IJMPR 2022, 6(1), 110-119

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Research Article
SJIF Impact Factor: 5.273

AN EVALUATION OF IN-VIVO DIABETES AMELIORATING POTENTIALITIES OF *PHYLLANTHUS EMBLICA* AGAINST NUMEROUS ALTERED PATHO-PHYSIOLOGICAL STATE EXPERIMENTAL RAT MODELS

Md. M. Alam*[1], S. Rahman[1], J. Ferdous[2], Md. R. Tahsin[2], Ahmemed U. Faisal[1], Monirul I. Daimond[1], Md. A. Rouf[1], A. Saha[3], Samia N. Tahiti[1], Ahmad U. Faisal[1], Jakir A. Chowdhury[4], S. Kabir[5], Abu A. Chowdhury[5], F. Aktar[5], T. Akter[6] and Md. S. Amran[5]

[1]Department of Pharmacy, University of Asia Pacific, Farmgate, Dhaka, Bangladesh.
[2]Department of Pharmaceutical Sciences, North South University, Plot # 15, Block # B, Bashundhara R/A, Dhaka 1229, Bangladesh.
[3]Department of Pharmacy, Faculty of Pharmacy, University of Dhaka, Dhaka 1000, Bangladesh.
[4]Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Dhaka, Dhaka 1000, Bangladesh.
[5]Molecular Pharmacology and Herbal Drug Research Laboratory, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka, Dhaka 1000, Bangladesh.
[6]Department of Physiology, Dhaka Medical College, Dhaka-1000, Bangladesh.

Received on: 15/12/2021
Revised on: 05/01/2022
Accepted on: 25/01/2022

***Corresponding Author**
Md. Mahbub Alam
Department of Pharmacy, University of Asia Pacific, Farmgate, Dhaka, Bangladesh.

ABSTRACT

Diabetes mellitus (DM) is a disorder caused by improper glucose, protein, and lipid metabolism. It is caused by insulin insufficiency, which is frequently accompanied by insulin resistance. Plants have long been an excellent source of medications, and many of the drugs that are currently available were produced directly or indirectly from them. The *Phylanthus emblica* plant is said to have anti-diabetic effects as well as other health benefits such as increased immunity, improved skin and eyesight, improved liver, heart, and brain function, and so on. In this study, the antidiabetic activity of *Phylanthus emblica* plant in alloxan induced diabetic rats was evaluated against metformin. Here, rats were kept in lab for 7 days for habituating them in the lab environment and treatment period was 42 days. Alloxan was given in fasting condition in a dose of 150 mg/kg/body/day weight and 14 days were waited after administration of alloxan. For the evaluation of antidiabetic activity, body weigh, blood sugar level, liver function (SGPT &SGOT level), creatinine and urea level were tested. The ethanolic extract of *P. emblica* fruit has a promising anti-diabetic impact on the animal model (p0.05/p0.01), but only in a dose-dependent way. The lower dose of *P. emblica* was found to be significantly capable of restoring the altered physiological state (p0.05). A higher dose of *P. emblica*, on the other hand, has better anti-diabetic therapeutic effects. This study found that different doses of *P. emblica* extracts have comparable therapeutic effects to established marketed medications in the treatment of hyperglycemia.

KEYWORDS: Diabetes mellitus, Hyperglycemia, SGPT, SGOT, Creatinine, Alloxan.

INTRODUCTION

Diabetes is thought to be the most widespread occurrence over the world.[1] Diabetic patients are expected to grow from 171 million in 2000 to 366 million in 2030, according to estimates.[2] Although, according to the International Diabetes Federation, the latter threshold was already reached in 2011. In Asia, particularly China and India, accounted for a large portion of this rise.[3]

Diabetes is a category of metabolic illnesses characterized by hyperglycemia as a result of insufficient insulin synthesis (type-I) or inadequate insulin use (type-II).[4] Diabetes is caused by a number of different pathogenic mechanisms. These can range from autoimmune destruction of the pancreas'- cells, resulting in insulin insufficiency, to anomalies that lead to insulin resistance. Diabetes causes anomalies in glucose, lipid, and protein metabolism due to insulin's ineffective action on target tissues.[5] Diabetes mellitus (DM) causes chronic hyperglycemia, which causes organ damage, malfunction, and failure in organs and tissues such as the retina, kidney, nerves, heart, and blood vessels.[6]

Oral antidiabetic medicines such as Metformin, sulfonylureas (SU), thiazolidinediones (TZD), and dipeptidyl peptidase-IV (DPP-4) inhibitors, as well as insulin injections (in severe cases) along with standard diet and physical activity, were all extensively used

therapies for diabetes.[7] Nonetheless, these synthetic drugs have negative side effects, and they are frequently blamed for the ineffectiveness of chronic diabetes patients.[8]

As a result of globalization and the current medical environment the expense of synthetic medications are increasing day by day. Furthermore, despite considerable progress in biomedicine, with greater understanding and possibly successful therapeutic techniques to treat many diseases, diabetes therapy remains a major challenge. The negative side effects of several synthetic medications have rekindled interest in ancient medical methods for the treatment of diabetes.[9] Medicinal plants continue to be of critical therapeutic value in the treatment of human illnesses because they include a variety of natural active ingredients that serve a variety of pharmacological effects.[10] Because most herbal medicines appear to be increasingly effective via genetic alteration of active ingredients, safe, and have no high-risk relationship because there are minor or nearly no side effects, the influence and worldwide demand for natural cures cannot be ignored. Organically produced natural healthcare remedies have long been viewed as promising means to controlling chronic disorders.[11]

Phyllanthus emblica (*Euphorbiaceae*) is also locally known as 'amla' or 'amalaki', a plant that thrives in subtropical and tropical locations in China, India, Asia, Indonesia, and the Malay Peninsula. Plant components such as roots, stems, leaves, and fruits are utilized both fresh and dried.[12] Every parts of this plant has been used traditionally for the treatment of anorexia, constipation, piles, leucorrhea, inflammatory bowls, cough, hemorrhoids, fever, thirst, toxicity of blood and atherosclerosis diabetic mellitus.[13]

