International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Evaluation of Antidiabetic Potential of A Novel Formulation from Prophetic Medicine in Streptozotocin-Induced Diabetic Balb/C Mice

Eman Elm .E. Elaswed[1], Moklesur Rahman Sarker[2]

[1]Faculty of Sciences, Lincoln University College Malaysia Mayang Jaya, 47301, Petaling Jaya, Selangor Darul Ehsan, Malaysia

[2]Faculty of Pharmacy, Lincoln University College Malaysia Mayang Jaya, 47301, Petaling Jaya, Selangor Darul Ehsan, Malaysia

Abstract: ***Diabetes is a common, chronic and expensive disease that is threatening the health of generations of people all around the world. Diabetes mellitus is a disorder that affects the body's ability to make or use insulin and it remains an incurable disorder in spite of intense research. Prophetic Medicine is the total authentic Hadith narrated by the Prophet (peace be upon him), which carries incredible values for the administration of diabetes. The present study aimed to develop a new formulation from Prophetic Medicine and to evaluate its therapeutic potential for the effective use in diabetes for avoiding major adverse effects in animal model. Towards this aim, diabetes was induced to Balb/c mice with the injection of streptozotocin (160 mg/kg). The mice were treated with the formulation of Prophetic medicine (PMFD) at the doses of 200, 400, 600 mg/kg and metformin at dose of 200 mg/kg orally. The glucose levels were measured on first day for 3 hours, second and third day for 2 hours and 2 weeks before and after treatment with the PMFD. Non-diabetic mice were used as a negative control and diabetic mice without treatment was used as a positive control .The formulation (PMFD) at the dose of 200, 400 and 600 mg/kg shows significant reduction in post-prandial plasma glucose level and body weight, whereas metformin of 200 kg/mg shows significant reduction of glucose level on second and third day.Thus, the present formulation of Prophetic medicine can be recommended for the prevention and treatment of diabetes. This data can support for biomedical research efforts that can lead to prevention, treatment and possibly even cures for diabetes.***

Keywords: Diabetes Multiuse, Prophetic medicine, Plasma Glucose level, Balb/c mice, Body Weight Streptozotocin , Metformin

1. Introduction

Diabetes mellitus (DM) is a clinical syndrome associated with deficiency of insulin secretion or action. It is considered one of the largest emerging threats to health in the 21st century. Insulin secretion is subject to control by nutrients, hormonal, neural, and pharmacological factors. Among these glucose is the most important regulator of insulin secretion machinery (Mosley et al., 2013). It is estimated that there will be 380 million persons with DM in 2025 (Atkins & Zimmet, 2010). Despite considerable progress in the treatment of diabetes by hypoglycemic agents, search for newer drugs continues because the existing synthetic drugs of diabetes are associate with the increased risk of many complications, such as cardiovascular disease, cancer, renal impairment (Cassidy et al., 1999).

Many prophetic medicine plants have been used for the treatment of diabetes mellitus. Out of these only a few have been evaluated as per modern system of medicine. From many such plants, only extracts have been prepared and their usefulness evaluated in experimental diabetes in animals. Unfortunately, there is a lack of scientific investigations to discover and establish the effectiveness of Prophetic medicines for the treatment of different diseases. Towards, achieving this goal present study was performed. In the current study, streptozotocin (STZ)-induced diabetic mice were treated by Prophetic medicine formula for Diabetic (PMFD) and subjected to management of blood glucose level and body weight.

The aim of the present study is to investigate or evaluate the therapeutic potential of PMFD for management and treated streptozotocin (STZ)-induced diabetic mice with avoiding major adverse effects. This study hypothesize that diabetic mice treated with PMFD will significantly reduce fasting plasma glucose FPG and post-prandial blood glucose PPBG levels. The result from this study might be significantly contribute for the management of plasma blood glucose of STZ- induced diabetic Balb/c mice or minimizing the side-effects of diabetic medication. Thus, it can be a clue of new drug for the effective management of diabetes improving the quality of life for diabetic patients.

2. Objectives

The aim of the current research is to develop a new formulation from Prophetic medicines and to evaluate its therapeutic potential for the effective management of plasma glucose STZ- induced diabetic Balb/c mice with avoiding major adverse- effects in animal model.

3. Methodology

3.1 Materials

3.1.1. Prophetic materials used in PMFD

The Essential Prophetic Medicine (PM) materials were selected based on literature survey and their use in traditional medicines. These materials were purchased from Arabian shops and Malaysian markets as well. The list of the prophetic materials used in the study are listed in Table 1.

Table 1: List of selected Prophetic medicine materials with their supplier

No.	Common name	Botanical name (Family)	Promotion Source
1	Pure Honey	Honey	Berkat Madinah (Selangor, Malaysia)
2	Black Seed	Nigella sativa	Berkat Madinah (Selangor, Malaysia)
3	Apple cider vinegar	Apple cider vinegar	Berkat Madinah (Selangor, Malaysia)
4	Ginger	Zingiber officinale	Hero market (Selangor, Malaysia)
5	Cinnamon	Cinnamomum zeylanicum (NEES)	Berkat Madinah (Selangor, Malaysia)
6	Olive leaves	Olea europaea L	Berkat Madinah (Selangor, Malaysia)
7	Extra virgin olive oil	Olea europaea L	Berkat Madinah (Selangor, Malaysia)
8	Barley	Hordeum vulgare L	Hero market (Selangor, Malaysia)

3.1.2.Chemicals

The chemicals used in this study are listed in Table 2 together with their source of manufacturer.

