Evaluation and comparison of blood glucose lowering material from different parts of the mango (leaf, peel, fruit)

Susan Khosroyar[1]*, Tahmineh Hasanzadeh[1], Farzad Kaj[2]

[1]*Department of Chemical Engineering, Quchan Branch, Islamic Azad University, Quchan, Iran.*
[2]*Department of Agriculture and Environmental Enginnering, Rostock University, Rostock, Deutschland.*

***Corresponding author:** susankhosroyar@yahoo.com

Original Research

Abstract:

Diabetes mellitus is a common disease that currently affects more than 3 million people in Iran. Many years ago, medicinal herbs have been used to treat many diseases. In this study, the evaluation and comparison of blood glucose lowering agents from different parts of mango (leaf, peel, and fruit) was studied. In this experimental study, 30 adult male rats weighing 220-250 gr of Wistar were selected and randomly divided into 5 case, control, diabetic controls. In diabetic and control groups, streptozotine (55 mg / kg) was injected intraperitoneally to produce diabetes. Then the case groups received mango leaves, fruit and skin (400 mg / kg) for 30 day and orally. The consumption of aqueous extract of mango leaves, fruit and skin in the case group was significantly reduced compared to the control group of diabetic patients. the antidiabetic effect of mangiferin possess antidiabetic activity against stz-induced diabetic rats. This current research affirms prominent cytotoxic and moderate hypoglycemic potential of M. indica . Further bioactivity guided isolation of phytoconstituents and investigation on higher animals can lead to development of new drug molecules.

1. Introduction

Diabetes mellitus is a systemic disease characterized slightly higher (79 kcal per 100 g) [1]. The mango leaves by abnormal metabolic regulation of glucose, resulting in have powerful antioxidant properties as it has high hyperglycemia. The standard method of inducing diabetes flavonoids and phenol contents. Nowadays, most of in animal models is with alloxan, a toxic glucose analogue, researches and investigations have been carried out to which selectively destroys insulin-producing (beta) cells find out the benefits of mango leaves as soon as it in the pancreas when administered to rodents this contains valuable polyphenolic compounds. The amounts causes an insulin-dependent diabetes mellitus called of the different polyphenolic compounds in the mango "stz" in these animals [2–4]. As traditional medicine, the use of plant for the treatment of different diseases has been going on since the dawn of human history,

owing to the presence of different phytoconstituents. These phytoconstituents, also known as secondary metabolites, are a huge source of molecules with outstanding diversity which helps to continue the drug discovery process [5, 6]. Mangifera indica (M. indica) is a large spreading evergreen tree which belongs to the family Anacardiaceae. This plant is indigenous in India and Myanmar. Apart from its application as food, the different parts of this plant possess different activities. For example, the bark is well known for its use in the treatment of diarrhea; ripe fruit is used to treat habitual constipation; the seeds are used as astringent to the bowels and leaves are used to treat piles [7, 8]. The mango leaves have powerful antioxidant properties as it has high flavonoids and phenol contents. Nowadays, most of researches and investigations have been carried out to find out the benefits of mango leaves as soon as it contains valuable polyphenolic compounds. The amounts of the different polyphenolic compounds in the mango vary from

part to part (pulp, peel, seed, bark, leaf and flower) with most polyphenols being found in all the parts [2, 9]. Like other pharmacological activities, the hypoglycemic activity is also exhibited by medicinal plants, and glucose tolerance test is usually done for the hypoglycemic activity. It is a therapeutic test where glucose is given followed by testing the blood to determine the time it takes to be cleared from the blood. The test is typically used to test for diabetes, insulin resistance, reactive hypoglycemia and rarer issue of starch digestion system.

There have also been manyreported bioactivities like antioxidant, immunomodulatory, antiinflammatory, anti-allergic, antiviral, antibacterial, antifungal and monoamine oxidase inhibitory activities of this plant [7–11]. In this current research, the objectives were to prepare methanolic extract of the peels of M. indica and analyze its cytotoxic and hypoglycemic effects. In modern medicine, there is no satisfactory ef-fective therapy to cure diabetes mellitus. There have also been many reported bioactivities like antioxidant, immunomodulatory, anti inflammatory, anti-allergic, antiviral, antibacterial, antifungaland monoamine oxidase inhibitory activities of this plant. In this current research, the objectives were to prepare methanolic extract of the peels of M. indica and analyze its cytotoxic and hypoglycemic effects [7–11].The man-agement of diabetes mellitus by insulin therapy, have several drawbacks like insulin resistance and in chronic treatment cause anorexia nervosa, brain atrophy, and fatty liver. The oral hypoglycaemic drugs are sulphony-lureas and biguanide groups have been used in the treatment of diabetes mellitus. The sulfonylureas (e.g., glibenclamide, glipizide) stimu-late the insulin secretion from the existing pancre-atic β cells. Glibenclamide inhibits the adenosine tri phosphate (ATP) sensitive K^+ (KATP) channels in the plasma membrane. This leads to membrane de-polarization, activation of voltage gated Ca^{2+} chan-nels, a rise in cytosolic (Ca^{2+}), and release of the insulin. The streptozotocin (STZ)-induced diabetes is treated by gilbenclamide and used as a standard drug to compare the antidiabetic activity of various compounds. Ethnobotanical information indicates that more than 800 plants are used as traditional remedies for the treatment of diabetes,but many plants do not have a scientific scruting. Herbal medicines are used for primary health care, by about 80% of the world population particularly in the developing countries, because of better cultural acceptability, safety, efficacy, potent, inexpensive, and lesser side effects.The plant drugs are frequently considered to be less toxic when compared to synthetic drugs. More than 1123 plant species have been used to treat diabetes and more than 200 pure compounds have showed, lowering blood glucose activity [1, 3, 4, 7, 12, 13].

