Investigation of Pharmacological Screening Techniques for Diabetes Mellitus

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KEYWORDS

Health, Health care, pharmacist, pharmaceutical care

ABSTRACT

Diabetes is the medical term for a condition in which the body fails to generate or use insulin as intended, leading to high blood sugar levels. Both in-vitro and in-vivo techniques are employed to assess the antidiabetic potential of synthetic or natural compounds that have been extracted from conventional plants. The rat paw oedema method is frequently used to screen anti-inflammatory medications. The use of animals in this procedure has drawbacks related to ethical concerns. We proposed an in vitro system in this context that would not have these drawbacks. Rat in vivo experiments are frequently used to screen anti-hyperlipidemic medications. Pharmacological screening currently entails testing novel chemical entities as plant extracts or any other type of material (synthetic or semisynthetic) in isolated preparations before testing on entire animals. Rats and mice are typically used, but occasionally higher animals like dogs and monkeys are as well. These techniques have been used to assess the majority of medications now used in therapy. Wherever possible, non-animal alternatives are being developed. Pharmacologists' constant struggle is to reconcile in vitro and in vivo results. A thorough grasp of the in vivo performance is one of the main objectives of pharmacological screening. Therefore, it would be praiseworthy to establish in vitro assessments that might be connected to in vivo performance.

1. Introduction

Diabetes mellitus is a complex condition linked to numerous illnesses, particularly vascular problems [1]. The primary causes of this illness are modern lifestyle choices including eating a lot of fast food, drinking a lot of alcohol, and not exercising. Diabetes is more common in today's world. Diabetes may result from an imbalance in various substances, including oestrogens, corticosteroids, glucagon, pituitary hormones, thyroid hormones, adrenaline, and so on. Elevation of blood glucose is caused by these substances' alteration. GLP1 stimulates the pancreatic beta cells, which then release more insulin [2]. Diabetes has several side effects, such as poor blood flow to the legs, cardiac problems, renal failure, pain, loss of feeling, numbness, etc. Diabetes is a common cause of vision problems. Long-lasting consequences eventually result in blindness and, more prominently, kidney damage. Diabetes patients have a twofold increased risk of heart attacks compared to healthy individuals [3][12]. If a woman has diabetes, the children will also have diabetes. Although diabetes cannot be totally treated, its effects can be minimised with early detection. Diabetes can successfully prevent or lessen the subsequent issues it causes. One of the key treatments for lowering the consequences of diabetes is diet control. Preserving body weight is another diabetes control strategy [4]. Diabetes patients should avoid getting married to other diabetic patients because this increases their chances of having children, maintaining good personal hygiene, getting regular exercise, cutting back on carbohydrate-rich foods, managing stress and emotions, etc. Numerous antidiabetic medications with varying pharmacological activities are on the market, including sulfonylurea, biguanides derivatives, and alpha glycosidase inhibitors. [11].

2. Literature Review

Analysing the effects of synthetic or natural compounds on haemoglobin glycosylation, glucose absorption, and the inhibition of alpha-glucosidase and alpha-amylase enzymes are some in-vitro techniques used to assess their antidiabetic qualities. Alpha-amylase is the enzyme that breaks down alpha-bond connected polysaccharides into disaccharides, including starch and glycogen [6]. Because glucose is not readily available via the gastrointestinal system, the test compound's inhibitory character reflects its anti-diabetic efficacy. The hydrolysis of sucrose and isomaltose is catalysed by the bifunctional enzyme sucrase-isomaltase [5]. The sample's impact on sucrose activity is measured using Honda and Hara's methodology. Numerous labs have been paying closer attention to the features of the yeast sugar transport system [14]. As their primary source of carbon and energy, one or more sugars can be used by all known yeasts. Yeast produces ethanol from this sugar. Research has been done on how insulin affects rats' soleus muscles' ability to absorb glucose during hemorrhagic shock [7]. D(U-

14C) glucose is treated with adipocytes for 20 minutes at a final concentration of 0.2 mM. Cells are taken out and their radioactivity is quantified after being centrifuged on silicon oil to extract them from the media. There are several techniques used to accomplish this, including chemical, surgical, and genetically induced diabetes models. Key diabetogenic agents that cause diabetes include streptozocin, alloxan, and other chemicals that damage pancreatic cells to cause diabetes in rats, a single injection of streptozocin (typically 60 mg/kg) is required. Following three days of injection, the animal may develop diabetes as a result of degenerative alterations in the pancreatic Langerhans cells [8].