Table 2: List of chemicals and reagents used in the study

No	Chemicals and Reagent	Source
1	Ethanol	Dhe tech enterprise Taman Mayang, PJ Malaysia
2	Citric acid	R &N Marketing, Essex, U.K.
3	Sodium citrate	Alpha Chemika, India.
4	Streptozotocin	Sigma Aldrich, U.S.A.
5	Metformin	Santa Crutz, German.

3.1.3 Experimental Balb/c mice

Total 18 male Balb/c mice were used for the experimental, which were purchased from "Pets Wonderland Paradigm Mall" Selangor Malaysia (Their source: Envigo, USA). The approximate weight of each mouse was 18–30 g and the age was in between 7-9 weeks. All mice were kept under standard conditions at animal house of Lincoln University college. Balb/c mice were fed with normal diet for 10 days before proceed in the experiments.

3.2 Methods

3.2.1 Collection of materials used for the formulation of antidiabetic of Prophetic medicine.

The materials that have been used in this study are Cinnamon (Cinnamomum zeylanicum), Ginger (Zingiber officinale), Black seed (Nigella sativa), Olive leaves (Olea European), Barley (Hordeum vulgare L), Olive oil, Apple cider vinegar and Pure Honey. Most of materials were dried and crushed into powder and measured, whereas ginger was washed, cut into small pieces and dried under sun light for one week then crushed into powder and measured.

3.2.2 Extraction of materials used in the formulation of antidibetic Prophetic medicine

The Extraction of materials performed by grinding and drying of each material into the powder and proceeds with extraction. All flasks containing the mixture of material powders in ethanol were kept in a dark place for all extraction processing.

3.2.2.1 Extraction of cinnamon

The extraction of Cinnamon was performed by adding 300 g cinnamon powder to 500 ml of 80 % ethanol and by shaking the flask twice a day to mix the material with each other. Alcohol was changed every two days for two weeks. At last day of extraction, all cinnamon extract was filtered using filter paper. Finally, extracted cinnamon was dried by using heating mantle at 40 0C temperature.

3.2.2.2 Extraction of black seed

Black seed powder of 200 g was added to 500 ml of 80 % ethanol and shaking the flask twice a day to mix the material with each other and alcohol changed every two days for two weeks to get the extraction. At last day of extraction, all black seed extract was filtered using filter paper. Finally, the extracted black seed were dried by using heating mantle at 40 0C temperature.

3.2.2.3 Extraction of barley

Barley powder of 300 g was added to 700 ml of 80% ethanol and the flask was shaked twice a day to mix the material with each other and alcohol changed every two days for two weeks. At last day of extraction, all barley extract was filtered using filter paper. Finally, extraction of barley was dried by using heating mantle at 400C temperature.

3.2.2.4 Extraction of olive leaves

Olive leaves powder of 200 g was added to 500 ml of 80% ethanol and shake the flask twice a day to mix the material with each other and alcohol changed every two days for two weeks. At last day of extraction, all olive leaves extract was filtered using filter paper. Finally, extraction was dried by used heating mantle at 400C temperature.

3.2.2.5 Extraction of ginger

Ginger powder of 150 g was added to 400 ml of 80 % ethanol and shake the flask twice a day to mix the material with each other and alcohol changed every two days for two weeks. At last day of extraction, all ginger extract was filtered using filter paper. Finally, extracted ginger was dried by using heating mantle at 40 0C temperature. All extracted samples of PMFD kept in fridge until it prepared the formulation.

3.2.3 Preparation of formulated Prophetic medicine

After three weeks of processing PMFD materials, different quantity of each PM extracted material was measured separately by using electrical balance. Cinnamon (2 g),

Black seed (2 g), Barley (1 g), Olive leaves (2 g), Ginger (3 g), Olive oil (5ml), Apple cider vinegar (1 ml), and Pure Honey (15 ml) were mixed together in a beaker. Finally, mixer of formulation was kept in the fridge until further use.

3.2.4 Induction of diabetes in Balb/c mice by streptozotocin

Diabetes was induced in Balb/c mice by a single intraperitoneal injection of 160 mg/kg weight of 0.1 M streptozotocin. STZ was prepared in 0.1 M citrate buffer by dissolving 2.1 g of citric acid and 2.94 g of sodium citrate in 100 ml of distilled water. The pH was adjusted to 4.5 by proper addition of concentrated NaOH/HCL using a calibrated pH meter (Ballester et al., 2004). After 48 hours of induction of diabetes, One touch Glucometer and compatible glucometer strips were used for the determination of blood glucose levels in over-night fasted mice.

Blood samples were collected from dorsal vein of the tail of conscious mice. Diabetes was allowed to stabilize for 5 days before the commencement of intervention. Thereafter, the blood glucose level of all animals in each experimental group was assessed. Animals were checked for clinical signs of drug toxicity such as tremors, diarrhea, weakness, weight loss and death.