2. Materials and methods

2.1 Materials

2.1.1 Chemical materials

The analytical graded chemicals were used for all the experiments. The STZ was purchased from Sigma Chemicals, St. Louis, MO, U.S.A.

2.1.2 Plant material

Mangifera indica Mango fruit, M. indica, and its leaf was bought from the market of fruits and vegetables in Mashhad in March 2017 and was transferred to the laboratory for preparation and continuation of the testing process.

2.1.3 Experimental animal

Male Wistar albino rats (220–250 g) were procured from Ferdowsi University of Faculty of Medicine mashhad, Iran and were housed in polycarbonate cages in an animal room with 12 hr day-night cycle at tem-perature of 22 ± 2 °C and humidity of 45–60%. They were fed with commercial pelleted rats chow and free access water during the experiment.

The blood glucose level of 30 Wistar rats was measured and blood samples were taken from the tail by the Easy Gluco device before streptozotocin injection. The rats were randomly assigned into 5 groups with 5 members. The members of each group were labeled with picric acid in different areas of the body.[6]
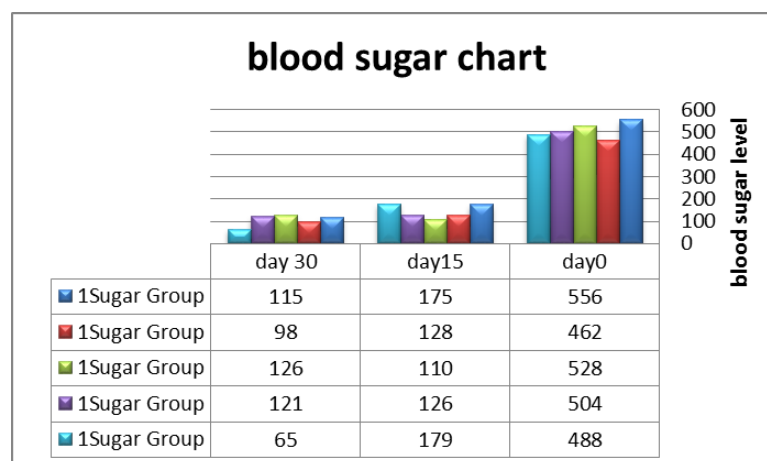

	day 30	day15	day0
■ 1Sugar Group	115	175	556
■ 1Sugar Group	98	128	462
■ 1Sugar Group	126	110	528
■ 1Sugar Group	121	126	504
■ 1Sugar Group	65	179	488

Diagram 1. For the treatment of this group, the amount of 400 mg / kg of mango skin (peel) extract was mixed with 0.5 cc distilled water twice, and then fed to mice in gavage.
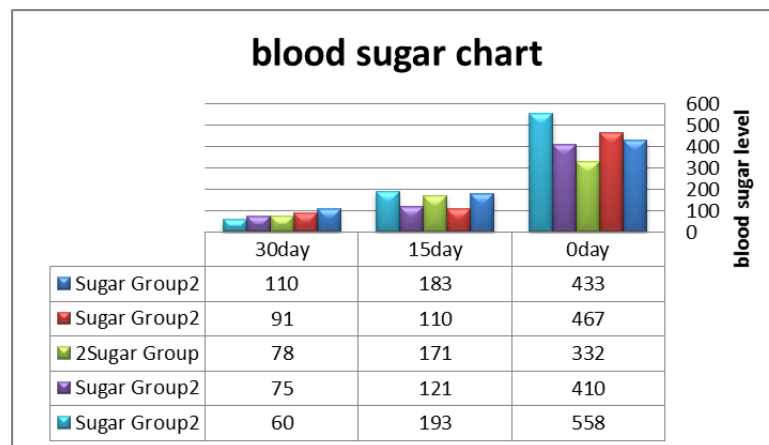
blood sugar chart

	30day	15day	0day
Sugar Group2	110	183	433
Sugar Group2	91	110	467
2Sugar Group	78	171	332
Sugar Group2	75	121	410
Sugar Group2	60	193	558

Diagram 2. For the treatment of this group, the amount of 400 mg / kg of mango leaf extract with 0.5 cc distilled water was mixed twice and then served as gavage in rats.