Phytochemical screening of *P. emblica* shows that it is high in vitamin C and gallic acid. It also includes ellagic acid, phenolic compounds, corilagin, furosin, flavonoids, glycosides, and tannins that posseses with anti-inflammatory, antibacterial, anti-ulcer, nephroprotective, analgesic, antipyretic, anti-tussive, and immune modulating actions.[14,15,16,17]

The fruit and leaves' decoctions of *P. emblica* is used in the prevention and treatment of diabetes, according to a study issued by the Central Council for Research Ayurvedic Sciences.[18] It works by blocking glycogenolysis, hepatic glucogenesis, and gastrointestinal glucose absorption. It also stimulates insulin release, which improves peripheral glucose absorption.[19] In study of various ethnophytomedicinal reports for diabetes, *P. emblica* has been found the most active plant. In nine traditional recipes, *P. emblica* has been used in different forms viz. herbal mixtures, fruits, seeds, flour, powders, extracts and so on.[20] *P. emblica's* anti-hyperglycemic action has been substantiated by a number of clinical and non-clinical research. In a 21-day clinical trial, *P. emblica* not only considerably lowered fasting and 2 hours' post-prandial blood glucose levels in diabetic patients, but it also significantly reduced total cholesterol and triglyceride (TG) levels in participants.[21]

This review systematically encapsulates the role of different active phytochemical compounds of *P. emblica* against Diabetes mellitus. Adequate outcome regarding pharmacological activity may give persuasive rationale for the scientist to pursue additional research to isolate the active chemicals and develop a new medicine via molecular modification for the respective diseases.

METHOD AND MATERIALS

Plant Collection and Extract Preparation

The *Phyllanthus emblica* bark was collected from the garden of the department of pharmacy, Jahangirnagar University.

Botanical authentication

We submitted the sample of each part of our plant species in accordance with the requirements of our National Herbarium, and the herbarium authorities took the appropriate steps. But due to COVID-19 pandemic situation, the herbarium authority made the institute restrict to the outsiders for a long time. For all these reasons, so we couldn't receive the botanical authentication (accession number) yet.

Drugs and Chemicals

Alloxan was purchased from the Sigma Company in the United States. Metformin, a common anti-diabetic medicine, was sent as a gift sample by Incepta Pharmaceutical Ltd. Chemical.co.uk provided the acid.

Experimental Animal Procurement, Nursing, and Grouping

Total 140 male rats were purchased from Jahangirnagar University, Savar, Dhaka, Bangladesh. The rats are weighing between 120-150 gm. Each of them was kept in the Institute of Nutrition & Food Science in a well-controlled environment (temperature 25±2°C, relative humidity 55±6%, and 12 hours light/dark cycle) at the Jahangirnagar University. They were given a conventional diet and were given access to clean water. Before the trial all of the animals were nursed in this conditions for at least one week before the experiment. All of the experimental methods were accomplished under the Institutional Animals Ethics Committee (IEAC)

Dose selection for respective study

Before initiating the study a pilot study was conducted. The test extract began to exhibit pharmacological activity at a dose of 500mg/kg according to the findings, indicating the minimum effective concentration (MEC) value at above 500mg/kg. In addition, the activity was continuous with the increase of dose. When the dose was increased from 1000mg/kg to 1200mg/kg, the effect didn't increase significantly. It indicating that the

receptors associated with concern pharmacological activity was started being saturated at a dose of 1000mg/kg. Also, the doses of standard drugs were selected in the same manner.

Evaluation of Anti-diabetic Activity

For this experiment, 140 rats were randomly picked and equally divided into fourteen groups.

Group Number	Group Specification	Treatment species	Dose Treatment species (mg/kg)	Abbreviation of Groups
1	Negative Control	Physiological Saline	10ml/kg	N
2	Alloxan Control	N/A	N/A	A
3	Alloxan+ Metformin	Metformin	100	$A+M_{100}$
4	Alloxam+ Metformin	Metformin	200	$A+M_{200}$
5	Alloxan + Metformin	Metformin	400	$A+M_{400}$
6	Alloxan + *Phyllanthus emblica*	*Phyllanthus emblica*	300	$A+PE_{300}$
7	Alloxan + *Phyllanthus emblica*	*Phyllanthus emblica*	500	$A+PE_{500}$
8	Alloxan + *Phyllanthus emblica*	*Phyllanthus emblica*	800	$A+PE_{800}$
9	Metformin	Metformin	100	M_{100}
10	Metformin	Metformin	200	M_{250}
11	Metformin	Metformin	400	M_{500}
12	*Phyllanthus emblica*	*Phyllanthus emblica*	300	PE_{300}
13	*Phyllanthus emblica*	*Phyllanthus emblica*	500	PE_{500}
14	*Phyllanthus emblica*	*Phyllanthus emblica*	800	PE_{800}

To induce diabetes in the rats of the group (2-8) alloxan was injected intraperitoneally at a dose of 150 mg/kg. But at the other, alloxan was not injected into the rats of group in 1 and 9-14. Then blood glucose level was checked in all groups to ensure whether diabetes was induced or not. Blood glucose level was measured once a week in the fasting condition. The duration of treatment was six weeks. Both the extracts and the drugs were given orally.

Statistical Analysis

All of our findings (raw data) belong to several groups concerning numerous research parameters recorded. It had been analyzed on a broadsheet using MS excel program. Data were subjected to descriptive statistics and the results were represented as mean ± SD. We engaged the "One Way Anova Test" of SPSS 16" software for explaining the inter-group heterogeneity in terms of different biological characteristics to determine the statistical significance. We consider the events as statistically important while the 'p' value was found as less than 0.05 ($p<0.5$).