3.2.5 Treatment of mice with prophetic medicine formula (PMFD)

After preparation of final prophetic medicine formula (PMFD) then, all Balb/c mice were divided into 6 experimental groups and different doses of PMFD was given as listed below.

Group 1: Non-diabetic Mice (negative control-1)
Group 2: Diabetic Mice without treatment (positive control-2)
Group 3: Diabetic mice treated with PMFD (200 mg/kg)
Group 4: Diabetic mice treated with PMFD (400 mg/kg)
Group 5: Diabetic mice treated with PMFD (600 mg/kg)
Group 6: Diabetic mice treated with metformin (standard. Antidiabetic drug) at dose of 200 mg/kg.

Nondiabetic (group-1) and diabetic (group-2) mice was administrated with distilled water daily and group 3, 4 & 5 was administrated orally with (PMFD) with 200, 400 and 600 mg/kg doses. Metformin group-6 mice was treated with metformin drug orally. Each dose of PMFD and metaformin was diluted
with 4 ml of distilled water.

3.2.6 Measurement of blood glucose levels

Blood glucose level of each mice of all groups was measured by using one touch glucometer. The blood samples were collected from the tail vein of mice by using sterile needle . Blood glucose level of each mice was measured before and after the treatment of diabetic mice with PMFD. Blood glucose levels was measured also for non-diabetic, diabetic and metformin group. For all the 6 groups blood glucose level were measured on first day before and after 3 hours, second and third days before and after 2 hours and 2 weeks before and after treatment in administrated mice.

3.2.7 Measurement of body weight

Body weight of mice was measured on the first and last days of the experiment (before and after treatment with PMFD) by using Electric balance.

3.3 Data analysis

Statistical Analysis was performed by using IBM SPSS 22 version software. The results for blood glucose level were presented as mean ± S.D (standard deviation). One way analysis of variance (ANOVA) test was used in this study. Differences were considered statistically significant at $P < 0.05$.

4. Results

The current research was done in lab environment at Lincoln University. Total 18 mice were used in this project, which were equally divided into 6 different groups that is 3 mice each group.

Diabetes was induced in Balb/c mice with the i.p. administration of streptozotocin. The administration of prophetic medicine formula (PMFD) given to group 3, 4 and 5 groups as 200, 400 and 600 mg/kg dose. Group 6 diabetic mice were treated with metformin at dose of 200 mg/kg. Non-diabetic Mice (group-1) used as a negative control and diabetic mice without treatment was used as a positive control (group-2). Blood glucose levels of each mice of all the groups were measured on first day before and after treatment of 3 hours, second and third day before and after treatment of 2 hours, and after 2 weeks. Body weight of mice were measured on 2nd week before and after treatment with PMFD.

4.1 Result of PMFD on blood glucose levels in STZ-induced Balb/c mice 3 hours after treatment of diabetic mice

The STZ-induced Balb/c mice were treated with PMFD and blood glucose level was recorded at on first day before and after 3 hours of treatment. The data on (figure 1) clearly shows that the glucose level was decreased in all the mice of each group. The positive control mice blood glucose level was found to be increased. However, the statistical significance test shows that only results of group 3, 4 and 5 were significant and group 6 results were insignificant (Table 3).

Table 3: Effect of PMFD on blood glucose levels in STZ-induced Balb/c mice after 3 hours treatment (1st day) to diabetic mice

No.	Non-diabetic Control Group		Diabetic Control Group		Diabetic mice + Metformin (200 mg/kg)		PMFD (200 mg/kg)		PMFD (400 mg/kg)		PMFD (600 mg/kg)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	5.1±0.14	4.3±0.21	8.2±0.35	11.1±0.14	23.45±0.35*	20.1±0.14*	5.3±0.28*	4.15±0.21*	10.45±0.21*	10.25±0.35*	8.7±0.28	7.5±0.28
2	4.6±0.21	5.6±0.14	10.25±0.35	12.15±0.21	12.3±0.42*	10.1±0.14*	32.1±0.14*	27.15±0.21*	24.3±0.42*	20.15±0.21*	7.15±0.21	7.2±0.28
3	3.8±0.28	4.9±0.57	8.2±0.35	11.25±0.35	16.15±0.21*	13.2±0.28*	24±0.14*	21.1±0.14*	11.1±0.28*	10.1±0.28*	7±0.14	6.3±0.28

(An asterisk signifies a statistically significant difference change in glucose level in PMFD Balb/c mice before and after 3 hours of administration at $P < 0.05$.).

