Article

JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Special Issue 2: Proceedings of Al-Muthanna University's First Conference/Directing Scientific Research Towards Achieving Sustainable

Vol, 33; S.2 | 2025

Determining the Antidiabetic Effect of Nanoliposomal Metformin on Pancreatic tissueTissue in Male Albino Rats Induced with Diabetes by Alloxan

Baha Sihab Saleh[1]*, Buthaina Abdul Hamid Abdullah[1]

[1,2,]*Department of Biology, College of Education for Pure Sciences, Al-Muthanna University, Samawah, 66001, Iraq*

***Corresponding author email:** dr.yassiralasadiy@mu.edu.iq

[1]*Department of Pharmaceuticals, Physiology, and Biochemistry, College of Veterinary Medicine, Tikrit University, Salah al-Din, Iraq.*

*Corresponding Author: bahaasahab73@gmail.com

DOI:

Received 00 Month 2000; Accepted 01 Month 2000; Available online 02 Month 0000

Published:31/08/2025

ABSTRACT:

Background: One of the most important treatments for patients with type 2 diabetes mellitus (T2DM) is metformin. This drug primarily works by preventing the pancreas from producing glucose, which leads to reduced fasting glucose levels. Nanolipid technology was used to enhance the action of metformin. Nanotechnology, such as Nano-lipid, is a unique approach that can effectively boost the topical delivery of medications without changing their molecular structure.

This study aims: to determine the harmful side effects of metformin and its efficacy against diabetes induced by alloxan in adult male albino rats.

Methods: Using the nanolipid technique after loading metformin onto nanoscale lipids (structured nanolipids). The loading was confirmed through several tests, including entrapment efficiency, transmission electron microscopy, and Fourier-transform infrared spectroscopy (FTIR), as well as X-ray diffraction (XRD). The experiment was conducted at the College of Veterinary Medicine at Tikrit University in the college's animal house. Fifty adult male albino rats weighing between 200 and 250 grams were used to determine the effect of metformin on liver cell tissue. The rats were divided into five groups: the first group received no drug, the second group was given alloxan (150 mg/kg) only, the third group received only nanoliposomal formulation without any drug, the fourth group was given alloxan with nanoliposomal metformin, and the fifth group received metformin (500 mg) along with alloxan.

Results: The fourth group (Aloxan + fatty metformin nano) exhibited considerable recovery, with minimal changes in pancreatic islets, suggesting the effectiveness of lipid nanotechnology in preserving pancreatic function. Similarly, the fifth group (Aloxan + metformin 500 mg/kg) showed significant improvement, aligning with previous research findings.

Conclusion: These results highlight the potential of nanotechnology-based treatments, particularly lipid nanoformin, in mitigating Aloxan-induced pancreatic damage and restoring islet cell integrity.

Keyword: Metformin, Nanol-ipid, Pancreatic tissue, diabetes.

Article

JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Special Issue 2: Proceedings of Al-Muthanna University's First Conference/Directing Scientific Research Towards Achieving Sustainable

Vol, 33; S.2 | 2025

info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com ISSN: 2312-8135 | Print ISSN: 1992-0652

1. INTRODUCTION

One of the most important treatments for patients with type 2 diabetes mellitus (T2DM) is metformin, which was recently recognized by the American Diabetes Association (2017) (Rojas & Gomes, 2013). This drug primarily works by preventing the pancreas from producing glucose, which leads to reduced fasting glucose levels (Liang et al., 2013). Additionally, metformin has been found to act as an antioxidant, thereby reducing the risk of cancer and improving insulin sensitivity (Buczyńska, Sidorkiewicz, Krętowski, Zbucka-Krętowska, & Adamska, 2022). Metformin also has positive effects on blood disorders, blood clotting, triglycerides, and inflammation, making it beneficial for vascular functions (Grant, 2003). Some studies have described how metformin lowers very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), triglycerides, clotting factors, plasminogen activators, and C-reactive protein, and increases high-density lipoprotein (HDL) cholesterol, particularly in abnormal cases (Al-Majali, 2004). Other studies have shown a significant effect of metformin on blood lipids. In 1994, metformin was approved by the Food and Drug Administration (FDA), and in the guidelines for type 2 diabetes patients, it is recommended as the first-line medication due to its low cost, safety, and association with a reduced risk of vascular and cardiac diseases (Lorber, 2014). Metformin does not bind to plasma proteins and is excreted unchanged in urine via active secretion by renal tubular cells (approximately 78.9–99.9%) (Zhang et al., 2019). Some studies have indicated that this drug is significant in lowering androgen levels in the blood when used by patients with polycystic ovary syndrome, thus becoming important for regulating menstrual cycles (Jayasena & Franks, 2014). It also helps reduce body weight by suppressing appetite (Woods & D'Alessio, 2008).

