

## Research Article

**Single Blind Placebo Control Study on Hypoglycemic Potential of Pakistani Fruit: FIGS**Shah Murad<sup>1\*</sup>, Nusratullah Khan<sup>2</sup>, Saleemullah Abro<sup>3</sup>, Azizullah Khan Dhilloo<sup>4</sup>, Quratulain Saleem<sup>5</sup>, Nazima Zain<sup>6</sup>, Seema Shah Murad<sup>7</sup>, Hafiz Moeen-Ud-Din<sup>8</sup> and Farid-Ud-Din<sup>9</sup><sup>1</sup>Professor of Pharmacology, IMDC, Islamabad, Pakistan<sup>2</sup>Nusratullah Khan, Assistant Prof of Biochemistry at Bolan University of Medical and Health Sciences, Quetta, Pakistan<sup>3</sup>Saleemullah Abro, Assistant Professor of Physiology at Baqai Medical University, Karachi Pakistan<sup>4</sup>Azizullah Khan Dhilloo, AP in Infectious Diseases, Dow University of Health Sciences Karachi, Pakistan<sup>5</sup>Quratulain Saleem, AP at Community Medicine Department, Karachi Medical & Dental College (KMDC), Karachi, Pakistan<sup>6</sup>Nazima Zain, Consultant Gynecologist at DUHS/Civil Hospital Karachi Pakistan<sup>7</sup>Seema Shah Murad, Gynecologist at NMC Karachi Pakistan<sup>8</sup>Hafiz Moeen-Ud-Din, Associate Prof of Anatomy at King Edward Medical University, Lahore Pakistan<sup>9</sup>Farid-Ud-Din, Lecturer Pharmacology at DANTH Islamabad Pakistan**\*Corresponding author**

S Murad, HOD Pharmacology at IMDC Islamabad Pakistan, Tel: +923338124611

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**Abstract**

Adverse consequences from hyperglycemia may reflect effects of glucose as well as hyperinsulinemia. Glycemic effects include elevations in reactive oxygen species and formation of advanced glycation products. Hyperinsulinemia has been associated with mitogenic effects on vascular smooth muscle cells. Because elevated blood glucose is a common and potentially treatable condition, characterization of whether higher blood glucose may contribute to CAD is of particular clinical consequence. Coronary artery disease (CAD) is a major determinant of the long-term prognosis among patients with diabetes mellitus (DM). DM is associated with a 2 to 4-fold increased mortality risk from heart disease. Near-normal glycemic control for a median of 3.5 to 5 years does not reduce cardiovascular events. Diabetes mellitus is a chronic, lifelong condition that affects your body's ability to use the energy found in food. There are three major types of diabetes: type 1 diabetes, type 2 diabetes, and gestational diabetes. Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves. Too much sugar in your blood can lead to serious health problems. Type-2 diabetes mellitus, which accounts for 90–95% of those with diabetes, previously referred to as non-insulin-dependent diabetes, or adult-onset diabetes, encompasses individuals who have insulin resistance and usually have relative, rather than absolute, insulin deficiency. At least initially, and often throughout their lifetime, these individuals do not need insulin treatment to survive. Metformin is oral antidiabetic drug having lesser morbid effects as compared to other oral antidiabetic agents. We have compared hypoglycemic potential of herbal hypoglycemic agent Figs or INJEER with Metformin. It was single blind correlational research conducted at Jinnah Hospital Lahore-Pakistan from April to August 2018. Fifty diabetic type-II patients were selected for research. Approved and explained consent was taken by all patients. They were divided in two groups, 25 patients in each group. Group-I patients were advised to take 250 mg Metformin thrice daily for two months. Group-II patients were advised to take 10 grams of Injeer (Figs) in three divided doses for two months. Their base line fasting blood glucose level was taken and kept in record. They were advised to visit the OPD of the hospital fortnightly. They were also advised to check their fasting plasma glucose level daily at the morning by using Glucometer (provided by Acon Pharmaceuticals Ltd). After two months when results were compiled and statistically analyzed, it was observed that Metformin decreased blood sugar level 27.6 % and Figs decreased 13.5 %. It was concluded from the study that Figs can decrease blood glucose level significantly, but when compared to Metformin, this change is about half fraction of the Metformin.