2.2 Methods

2.2.1 Extract preparation

2.2.1.1   Extract preparation of mango leaves

The collected leaves were approved by the Ferdowsi University of Mashhad. New mango leaves were collected from the town of Negun, Assam. Phytochemical quality initial experiments were carried out using coloring and precipitation of chemical reaction on ethanolic extract of leaves. For the extraction of ethanolic leaves, fresh leaves for about 2 weeks were dried at about 32 °C (room temperature).

The amount of 100 grams of mango leaves was minced by a mill (Model PX-MFC 90 D), and poured into 2000 ml of eagle and 1000 ml of 96% ethanol was added to it and extracted for 6 hours by a Soxhlet apparatus. After the mentioned time, a solid and liquid phase was separated by the Buchner funnel and the vacuum pump (FJ model). The separated liquid phase, containing solvent and extract, was condensed with a rotary evaporator (Hbcontrol model) at 50 °C and vacuum 50 milligrams and the solvent was removed as far as possible.

Compared to the practice of Chandra and Hazarika (2012)[2], an attempt was made to investigate the antidiabetic effect of mango leaf extract on albino mice, and conducted phytochemical experiments with an ethanolic extract of mango leaves. Albino mice were treated with ethanolic extract at 100, 200 and 400 mg / kg body weight. Another group of diabetic rats was treated as a standard insulin hypoglycemic drug. Blood glucose levels were monitored for different groups at different times. A significant decrease in blood glucose levels was observed after four hours of extract of leaf extract at 200 mg / kg. This suggests that mango leaves have almost the same strength with insulin in reducing blood glucose and significantly reduces it [2, 14].

2.2.1.2   Extract preparation of mango peel

Mango M indica was purchased from the fruit market in Mashhad and confirmed by the Ferdowsi University of Mashhad's botanical group. The yellow skin of the mangoes is isolated and then thoroughly washed with water and dried for one week at room temperature for sterilization to convert it to a powder using a mill.The amount of 100 g of skin was
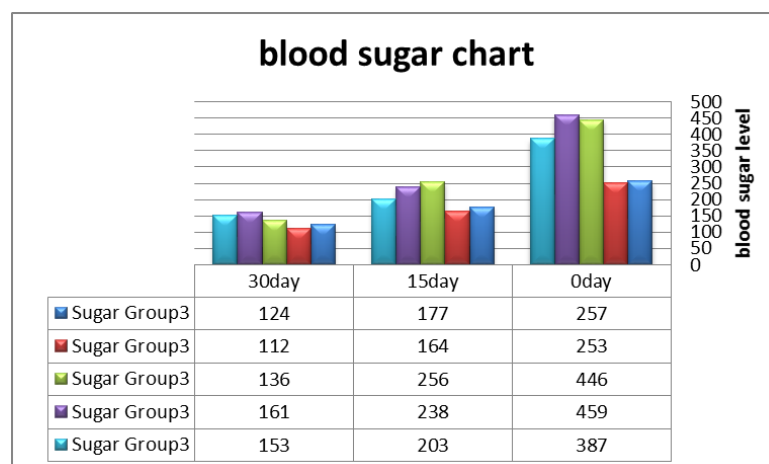
blood sugar chart

	30day	15day	0day
Sugar Group3	124	177	257
Sugar Group3	112	164	253
Sugar Group3	136	256	446
Sugar Group3	161	238	459
Sugar Group3	153	203	387

Diagram 3. For treatment of this group, 400 mg / kg of mango powder was mixed with 0.5 cc distilled water twice, and then fed to mice in gavage.
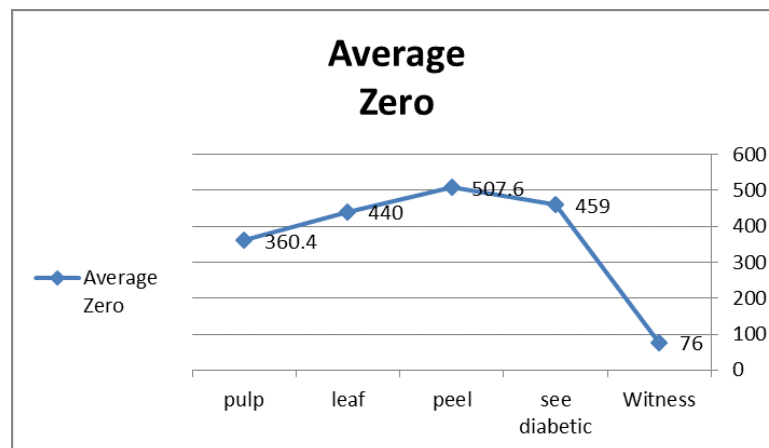
Diagram 4. Blood glucose average of all tested groups before intervention.

milled by the mill (model PX-MFC 90 D) and added to the 2000 ml of eagle and 1000 ml of 96% ethanol was added and extracted for 6 hours by the Soxhlet apparatus and after The time elapsed with the aid of the Buchner funnel and the vacuum pump (FJ model) was separated from the solid and liquid phase. The separated liquid phase, containing solvent and extract, was condensed with a rotary evaporator (Hbcontrol model) at 50 °C and vacuum 50 milligrams and the solvent was removed as far as possible [9].