1.1 Objective of the Study

To minimize the side effects of metformin treatment on Pancreatic tissue at lower doses and its impact on liver tissue.

2. MATERIALS AND METHODS

2.1 Experimental Animals

Fifty mature male rats were used, obtained from the Veterinary Medicine College at the animal house of Tikrit University. The rats were aged between 10 and 12 weeks, with an average weight ranging from 200 to 250 grams. The experiment was conducted from February 1 to March 1, 2024, at the animal house of the Veterinary Medicine College at Tikrit University. The animals were housed in standard plastic cages measuring 46 × 28 × 13 cm, with appropriate lighting, ventilation, and controlled temperature (20 to 25 degrees Celsius). To maintain hygiene, the cage floors were covered with sawdust, replaced two to three times a week, with unrestricted access to food and water, and artificial lighting.

2.1 Sample Collection

At the end of the designated experimental period of 30 days, after inducing diabetes in male rats and administering metformin and lipid-based nanometformin, the animals were fasted again. Blood samples were drawn every 4 days for a total of 6 times. Blood was collected directly from the cardiac vein or the tail vein and placed in test tubes free of anticoagulants. Serum was separated using a centrifuge for 15 to 30 minutes and then transferred to a refrigerator for storage at -20°C

Article

JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Special Issue 2: Proceedings of Al-Muthanna University's First Conference/Directing Scientific Research Towards Achieving Sustainable

Vol, 33; S.2 | 2025

until clinical tests were conducted for biochemical groups (triglycerides, glucose, cholesterol, HDL-C, LDL-C, antioxidants, creatinine, and insulin). The animals were then dissected, and the liver, kidneys, and pancreas were removed for histological sectioning to observe changes in the tissue during the study period when diabetes was induced and treated with metformin and lipid-based nanometformin, as well as to assess differences.

2.2 Experimental animal design

The average weight of an adult human is 70 kg, and the typical dosage administered is 500 mg or 850 mg of the glucose-regulating drug. Since the average weight of the animals was around 250 grams, the resulting dosage was calculated by multiplying the drug quantity by the average weight of the animals in a group and dividing the result by 7,000, which is the average body weight of an adult human in grams. To obtain the concentration for a single dose for each group of animals, we multiply by 0.0357 (10^3), resulting in 0.3571 grams for a concentration of 500 mg.

Each group of animals received one of the drugs after taking 10 tablets of solid metformin, which were ground using a designated mortar and pestle, weighed, and dissolved in 50 ml of distilled water. Each animal was given 1 ml of the drug administered orally using a specialized syringe, and this process continued throughout the dosing days. The control and induction groups were left untreated.