Experimental Guideline

All the experiments were performed in accordance with the ethical standards laid down in the Declaration of Helsinki 2013. Animals were treated by following the principles of the Swiss Academy of Sciences and Swiss Academy of Medical Sciences. Animals were euthanized by following the Guidelines for the Euthanasia of Animals: 2013 edition.

RESULTS

The negative control group had a significant increase in bodyweight, whereas the alloxen-treated group had a decrease. Metformin reduced body weight in diabetic rats induced by alloxen in a dose-dependent manner. However, after administration of *P. emblica* to alloxan-induced diabetic rats, body weight increased in a dose-dependent manner. Metformin and *P. emblica* had the same effects in non-diabetic rats that they did in diabetic rats [Figure 1]

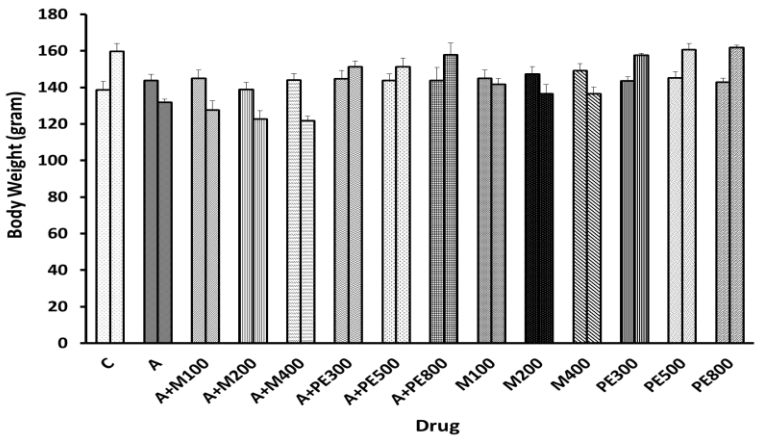

Figure 1: Body weight of rats of 14 groups before and after completing the experiment in diabetic rats.

Non-diabetic rats which were given metformin and plant extract had blood glucose levels similar in comparison to the negative control group. Alloxen-induced diabetic rats had elevated blood glucose levels that grew over time. Metformin and *P. emblica* extract significantly reduced blood glucose levels in diabetic rats in a dose-dependent manner. However, metformin outperformed the plant extract in terms of response[Figure 2].

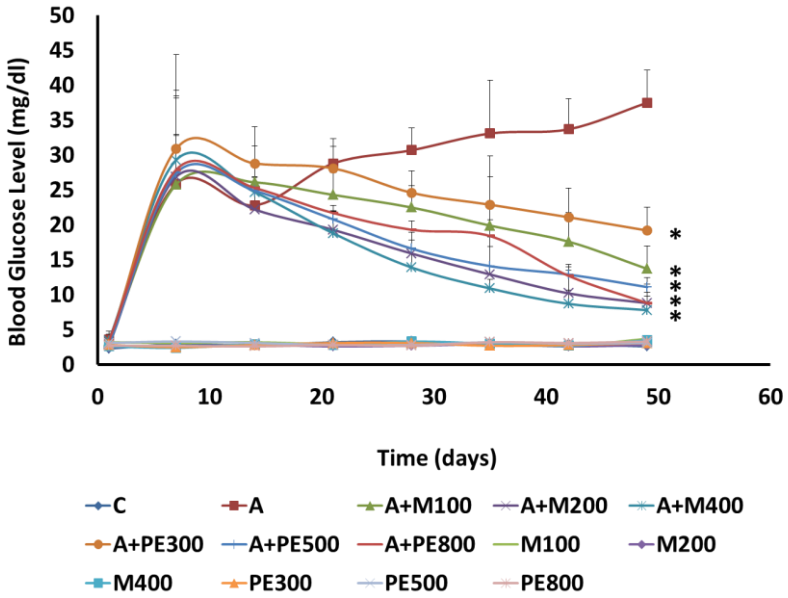

Figure 2: The blood glucose level (mmol/dl) of rats of 14 groups after receiving 42 days of respective treatments. The data were expressed as mean± standard deviation. (*indicates statistically significant change)

Total cholesterol level was low in the negative control group but high in the alloxan-induced diabetic rats. In alloxan-induced diabetic rats, total cholesterol gradually decreased as metformin doses were gradually increased. In alloxan-induced diabetic rats, cholesterol levels decreased in a dose-dependent manner after administration of *P. emblica* extract. In non-diabetic rats, cholesterol levels remained roughly the same after administration of metformin and *P. emblica* extract. The negative control group's HDL level was low. Alloxan-induced diabetic rats had impaired HDL levels. Metformin and *P. emblica* administration normalize the HDL level in diabetic rats. Metformin and *P. emblica* had the same effect on non-diabetic rats. LDL cholesterol levels were low in the negative control group. Alloxan-induced diabetic rats had high LDL levels. Metformin and *P. emblica* administration reduced LDL levels in alloxan-induced diabetic rats in a dose-dependent manner. Metformin and *P. emblica* had comparable effects in non-diabetic rats. The triglyceride level in the negative control group was low. Triglyceride levels were elevated in diabetic rats induced by alloxan. Metformin and *P. emblica* both reduced triglyceride levels gradually as the dose was increased in alloxan-mediated diabetic mice. On non-diabetic rats, metformin and *P. emblica* had the same effect[Figure 3-6].