Compared to the practice of Streptozotocin treatment caused significant weight reduction in rats as compared to the vehicle treated normal rats at day 30 of injection (163.33 ± 10.54 g versus206.67 ± 13.18 g). However, the chronic treatment of mangiferin (10 and 20 mg/kg, i.p.) for 28 days significantly(P < 0.05) restored the body weight loss as compared to the vehicle treated diabetic control rats observed at the end of 28 days of treatment period (191.67 ± 15.35 g and 200 ± 10.72 g versus 130 ± 5.16 g, respectively). However, the standard drug insulin (6 U/kg, i.p.) also exhibited significant improvement in body weight loss of the diabetic animals following 28 days of treatment (196.67 ± 8.37 versus 130 ± 5.16). Streptozotocin treatment resulted in significant elevation of plasma glucose, triglycerides, total cholesterol, LDL-C and reduction in HDL-C levels as compared to the normal control rats as

noted at different periods of the study . The chronic administration of mangiferin (10 and 20 mg/kg, i.p.) resulted in significant (P < 0.05) reduction in plasma glucose level at different periods in the experimental duration of 28 days in STZ-diabetic rats with the maximum percent reduction of plasma glucose being 49.77 and 51.89, respectively on 28th day of treatment. However, the standard drug insulin (6 U/kg, i.p.) exhibited significant and more potent antidiabetic activity with maximum percent reduction of plasma glucose 67.54 on 28th day as compared to the diabetic control group [7–9, 15].

2.2.1.3   Preparation of mango pulp powder

Angica fruit M indica was purchased from the fruit market in Mashhad and confirmed by the botanical group Ferdowsi University of Mashhad. It was washed, peeled, and cut into pieces of about 3 × 3 cm and dried at 55 to 60 °C. Dried specimens in the PX-MFC 90 D grinding mill are used to prepare flour crushed [16].

2.2.2 Induction of experimental diabetes

Diabetes was induced by administering intraperitonial injection of a freshly prepared solution of STZ (55 mg/kg of body weight) in 0.1 M cold citrate buffer (pH 4.5) to the over night fasted rats. Because of the instability of STZ
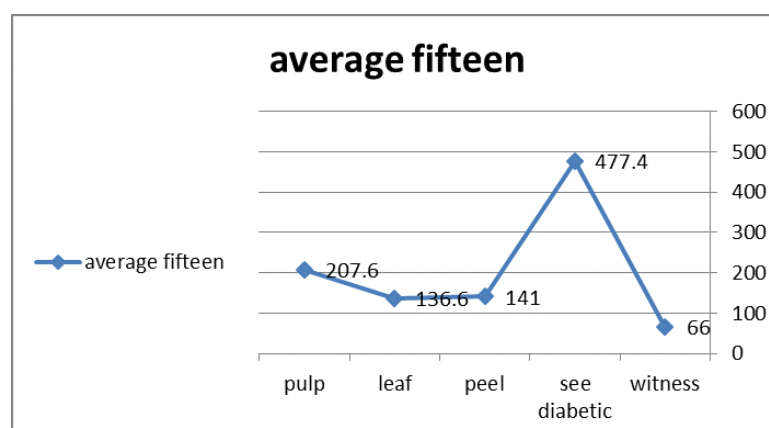

Diagram 5. Average blood glucose of all tested groups 15 days after intervention.

Table 1. Designing a test based on variables.

at	repeat	the plant (in code)	treatment groups
1	mice with a colored part on the left side	1	healthy witness
2	mice with the colored part on the right side	1	healthy witness
3	mice with a colored part in the head	1	healthy witness
4	mice with a colorful part in the tail	1	healthy witness
5	the mouse has no colored part	1	healthy witness
1	mice with a colored part on the left side	2	see diabetic
2	mice with the colored part on the right side	2	see diabetic
3	mice with a colored part in the head	2	see diabetic
4	mice with a colorful part in the tail	2	see diabetic
5	the mouse has no colored part	2	see diabetic
1	mice with a colored part on the left side	3	extract of the skin
2	mice with the colored part on the right side	3	extract of the skin
3	mice with a colored part in the head	3	extract of the skin
4	mice with a colorful part in the tail	3	extract of the skin
5	the mouse has no colored part	3	extract of the skin
1	mice with a colored part on the left side	4	leaf extract
2	mice with the colored part on the right side	4	leaf extract
3	mice with a colored part in the head	4	leaf extract
4	mice with a colorful part in the tail	4	leaf extract
5	the mouse has no colored part	4	leaf extract
1	mice with a colored part on the left side	5	pulp
2	mice with the colored part on the right side	5	pulp
3	mice with a colored part in the head	5	pulp
4	mice with a colorful part in the tail	5	pulp
5	the mouse has no colored part	5	pulp

