Antidiabetic and hypolipidemic investigation of *Momordica charantia* and *Azadirachta indica* extract in streptozotocin-induced diabetic albino rats

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Abstract- Diabetes Mellitus is a serious health problem and is characterized by hyperglycemia, caused by the low level of insulin or its abnormal functions. Among various measures to control diabetes, medicinal plants, showing anti-diabetic activity are in great concern to control blood glucose level. Anti-diabetic and

hypolipidemic effects of *Momordica charantia* and *Azadirachta indica* extracts was evaluated in the streptozotocin-induced diabetic male albino rats. Total 30 male Wistar rats were divided randomly into 5 treatment groups (n=6). Diabetes was induced in rats using single dose of Streptozotocin (55mg/kg). Group A was treated as normal and group B was treated as diabetic control. Group C and D were given an extract of *M. charantia* and *A. indica* respectively (100mg/kg BW), whereas, group E was treated with extract of both plants. After 21 days blood samples were collected for the biochemical analysis. The treatment with both plants extracts showed a significant ($p<0.05$) reduction in glucose level and body weight of rats. Similarly, Level of cholesterol, low-density lipoprotein, triglycerides, and very low-density lipoproteins were decreased, whereas, high-density lipoprotein was increased significantly ($p<0.05$) in rats of group E. Extract of both plants showed an effective anti-diabetic and hypolipidemic effects on diabetic rats. A combination of both *Momordica charantia* and *Azadirachta indica* extract can be used for the management of diabetes.

***Index Terms*:** Diabetes mellitus, *Momordica charantia*, *Azadirachta indica*, Anti-diabetic, hypolipidemic

I. INTRODUCTION

Diabetes mellitus is a chronic disorder causing serious health issues and globally increasing day by day (Verma *et al.,* 2018). Among different types of diabetes, Type 1 causes damage to the pancreatic β-cells by auto-reactive immune cells. This damage resulted in the loss of function of islets of Langerhans (Punthakee *et al.,* 2018; Pang *et al.,* 2019). This type affected 5%-10% of all diabetic patients and mostly at the age of 20 years (Gordon *et al.,* 2019). Type 2 diabetes is a multifarious disease, due to the insufficiency of insulin secretions by pancreatic β-cells (Kosteria *et al.,* 2019). Insulin production is insufficient enough to meet the body requirements, thus leading to a hyperglycemic state (Bhowmik *et al.,* 2018). Cortisol (Glucocorticoid) hormones, secreted by the adrenal cortex also play a significant role in the establishment of diabetes. Its elevated level inhibits insulin secretions and hence leads to type 2 diabetes (Elalfy *et al.,* 2019). Anti-diabetic drugs show certain adverse effects on human physiology such as metformin stimulating insulin secretions but also showing other adverse effects. Due to these reasons, traditional remedies are used. According to the World Health Organization (WHO), about 80% of diabetic people are using medicinal plants for treatment (Ostovan *et al.,* 2017). Medicinal plants contain phytochemicals that show anti-glycemic properties (Phimarn *et al.,* 2018).

Momordica charantia also known as bitter melon is a traditional medicinal plant, exhibits hypoglycemic, anti-fungal, anti-parasitic, anti-viral, anti-bacterial, anti-carcinogenic and anti-tumorous properties (Chanda *et al.,* 2019; Fachinan *et al.,* 2017). It contains many chemical compounds like glycosides vicine, karavilosides, charantin, and polypeptide-p that show hypoglycemic effects (Hosseini *et al.,* 2015; Khan *et al.,* 2019). It has been used for the treatment of various diseases like hepatitis, peptic ulcer and diabetes. It has various biochemical and physiological regulating properties like glucose uptake by muscular cells

(Mahwish *et al.,* 2017), suppression of gluconeogenesis and increase in the production of pancreatic β cells in diabetic treatment (Hosseini *et al.,* 2015). It has the capability to regenerate the pancreatic β-cells to stimulate the secretion of insulin (Khan *et al.,* 2019) and accumulation of glycogen in the liver (Phimarn *et al.,* 2018; Aljohi *et al.,* 2016) and thus significantly reduces the blood glucose level in diabetic patients (Laleye *et al.,* 2015).