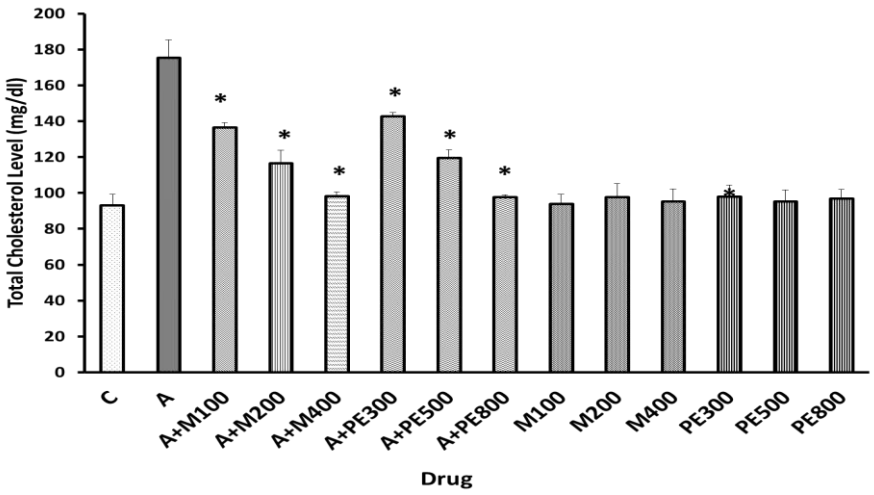

Figure 3: Total Cholesterol (mg/dl) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

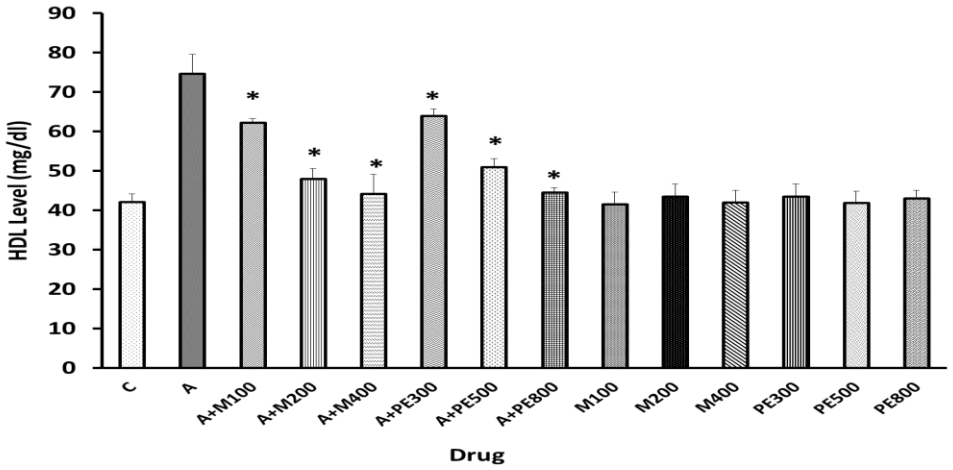

Figure 4: HDL (mg/dl) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

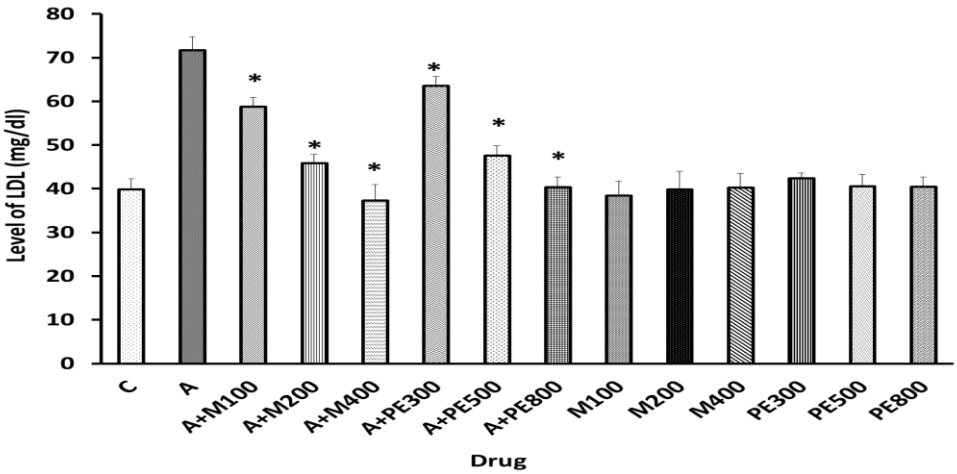

Figure 5: LDL (mg/dl) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

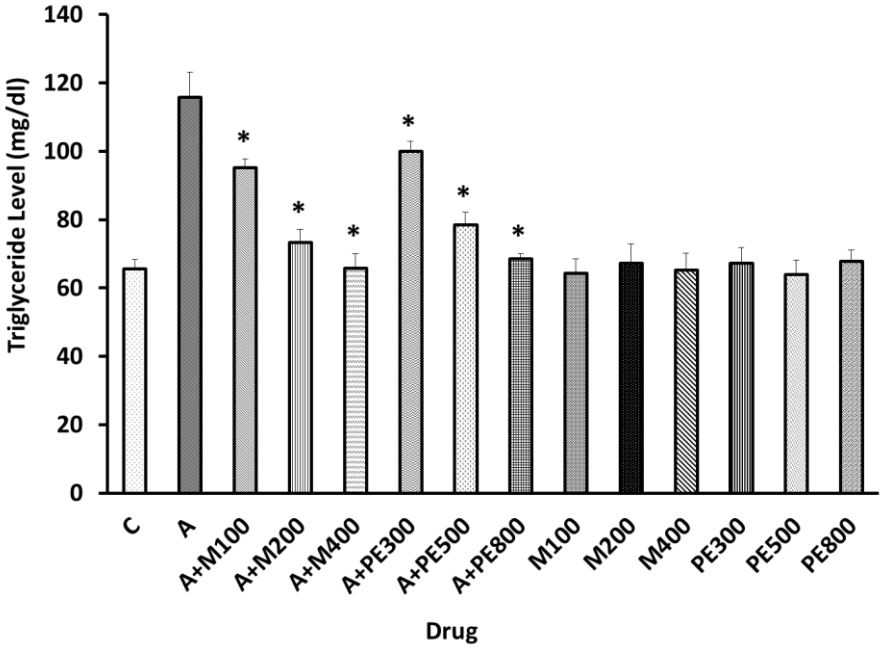

Figure 6: Triglyceride (mg/dl) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

SGPT level was low in the negative control group but elevated in the alloxan-induced diabetic rats. In alloxan-induced diabetic rats, SGPT dropped gradually as metformin dose was enhanced. SGPT levels lowered in alloxan-induced diabetic rats after administration of *P. emblica* extract in a dose-dependent manner. The SGPT level in non-diabetic rats remained roughly the same after metformin and *P. emblica* extract administration.