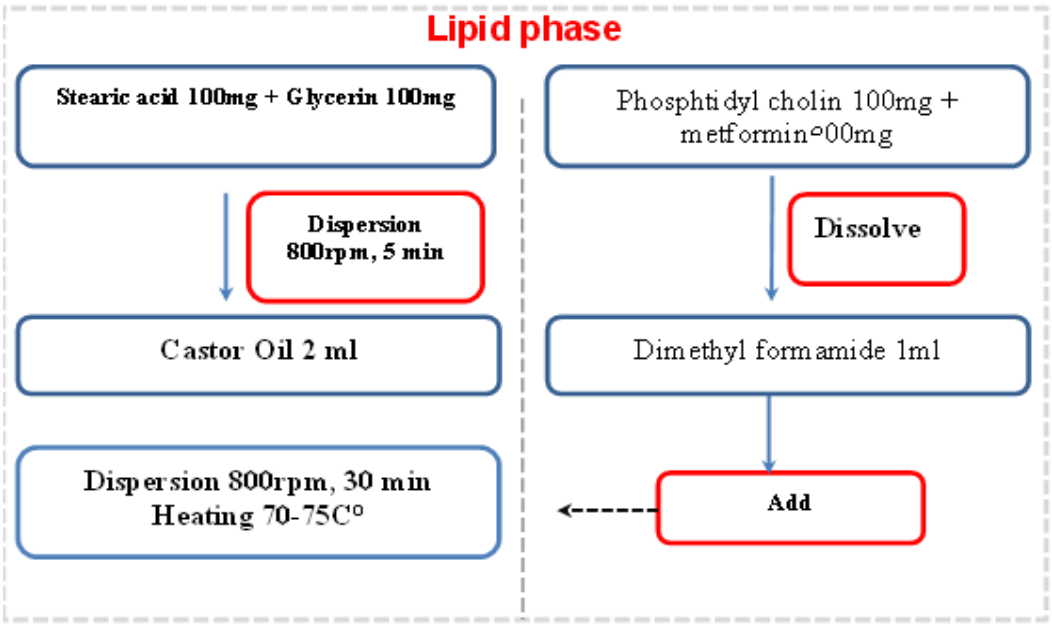
2.3 Experimental Design

The experiment was divided into two main parts:

1. Preparation of Lipid-Based Nanometformin Using Solvent Evaporation and Standardization.
2. Determining the Effects of Lipid-Based Nanometformin and Regular Metformin on the Pancreatic tissue of Adult Male Rats.

Preparation of Lipid-Based Nanometformin

Protocol for preparing the lipid nanostructure:



مجلة جامعة بابل للعلوم الصرفة والتطبيقية مجلة جامعة بابل للعلوم الصرفة والتطبيقية مجلة جامعة بابل للعلوم الصرفة والتطبيقية

info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com ISSN: 2312-8135 | Print ISSN: 1992-0652

The diagram illustrates how to prepare lipid-based nano metformin. The lipid phase consisted of two forms:

- Lipid Form: The lipid state was created by dispersing at 800 RPM with 2 mL of castor oil after dissolving 100 mg of fatty acid with 100 mg of glycerol monostearate, and the mixture was vortexed at 1500 RPM for 30 minutes.
- Dissolved Form: The growing lipids were dissolved in 100 mg of phosphatidylcholine, requiring 800 RPM of loaded and dispersed metformin for 30 minutes. After that, the dissolved mixture was blended with the lipid form for one hour at 800 RPM and cooled overnight at 8 degrees Celsius until needed. Before use, mix for 30 minutes while spinning at 800 RPM.

3. RESULTS AND DISCUSSION

The results are shown through Figure (1) and according to the relative study of this tissue section. There is, in the first group, which has not been given treatment, the presence of clearly the pancreatic capsule, soft pancreatic fascia, and interlobular goyzers as well as gland samples, while the second group was given Aloxan at significant differences (R≤0.01) when reading the tissue sections of the pancreas. The reading showed, as in Figure (2) that there is hyperplasia in the endocrine cells of the islets of Lankerhans and there is vesicular cytodecay as well as separation in samples of lobular tissue as well as infiltration in the blood between the fine capillaries as in Figure (3).

Figure (4) of the third group, which was given aloxan with fatty nanotechnology only at significant differences (R≤0.01), showed the presence of intraplatelet channels lined with cuboid cells and compact external secretory samples with the presence of phagocytes around these samples, as well as in the fibrous tissue of vesicles with a vessel blood vessel and also infiltration in blood cells.