Azadirachta indica, commonly known as neem is a medicinal plant and has therapeutic potential for controlling different diseases. It has anti-diabetic, anti-viral and antibacterial properties (Shori and Baba, 2015; Keta *et al.,* 2019). It contains certain phytochemicals *i.e.* nimbidin, nimbin, limonoids, nimbolide, and charatin, that display anti-glycemic properties (Okpe *et al.,* 2019). The plants' extract show anti-hyperglycemic activity along with its role as anti-hypercholestrolemic agent in induced diabetic models (Mohamed *et al.,* 2016; Ayodhya *et al.,* 2010). Ethanolic extract of *A. indica* has the potential to regenerate β-cells (Mandle *et al.,* 2019) and has shown improvement in pancreatic islets of induced diabetic rats (Oluwole *et al.,* 2010); Pitipanapong *et al.,* 2007). It provides protection against hepatic dysfunctions (Gutierrez *et al.,* 2011). Its' leaves significantly decrease the blood adrenaline and reduce hyperglycemia by lowering blood glucose level (Pang *et al.,* 2019; Shori and Baba, 2015; Surya *et al.,* 2014; Arika *et al.,* 2017). Many studied have been reported about the usage of medicinal plants in curing diabetes but meager data is available about *M. charantia* and *A. indica,* so this study was designed to check anti-diabetic and hypolipidemic effects of *M. charantia* and *A. indica* extracts in streptozotocin-induced diabetic male albino rats.

II. MATERIAL AND METHODS

Collection of plants

The fruit of *M. charantia* and leaves of *A. indica* were bought from the local market, washed, dried under the shade and powdered in a mechanical grinder. The extract was prepared by the ratio of 10mg/100ml in 70% ethanol using succinate apparatus. The extract was further dried using a rotary evaporator. The extract was collected and stored in glass vials till further use.

Dose calculation and preparation

Dose of *M. charantia* and *A. indica* extracts was prepared according to bodyweight of animals (100mg/kg BW). For the combined dose, 50% extract of *M. charantia* extract was mixed with 50% extract of *A. indica*. Extracts were given to animals orally using the gauge method.

Test animals

Albino rats (150±20g) were obtained from the animal house of The University of Lahore. They were acclimatized in the lab environment for one week before the experiment at standard environmental conditions of temperature (25±2ºC) and humidity (55-58%) under 12 hrs. light to dark cycle. Food and water were given *ad-libitum*.

Induction of diabetes

Diabetes was induced in the overnight fasted 25 male rats by intra-peritoneal injection (I.P) of streptozotocin (55 mg/Kg). After 48hrs of STZ administration, glucose level of the animals was monitored. Blood glucose level was checked by glucometer (On Call® Plus) and animals with blood glucose levels up to 200mg/dl were considered as diabetic and suitable for use in the experiment.

Experimental design

30 rats were divided into 5 treatment groups A, B, C, D, and E (n=6). Group A was having rats, not injected streptozotocin, hence considered as control and group B was treated as diabetic control, however, Rats of group C were given extract of *M. charantia*, group D extract of *A. indica* and group E were treated with extracts of both plants for 21 days.

Dissection and Blood collection

At the end of the experiment, glucose level and body weight of animals were recorded and killed for tissue collection. Blood samples were collected, centrifuged and serum separated in aseptic vials for analysis of lipid profile. The body organ (pancreas) was collected, weighed, and preserved in formalin for further histological examination.

Statistical Analysis

Validity of data was confirmed by one-way analysis of variance (ANOVA) using SAS for windows.

III. RESULTS

Effect of treatment on body weight and glucose level

Comparison of initial body weight and final body weight (FBW) (Fig.1) of albino rats showed that FBW of rats in diabetic control group (B) was significantly ($p<0.05$) higher than other treatment groups. However, FBW was normal in group treated with a combination of extracts of plants, *M. charantia* and *A. indica*. Similarly, comparison of initial glucose level (IG) and final glucose level (FG) of all experimental groups (Figure 2) showed that FG level was significantly ($p<0.05$) different in all feeding groups. FG level of the diabetic control group was non-significantly ($p<0.05$) higher than all other treatment groups, whereas all other experimental groups had normal glucose levels. Group treated with a combination of extracts of plants, *M. charantia* and *A. indica* showed effectively decreased FG level.

Effect of treatment on Lipid profile

It was observed in this study that cholesterol level was distinctly different among all treatment groups. The diabetic control group had a higher level of cholesterol as compared to other groups, while animal treated with a combination of extracts of both plants i.e. *M. charantia* and *A. indica* had lower level of cholesterol (Figure 3). The results showed that there was a significant ($p<0.05$) increase in HDL levels in the treatment groups than the diabetic control, however, HDL level of the diabetic groups was littlebit lower than the normal control (Figure 4).