Treatment of alloxan-induced rats with metformin or plant extract showed a dose-dependent reduction in SGOT levels, with metformin having a somewhat higher reducing influence than the plant. The SGOT levels of the other six non-alloxan treated groups did not change substantially from the negative control group [Figure 7,8].

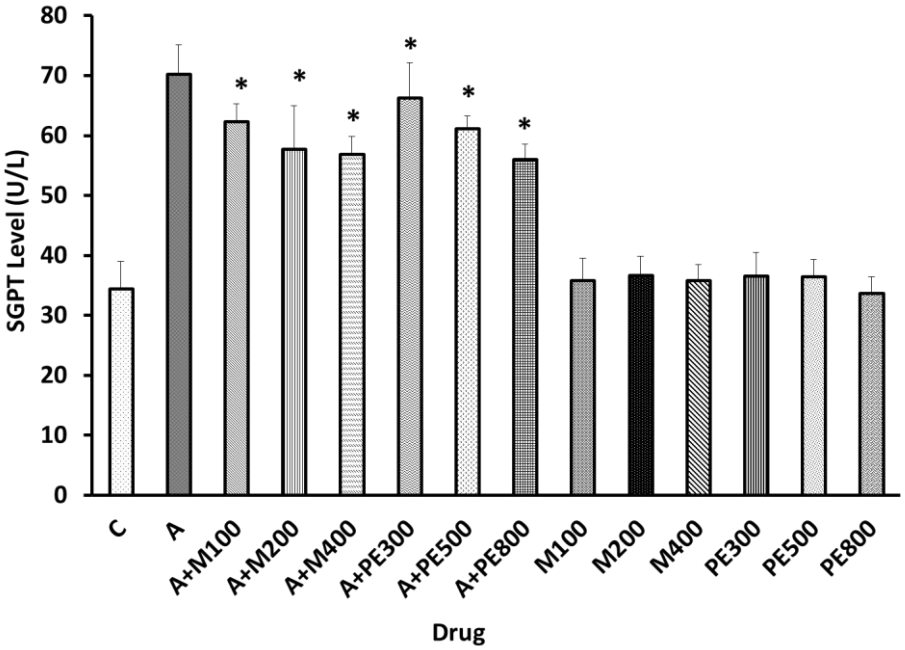

Figure 7: SGPT (U/L) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

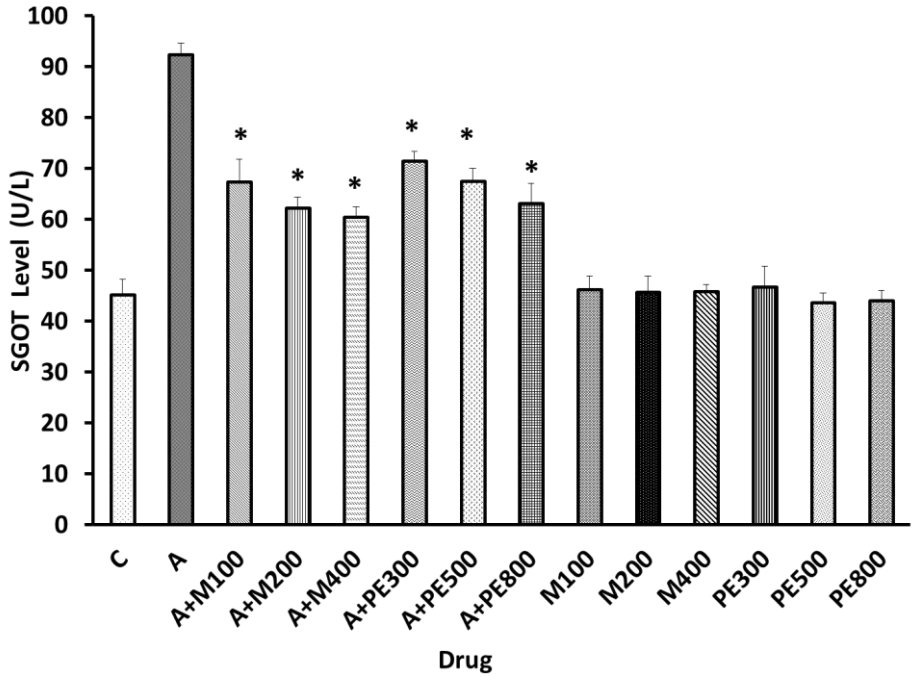

Figure 8: SGOT (U/L) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

Creatinine level was low in the negative control group and elevated in the alloxan group. The prescription of metformin lowers creatinine levels. Creatinine levels fell as the dose was increased. The creatinine level in non-diabetic rats treated with metformin and plant extract was the same as in the negative control group [Figure 9]