Figure (5) of the fourth group that was given luloxan with metformin fatty nanotherapy at significant differences (R≤0.01) showed that there are samples of external secretion of equal shape lined with pyramidal cells with the presence of an intralobule channel with the presence of endocrine cells in the islets of Lankerhans with capillaries inside the islands and the presence of the blood vessel and Figure (6) of the fifth group that was given aloxan with metformin 500 mg / kg at significant differences (R≤0.01) the presence of endocrine cell hyperplasia in the islets of Lankerhans With capillaries with a fascia of fibrous specimens and lining blood cells

It was observed through the forms that the pancreatic tissue was normal in the first group compared to the other groups, while in the second group, large abnormalities and secretions were observed in the cells of the islets of Lankerhans and beta cells after being injected into Aloxan, as well as in the third group, which was injected into Aloxan with fatty nano-only.

An improvement was observed in the fourth group that was injected with aloxan with fatty metformin nano, where it was noted that there were no significant changes or damage in the islet cells in the pancreas after giving them doses of lipid nanoformin, due to the advantages of lipid nanotechnology in reaching and returning the affected tissues.

When comparing the fifth group with other groups, we note that there is an improvement in pancreatic cells and islet cells after giving them aloxan followed by metformin 500 mg / kg and this study is consistent with the results of the study of (Balamash and ALkreathy). (Balamash, 2018)

مجلة جامعة بابل للعلوم الصرفة والتطبيقية | مجلة جامعة بابل للعلوم الصرفة والتطبيقية | ISSN: 2312-8135 | Print ISSN: 1992-0652
info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com

Article

JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Special Issue 2: Proceedings of Al-Muthanna University's First Conference/Directing Scientific Research Towards Achieving Sustainable

Vol, 33; S.2 | 2025

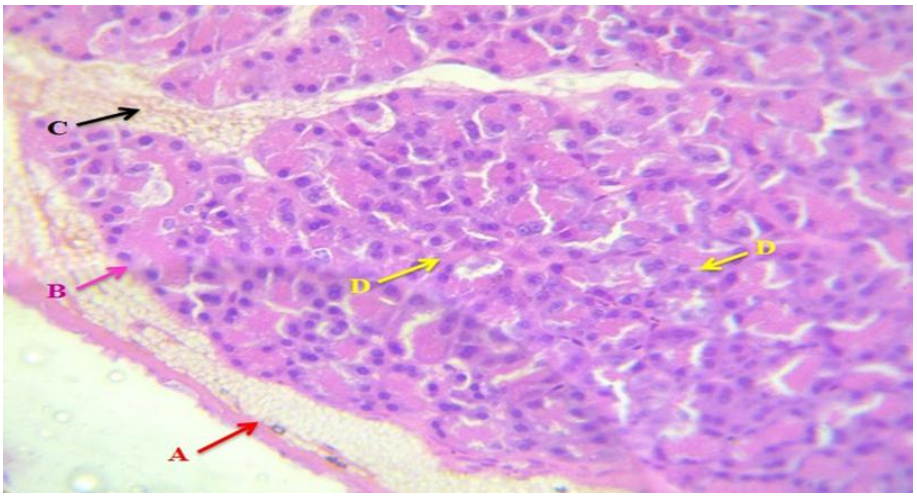


Figure (1): Pancreatic filters, pancreatic capsule (A) Soft pancreatic fascia, (B) Interlobular vesicles, (C) Samples, (D) Gland CH2EX40.