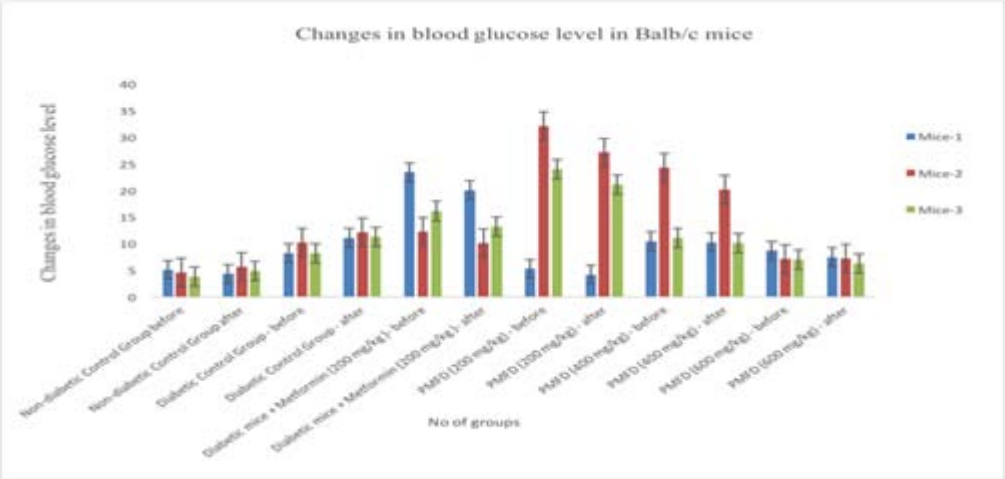

Figure 1: Comparison of change in blood glucose level in STZ-induced Balb/c mice before and after 3 hours of PMFD treatment(1st day)

4.2 Result of PMFD on blood glucose levels in STZ-induced Balb/c mice 2 hours after treatment (2nd day) to diabetic mice.

The blood glucose level was measured for each mice of all groups on second day before and after 2 hours of PMFD treatment to diabetic mice. The positive control mice blood glucose levels were found to be increased. The results show that the blood glucose level in all the mice were reduced (Figure 2). All the results found to be statistically significant (Table 4).

Table 4: Effect of PMFD on blood glucose levels in STZ-induced Balb/c mice after 2 hours treatment (2nd day) to diabetic mice

No.	Non-diabetic Control Group		Diabetic Control Group		Diabetic mice + Metformin (200 mg/kg)		PMFD (200 mg/kg)		PMFD (400 mg/kg)		PMFD (600 mg/kg)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	4.9±0.14	5±0.14	6.9±0.14	9.5±0.28*	22±0.14*	13.15±0.21*	6.15±0.21*	4.8±0.21*	7.6±0.14*	7.15±0.21*	4.2±0.28*	3.4±0.14*
2	4.4±0.14	3.8±0.28	7.4±0.14	9.05±0.07*	12.9±0.14*	10.35±0.21*	19.75±0.35*	17.1±0.14*	31.85±0.21*	26.9±0.14*	8.85±0.21*	7.15±0.21*
3	4.15±0.21	3.2±0.28	8±0.14	11.1±0.14*	18.25±0.21*	15.2±0.28*	25.15±0.21*	20.2±0.28*	3.85±0.21*	3.2±0.28*	9.25±0.21*	6.2±0.28*

(An asterisk signifies a statistically significant difference change in glucose level in PMFD Balb/c mice before and after 2 hours of administration at $P < 0.05$.).

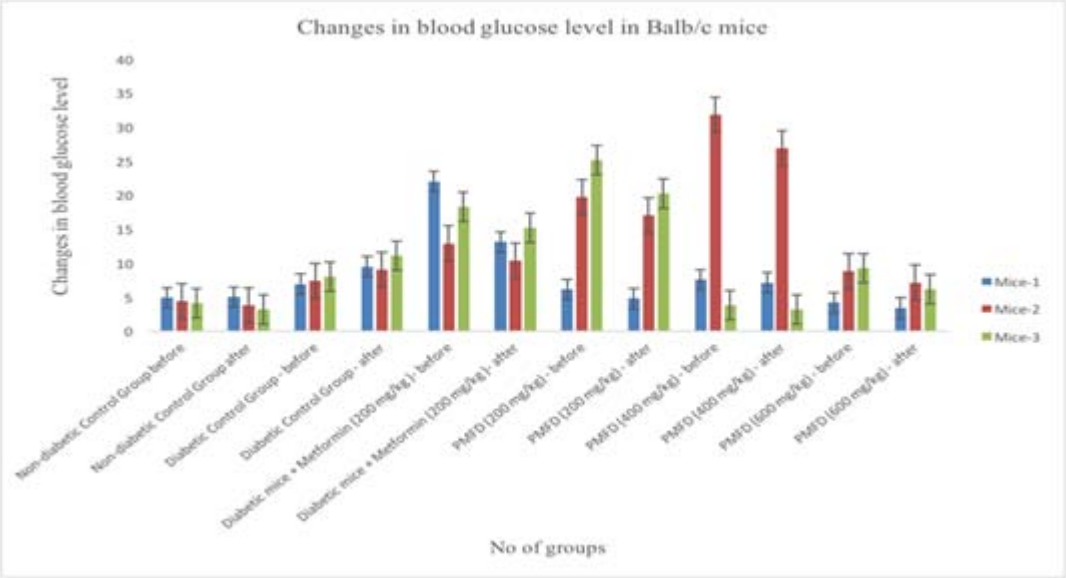

Figure 2: Comparison of change in blood glucose level in STZ-induced Balb/c mice before and after 2 hours of PMFD treatment (2nd day)

4.3 Result of PMFD on blood glucose levels in STZ-induced Balb/c mice 2 hours after treatment (3th day) to diabetic mice.