3. Methodology

Metformin hydrochloride is the material utilized in this investigation, while Design Expert is the equipment and software used. In this study, we used alloxan-induced diabetes rats to gather in vivo data on the antidiabetic action of metformin, the conventional medication of choice [13]. Using Microsoft Excel software, the estimated fasting blood glucose readings were calculated from the provided graph. The majority of published in vivo blood glucose level data were collected using glucometers, which supported the use of glucometers in the in vitro investigations. Plasma glucose concentration can be simulated by properly arranging compartments to mimic physiological systems (CG). The main goal of the study was to develop a tool that could mimic plasma concentrations similar to the in vivo response of anti-diabetic drugs, and then to correlate results from in vitro and in vivo experiments [10]. The sample compartment is a glass chamber, or any other suitable material of construction, with a volume capacity of approximately 1000 mL. The end of a silicone tube that is connected to a peristaltic pump can be fastened to the compartment's fitting. The other end of the silicone tube is placed inside the plasma compartment. In order to stop yeast and insoluble residue from being pumped into the reservoir compartment, there can be a filter connection point on the silicon tube end [9]. In the course of the current investigation, we did not use any filters. The filtered sample is pumped from the sample container into the reservoir compartment. An infusion bottle was used as the reservoir compartment in this study. Blood glucose concentration in vivo is simulated via a plasma compartment chamber. About 100 mL of glucose at a concentration of 80–120 mg/dL make up the plasma compartment; the precise amount chosen depends on the chosen in vivo response. The same as in vivo investigations, samples (one or two drops) are taken at predefined intervals. There is an outlet in the chamber that controls the fixed volume of the plasma compartment. Using a magnetic stirrer guarantees that the fluid in the plasma compartment is properly mixed. The delivered sample compartment fluid and the plasma compartment fluid are instantly mixed thanks to the churning. Figure 1 shows a schematic illustration of the in vitro apparatus that was developed for the investigation.

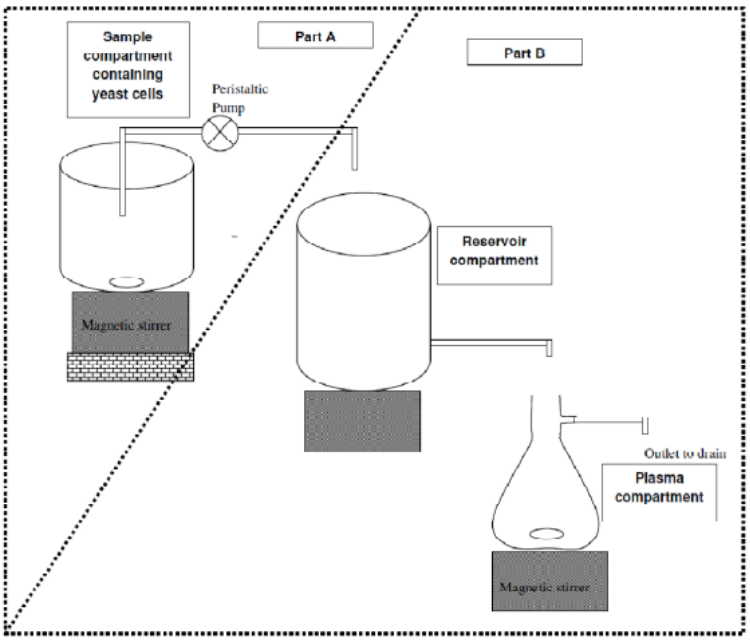

Figure 1. system flow

An IVIVC plot was created. It was discovered during the early research that the length, intervals, and total time needed for the assessment of the anti-inflammatory drugs must be fixed or optimised. It should be easier to track the variations in the outcomes during the chosen periods.