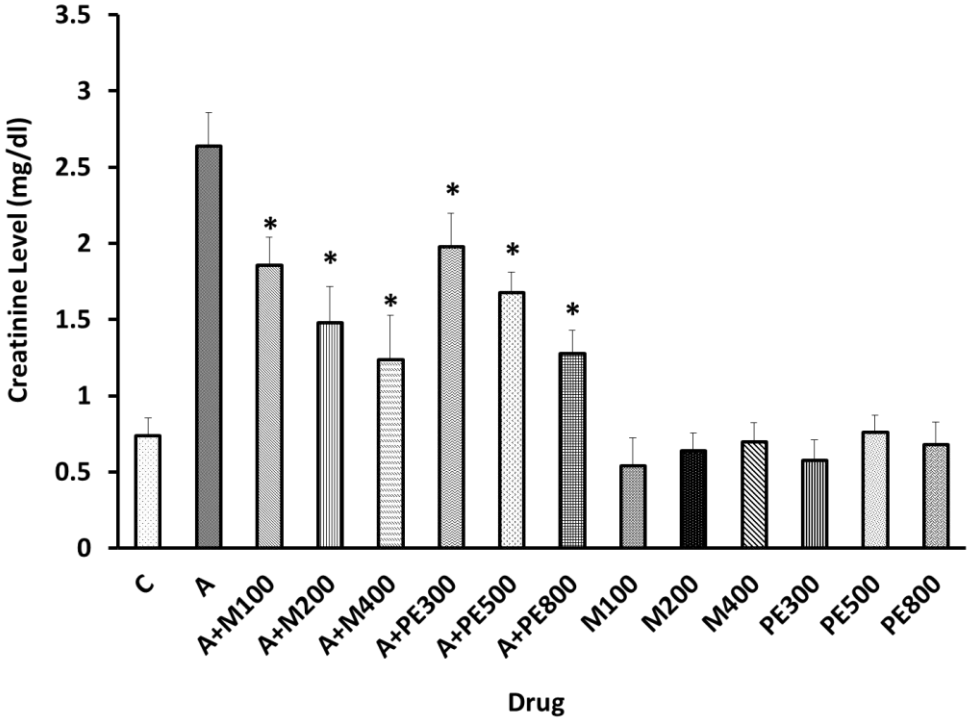

Figure 9: Creatinine (mg/dl) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

In alloxan-mediated diabetic rats, urea levels were raised. The urea level was reduced in a dose-dependent manner after metformin and plant extract delivery. However, the drop for metformin was more than the reduction for the plant. In non-diabetic rats, the effects of metformin and plant were nearly identical, and urea levels appeared to be comparable to the negative control group [Figure 10]

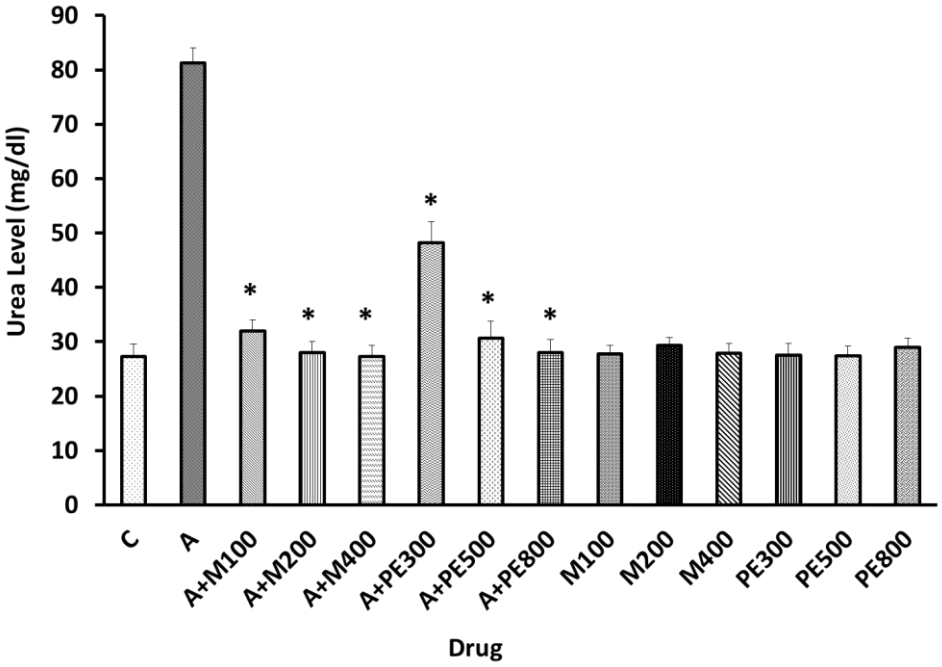

Figure 10: Urea (mg/dl) Level of rats from 14 groups. The data were expressed as mean± standard deviation. (* indicates statistically significant change)

DISCUSSION

The fruits of E. officinalis are widely known for their pharmacological and anti-diabetic activities.[23-25] Diabetes is one of the world's most serious health issues. Diabetes in the rat model can be assessed using a variety of procedures. Alloxan is commonly utilized for inducing diabetes in animal models due to its relative price and availability. The antidiabetic activity of *Phyllanthus emblica* is evaluated in this study.

Negative control group showed significant increase in bodyweight on the other side alloxen treated group showed decrease. Metformin lowered the body weight in alloxen induced diabetic rats in a dose dependent manner. But body weight increased in a dose dependent manner after administration of *P. emblica* in alloxan induced diabetic rats. Metformin and *P. emblica* both produced same effects in non-diabetic rats as they were induced in diabetic rats.

Total cholesterol level was low in negative control group on the other hand high in alloxan induced diabetic rats. Total cholesterol decreased gradually with the gradual increase in metformin dose in alloxan induced diabetic rats. Cholesterol level also decreased in alloxan induced diabetic rats after administration of *P. emblica* extract in a dose dependent manner. In non-diabetic rats, cholesterol level remains approximately same for metformin and *P. emblica* extract administration. It can be concluded that there is no associated massive lethality. For 56-day treatment period in streptozotocin induced diabetic rats, cholesterol level wasn't changed by *E. officinalis.*[24,26]

HDL level was low in negative control group. Alloxan induced diabetic rats showed high HDL level. Administration of metformin and *P. emblica* similarly decreased the HDL level in alloxan mediated diabetic rats gradually with increasing dose. Metformin and P. emblica affect the non-diabetic rats similarly.

In the negative control group, LDL levels were low. High LDL levels were found in diabetic rats produced by alloxan. Metformin and *P. emblica* administration similarly reduced LDL levels in alloxan-mediated diabetic rats with increasing dose. Metformin and *P. emblica* had similar effects in non-diabetic rats.