From the results, the effect of PMFD treatment on change in glucose level in diabetic Balb/c mice before and after 2 hours of administration on third day shows that the glucose levels were reduced after the treatment of PMFD in group 3, 4, 5 and 6 compared to before treated mice (Figure 3). The positive control mice blood glucose level was found to be increased. All the results found to be statistically significant (Table 5).

Table 5: Effect of PMFD on blood glucose levels in STZ-induced Balb/c mice after 2 hours treatment (3^{th} day) to diabetic mice

No	Non-diabetic Control Group		Diabetic Control Group		Diabetic mice + Metformin (200 mg/kg)		PMFD (200 mg/kg)		PMFD (400 mg/kg)		PMFD (600 mg/kg)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	3.15±0.21	4.9±0.14	6.15±0.21*	10.2±0.28*	16.15±0.21*	11.8±0.28*	8.2±0.28*	5.8±0.28*	9.15±0.21*	8.1±0.14*	11.95±0.07*	5.2±0.14*
2	3.8±o.28	4.1±0.14	10.35±0.21*	12.95±0.21*	19.1±0.14*	17.95±0.07*	31.15±0.21*	27.1±0.14*	14.15±0.21*	10.1±0.14*	8.1±0.14*	6.2±0.28*
3	4.15±0.21	4.1±0.14	12.25±0.21*	15.85±0.21*	16.9±0.14*	14.2±0.28*	28.1±0.14*	24.35±0.21*	12.15±0.21*	11.8±0.28*	7.2±0.14*	4.1±0.14*

(An asterisk signifies a statistically significant difference change in glucose level in PMFD Balb/c mice before and after 2 hours (3th day) of administration at $P < 0.05$.)

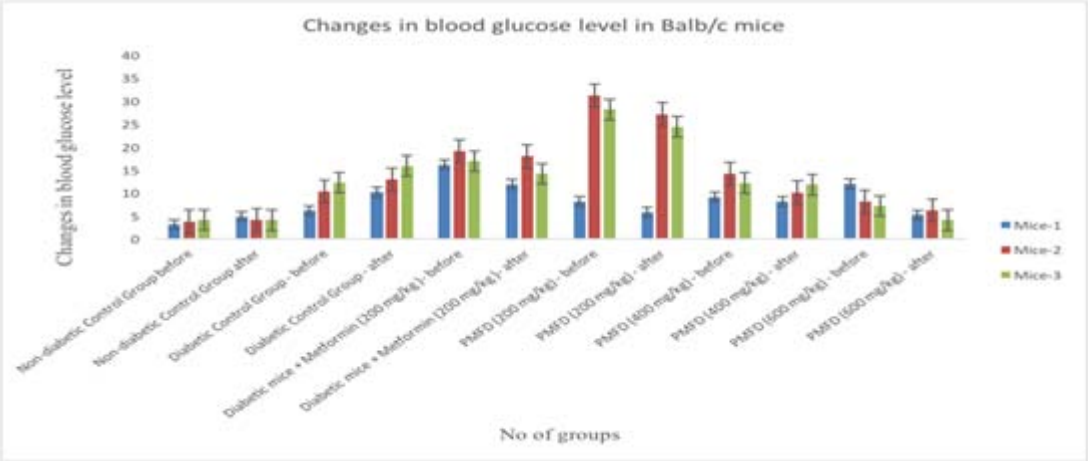

Figure 3: Comparison of change in blood glucose level in STZ-induced Balb/c mice before and after 2 hours of PMFD treatment (3th day)

4.4 Result of PMFD on blood glucose levels in STZ-induced Balb/c mice after 2 week's treatment to diabetic mice

The blood glucose level in diabetic Balb/c mice after 2 weeks of administration of PMFD shows reduction in all the groups compared to before treatment mice (Figure 4). The positive control mice blood glucose level was found to be increased. All the group's results show statically significant reduction in blood glucose level (Table 6).

Table 6: Effect of PMFD on blood glucose levels in STZ-induced Balb/c mice after 2 weeks treatment to diabetic mice

No	Non-diabetic Control Group		Diabetic Control Group		Diabetic mice + Metformin (200 mg/kg)		PMFD (200 mg/kg)		PMFD (400 mg/kg)		PMFD (600 mg/kg)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	5.1±0.14*	4.9±0.14	8.6±0.21*	10.1±0.14*	15.25±0.07*	10.2±0.28*	9.2±0.28*	5.85±0.21*	8.05±0.07*	5.85±0.21*	10.1±0.14	4.25±0.07*
2	3.9±0.14*	4.05±0.07	13.35±0.21*	16.1±0.14*	16.95±0.07*	10.7±0.14*	13.1±0.14*	7.05±0.07*	11.15±0.21*	5.3±0.14*	9.1±0.14	2.5±0.14*
3	2.35±0.21*	4.75±0.21	12.15±0.21*	13.95±0.07*	18.85±0.21*	12.15±0.21*	15.75±0.21*	7.9±0.28*	16.95±0.21*	10.05±0.07*	10±0.14	4.4±0.28*

(An asterisk signifies a statistically significant difference change in glucose level in PMFD Balb/c mice before and after 2 weeks of administration at $P < 0.05$.).