4. Results and Discussion

A diabetic rat model produced by alloxan was used for the in vivo evaluation. Figure 2 displays the glucose level of the rats following different treatments.

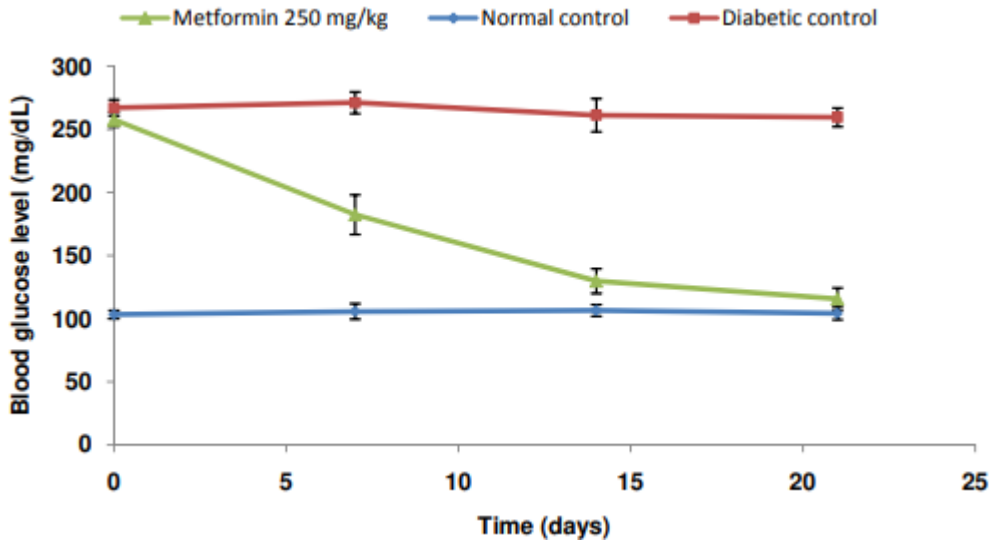

Figure 2. Blood glucose level of rats after treatment

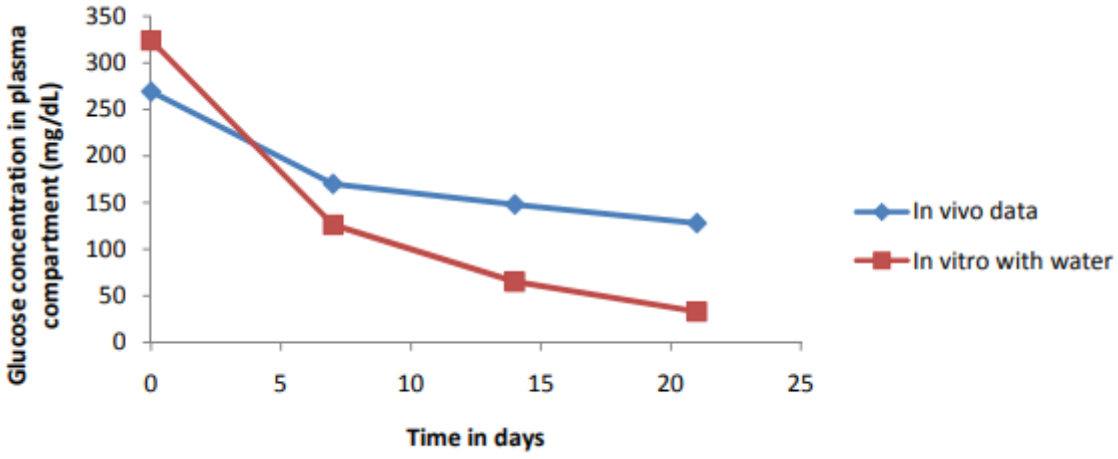

Figure 3. Initial assessment

The sample compartment needed to be ready in order to fill the reservoir compartment with an optimally concentrated glucose solution, which was the following stage in the investigation. It was vital to assess how the presence of metformin affected the change in glucose concentration before setting a time.