The negative control group had a low triglyceride level. Alloxan-induced diabetic rats had high triglyceride levels. Metformin and *P. emblica* both gradually reduced triglyceride levels in alloxan-mediated diabetic mice as the dose was increased. Metformin and *P.emblica* had the same effect on non-diabetic rats. In case of 8 week treatment period *E. officinalis* reduces triglycerides 14%.[24,26]

SGPT level was low in negative control group on the other hand high in alloxan induced diabetic rats. SGPT decreased gradually with the gradual increase in metformin dose in alloxan induced diabetic rats. SGPT level also decreased in alloxan induced diabetic rats after administration of *P. emblica* extract in a dose dependent manner. In non-diabetic rats, SGPT level remained approximately same for metformin and *P. emblica* extract administration. As a result, it was possible to infer that metformin or the plant did not appear to have any major adverse consequences. Similar result has been observed for *Tithonia diversifolia*, Anacardium *occidentale* L, *Sargassum longiotom, Streblus asper.*

The treatment of alloxan-induced rats with metformin or plant extract resulted in a dose-dependent decrease in SGOT levels, however the lowering impact was slightly larger in the case of metformin than in the case of the plant. When compared to the negative control group, the SGOT levels of the other six non-alloxan treated groups did not differ significantly, ruling out the likelihood of severe effects from metformin or the plant consumption. *T. arjuna, Anacardium occidentale L, Sargassum longiotom, Tithonia diversifolia,* and *Streblus aspera* all yielded similar findings.[27-30]

Creatinine level was low in negative control group and high in alloxan group. Creatinine levels decreases with the administration of metformin. Creatinine level decreased with the increase in dose. In the metformin and plant extract treated non-diabetic rats, the creatinine level was same as in the negative control group indicating no toxic effects in body. In case of treatment period of 56 days, Streptozotocin induced diabetic rats did not show any significant change in serum creatinine level.[31,32]

Urea level was elevated in alloxan mediated diabetic rats. After the administration of metformin and plant extract, the urea level showed reduction in a dose dependent manner. But the reduction for metformin was better than that for the plant. In non-diabetic rats the effect of metformin and plant was almost same and urea level seemed to be similar to the negative control group. It can be concluded that the plant extract has no severe effect.

The metformin and plant extract treated non-diabetic rats had similar blood glucose level to the negative control group. Alloxen induced diabetic rats showed high blood glucose level that increased with time. Metformin and *P. emblica* extract reduced the blood glucose level significantly in diabetic rats in a dose dependent manner. But the response of metformin was better than the plant extract. Methanolic extract of *Operculina turpethum* stem and roots also reduce the blood glucose level significantly in Streptozotocin induced diabetic rats.[33]

Amlaki has also given antidiabetic effect by lowering blood glucose in both streptozotocin induced diabetic rats and non-diabetic rats.[34] Some study ensure about the antihyperglycemic effect of amlaki.[35]

CONCLUSION

Our findings regarding the responses of rat models to several test batteries provide a number of indications that the ethanolic extract of *Phyllanthus emblica* may be capable of restoring multiple disrupted pathophysiological states to a healthy state. The dose-dependent improvements in responses also suggested that adequate and precise extract dosing via justifiable isolation of target therapeutic specimen from the overall extract could amplify the therapeutic impact to a reasonable degree. T. in silico research Amlaki's natural ingredients corroborate our findings to some extent and open up opportunities to investigate the therapeutic plant at the molecular level. As a result, it may be inferred that future research into *Phyllanthus emblica's* pharmacological response and phytochemical analyses may open up new avenues in disease management.