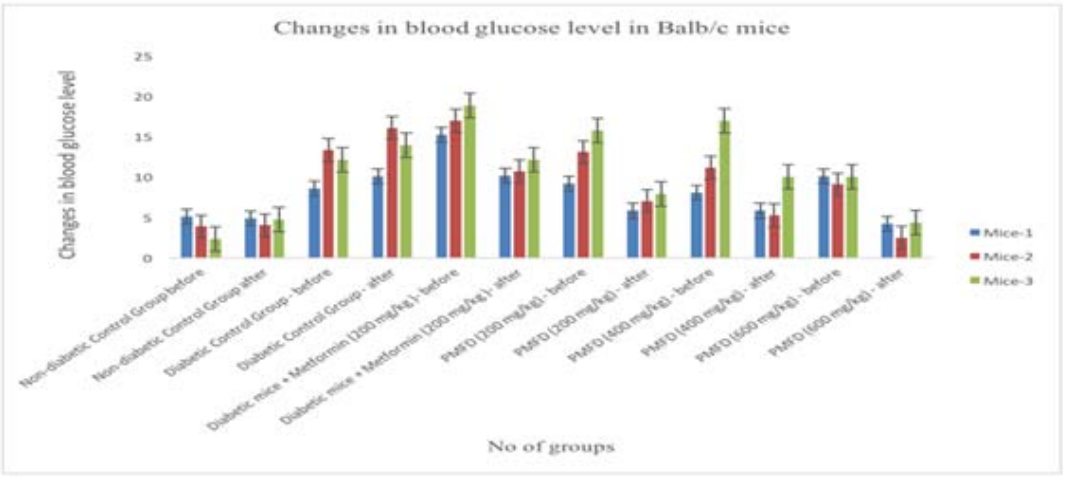

Figure 4: Comparison of change in blood glucose level in STZ-induced Balb/c mice before and after 2 weeks of PMFD treatment

4.5 Result of PMFD on body weight in STZ-induced Balb/c mice after 2 week's treatment to diabetic mice.

The body weight of diabetic mice was measured before and after PMFD treatment at 2 weeks. The positive control mice blood glucose levels were found to be increased. (Table 7) shows that there was significant reduction in group 3, 4, and 5, but group 6 (diabetic mice were treated with metformin at dose of 200 mg/kg) did not appear statistical significant (Figure 5).Overall results prove that that PMFD treatment help in reducing blood glucose level and body weight in most of the mice in all groups. Comparisons of blood glucose level and body weight of all 18 mice compared with control group (untreated mice) were done using the Student's t-test. Most of the results found to be statistically significant difference compared to the control (untreated seedlings) at $P < 0.05$).

Table 7: Effect of PMFD on body weight in STZ-induced Balb/c mice after 2 weeks treatment to diabetic mice (An asterisk signifies a statistically significant difference change in body weight in PMFD Balb/c mice before and after 2 weeks of administration at $P < 0.05$.)

No	Non-diabetic Control Group		Diabetic Control Group		Diabetic mice + Metformin (200 mg/kg)		PMFD (200 mg/kg)		PMFD (400 mg/kg)		PMFD (600 mg/kg)	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	13.88±*	12.03±0.04*	24.38±0.31*	27.46±0.28	13.98±0.28*	15.41±0.32*	23.24±0.33*	20.21±0.14*	20.77±0.32*	18.09±0.13*	27.72±0.35*	19.54±0.35
2	17.99±0.00*	19.95±0.07*	18.37±0.16*	28.54±0.33	19.04±0.07*	19.93±0.09*	22.96±0.05*	19.92±0.1*	19.32±0.26*	18.17±0.23*	28.09±0.31*	20.77±0.31
3	13.97±0.03*	21.07±0.26*	19.72±0.17*	26.41±0.12	16.54±0.25*	15.03±0.04*	19.83±1.170*	14.96±0.04*	32.93±0.09*	28.9±0.15*	21.89±0.15*	19.82±0.24

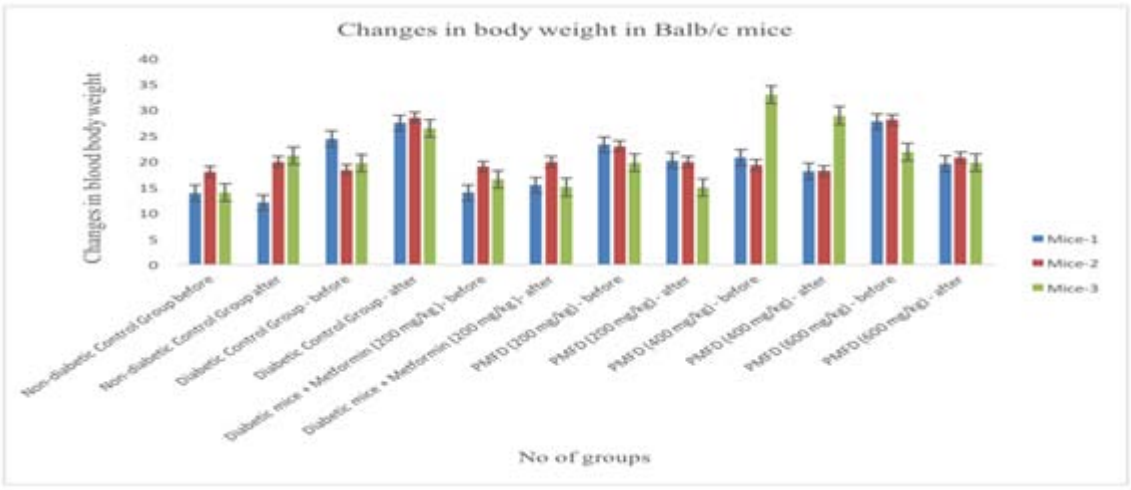

Figure 5: Comparison of change in body weight in STZ-induced Balb/c mice a before and after 2 weeks of PMFD treatment .