The diabetic group had the highest level of LDL from all other treatment groups although both groups treated with *M. charantia* and group received combination of extracts of both plants had the same level of LDL (Figure 5). The TG levels were significantly ($p<0.05$) higher in the diabetic control group as compared to other treated groups. The normal group showed a decreased level as compared to the diabetic control group. Group treated with a combination of extracts of both plants *M. charantia* and *A. indica* exhibited lower levels of TG as compared to the diabetic control group (Figure 6). The Group treated with a combination of both plants *M. charantia* and *A. indica* showed the lowest level of VLDL among all other groups although the diabetic control group had the highest level. The diabetic control group showed a higher level as compared to the normal group (Figure 7).

Effect of treatment on the of organs' weight

The results showed that the liver weight of the rats of diabetic control group was significantly ($p<0.05$) higher than all other groups. The weight of the pancreas remained nearly constant in all feeding groups. Weight of kidney was recorded highest in the diabetic control group (Figure 8)

Effect of treatment on histology of pancreas

Are mentioned in Fig. No. A, B, C, D, E

V. DISCUSSION

Herbal plants have been effectively used in the treatment of different diseases since ancient times ((Verma *et al.,* 2018). In this study, *M. charantia* and *A. indica* were used to investigate their effect in reducing glucose levels and improving the lipid profile. In our results, a noticeable increase in body weight was observed in the diabetic control group. This increase in body weight might be due to less metabolic activity and accumulation of proteins and carbohydrates in the body by less insulin production. These results are in accordance with findings of (Lakshmi *et al.,* 2013). The direct relation between the diabetes and weight gain was also reported by (Oluwole *et al.,* 2010), who studied that hunger and thirst increased in diabetic animal, thus more insulin is required to convert glucose into glycogen. Deposition of fats occurs in the body this high glucose level cause's β-cells dysfunction (Verma *et al.,* 2018; Kosteria *et al.,* 2019) suggested the same beneficial effects of *A. indica* as an anti-diabetic agent. The decrease in body weight of rats in the groups treated with a mixture of both plant extracts was observed and this is also reported by (Ibrahem and Abassi, 2010). The diabetic control group showed higher levels of glucose while all other experimental groups showed normal blood glucose levels. Our results showed that both plants effectively lower the glucose levels, due the presence of chemical compounds such as ß-sitosterol, quercetin, polyphenolic, flavonoids charantins, P-insulin, and vicine and becomes beneficial in controlling the glucose level (Artha *et al.,* 2019). Elevated levels of LDL cholesterol; VLDL, and decreased levels of HDL are major changes in lipid fractions in diabetic patients (Sarhadi *et al.,* 2019).

In our study, CHOL level was lowest in the group that received a mixture of extracts of both plants, while the diabetic control group had the highest level of CHOL. These results are in accordance with some earlier researchers, who reported that *M. charantia* and *A. indica* may have some anti-hyperglycemic activity along with its role as anti-hypercholestrolemic agent in induced diabetic models (Mohamed *et al.,* 2016; Ayodhya *et al.,* 2010). In our study both plants showed anti-hypercholesterolemic properties which are in accordance with the work carried out by (Phimarn *et al.,* 2018). In another study, it was reported that *M. charantia* and *A. indica* are helpful in the reduction of the CHOL level separately (Ibrahem and Abassi, 2010) which support our study. So herbal remedies not only lower the glucose level but also control the other induced diseases by so, these remedies can be used for the treatment of diabetes and its associated disorders. HDL level is recognized as good cholesterol and in diabetic patients the values of HDL become low. In our study combine remedy of both plants *M. charantia* and *A. indica* showed a significant role in increasing HDL level as compared to the diabetic control. Our results are in accordance with (Phimarn *et al.,* 2018; Baonda *et al.,* 2019) which showed an increased level of HDL with the treatment of *M. charantia* and *A. indica* individually.