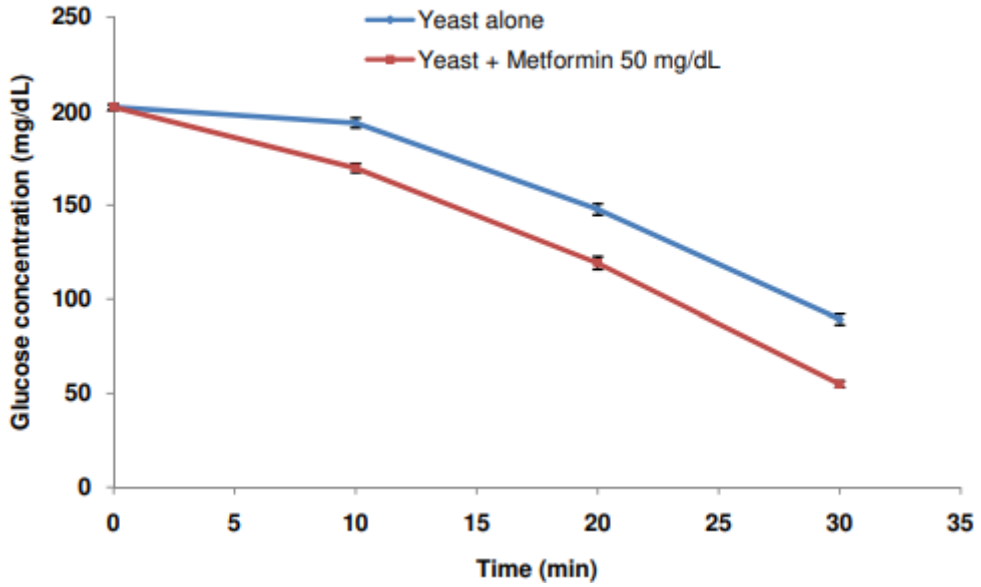

Figure 4. Yeast suspensions' glucose concentrations with and without metformin

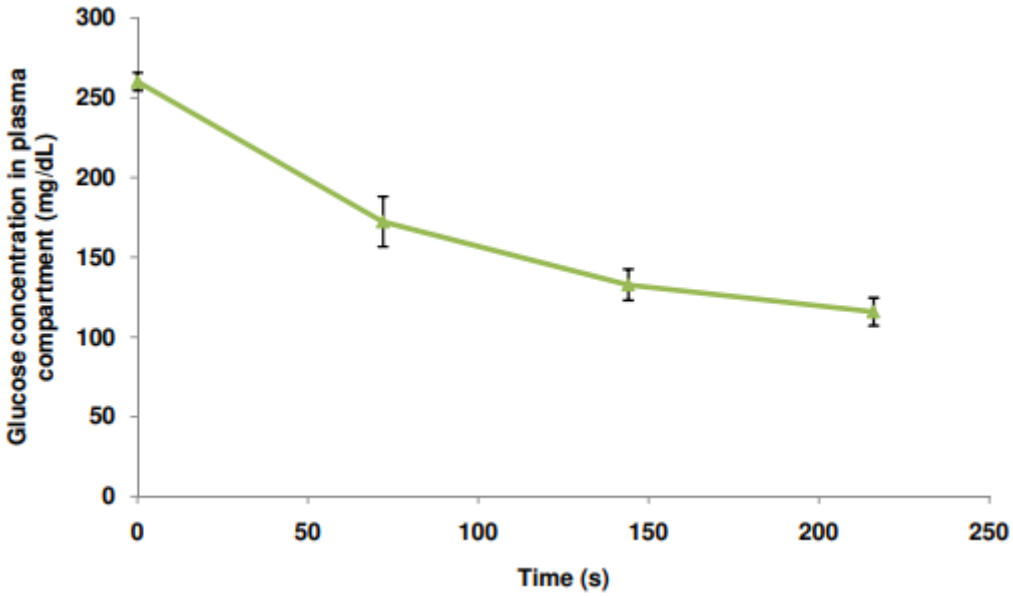

Figure 5. The amount of glucose in the plasma section

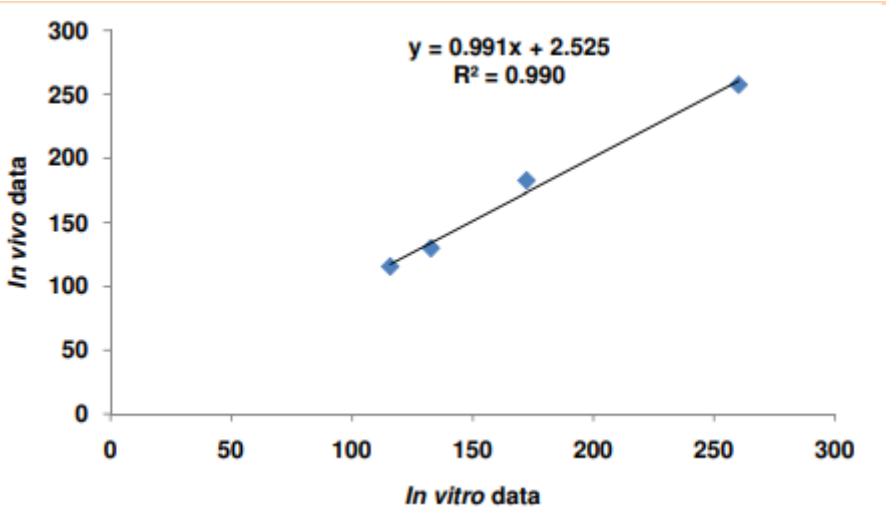

Figure 6. IVIVC plot (anti-diabetic activity)

A successful IVIVC is indicated by the IVIVC plot, which shows a strong connection between in vitro and in vivo data.

5. Conclusion

Under the current circumstances, the development of reliable in vitro screening or evaluation methods that could serve as stand-ins for animal research may be worthwhile. These in vitro methods may take the place of laborious and unresolved animal experiments. They also steer clear of moral dilemmas with the care and use of animals in research. It could be very helpful to correlate in vitro activity with an animal pharmacodynamic screening strategy. The study's findings demonstrated that metformin increases yeast cells' uptake of glucose, which causes a drop in the amount of glucose in the sample compartment. Therefore, it was anticipated that medications that resembled metformin would alter the sample compartment in a comparable way, making it possible to screen for their anti-diabetic effects.

Reference

[1] Meng, Fan-Cheng, Zheng-Feng Wu, Zhi-Qi Yin, Li-Gen Lin, Ruibing Wang, and Qing-Wen Zhang. "Coptidis rhizoma and its main bioactive components: recent advances in chemical investigation, quality evaluation and pharmacological activity." Chinese Medicine 13 (2018): 1-18.

[2] Tătaru, Iulian, Oana M. Dragostin, Iuliu Fulga, Florentina Boros, Adelina Carp, Ariadna Maftei, Carmen L. Zamfir, and Aurel Nechita. "The modern pharmacological approach to diabetes: innovative methods of monitoring and insulin treatment." Expert Review of Medical Devices 19, no. 7 (2022): 581-589.

[3] Ajebli, Mohammed, and Mohamed Eddouks. "Buxus sempervirens L improves streptozotocin-induced diabetes mellitus in rats." Cardiovascular & Haematological Disorders-Drug Targets (Formerly Current Drug Targets-Cardiovascular & Hematological Disorders) 17, no. 2 (2017): 142-152.