5. Discussion

Diabetes is a metabolic disorder and major global health problem worldwide. As per evaluation, one person is detected with diabetes every five second in the world whereas one patient dies of in every 10 second (Colagiuri, 2010). Most of prophetic plants contain carotenoids, flavonoids, terpenoids, alkaloids, glycosides and can often have anti-diabetic effects (Afrisham et al., 2015). Numerous studies have substantiated the beneficial effects of medicinal herbs for controlling glycaemicstatus (Campbell-Tofte et al., 2012; Abdelwahab et al., 2013; El-Abhar & Schaalar, 2014). Scientific evaluation of Prophetic medicine recommended for the management of diabetes is lacking. We designed a study to evaluate a formulation of Prophetic medicine for the reduction of blood glucose levels to the significantly lower levels. Our investigation demonstrated that this innovative formulation of Prophetic medicine effectively reduced blood glucose levels (post prandial and random blood glucose levels as well). From our investigation, we found that diabetic mice treated with PMFD at the doses of 200, 400 and 600 mg/kg body weight significantly reduced plasma glucose levels on first day at 3 hours (Table 3), second and third day at 2 hours after treatment of diabetic mice (Table 4 and 5) and after 2 weeks (Table 6) . Metformin as a positive control also reduced plasma glucose levels .The levels of glucose reduction by (PMFD) were strongly comparable with metformin group or higher than that of metformin group reduction. But in case of the diabetic untreated group, the glucose levels were increased in each time of 2, 3 days and 2 weeks after treatment. This indicates that in case of normal diabetes mice, the condition of diabetes was deteriorated with the increasing of glucose levels without treatment. This proves the effectiveness of (PMFD) as it could effectively control

the diabetic disease status with effective control of blood glucose levels in the treated group.

Many similar previous studies have shown that cinnamon, black seed, olive leaves and ginger had effects for treatment of diabetes. The therapeutic potentials of α-lipoic acid (α-LA), L-carnitine and *N. sativa* or combination of them in carbohydrate and lipid metabolism was evaluated in a rat model of diabetes which was induced by single *i.p.* injection of streptozocin (STZ) 65 mg/kg. For evaluation of glucose metabolism, fasting blood glucose, insulin, insulin sensitivity, HOMA, C-peptide, and pyruvate dehydrogenase activity were determined. Either α-LA or *N. sativa* significantly reduced the elevated blood glucose level. The combination of 3 compounds significantly increased the level of insulin and C-peptide. Combination of α-LA, L-carnitine and *N. sativa* will contribute significantly in improvement of the carbohydrate metabolism in diabetic rats, thus increasing the rate of success in management of DM (Salama, 2011). The stretpozotocin induced diabetic in rat model has demonstrated the ability of cinnamon to normalize glucose metabolism, lipid abnormalities and weight changes associated with diabetes. Most of the trials on animal studies showed the ability of cinnamon to reduce FPG, postprandial glucose and or HbA1c (Subash Babu et al., 2007; Anand et al., 2010; Shihabudeen et al., 2011). Previous study used cinnamaldehyde extracted from *Cinnamomum zeylanicum* to demonstrate a significant reduction of plasma glucose and HbA1c levels in streptozotcin induced diabetic rats. This study was carried out to isolate and identify the putative anti-diabetic compounds based on bioassay-guided fractionation. Cinnamaldehyde thus isolated was orally fed to diabetic rats, which caused significant reduction of plasma glucose and increased insulin levels. The authors concluded that cinnamaldehyde is responsible for increasing insulin secretion from pancreatic β cells and thus ameliorating glucose levels (Subash Babu et al., 2007).

Succeeding studies evidenced a strong link of the antidiabetic action with the antioxidant effects of Oleuropin (OL). By treating alloxan-diabetic rabbits with OL, Al-Azzawie and Alhamdani obtained a significant hypoglycemic effect as compared with diabetic control animals, associated with restoration of the levels of malondialdehyde and most of the enzymatic and non-enzymatic endogenous antioxidants (AL-Azzawie & Alhamdani, 2006). An important finding based on in STZ treated type 1 diabetic rat model reported that, oral administration of ethanolic extract of ginger significantly decrease fasting blood glucose level (Ojewole, 2006). Our study showed that with diabetic mice treatment with PMFD significantly reduces the glucose levels after 3 hours, 2 hours and two weeks of time duration at different concentration of doses.