in aqueous media, the solution is made using cold citrate buffer (pH 4.5) immediately before administration. Control rats were injected with citrate buffer alone. The rats were allowed to drink 5% glucose solution overnight to overcome the drug-induced hypoglycemia. The blood glucose values above 250 mg/dl on the third day after STZ injection, were considered as diabetic rats. Then the treatment was started on the fifth day after STZ injection and it was considered as first day of treatment [16, 17].

2.2.3 Treatment of diabetic rats

2.2.3.1 Treatment of the first group with extract of mango peel

For the treatment of this group, 400 mg / kg weight, 0.5 cc distilled water was mixed twice, and was fed to streptozotocin-induced diabetic rats by oral gavage daily. This procedure continued for 30 days. Blood sampling was performed once before treatment (time zero) once a day 15 days after treatment and the last blood collection was performed 30 days after treatment (Diagram 1) [7–9, 15].

2.2.3.2 Treatment of the second group with the extract of mango leaves

To treat this group, the amount of 400 mg / kg of mango leaves extract was mixed with 0.5 cc distilled water and then fed to mice for gavage. This action lasted for 30 days. The blood samples were taken one time before treatment (time zero) once a day, 15 days after treatment, and the last

blood sample was taken 30 days after treatment. (Diagram 2) [2, 14].

2.2.3.3 Treating the third group with mango fruit (pulp)

To treat this group, 400 mg / kg of mango powder with 0.5 cc distilled water was mixed twice and then was fed to mice in gavage. This action lasted for 30 days. The blood samples were taken one time before treatment (time zero) once a day 15 days after treatment and the last blood collection was also performed 30 days after treatment. (Diagram 3) [7, 8, 11, 16, 18].

2.2.4 Comparison of three treatment groups with diabetic control and positive control group

2.2.4.1 Statistical analysis method

In order to analyze the data, a factorial design was used. The results from different parts of the plant were compared by ANOVA ANOVA using oneway method. The design of the test for independent variables includes different parts of the plant and the different mice in Table 1.

3. Results

3.1 Design of the factorial model

To investigate the relationship between the obtained results and the process variables, then the comparison of the results obtained with the MSTC software was used.
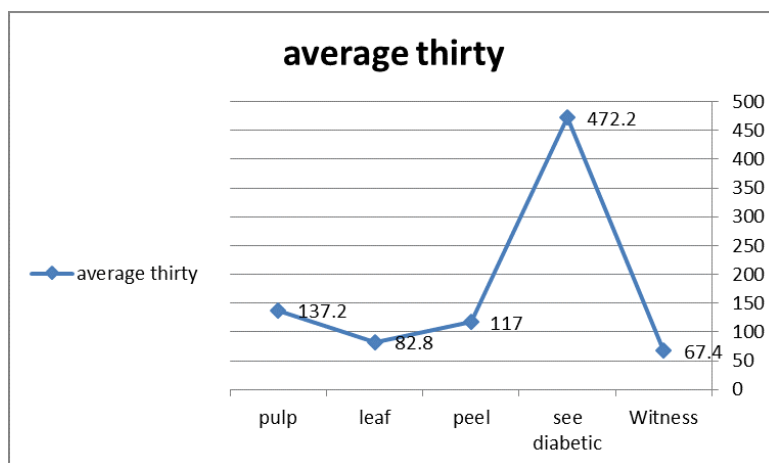
Diagram 6. Average blood glucose in all tested groups 30 days after intervention.

3.2 Statistical analysis of selected model

In order to evaluate the validity of fitted models, fit fitness weakness, coefficient of variation, values of R^2, R^2 (adj) were determined. The most important part of the statistical analysis table in the analysis section of variances is the Lack of Fit parameter and the statistic is a suitable model for which its fit fitness test is not meaningful, this parameter indicates the suitability or inappropriateness of the model and If it is less than 0.05, then the model should generally be discarded [19]. Also, for a good fit model, the R-Squared and Adj R-Squared values should be closer to 1.