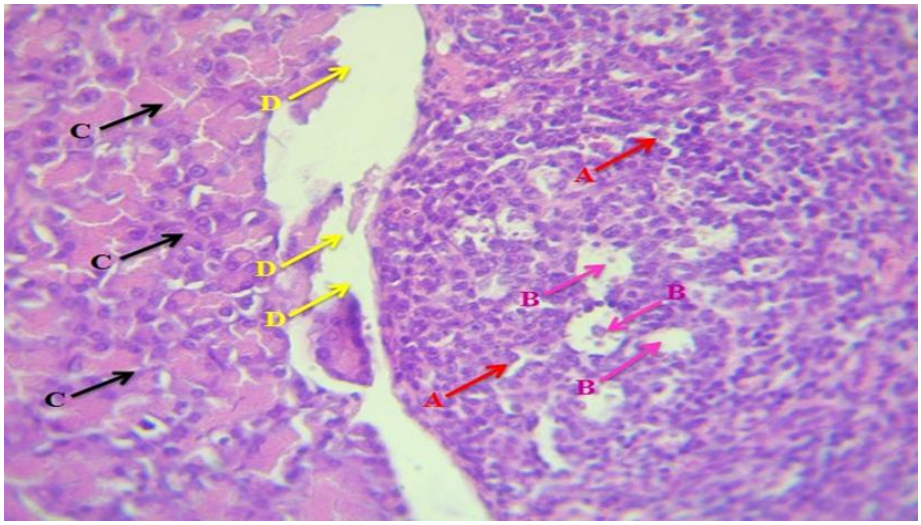


Figure (2): Pancreatic tissue, endocrine cell hyperplasia of the Lankerhans islets (A) Vesicular cytodecay, (B) Separation of samples from lobular tissue, (C) CH2EX40.

مجلة جامعة بابل للعلوم الصرفة والتطبيقية مجلة جامعة بابل للعلوم الصرفة والتطبيقية

info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com ISSN: 2312-8135 | Print ISSN: 1992-0652

Article

JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Special Issue 2: Proceedings of Al-Muthanna University's First Conference/Directing Scientific Research Towards Achieving Sustainable

Vol, 33; S.2 | 2025

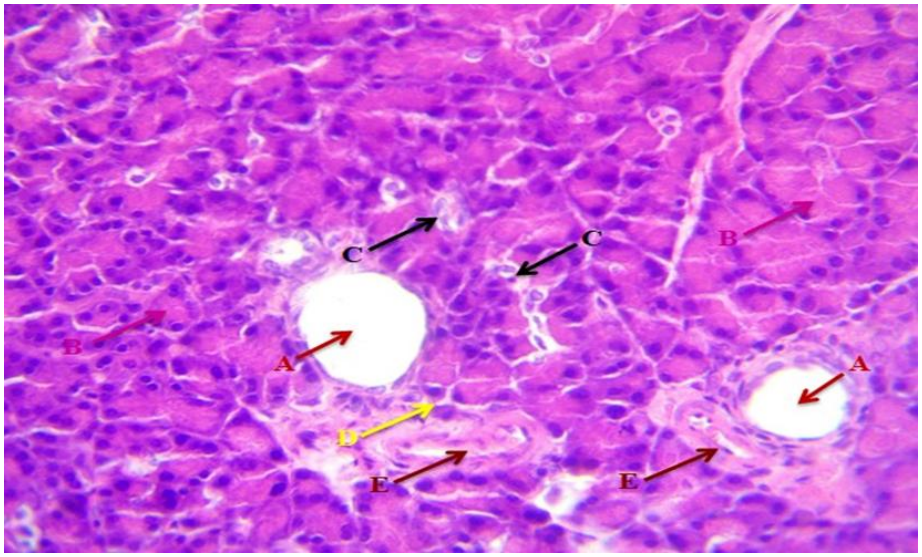


Figure (3): Pancreatic tissue, intraplatelet channels lined with cubic cells (A) Compactic external secretory samples, (B) Phagocytes around samples, (C) and in the fibrous tissue of vesicles, (D) Vesicular blood vessel, (E) CH2EX40.