6. Conclusion

From this study, it can be concluded that the formulation of Prophetic medicine PMFD significantly reduced the plasma glucose levels in STZ induced diabetic mice without major side-effects. This result proves that diabetic mice treated with PMFD was significantly able to reduce fasting plasma glucose FPG and post-prandial blood glucose PPBG levels. The outcomes from this study could be contribute for the management of plasma blood glucose of STZ- induced diabetic Balb/c mice or minimizing the side-effects of diabetic medication. Thus, it can be used as a raw data for manufacturing new drug for the effective management of diabetes improving the quality of life for diabetic patients. Development of new medications from natural sources especially from Prophetic medicine sources will be very useful as can ensure the long-term affectivity of antidiabetic drugs, minimizing or diminishing apparent side-effects.

7. Recommendations and Further Studies

Based on the findings of this study the following recommendations are suggested:

The formulation of Prophetic medicine (PMFD) can be used for the management of diabetes. However, further *in vivo* studies to assess the active of the formulation on insulin, lipids, HbA1c levels may confirm its therapeutic effectiveness. Besides, clinical studies of this formulation on diabetic patients for long period are also recommended. The present study on formulation of Prophetic medicine can be recommended for the prevention and treatment of diabetes.

References

[1] Al-Azzawie, H. F., & Alhamdani, M. S. (2006). Hypoglycemic and antioxidant effect of oleuropein in alloxan-diabetic rabbits. Life Sci. 78:1371–1377.
[2] Abdelwahab, S. I., Sheikh, B.Y., Taha, M. M. E., How, C. W., Abdullah R., Yagoub, U., et al. (2013). Thymoquinone-loaded nanostructured lipid carriers: preparation, gastroprotection, in vitro toxicity, and pharmacokinetic properties after extravascular administration. Int J Nanomedicine. p. 2163.
[3] Afrisham, R., Aberomand, M., Ghaffari, M.A., Siahpoosh, A., & Jamalan, M. (2015). Inhibitory Effect of Heracleum persicum and Ziziphus jujuba on Activity of Alpha-Amylase. Journal of Botany. 1–8.
[4] Atkins, R. C., & Zimmet, P. (2010). Diabetic kidney disease: Act now or pay later. Saudi J Kidney Dis Transpl. 21:217-21.
[5] Anand, P., Murali, K., Tandon, V., Murthy, P. S., & Chandra, R. (2010). Insulinotropic effect of cinnamaldehyde on transcriptional regulation of pyruvate kinase, phosphoenolpyruvate carboxykinase, and GLUT4 translocation in experimental diabetic rats. Chemico-Biolog Interact. 186:72–81.
[6] Ballester, J., Munoz, M. C., Dominguez, J., Rigau, T., Guinovart, J. J., & Rodriguez-Gil, J. E. (2004). Insulin-dependent Diabetes Affects Testicular Function by FSH- and LH-Linked Mechanism. J. Androl. 25: 706-719.
[7] Campbell-Tofte, J.I., Mølgaard, P., & Winther, K. (2012). Harnessing the potential clinical use of medicinal plants as anti-diabetic agents. Bot Targets

Ther. 2 pp. 7–19.
[8] Colagiuri, R. (2010). Diabetes: A pandemic, a development issue or both? Expert Rev Cardiovasc Ther. 8: 305-9.
[9] Cassidy, F., Ahearn, E., & Carroll, J. (1999). Elevated frequency of diabetes mellitus in hospitalized manic-depressive patients. Am J Psychiatry.156(9): 1417-1420.
[10] El-Abhar, H. S., & Schaalan, M. F. (2014). Phytotherapy in diabetes: review on potential mechanistic perspectives. World J Diabetes. 5.p. 176.
[11] Kaneto, H. (2015). Pancreatic b-cell glucose toxicity in type 2 diabetes mellitus. Curr Diabetes Rev. 11:26.
[12] Mosley, A.L., Corbett, J.A., & O¨ zcan, S. (2013). Glucose regulation of insulin gene expression requires the recruitment of p300 by the b-cell-specific transcription factor Pdx-1. Mol Endocrinol.22,39-44.
[13] Ojewole, J.A.O. (2006). Analgesic, anti-inflammatory and hypoglycaemic effects of ethanol extract of Zingiber officinale (Roscoe) rhizomes (Zingiberaceae) in mice and rats. Phytother Res. 20: 764-77.
[14] Subash Babu, P., Prabuseenivasan, S., & Ignacimuth, S. (2007). Cinnamaldehyde-A potential antidiabetic agent. Phytomedcine. 14:15–22.
[15] Shihabudeen, M. S., Hansi Priscilla, D., & Thirumurugan, K. (2011). Cinnamon extract inhibits alpha-lucosidase and dampens posprandial glucose excursions in diabetic rats. Nutr Metab (Lond), 8:46.
[16] Subash Babu, P., Prabuseenivasan, S., & Ignacimuthu, S. (2007). Cinnamaldehyde--a potential antidiabetic agent. Phytomedicine. 14(1):15–22.
[17] Salama, R. H. (2011). Hypoglycemic effect of lipoic acid, carnitine and Nigella sativa in diabetic rat model. Int J Health Sci (Qassim). 5(2):126–134.

Author Profile

Eman Elaswed, received the (higher professional diploma) degrees in Branch of Medical Analysis from The higher Institute for medical Professions at AlJMAIL in the academic year 2009/2010. She pursued study for the Master's degree in Biotechnology in the Department of Biotechnology in Lincoln University College, Malaysia, and this paper is part of her thesis results in Biotechnology.