**Keywords:** High serum glucose, Lipids, Mortality, CAD, CCF, Hyperlipidemia, Morbidity, Cardiac arrhythmias, Fats, LDL-Cholesterol, Diabetes mellitus

## Introduction

Pathologic consequences from modest elevations of glucose are plausible since impaired glucose tolerance and impaired fasting glucose have been associated with macrovascular disease and greater mortality. Patients presenting with acute coronary syndrome frequently have glucose intolerance, and it has been reported that glucose intolerance but not impaired fasting glucose may be associated with CAD. In contrast, meta-analysis indicates that glucose above a threshold of 100 mg/dl may also be a significant risk. Since impaired fasting glucose is increasingly common, affecting >35 million adults in the U.S., and CAD affects a majority of older adults, associations between these common, morbid, and potentially fatal conditions are of clinical importance. A triglyceride is a type of fat you get mostly from the food you eat. Your body also produces it when it converts excess calories to fat for storage. Some triglycerides are necessary for certain cell functions, but too much is unhealthy. As with LDL, lower levels of triglycerides are considered healthier. The most common form of diabetes is called type 2, or non-insulin dependent diabetes. This is also called "adult onset" diabetes, since it typically develops after age 35. However, a growing number of younger people are now developing type 2 diabetes. People with type 2 are able to produce some of their own insulin. Often, it's not enough. And sometimes, the insulin will try to serve as the "key" to open the body's cells, to allow the glucose to enter. But the key won't work. The cells won't open. This is called insulin resistance. Often, type 2 is tied to people who are overweight, with a sedentary lifestyle. Patients with high blood sugar will typically experience polyuria (frequent urination), they will become increasingly thirsty (polydipsia) and hungry (polyphagia). Normally, body breaks down the sugars and carbohydrates eat into a special sugar called glucose. Glucose fuels the cells in body. But the cells need insulin, a hormone, in bloodstream in order to take in the glucose and use it for energy. With diabetes mellitus, either body doesn't make enough insulin, it can't use the insulin it does produce, or a combination of both [1,2]. Since the cells can't take in the glucose, it builds up in blood. High levels of blood glucose can damage the tiny blood vessels in kidneys, heart, eyes, or nervous system. That's why diabetes -- especially if left untreated -- can eventually cause heart disease, stroke, kidney disease, blindness, and nerve damage to nerves in the feet [3]. Currently, six classes of oral antidiabetic drugs (OADs) are available: biguanides (e.g., metformin), sulfonylureas (e.g., glimepiride), meglitinides (e.g., repaglinide), thiazolidinediones (e.g., pioglitazone), dipeptidyl peptidase IV inhibitors (e.g., sitagliptin), and  $\alpha$ -glucosidase inhibitors (e.g., acarbose) [4]. Metformin marketed under the trade name Glucophage among others, is the first-line medication for the treatment of type 2 diabetes. This is particularly true in people who are overweight. It is also used in the treatment of polycystic ovary syndrome. Limited evidence suggests metformin may prevent the cardiovascular disease and cancer complications of diabetes. It is not associated with weight gain. It is taken by mouth [5]. Metformin is generally well tolerated. Common side effects include diarrhea, nausea, and abdominal pain. It has a low risk of developing low blood sugar. High blood lactic acid levels is a concern if prescribed inappropriately and in overdose. It should not be used in those with liver disease or kidney problems. While there is no clear harm if used during pregnancy insulin is generally preferred for gestational diabetes. Metformin is in the biguanide class. It works by decreasing glucose production by the liver and increasing glucose use by body tissues [6-9]. Fig is a tree. The fruit is commonly eaten. The fruit and leaves are used to make medicine [10]. Raw figs are a good

source (14% of the Daily Value, DV) of dietary fiber per 100 gram serving (74 calories), but otherwise do not supply essential nutrients in significant content. In a 100 gram serving providing 229 calories, dried figs are a rich source (> 20% DV) of dietary fiber and the essential mineral, manganese (26% DV), while several other dietary minerals are in moderate-to-low content [11]. Figs contain diverse phytochemicals, including polyphenols such as gallic acid, chlorogenic acid, syringic acid, (+)-catechin, (-)-epicatechin and rutin [12]. Trans-fatty acids, are worse than saturated fats because they can raise your LDL levels and lower your HDL levels. Some trans fats are found naturally in animal products. Others are found in processed foods that have undergone a process called hydrogenation, such as some kinds of margarine and potato chips. With diabetes mellitus, either body doesn't make enough insulin, it can't use the insulin it does produce, or a combination of both [2]. Since the cells can't take in the glucose, it builds up in blood. High levels of blood glucose can damage the tiny blood vessels in kidneys, heart, eyes, or nervous system. That's why diabetes -- especially if left untreated -- can eventually cause heart disease, stroke, kidney disease, blindness, and nerve damage to nerves in the feet [13-17].