The LDL is bad cholesterol and diabetic patients have elevated levels of LDL which leads to various cardiovascular diseases in diabetic patients. LDL level was highest in the diabetic control group. Group treated with a mixture of both plants *M. charantia* and *A. indica* had a lower level of LDL as compared to the other treatment groups. The lowest LDL level was observed in the group treated with both plants. Study findings suggested the anti-diabetic and anti-hyperlipidemic properties of these two plants are involved in the significant reduction of LDL levels (Artha *et al.,* 2019; Baonda *et al.,* 2019). Diabetic patients have higher levels of TG due to the presence of the excess amount of carbohydrates in the diabetic patients that is associated with the prevailing condition of diabetes as compared to non-diabetic patients. The diabetic control group showed significantly increased levels of TG as compared to other treated groups. Group treated with extract of both plants *M. charantia* and *A. indica* had the lowest value of TG. (Chanda *et al.,* 2019; Mendle *et al.,* 2019) suggested that *M. charantia* contains some fatty acids like myriaatic, lauric, palmitic, linoleic acids and stearic acid and (Phimam *et al.,* 2018) reported that increase in the TRIGL level results in the reduction of protein contents in lipoproteins that causes dyslipidemia a characteristics feature of diabetes. In our results, VLDL was higher in diabetic control group. Group treated with extract of both plants *M. charantia* and *A. indica* had the lowest level of VLDL as compared to the diabetic control group which had the highest level of VLDL. These results suppoots the findings of (Rahmoun *et al.,* 2019) who recommended that *M. charantia* possessed lipogenic and anti-lipolytic properties due to presence of certain compounds such as momordin, glycosides, cucurbitane.

Effect of treatment on body organs showed that weight of liver significantly increased in the diabetic control group due to the inflammation. No significant changes in the weight of the pancreas were observed in the treated groups. Weight of kidney was increased in the diabetic control group due to the increase in

glomerular and tubule length also reported by (Rasch *et al.*, 2010). The pancreas contains Islets of Langerhans which produce β-cells that are involved in insulin production (Adinortey *et al.*, 2019). Histological examination showed that no prominent changes were observed in the pancreas of normal group whereas diabetic pancreas contained lesser number of acinar and β-cells and degradation also occurred. Group treated with *M. charantia* and group treated with extract of both plants *M. charantia* and *A. indica* showed no histological changes in pancreas while the diabetic control group showed mild changes in the pancreas due to increase in LDL, TG, and CHOL level.

V. CONCLUSION

It was observed that both plants' extracts showed a significant reduction in glucose level and a significant decrease in body weight of the induced diabetic rats. Level of CHOL, TG, , LDL, and VLDL were significantly lower in the treatment groups as compared to diabetic control, whereas, HDL level was significantly higher in the group treated with the mixture of both plant extracts. Mixing of extracts of both plants showed an effective anti-diabetic and hypolipidemic effect. No evidence of inflammation or any degeneration was observed in the pancreas, however regeneration of pancreatic cells was observed in the treated groups. Keeping in view the findings of this study, it is concluded that these plants' extracts can be used for the cure of diabetes.

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CONFLICTS OF INTEREST

All the authors declare that they have no conflict of interest.