REFERENCES

1. Qureshi, S.A., Asad, W. and Sultana, V., 2009. The effect of Phyllantus emblica Linn on type-II diabetes, triglycerides and liver-specific enzyme. *Pakistan Journal of Nutrition*, 8(2): 125-128.
2. Wild, S., Roglic, G., Green, A., Sicree, R. and King, H., 2004. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes care*, 27(5): 1047-1053.
3. Liu, Y., Sun, J., Rao, S., Su, Y. and Yang, Y., 2013. Antihyperglycemic, antihyperlipidemic and antioxidant activities of polysaccharides from Catathelasma ventricosum in streptozotocin-induced diabetic mice. *Food and Chemical Toxicology*, 57: 39-45.
4. Marshal, J.W. and S.K. Bangert, 2004. *In: Clinical Chemistry: Disorders of carbohydrates metabolism.* 5th edn. Elsevier Limited, 191-217.
5. Mellitus, D., 2005. Diagnosis and classification of diabetes mellitus. *Diabetes care*, *28*(S37): S5-S10.
6. Whiting, D.R., Guariguata, L., Weil, C. and Shaw, J., 2011. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes research and clinical practice*, 94(3): 311-321.
7. Vats, V., Grover, J.K. and Rathi, S.S., 2002. Evaluation of anti-hyperglycemic and hypoglycemic effect of Trigonella foenum-graecum Linn, Ocimum sanctum Linn and Pterocarpus marsupium Linn in normal and alloxanized diabetic rats. *Journal of ethnopharmacology*, 79(1): 95-100.
8. Singh, S.K., Rai, P.K., Jaiswal, D. and Watal, G., 2008. Evidence-based critical evaluation of glycemic potential of Cynodon dactylon. *Evidence-Based Complementary and Alternative Medicine*, 5(4): 415-420.
9. Tiwari, N., Thakur, A.K., Kumar, V., Dey, A. and Kumar, V., 2014. Therapeutic targets for diabetes mellitus: an update. *Clin Pharmacol Biopharm*, 3(1): 1.
10. Tsay, H.S. and Agrawal, D.C., 2005. Tissue culture technology of Chinese medicinal plant resources in Taiwan and their sustainable utilization. *International Journal of Applied Science and Engineering*, 3(3): 215-223.
11. Valiathan, M.S., 1998. Healing plants. *Current science*, 75(11): 1122-1127.
12. Bashir, A., Mushtaq, A.A.M.I.R. and Mehboob, T., 2018. Evaluation of antioxidant and Antidiabetic activity of Phyllanthus emblica (fruit). *Biologia Pakistan*, 64(1): 85-91.
13. Sharma, P., Joshi, T., Joshi, T., Chandra, S. and Tamta, S., 2020. In silico screening of potential antidiabetic phytochemicals from Phyllanthus emblica against therapeutic targets of type 2 diabetes. *Journal of ethnopharmacology*, 248: 112268.
14. Nisha, P., Singhal, R.S. and Pandit, A.B., 2004. A study on degradation kinetics of ascorbic acid in amla (Phyllanthus emblica L.) during cooking. *International journal of food sciences and nutrition*, 55(5): 415-422.
15. Dang, G.K., Parekar, R.R., Kamat, S.K., Scindia, A.M. and Rege, N.N., 2011. Antiinflammatory activity of Phyllanthus emblica, Plumbago zeylanica and Cyperus rotundus in acute models of inflammation. *Phytotherapy Research*, 25(6): 904-908.
16. Kumaran, A. and Karunakaran, R.J., 2006. Nitric oxide radical scavenging active components from Phyllanthus emblica L. *Plant Foods for Human Nutrition*, 61(1): 1.
17. Zhang, Y.J., Tanaka, T., Iwamoto, Y., Yang, C.R. and Kouno, I., 2001. Novel Sesquiterpenoids from the Roots of Phyllanthus e mblica. *Journal of natural Products*, 64(7): 870-873.
18. Thakur, C.P. and Mandal, K., 1984. Effect of Emblica officinalis on cholesterol-induced atherosclerosis in rabbits. *The Indian journal of medical research*, 79: 142-146.
19. Mali, P.R., 2012. Study of Antidiabatic Activity of Phyllanthus emblica Linn. and Curcuma longa Linn. on Alloxan Induced Mice. *Trends in Biotechnolog y Research*, 1: 8-11.
20. Marwat, S.K., Khan, E.A., Khakwani, A.A., Ullah, I., Khan, K.U. and Khan, I.U., 2014. Useful ethnophytomedicinal recipes of angiosperms used against diabetes in South East Asian Countries (India, Pakistan & Sri Lanka). *Pakistan journal of pharmaceutical sciences*, 27(5).
21. Grover, J.K., Yadav, S. and Vats, V., 2002. Medicinal plants of India with anti-diabetic potential. *Journal of ethnopharmacology*, 81(1): 81-100.
22. Ahmad, I., Mehmood, Z. and Mohammad, F., 1998. Screening of some Indian medicinal plants for their antimicrobial properties. *Journal of ethnopharmacology*, *62*(2): 183-193.
23. Mehta, S., Singh, R.K., Jaiswal, D., Rai, P.K. and Watal, G., 2009. Anti-diabetic activity of Emblica

officinalis in animal models. *Pharmaceutical Biology*, *47*(11): 1050-1055.
24. Suryanarayana, P., Saraswat, M., Petrash, J.M. and Reddy, G.B., 2007. Emblica officinalis and its enriched tannoids delay streptozotocin-induced diabetic cataract in rats.
25. Qureshi, S.A., Asad, W. and Sultana, V., 2009. The effect of Phyllantus emblica Linn on type-II diabetes, triglycerides and liver-specific enzyme. *Pakistan Journal of Nutrition*, *8*(2): 125-128.
26. Yuneldi, R.F., Saraswati, T.R. and Yuniwarti, E.Y.W., 2018. Profile of SGPT and SGOT on Male Rats (Rattus norvegicus) Hyperglycemic After Giving Insulin Leaf Extract (Tithonia diversifolia). *Biosaintifika: Journal of Biology & Biology Education*, *10*(3): 519-525.
27. Aresta, M., Dibenedetto, A. and Quaranta, E., 2016. State of the art and perspectives in catalytic processes for CO2 conversion into chemicals and fuels: The distinctive contribution of chemical catalysis and biotechnology. *Journal of Catalysis*, *343:* 2-45.
28. Selvaraj, S. and Palanisamy, S., 2014. Investigations on the anti-diabetic potential of novel marine seaweed Sargassum longiotom against alloxan-induced diabetes mellitus: A pilot study. ||| *Bangladesh Journal of Pharmacology*|||, *9*(2): 194-197.
29. Karan, S.K., Mondal, A., Mishra, S.K., Pal, D. and Rout, K.K., 2013. Antidiabetic effect of Streblus asper in streptozotocin-induced diabetic rats. *Pharmaceutical biology*, *51*(3): 369-375.
30. Rao, T.P., Sakaguchi, N., Juneja, L.R., Wada, E. and Yokozawa, T., 2005. Amla (Emblica officinalis Gaertn.) extracts reduce oxidative stress in streptozotocin-induced diabetic rats. *Journal of medicinal food*, *8*(3): 362-368.
31. Ansari, A., Shahriar, M.S.Z., Hassan, M.M., Das, S.R., Rokeya, B., Haque, M.A., Haque, M.E., Biswas, N. and Sarkar, T., 2014. Emblica officinalis improves glycemic status and oxidative stress in STZ induced type 2 diabetic model rats. *Asian Pacific journal of tropical medicine*, *7*(1): 21-25.
32. Pulipaka, S., Challa, S.R. and Pingili, R.B., 2012. Comparative antidiabetic activity of methanolic extract of Operculina turpethum stem and root against healthy and streptozotocin induced diabetic rats. *International Current Pharmaceutical Journal*, *1*(9): 272-278.
33. Mehta, S., Singh, R.K., Jaiswal, D., Rai, P.K. and Watal, G., 2009. Anti-diabetic activity of Emblica officinalis in animal models. *Pharmaceutical Biology*, *47*(11): 1050-1055.
34. Paul, D.S., Walton, F.S., Saunders, R.J. and Stýblo, M., 2011. Characterization of the impaired glucose homeostasis produced in C57BL/6 mice by chronic exposure to arsenic and high-fat diet. *Environmental health perspectives*, *119*(8): 1104-1109.