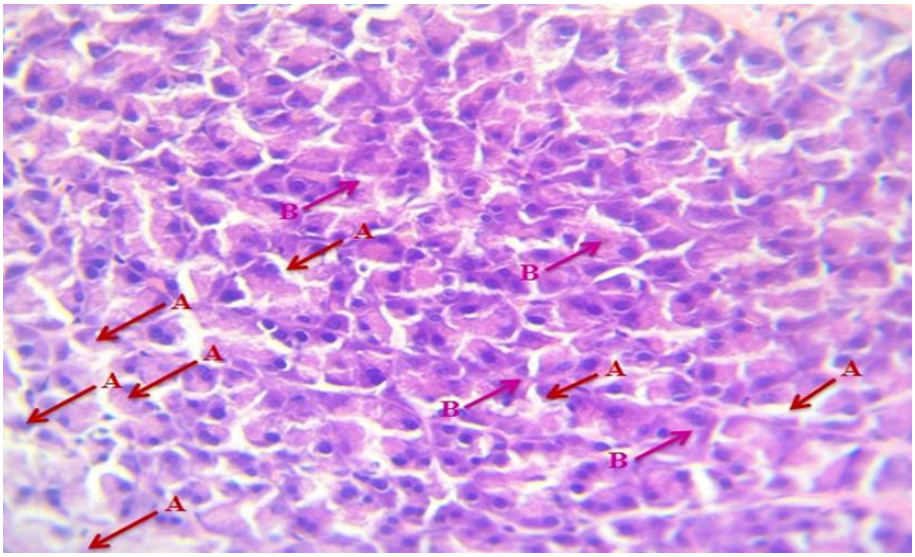


Figure (4): Pancreatic tissue, tissue fascia Pavement around the samples and in which the blood cells of the ventricle (A) External secretion samples, (B) CH2EX40.

مجلة جامعة بابل للعلوم الصرفة والتطبيقية مجلة جامعة بابل للعلوم الصرفة والتطبيقية

info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com ISSN: 2312-8135 | Print ISSN: 1992-0652

Article

JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Special Issue 2: Proceedings of Al-Muthanna University's First Conference/Directing Scientific Research Towards Achieving Sustainable

Vol, 33; S.2 | 2025

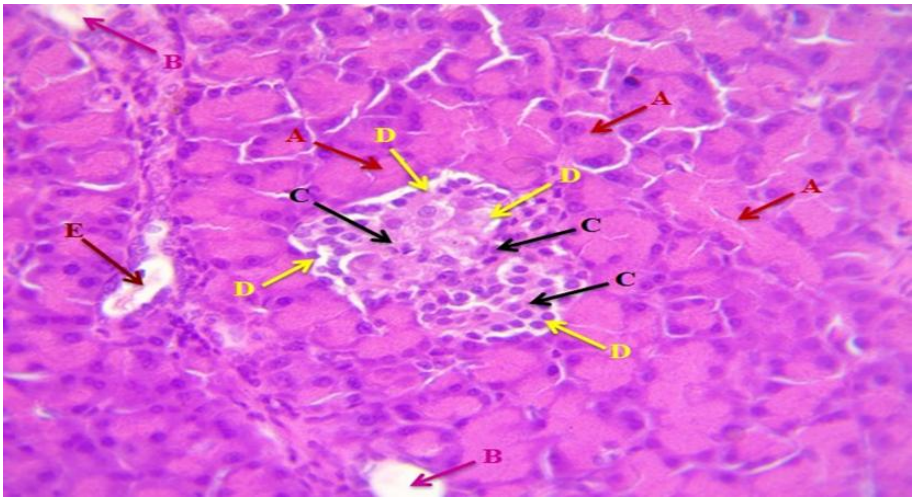


Figure (5): pancreatic tissue, Samples of exocrine are evenly shaped lined with pyramidal cells (A) Intralobule, Channel, (B) Lankerhans islets with endocrine cells, (C) Capillaries inside reflux, (D) CH2EX40, (E) blood vessel.