REFERENCES

1. Verma, S., Gupta, Popli, H. and Aggarwal G. (2018). Diabetes Mellitus Treatment Using Herbal Drugs. *International M Journal of Phytomedicine*, 10, 1-10. DOI:10.5138/09750185.2181
2. Punthakee, Z., Goldenberg, R. and Katz, P. (2018). Definition, Classification and Diagnosis of Diabet and Metabolic Syndrome. *Canadian Journal of Diabetes*, 42, 10-15. Doi:https//doi.ore/101016/icid.2017.10.003
3. Pang, GM., Li, FX., Yan, Y., Zhang, Y., Kong, LL., Zhu, P., Wang, KF., Zhang, F., Liu, B. and Lu, C. (2019). Herbal medicine in the treatment of patients with type 2 diabetes mellitus. *Chinese Medical Journal*, 132(1), 78-85. DOI: 10.1097/CM9.0000000000000006
4. Gordon, A., Buch, Z., Baute, V. and Coeytaux, R. (2019). Use of Ayurveda in the Treatment of Type 2 Diabetes Mellitus. *Global Advances in Health and Medicine*, 8,1-6. https://doi.org/10.1177/2164956119861094
5. Kosteria, I., Schwandt, A., Davis, E., Jali, S., Prieto, M., Rottembourg, D. and on behalf of the SWEET study group. (2019). Lipid profile is associated with treatment regimen in a large cohort of children and adolescents with Type 1 diabetes mellitus: a study from the international SWEET database. *Journal of Diabetic medicine,* 36, 1294-1303. https://doi.org/10.1111/dme.13963
6. Bhowmik, B., Siddiquee, T., Mujumder, A., Afsana, F., Ahmed, T., Mdala, I.A., Cristina, N., Moreira, N.C.V., Khan, A.K.A., Hussain, A., Ottesen, G.H. and Omsland, T.K. (2018). Serum Lipid Profile and Its Association with Diabetes and Prediabetes in a Rural Bangladeshi Population. *International Journal of Enviromental Research and Public Health*, 15, 231-243. https://doi.org/10.3390/ijerph15091944
7. Elalfy, M.M., Farag, A., Helmy, A.A., Metwaly, Z.E. and Ali F.R. (2019). Hematological, Biochemical and Cytotoxic Effect of Ethanolic Raw Extract of Egyptian C. colocynthis in Sprague Dawley Rats. *Journal of Enzyme Engeering*, *8,* 165-167. DOI: 10.4172/2329-6674.1000165
8. Ostovan, F., Gol, A. and Javadi, A. (2017). Investigating the effects of C. colocynthis pulp on oxidative stress in testes and epididymis in streptozotocin-induced diabetic male rats. *International Journal of Reproductive Biomedicine*,15, 41-48.
9. Phimarn, W., Sungthong, B., Saramunee, K. and Caichompoo, W. (2018). Efficacy of M. charantia L. on blood glucose, blood lipid, and body weight: A meta-analysis of randomized controlled trials. *Journal of Pharmacognosy*, 14, 351-358. DOI: 10.4103/pm.pm-215-17
10. Chanda, R., Samadder, A. and Banerjee J. (2019). Anti-diabetic Activity of Momordica Charantia or Bitter Melon: A Review. *Acta Scientific Pharmaceutical Sciences*, 3, 24-30.

11. Fachinan, R., Yessoufou, A., Nekoua, M.P. and Moutairou K. (2017). Effectiveness of antihyperglycemic effect of Momordica charantia: implication of t-cell cytokines. *Evidence-Based Complementary and Alternative Medicine*, *11*(3), 1-8. https://doi.org/10.1155/2017/3707046
12. Hosseini, A., Shafiee-Nick, R. and Ghorbani A. (2015). Pancreatic beta cell protection/regeneration with phytotherapy. *Brazilian Journal of Pharmaceutical Sciences*, *51*(9), 1-16. https://doi.org/10.1590/S1984-82502015000100001
13. Khan, M.F., Abutaha, N., Nasr, F.A., Alqahtani, A.S., Noman, O.M. and Wadaan, M.A. (2019). Bitter gourd (Momordica charantia) possesses developmental toxicity as revealed by screening the seeds and fruit extracts in zebrafish embryos. *BMC complementary and alternative medicine*, *19*(1), 1-13. https://doi.org/10.1186/s12906-019-2599-0
14. Mahwish., Saeed, F., Arshad, M.S., Nisa, M., Nadeem, M.T. and Arshad M.U. (2017). Hypoglycemic and hypolipidemic effects of different parts and formulations of bittergourd (Momordica Charantia). *Lipids in Health and Disease*, 16, 211-216. DOI 10.1186/s12944-017-0602-7
15. Aljohi, A., Matou-Nasri, S. and Ahmed, N. (2016). Antiglycation and antioxidant properties of Momordica charantia. *The Public Library of Science*, *11*(8), 541-550. https://doi.org/10.1371/journal.pone.0159985
16. Laleye, O.A.F., Ahissou, H., Assogba, M.F., Azando, V.B.E., Olounlade A.P., Agbo'Saga, K.F. and Laleye A. (2015). In vivo hypoglycemic activity and acute oral toxicity of ethanolic and aqueous leaves extract of Momordica charantia Linn (Cucurbitaceae) from Benin. *Journal of Chemistry and Pharmaceutical Research*, *7*(4), 376-385.
17. Shori, A.B. and Baba, A.S. (2015). Antioxidant activity and inhibition of key enzymes linked to type-2 diabetes and hypertension by Azadirachta indica-yogurt. *Journal of Saudi Chemical Society*, *17*(3), 295-301. https://doi.org/10.1016/j.jscs.2011.04.006
18. Keta, J.N., Suberu, H.A., Shehu, K., Yahayya, U., Mohammad, N.K. and Gudu, G.B. (2019). Effect of neem (Azadirachta indica) A. leaf extract on the growth of Aspergillus species isolated from foliar diseases of rice (Oryzea sativa). *Science World Journal*, *14*(1), 98-102.
19. Okpe, A.C., Shu, E.N., Nwadike, k. I., Udeinya, I. J., Nubila, N. I. and Aniagor, E. N. (2019). Effects of Fractionated Neem Leaf Extract (IRC) on Blood Glucose Level in Alloxan Induced Diabetic Wistar Rats. *International Journal of Diabetes and Clinical Research*, 6, 213-215. DOI: 10.23937/2377-3634/1410105
20. Mohamed, A.S., Soliman, A.M. and Marie, M.A.S. (2016). Mechanisms of echinochrome potency in modulating diabetic complications in liver. *Life sciences*, 151, 41-49. https://doi.org/10.1016/j.lfs.2016.03.007