3.3 Comparison of blood glucose levels after treatment with different parts of the mango

In this study, the effect of oral administration of leaf extract,peel, and mango fruit on the blood sugar of diabetic rats was evaluated and evaluated with healthy control group and diabetic group. The results of blood glucose measurement after 72 hours of streptozotocin injection in groups 2 to 5 showed that except for the healthy control group (group 1), all samples from groups 2 to 5 were infected with diabetes mellitus. Accordingly, one-way ANOVA test showed that there is a significant difference between blood sugar levels in the healthy control group and other groups ($P \leqslant 0.01$), which indicates that groups 2 to 5 have diabetes Candy and non-diabetic group 1 cases. (Diagrams 4 to 6). Regarding the changes in blood glucose samples in different groups before the start of treatment until thirty days after treatment, the results showed that the mean blood glucose of the kidneys in the three times before intervention, fifteen days after intervention and thirty days There was a significant difference between the two groups after intervention ($P < 0.01$) (Diagram 7).

3.4 Comparison of test results with control samples

The results of this study compared with the control and diabetic type showed that blood glucose in groups 2 to 5 was significantly decreased ($P < 0.01$), but the highest decrease was related to the group treated with mango leaf extract.
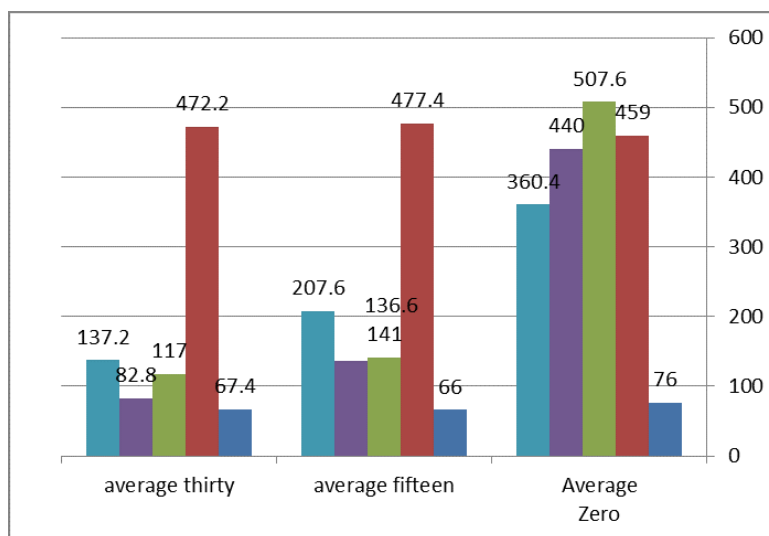

Diagram 7. Comparison of mean blood sugar of all groups in 3 times before intervention, 15 days and 30 days after treatment intervention.