## Patients and Method

Design of research work was correlational, and was conducted at Jinnah Hospital, Lahore from April to August 2018. Fifty diabetic patients (Diabetes Mellitus type-II) were selected from Jinnah hospital to conduct research study. Inclusion criteria was age limit from 25 to 70 years of both gender, male and female whose hyperglycemia was controlled and moderate in state. We excluded those diabetic patients whose hyperglycemia was uncontrolled, unstable, fragile due to use of allopathic or herbal hypoglycemic agents. Patients were divided in two groups. Group-I (25 diabetic patients) was advised to take 250 mg of Tablet Glucophage 250 mg (Metformin) half an hour before taking meal, thrice daily for two months. Group-II patients (25 diabetic patients) were advised to take Injeer (Figs) 10 grams daily in three divided doses half an hour after each meal for two months. Their baseline fasting glucose level was determined by Glucometer (On Call Extra made by ACON Lab 1190059) at start of research work. They were advised to check and keep in record their fasting blood glucose level every day early in the morning. They were advised to take their normal meal without any supplement or high glucose-contained baked or high glucose containing natural fruits. They were advised to come at hospital for follow up or any query regarding drug compliance. Data were expressed as the mean  $\pm$  SD and "t" test was applied to determine statistical significance as the difference. A probability value of <0.01 was considered as significant and P<0.001 was considered as highly significant.

## Results

Results of treatment with two different drugs on fasting blood glucose of DM-II patients are shown in following table. Two patients withdrew from group-I due to their personal problems so biostatistical data was applied for 23 patients in this group. In group-I which was on metformin 27.6% glucose reduction was observed which is statistically highly significant change in the parameter in estimated time.

In group-II which was on Figs treatment 13.5% glucose reduction was observed which is statistically significant change in the parameter in estimated time.

**Table 1: Explaining before and after treatment values, percentage change and statistical significance of diabetic patients with two different drugs**

Drug group	At day-0	At day-60	change	% change	p-value
Group-I (Metformin) n=23	230.04 $\pm$ 1.99	166.66 $\pm$ 2.05	63.4	27.6	<0.001
Group-II (Figs) n=25	219.22 $\pm$ 1.67	189.67 $\pm$ 1.04	29.5	13.5	<0.01

**Key:** All values were measured in mg/dl, Dose of Metformin was 250 mg thrice daily, dose of Figs was 10 grams in three divided doses, n= sample size, p-value <0.01 was considered as significant and p-value <0.001 was considered as highly significant change.

## Discussion

Chronic diabetes conditions include type 1 diabetes and type 2 diabetes. Potentially reversible diabetes conditions include prediabetes — when your blood sugar levels are higher than normal, but not high enough to be classified as diabetes — and gestational diabetes, which occurs during pregnancy but may resolve after the baby is delivered. Allopathic medications are just for good survival of the patients victimized. These drugs have adverse effects which can lead to less compliance of patients. Now a days herbal medications are going to replace allopathic drugs due to their ethnic related doctrine and having lesser adverse effects. In our research Metformin decreased fasting blood glucose 63.4 mg/dl in two months therapy which is equal to 27.6 % decrease. Biostatistically this change in mean values are highly significant which match with results of study conducted by Hubbard JK, et al. who proved almost same effects of Metformin on fasting blood sugar levels in 103 diabetic patients suffering from Diabetes Mellitus type-II [14]. Dunn CJ, et al. described that Metformin interrupt carbohydrates absorption from gastrointestinal tract [15]. Our results are in contrast with results of study conducted by Spiller HA, et al. who observed and proved only 24.8 mg/dl reduction in 22 diabetic male patients when Metformin was used at dose of 250 mg twice daily for three weeks [16]. This contrast in results may be due to less concentration of drug used. Hundal RS, et al. agrees with already accepted theory of Metformin's hypoglycemic mechanism that inhibition of hepatic gluconeogenesis is main cause for blood glucose level reduction [17]. Triggler CR, et al. labelled Metformin drug as first choice hypoglycemic agent in type-II diabetic patients [18]. In our research results Figs or Injeer decreased fasting blood sugar about 29.5 mg/dl in two months therapy in 25 diabetic patients of Type-II which is statistically significant decrease in the parameter. These results match with results of study conducted by Mawa S, et al. who proved that about 30.87 mg/dl of blood glucose may be decreased when Figs are used for three months with regular intake of this fruit with each meal i.e. thrice daily [19]. C Perez, et al. proved almost same changes in fasting blood glucose in 117 diabetic patients suffering from Type-II DM [20]. Perez C, et al. wrote that these fruits can lower fasting sugar level even more than this reduction proved, if used in enough amount and in research controlled environment [21]. Our results do not match with results of research work conducted by Serracarla, A et al. who proved very small amount of blood glucose reduction in 12 patients suffering from DM type-II, even they used 500 mg of Metformin thrice daily for one month [22]. Contrast in these results are or may be due to lesser exposure of drug and small sample size. Lyme WE, et al. warned in their research work's conclusion that Metformin can cause morbid effects if given concurrently with Insulin [23]. He has encouraged to use Metformin with Figs without any fear of morbid hypoglycemia.

## Conclusion

We concluded from this research that hypoglycemic agents of herb origin i.e. Figs may be good antidiabetic agent but these agents have half fraction of hypoglycemic effects when compared with allopathic drug Metformin.

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## Conflict of Interest

No conflict of interest regarding this work.

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