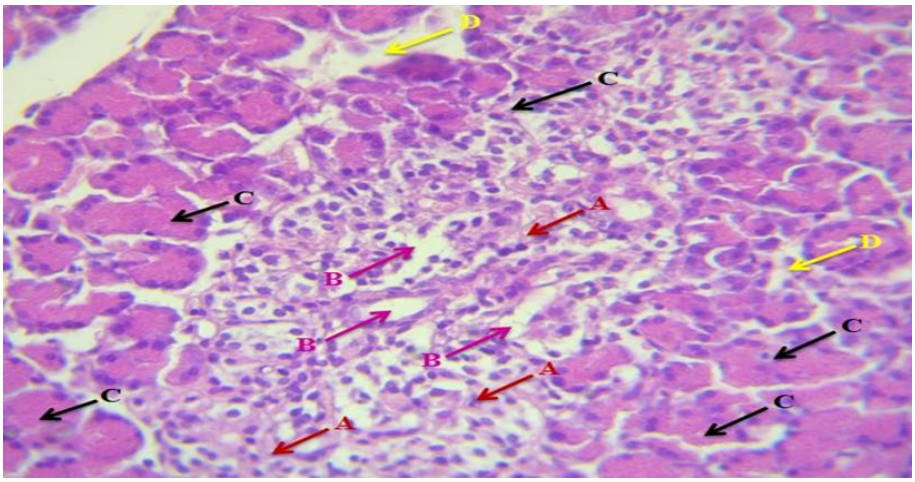


Figure (6): Pancreatic tissue, Lankerhans islets with endocrine cell hyperplasia in the middle of the circumference of the islands (A) Capillaries, (B) Exocrine samples, (C) Fibroblast fascia with lined blood cells, (D) CH2EX40.

مجلة جامعة بابل للعلوم الصرفة والتطبيقية مجلة جامعة بابل للعلوم الصرفة والتطبيقية

info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com ISSN: 2312-8135 | Print ISSN: 1992-0652

4. RECOMMENDATIONS

We suggest conducting studies to evaluate the biochemical mechanisms of metformin and how it can be utilized in a therapeutic context against oxidative damage.

5. CONCLUSIONS:

Notably, the (Nano-lipid metformin) exhibited considerable recovery, with minimal changes in pancreatic islets, suggesting the effectiveness of lipid nanotechnology in preserving pancreatic function. These results highlight the potential of nanotechnology-based treatments, particularly lipid nanoformin, in mitigating Aloxan-induced pancreatic damage and restoring islet cell integrity.

Conflict of interests.

There are non-conflicts of interest.

References

[1] Al-Majali, K. (2004). Postprandial lipaemia in type 2 diabetes: relationship to insulin sensitivity. University of London, University College London (United Kingdom).

[2] Buczyńska, A., Sidorkiewicz, I., Krętowski, A. J., Zbucka-Krętowska, M., & Adamska, A. (2022). Metformin intervention—a panacea for cancer treatment? Cancers, 14(5), 1336.

[3] Grant, P. J. (2003). Beneficial effects of metformin on haemostasis and vascular function in man. Diabetes & Metabolism, 29(4), 6S44-6S52.

[4] Jayasena, C. N., & Franks, S. (2014). The management of patients with polycystic ovary syndrome. Nature Reviews Endocrinology, 10(10), 624–636.

[5] Liang, J., Liu, C., Qiao, A., Cui, Y., Zhang, H., Cui, A., … Chen, Y. (2013). MicroRNA-29a-c decrease fasting blood glucose levels by negatively regulating hepatic gluconeogenesis. Journal of Hepatology, 58(3), 535–542.

[6] Lorber, D. (2014). Importance of cardiovascular disease risk management in patients with type 2 diabetes mellitus. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 169–183.

[7] Rojas, L. B. A., & Gomes, M. B. (2013). Metformin: an old but still the best treatment for type 2 diabetes. Diabetology & Metabolic Syndrome, 5, 1–15.

[8] Woods, S. C., & D'Alessio, D. A. (2008). Central control of body weight and appetite. The Journal of Clinical Endocrinology & Metabolism, 93(11_supplement_1), s37–s50.

[9] Zhang, G., Ma, Y., Xi, D., Rao, Z., Sun, X., & Wu, X. (2019). Effect of high uric acid on the disposition of metformin: in vivo and in vitro studies. Biopharmaceutics & Drug Disposition, 40(1), 3–11.

[10] Balamash, K. S., Alkreathy, H. M., Al Gahdali, E. H., Khoja, S. O., & Ahmad, A. (2018). Comparative Biochemical and Histopathological Studies on the Efficacy of Metformin and Virgin Olive Oil against Streptozotocin-Induced Diabetes in Sprague-Dawley Rats. Journal of diabetes research, 2018(1), 4692197.

info@journalofbabylon.com | jub@itnet.uobabylon.edu.iq | www.journalofbabylon.com ISSN: 2312-8135 | Print ISSN: 1992-0652