[4] Sofiene, M., Souhaila, B., & Souhir, C. (2024). Machine Learning for Early Diabetes Detection and Diagnosis. Journal of Wireless Mobile Networks, Ubiquitous Computing, and Dependable Applications (JoWUA), 15(1), 216-230.

[5] Ortiz-Martínez, Margarita, Mirna González-González, Alexandro J. Martagón, Victoria Hlavinka, Richard C. Willson, and Marco Rito-Palomares. "Recent developments in biomarkers for diagnosis and screening of type 2 diabetes mellitus." Current diabetes reports 22, no. 3 (2022): 95-115.

[6] Shah, V.D., Chauhan, B., Satani, B. Development and validation of HPTLC method for the estimation of Vasicine, Curcumin and Cucurbitacin B in an ayurvedic formulation: Panchtikta Ghrita(2018) International Journal of Pharmaceutical Research, 10 (2), pp. 138-142.

[7] Bobir, A.O., Askariy, M., Otabek, Y.Y., Nodir, R.K., Rakhima, A., Zukhra, Z.Y., Sherzod, A.A. (2024). Utilizing Deep Learning and the Internet of Things to Monitor the Health of Aquatic Ecosystems to Conserve Biodiversity. Natural and Engineering Sciences, 9(1), 72-83.

[8] Ojo, Oluwafemi Adeleke, Hannah Sokolayam Ibrahim, Damilare Emmanuel Rotimi, Akingbolabo Daniel Ogunlakin, and Adebola Busola Ojo. "Diabetes mellitus: From molecular mechanism to pathophysiology and pharmacology." Medicine in Novel Technology and Devices 19 (2023): 100247.

[9] Pathak, Rashmi, Neetu Sachan, and Phool Chandra. "Mechanistic approach towards diabetic neuropathy screening techniques and future challenges: A review." Biomedicine & Pharmacotherapy 150 (2022): 113025.

[10] S. Neelima, Manoj Govindaraj, Dr.K. Subramani, Ahmed ALkhayyat, & Dr. Chippy Mohan. (2024). Factors Influencing Data Utilization and Performance of Health Management Information Systems: A Case Study. Indian Journal of Information Sources and Services, 14(2), 146–152. https://doi.org/10.51983/ijiss-2024.14.2.21
[11] Akinyede, Kolajo Adedamola, Habeebat Adekilekun Oyewusi, Gail Denise Hughes, Okobi Eko Ekpo, and Oluwafemi Omoniyi Oguntibeju. "In vitro evaluation of the anti-diabetic potential of aqueous acetone helichrysum petiolare extract (AAHPE) with molecular docking relevance in diabetes mellitus." Molecules 27, no. 1 (2021): 155.
[12] Wang, Ying, Baichun Hu, Shasha Feng, Jian Wang, and Fengjiao Zhang. "Target recognition and network pharmacology for revealing anti-diabetes mechanisms of natural product." Journal of Computational Science 45 (2020): 101186.
[13] Sumiati., Penny, H., Agung, T., Afrasim, Y., & Achmad, S. (2024). Classification of Heart Disorders Using an Artificial Neural Network Approach. Journal of Internet Services and Information Security, 14(2), 189-201.
[14] Zhu, Chunyan, Tingting Cai, Ying Jin, Jiayun Chen, Guoqiang Liu, Niusheng Xu, Rong Shen et al. "Artificial intelligence and network pharmacology based investigation of pharmacological mechanism and substance basis of Xiaokewan in treating diabetes." Pharmacological research 159 (2020): 104935.
[15] Aziz, Namra, Biswajit Dash, Pranay Wal, Prachi Kumari, and Poonam Joshi. "New horizons in diabetic neuropathies: an updated review on their pathology, diagnosis, mechanism, screening techniques, pharmacological, and future approaches." Current Diabetes Reviews 20, no. 6 (2024): 25-43.