting glucose levels as well as decreased random glucose levels with HbA1C of less than 6%. The overall effects of this combination were similar to glibenclamide in terms of fasting glucose levels, also showing overall better random glucose levels than glibenclamide and HbA1C closer to standard drug. The excellent effects of this herbal combination may be due to synergistic effect as *Curcuma longa* produces its antidiabetic effect by decreasing hepatic glucose production (Watson and Preedy, 2012) while *Eugenia jambolana* stimulates peripheral utilization of glucose (Ford, 2006).

#### **CONCLUSION**

On the basis of above findings, it is concluded that *Curcuma longa* and *Eugenia jambolana*, when used in combination, has good treatment outcomes in managing diabetes mellitus. This combination in future can be of potential benefit in managing diabetes mellitus.

#### **REFERENCES**

- Araujo CAC and Leon LL (2001). Biological activities of curcuma longa L. *Memórias do Instituto Oswaldo Cruz.*, **96**(5): 723-728.
- Ashish B, Swapnil G and Baldi A (2011). Hypoglycemic Effect of Polyherbal Formulation in Alloxan Induced Diabetic Rats. *PhOL.*, **13**: 764-773.
- Ayyanar M and Subash-Babu P (2012). Syzygiumcumini (L.) Skeels: A review of its phytochemical constituents and traditional uses. *Asian Pac. J. Trop. Biomed.*, **2**(3): 240-246
- Bailey CJ and Day C (1989). Traditional plant medicines as treatments for diabetes. Source Department of Pharmaceutical Sciences, Aston University, Birmingham, United Kingdom. *Diabetes Care*, **12**(8): 553-564.
- Centre for Disease Control and Prevention (2011). National Diabetes fact sheet, retrieved from [http://www.cdc.gov/diabetes/pubs/pdf/ndfs\\_2011.pdf](http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf)
- Ford AM (2006). Focus on Diabetes Mellitus Research, 1<sup>st</sup> ed., Nova Science Publishers, p.11.

- Geetha G, Kalavalarasariel GP and Sankar V (2011). Anti diabetic effect of *Achyranthesrubrofusca* leaf extracts on alloxan induced diabetic rats. *Pak. J. Pharm. Sci.*, **24**(2): 193-199.
- Grover JK, Yadav S and Vats V (2002). Medicinal plants of India with anti-diabetic potential. *J. Ethnopharmacol.*, **81**(1): 81-100.
- Hussain HEMA (2002). Hypoglycemic, hypolipidemic and antioxidant properties of combination of cur cumin from *curcuma longa*, linn and partially purified product from *abromaAugusta*, linn. instreptozotocin induced diabetes. *Indian J. Clin. Biochem.*, **17**(2): 33-43.
- Malviya N, Jain S and Malviya S (2010). Antidiabetic potential of medicinal plants. *Acta. Pol. Pharm.*, **67**(2): 113-118.
- Pund KV, Vyawahare NS, Gadakh RT and Murkute VK (2012). Antidiabetic evaluation of *dalbergia Sissoo* against alloxan induced diabetes mellitus in wistar albino rats. *J. Nat. Prod. Plant. Resour.*, **2**(1): 81-88.
- Qadir MI and Malik SA (2010). Anti-diabetic activity of inorganic metals *Eugenia jambolana* Lam. (Myrtaceae) flowers. *PhOL.*, **2**: 979-985.
- Qazi N, Khan RA, Rizwani GH and Feroz Z (2014). Effect of *Carthamustinctorius* (Safflower) on fasting blood glucose and insulin levels in alloxan induced diabetic rabbits. *Pak. J. Pharm. Sci.*, **27**(2): 377-380.
- Rambiritch V, Maharaj B and Naidoo P (2014). Glibenclamide in patients with poorly controlled type 2 diabetes: a 12-week, prospective, single-center, open-label, dose-escalation study. *Clin Pharmacol.*, **6**: 63-69.
- Trinder P (1969). Determination of glucose in blood using glucose oxidase with an alternative oxygen receptor. *Ann. Clin. Biochem.*, **6**: 24-27.
- Trivedi MH, Lakshmi SM and Kumar AS (2010). Review on natural anti-inflammatory agents. *Int. J. Biol. Pharm. Res.*, **1**(1): 13-19.
- Tully TN (2012). A veterinary technician's guide to exotic animal care, 1<sup>st</sup> ed., American animal Hosp Assoc, p.151.
- Watson RR and Preedy VR (2012). Bioactive food as dietary interventions for diabetes, 1<sup>st</sup> ed., Academic Press, pp.281-282.
- WHO (2002). Traditional Medicine Strategy 2002-2005, World Health Organization, retrieved from <http://apps.who.int/medicinedocs/pdf/s2297e/s2297e.pdf>.
- WHO Fact sheet (2011). Diabetes, Fact sheet N°312 August 2011, retrieved from <http://www.who.int/mediacentre/factsheets/fs312/en>.
- WHO Geneva guidelines (2000). General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine, Geneva 2000, retrieved from [http://whqlibdoc.who.int/hq/2000/WHO\\_EDM\\_TRM\\_2000.1.pdf](http://whqlibdoc.who.int/hq/2000/WHO_EDM_TRM_2000.1.pdf).