4. Conclusion

Owing to the reported antidiabetic and hypolipidemic properties of mangiferin, a xanthone-C-glucoside in noninsulin dependent KK/Ay mice with hyperinsulinemia, the present study was carried out in an attempt to elucidate its effects on hyperglycemia and atherogenesis in STZ-diabetic rats. In the present study, STZ (55 mg/kg, i.v.) produced significant fasting hyperglycemia and body weight loss. Mangiferin showed significant and consistent reduction in fasting blood glucose levels and also significantly improved the body weight loss at different intervals throughout the period of experiment as compared to the vehicle treated diabetic controls indicating its potent antidiabetic activity. In our previous study, we showed that the chronic treatment of mangiferin(400 mg/kg, i.p.) caused significant as well as moderate reduction in the glycosylated hemoglobin levels in STZdiabetic rats further substantiating its potential in the long term glycemic control of diabetes mellitus [20]. Since STZ (55 mg/kg, i.v.) effectively destroys pancreatic cells and causes persistent hyperglycemia, the mechanism of antidiabetic action of mangiferin might involve actions other than pancreatic cells insulin release/secretion(insulinotropic effect), i.e. possibly through other extrapancreatic actions in these STZ-diabetic rats [21, 22]. The extrapancreatic actions perhaps might include the stimulation of peripheral glucose utilization or enhancing glycolytic and glycogenic processes with concomitant decrease in glycogenolysis and gluconeogenesis [23]. Furthermore, it is also likely that it might reduce blood glucose level by inhibiting the glucose absorption from the intestine. The latter hypothesis could be supported by the recent findings that mangiferin inhibits glucosidase enzymes (sucrase, isomaltase, maltase) [24] which are involved in the digestion of carbohydrate into simple sugars in the gut leading to delay or inhibition of carbohydrate breakdown and subsequent glucose absorption from the intestine [25]. Although, in the present study mangiferin was administered intraperitoneally, the inhibition of -glucosidase enzymes by the mangiferin excreted through bile into gut, i.e. through enterohepatic circulation cannot be ruled out. Also, in our preliminary investigation, we found that both the single and chronic administration of mangiferin did not have any significant effect on the basal fasting plasma glucose level in normal rats (data not shown). Nevertheless, chronic administration of mangiferin (400 mg/kg, i.p.) significantly improved oral glucose tolerance in glucose-loaded normal rats indicating its potent antihyperglycemic activity. This result is in accordance with the previous results conducted with the aqueous extract of Mangifera indica leaves further suggesting that the active principle, mangiferin might be responsible for the glucose lowering action on oral glucose tolerance test [18]. These evidences tempt us to speculate that apart from the aforementioned probable insulin independent extrapancreatic actions, the other possible pancreatic mechanism, i.e. stimulating insulin release from the pancreatic cells might contribute in improving oral glucose tolerance in the glucose-loaded normal rats. Taken together, it can be summarized as mangiferin might possess both pancreatic and extrapancreatic mechanisms in its antidiabetic action and such apparent dual pancreatic and extrapancreatic actions of mangiferin would be more advantageous to the existing oral antidiabetic monotherapy. In our study, STZ (55 mg/kg, i.p.) treated diabetic rats exhibited clear-cut abnormalities in lipid metabolism as evidenced from the significant elevation of plasma total cholesterol, triglycerides, LDL-C, atherogenic index and reduction of HDL-C levels. Treatment with mangiferin (10 and20 mg/kg, i.p.) for 30days significantly and greatly reduced plasma total cholesterol, TG and LDL-C associated with concomitant significant increase in HDL-C levels and decrease in atherogenic index in diabetic rats indicating its potent antihyperlipidemic and antiatherogenic activity. The glucose lowering action of the mangiferin can be due to the consequence of an improved lipid metabolism apart from the direct interaction with glucose homeostasis. The triglycerides lowering property of mangiferin could indirectly contribute to the over all antihyperglycemic activity through a mechanism of socalled glucose–fatty acid cycle [26]. mangiferin (400 mg/kg, i.p.) at the dose tested exhibits potent antidiabetic, anti hyperlipidemicand anti atherogenic activities in STZ-diabetic rats and also shows the improvement in oral glucose tolerance in glucose-loaded normal rats without inducing hypoglycemic state. The agent with these multiple advantageous properties viz., antidiabetic, antihyperlipidemic, antiatherogenic and antioxidant properties without causing hypoglycemia would be of greater therapeutic benefit in the management of DM associated with abnormalities in lipid profiles and merits further detailed investigation to find out its mechanism of action and to establish its therapeutic potential in the treatment of diabetes and diabetic complications. In spite of the better effect of mango leaves on blood glucose than peanut extract and mango, they can only be used as a supplement to common anti-diabetes medications. Also, herbal medicine may not only have a better effect on blood glucose control But rather likely to cause drug interactions and impacts. Mango leaves are well controlled by sugar levels. While research has proved its harmlessness, it is best to consult a physician before deciding on the amount of Mango.

The results emphasize that, despite the better effects of manganese leaf extract on blood glucose than mango peel extract, it can only be used as a supplement to common anti-diabetes medications. Also, in light of the results, it is suggested that more research into drug interactions be used to treat anti-diabetic herbal medicines.

paper.

Availability of Data and Materials
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interests
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Open Access
This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the OICCPress publisher. To view a copy of this license, visit https://creativecommons.org/licenses/by/4.0.

References

[1] G. Williams and J.C. Pickup. Book: Handbook of diabetes. *Wiley-Blackwell, Oxford*, **3**rd **ed**, 2004.

[2] P.C. Sarmah and R. Hazarika. Evaluation of hypoglycemic effect of mangifera leaf. *International Journal of Applied Biology and Pharmaceutical Technology*, **55**:114–120, 2012.

[3] S. Kumar, S. Narwal, V. Kumar, and O. Prakash. A-glucosidase inhibitors from plants: A natural approach to treat diabetes. *Pharmacogn Rev*, **5**:19–29, 2011.

[4] X. Hu, S. Wang, J. Xu, D.B. Wang, Y. Chen, and G.Z. Yang. Triterpenoid saponins from stauntonia chinensis ameliorate insulin resistance via the amp-activated protein kinase and ir/ irs1/pi3k/akt pathways in insulin-resistant hepg2 cells. *Int J Mol Sci*, **15**(6): 10446–58, 2014.

[5] C.N. Kunyanga, J.K. Imungi, M. Okoth, C. Momanyi, H.K. Biesalski, and V. Vadivel. Antioxidant and antidiabetic properties of condensed tannins in acetonic extract of selected raw and processed indigenous food ingredients from kenya. *J Food Sci*, **76**:C560–7, 2011.

[6] S. Khosroyar and S. Ghofranpour. The effect of walnut oil, septum and leaves aqueous extract in

alloxan-induced diabetic rats. *International Journal of PharmTech/ International Journal of ChemTech Research*, **10**(2/3), 2017.

[7] S. Muruganandan, K. Srinivasan, S. Gupta, P.K. Gupta, and J. Lala. Effect of mangiferin on hyperglycemia and atherogenicity in streptozotocin diabetic rats. *Journal of Ethnopharmacology*, **97**:497–501, 2005.