21. Ayodhya, S., Kusum, S. and Anjali, S. (2010). Hypoglycaemic activity of different extracts of various herbal plants. *International Journal of Research in Ayurveda and Pharmacy*, *1*(1), 212-224. URL : http://www.ijrap.net/first-issue/Saxe...
22. Mandle, K.S., Prashant, V. and Sahu, G.K. (2019). Comparison of fasting and non-fasting serum lipid profile in healthy population. *International Journal of Research in Medical Sciences*, *7*(3), 790-794.
23. Oluwole, B., Akinola., Ezekiel, A., Caxton, M. and Luciana D. (2010). Chronic Treatment with Ethanolic Extract of the Leaves of *Azadirachta indica* Ameliorates Lesions of Pancreatic Islets in Streptozotocin Diabetes. *International Journal of Morphology*, 28, 291-302. DOI: 10.4067/S0717-95022010000100043
24. Gutierrez, R.M.P., Gómez, Y.G.Y. and Guzman, M.D. (2011). Attenuation of nonenzymatic glycation, hyperglycemia, and hyperlipidemia in streptozotocininduced diabetic rats by chloroform leaf extract of Azadirachta indica. *Pharmacognosy magazine*, *7*(27), 254-259. doi: 10.4103/0973-1296.84243
25. Gupta, N.K., Srivastva, N., Bubber, P. and Garg, S. (2017). Protective Potential of Azadirachta indica Leaf Extract in Diabetic Rat Liver. *International Journal of Pharmacognosy and Phytochemical Research, 9*(1), 174-180.
26. Fachinan, R., Yessoufou, A., Nekoua, M.P. and Moutairou K. (2017). Effectiveness of antihyperglycemic effect of Momordica charantia: implication of t-cell cytokines. *Evidence-Based Complementary and Alternative Medicine, 11*(3), 1-8. https://doi.org/10.1155/2017/3707046
27. Okpe, A.C., Shu, E.N., Nwadike, K.I., Udeinya, I.J. and Nubila, N.I. (2019). Effects of fractionated neem leaf extract (IRC) on blood glucose level in alloxan induced diabetic wistar rats. *International Journal of Diabetes and Clinical Research, 6*(105), 213-215. DOI: 10.23937/2377-3634/1410105
28. Pitipanapong, J., Chitprasert, S., Goto, M., Jiratchariyakul, W., Sasaki, M. and Shotipruk A. (2007). New approach for extraction of charantin from Momordica charantia with pressurized liquid extraction. *Separation and Purification Technology*, *52*(3), 416- 422. https://doi.org/10.1016/j.seppur.2005.11.037
29. Surya, S., Salam, A.D., Tomy, D.V., Carla, B., Kumar, R.A. and Sunil, C. (2014). Diabetes mellitus and medicinal plants-a review. *Asian Pacific Journal of Tropical Disease*, *4*(5), 337-347. DOI : 10.1016/S2222-1808(14)60585-5
30. Arika, W.M., Nyamai, D.W., Agyirifo, D.S., Ngugi, M.P. and Njagi E.N.M. (2016). In vivo antidiabetic effect of aqueous leaf extract of Azardirachta indica, in alloxan induced diabetic mice. *Journal of Diabetic Complications & Medicine, 1*(2), 1-6. http://dx.doi.org/10.4172/jdcm.1000.106