[8] S.S. Periyar, P.S. Sellamuthu, P.M. Balu, and B.P. Muniappan. Antihyperglycemic effect of mangiferin in streptozotocin induced diabetic rats. *Journal of Health Science*, **55**(2):206–214, 2009.

[9] S. Chowdhury, S.K. Poddar, S. Zaheen, F.A. Noor, N. Ahmed, S. Haque, A. Sukul, S.B. Sunjida, M.U. Mazumder, and N. Akbar. Phytochemical screening and evaluation of cytotoxic and hypoglycemic properties of mangifera indica peels. *Asian Pac J Trop Biomed*, **7**(1):49–52, 2017.

[10] C.M.P. Gourgue, M.M.J. Champ, Y. Lozano, and J.D. Laval. Dietary fiber from mango byproducts: Characterization and hypoglycemic effets determined by in vitro methods. *J Agric Food Chem*, **40**:1864–1868, 1992.

[11] A.O. Aderibigbe, T.S. Emudianughe, and B.A. Lowal. Antihyperglycemic effect of mangifera indica in rat. *Phytotherapy Research*, **13**:504–507, 1999.

[12] I. Torsdottir, M. Alpsten, G. Holm, A. Sandberg, and J. Tolli. A small dose of soluble alginate – fiber affects postprandial glycemia and gastric emptying in humans with diabetes. *J Nutr*, **121**:795–799, 1991.

[13] P. Bwititi, C.T. Musabayane, and C.F.B. Nhachi. Effects of opuntia megacantha on blood glucose and kidney function in streptozotocin diabetic rats. *Journal of Ethnopharmacology*, **69**:247–252, 2000.

[14] A. Kashyap. Extraction and analysis of mango leaf components and testing. *Helix-the scientific Explorer*, **12**(5):16–20, 2022.

[15] J. Mistry, M. Biswas, S. Sarkar, and S. Ghosh. Antidiabetic activity of mango peel extract and mangiferin in alloxan-induced diabetic rats. *Future Journal of Pharmaceutical Sciences*, **9**:22, 2023.

[16] G.F. Perpétuo and J.M. Salgado. Effect of mango (mangifera indica, l.) ingestion on blood glucose levels of normal and diabetic rats. *Plant Foods for Human Nutrition*, **58**:1–12, 2003.

[17] A. Akbarzadeh, D. Norouzian, M.R. Mehrabi, S.H. Jamshidi, A. Farhangi, A.A. Verdi, S.M.A. Mofidian, and B.L. Rad. Induction of diabetes by streptozotocin in rats. *Indian Journal of Clinical Biochemistry*, **22**: 60–64, 2007.

[18] A.O. Aderibigbe, T.S. Emudianughe, and B.A. Lowal. Evaluation of antidiabetic action of mangifera indica in mice. *Phytotherapy Research*, **15**:456–458, 2001.

[19] A.C. Atkinson and A.N. Donev. Book: Optimum experimental designs. *Oxford University Press, Oxford*, 1992.

[20] S. Muruganandan, S. Gupta, M. Kataria, J. Lal, and P.K. Gupta. Mangiferin protects the streptozotocin-induced oxidative damage to cardiac and renal tissues in rats. *Toxicology Journal*, **176**(3):165–173, 2002.

[21] P. Bwititi, C.T. Musabayane, and C.F.B. Nhachi. Effects of opuntia megacantha on blood glucose and kidney function in streptozotocin diabetic rats. *Journal of Ethnopharmacology*, **69**(3):247–252, 2000.

[22] H. Jouad, M. Eddouks, M.A. Lacaille-Dubois, and B. Lyoussi. Hypoglycaemic effect of spergularia purpurea in normal and streptozotocin-induced diabetic rats. *Journal of Ethnopharmacology*, **71**(1-2):169–177, 2000.

[23] A. Saxena and N.K. Vikram. Role of selected indian plants in management of type 2 diabetes. *The Journal of Alternative and Complementary Medicine*, **10**(2), 2004.

[24] Y. Yoshikawa, E. Ueda, H. Miyake, H. Sakurai, and Y. Kojima. Insulinomimetic bis (maltolato) zinc (ii) complex: Blood glucose normalizing effect in kk-ay mice with type 2 diabetes mellitus. *Biochemical and Biophysical Research Communications Journal*, **281** (5):1190–1193, 2001.

[25] G. Emilien, J.M. Maloteaux, and M. Ponchon. Pharmacological management of diabetes: Recent progress and future perspective in daily drug treatment. *Pharmacology & Therapeutics Journal*, **81**(1):37–51, 1999.

[26] P.J. Randle, P.B. Garland, C.N. Hales, and E.A. Newsholme. The glucose fatty-acid cycle its role in insulin sensitivity and the metabolic disturbances of diabetes mellitus. *The Lancet*, **13**(1(7285)):785–789, 1963.