31. Lakshmi, B., Sendrayaperumal, V. and Subramanian S. (2013). Beneficial Effects of *Citrullus colocynthis* Seeds Extract Studied in Alloxan-induced Diabetic Rats. *International Journal of Pharmaceutical Sciences*, 19, 47-55.
32. Ibrahem, A.M.S. and Abassi, N.A. (2010). Study Antidiabetic Effect of *Momordica Charantia* (bitter gourd) seeds on Alloxan Induced Diabetic Rats. *Iraqi Journal of Veterinary Sciences*, 34, 165-170.
33. Artha, M.J.R., Bhargah, A., Dharmawan, N.K., Pande, U.W., Triyana, K.A., Mahariski, P.A, Yuwono, J., Bhargah, V., Prabawa, P.Y., Putra, I.B.A. and Rina, M.K. (2019). High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. *Vascular Health and Risk Management*, 15, 149-157. http://doi.org/10.2147/VHRM.S209830
34. Sarhadi, N.A., Fakhreddin-nejad, M.E., Rajabi, M.H., Mokarrari, S., Naghipour, E., Karkon, H. and Hashemi, M.M. (2019). Evaluation of Fasting Blood Sugar and Lipid Profile in Patients with Type 1 and Type 2 Diabetes and Normoglycemic Individuals in Gorgan, Northeastern Iran. *Journal of Clinical and Basic Research*, 3, 6-10. doi 10.29252/jcbr.3.1.6
35. Baonda, S.M., Loumpangou, C.N., Ampa, R., Ndinga, A.M.E., Milandou, L.J.C.B., Bonose, M. and Ouamba J.M. (2019). Evaluation of antidiabetic activity of the ethanol extract of Momordica charantia L. and the identification of charantine by gas chromatography coupled with Mass spectrometry. *Journal of Medicinal Plants Research*, 13, 321-328. https://doi.org/10.5897/JMPR2019.6750
36. Mandle, K.S., Prashant, V. And Sahu, G.K. (2019). Comparison of fasting and non-fasting serum lipid profile in healthy population. *International Journal of Research in Medical Science*, 7, 790-794.
37. Rahmoun, M.N., Ghembaza, C.E. and Ghembaza, M.E. (2019). Lipid profile in type 2 patients with diabetes from Tlemcen: A Western Algerian population. *International Journal of diabetes*, 13, 1347-135. https://doi.org/10.1016/j.dsx.2019.02.008
38. Rasch, R. and Dorup, J. (2010). Quantitative morphology of the rat kidney during diabetes mellitus and insulin treatment. *Diabetologia*, 40, 802-810. https://doi.org/10.1007/s001250050752
39. Adinortey, M.B., Agbeko, R., Boison, D., Ekloh, W., Kuatsienu, L.E., Biney, E.E., Affum, O.O., Kwarteng, J. and Nyarko, A.K. (2019). Phytomedicines Used for Diabetes Mellitus in Ghana: A Systematic Search and Review of Preclinical and Clinical Evidence. *Evidence-Based Complementary and Alternative Medicine*, 1-23. https://doi.org/10.1155/2019/6021209

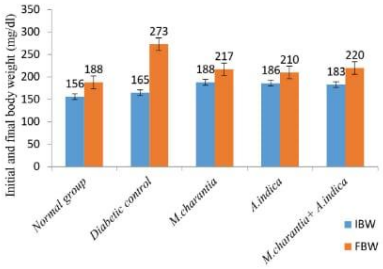

Figure 1 Comparison of Initial and final body weight (g) among all experimental groups after 21days of treatment.

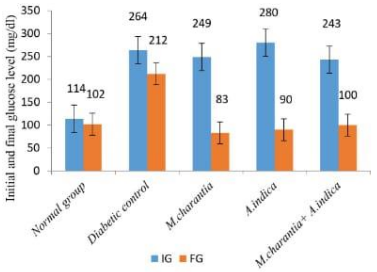

Figure 2 Comparison of Initial and final Glucose level among all experimental groups after 21days of treatment

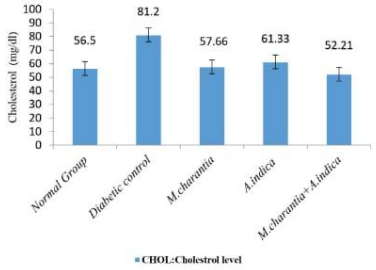

Figure 3: Comparison of cholesterol level among all experimental groups after 21days of treatment

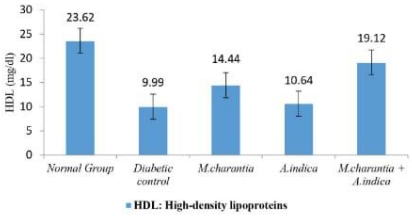

Figure 4: Comparison of HDL level among all experimental groups after 21days of treatment

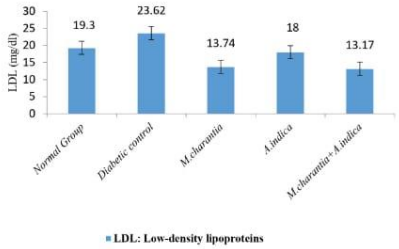

Figure 5: Comparison of LDL level among all experimental groups after 21days of treatment.

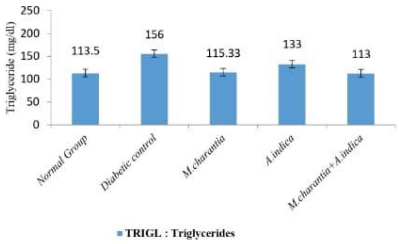

Figure 6: Comparison of TRIGL level among all experimental groups after 21days of treatment.

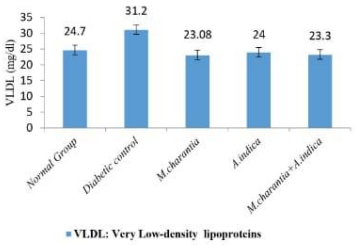

Figure 7: Comparison of VLDL level among all experimental groups after 21days of treatment.

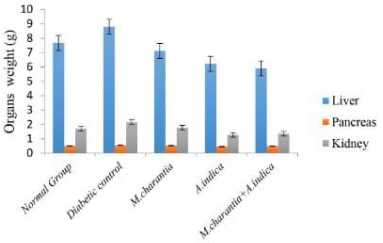

Figure 8: Comparison of the organs' weight (liver, pancreas, and kidney) in all experimental groups after 21 days of treatment

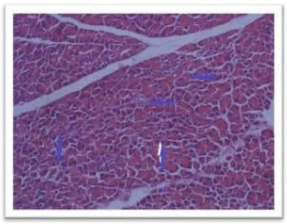

Figure (A); Photomicrograph of the pancreas from control group showing Islets of Langerhans contain normal acinar and β-cells concentrations no evidence of inflammation and degeneration occurs (H&E Staining 400X).

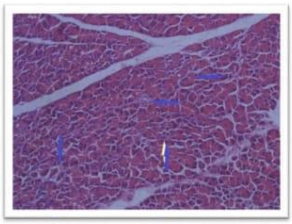

Figure (B); Photomicrograph of the pancreas from the diabetic control group (B) showing Islets of Langerhans contain lesser number of acinar and β-cells. Degeneration of β-cells occurs. Inflammation and malignancy observe (H&E Staining 400X).

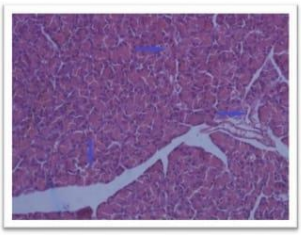

Figure (C); Photomicrograph of the pancreas from the group (C) treated with extract of *M. charantia* showing Islets of Langerhans contain normal acinar and β-cells concentrations (H&E Staining 400X).

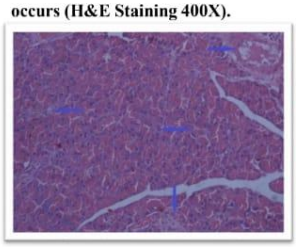

Figure (D); Photomicrograph of the pancreas from the group (D) treated with extract of *A. indica* showing Islets of Langerhans contain lesser number of acinar and β-cells and no evidence of inflammation occurs (H&E Staining 400X).

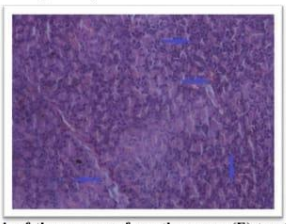

Figure (E); Photomicrograph of the pancreas from the group (E) treated with extract of both plants *M. charantia* and *A. indica* showing Islets of Langerhans contain normal acinar and β-cells concentrations. Pancreatic tissue revealed normal-looking endo-and exocrine elements of the pancreas. No evidence of inflammation was observed (H&E Staining 400X).