Bionatura
Latin American Journal of Biotechnology and Life Sciences

Bionatura Issue 3 Vol 8 No 1 2023

Article

Evaluation of some Herbal Agents in the treatment of Diabetes in Comparison to Insulin

Jawad F. H. Al-Musawi
Thi-Qar Medical College of Thi-Qar University, Department of Pharmacology and Therapeutic, Iraq.
*Correspondence: jwad-f@utq.edu.iq, https://orcid.org/0000-0002-8896-0334
Available from: http://dx.doi.org/10.21931/RB/CSS/2023.08.03.49

Abstract
We conducted an experimental investigation in which hyperglycemia was created in rats using Alloxan; we then employed an herbal drug that could reverse the hypoglycemic effects of insulin, which is to say, we used Alloxan to induce hyperglycemia in the rats. Research conducted on 24 Black rats over 28 days (split into four groups of six rats each on days 1, 7, 14, and 28) shows that ALLOXAN can induce hyperglycemia with statistical significance (P0.0001). HERBAL DRUGS (Momordica Charantia L) have effectively reduced hyperglycemia brought on by Alloxan, with statistically significant results (P0.0001) but not as strong as those produced by insulin. Momordica Charantia L for its insulin-like effects on blood sugar levels in the context of hyperglycemia produced by Alloxan. Through the use of "Black rats," we were able to successfully visualize a model for inducing hyperglycemia via intraperitoneal injection of ALLOXAN. The effectiveness of Momordica charantia L in bringing down hyperglycemia was then compared to that of insulin. Comparing Momordica charantia L to insulin for the treatment of type 1 diabetes in rats, the following results were found: - On days 7, 14, 21, and 28, with a total of 6 animals (Black rats) in each group, the mean S.D. of the hypoglycemic effect of Momordica charantia L was (148.42 +/-3.65), (127.66 +/-2.520), (95.78 +/-1.18), and (86.54 +/3.55). To put it another way, the herbal remedy effectively lowers blood sugar levels in those who suffer from hyperglycemia. The present findings highlight that Momordica charantia L effectively treats type 1 diabetes mellitus in rats and has the same effect on blood glucose levels as pharmaceutical insulin.

Keywords: Alloxan, Hypoglycemia, Insulin, Momordica charantia L, Hyperglycemia.

Introduction

Momordica charantia L., commonly called the bitter melon, falls under the Cucurbitaceae family. It originated in East India and is now grown, processed, and eaten all throughout the world, even in the Arctic and the tropics. The vegetable, which is light green and has the shape of a long cone, has a harsh taste but is widely consumed because of its various nutritional and functional benefits [1].

Bitter gourd is an economically and nutritionally significant vegetable in Asia, where 340,000 hectares are devoted to its cultivation [2]. Diabetes Mellitus (Type 1) is considered a chronic disease where the pancreas significantly induces insulin production in a meager amount or does not produce it. It is a condition that typically affects adolescents and is characterized by several symptoms, including increased thirst, wound-healing difficulties, frequent urination, excessive hunger, unintentional weight loss, blurred vision, fatigue, and weakness. (ALSHAYBAN, D., & JOSEPH, R., 2020; Pisoschi, C., Darie, V., & Serban, M., 1998; QASIM, M. J., & FALIH, I. Q., 2020; YUMASHEV, A., MATVEEVA, E., TAMBOVTSEVA, N., LI, J., & YANG, B., 2019). The fruit is widely utilized throughout Asia and its surrounding regions in South and East Asia for various purposes [3].

At full ripeness, the fruit turns orange and becomes mushy. It also separates into portions that curl backward, displaying brilliant crimson pulp encasing seeds. [40].

Momordica charantia is a fruit used to cure various clinical problems, including cancer, diabetes, fever, HIV, and AIDS (Ray RB, Raychoudhuri A, and Steele R 2010). Persistent Diarrhea, stomach discomfort, high temperature, hypoglycemia state, difficulty with urine flow, atypical pain, and uncomfortable chest are some of the indications and symptoms associated with using Momordica charantia. Nevertheless, the clinical symptoms are minimal, do not necessitate therapy, and are recoverable via rest. [4].

Bitter melon is contraindicated during pregnancy due to its potential to cause bleeding, contractions, and miscarriage [5].

The anti-diabetic activity of M. charantia L. in numerous animal models of type 2 diabetes mellitus has been investigated. [6, 8]

In mice and other animals, a poisonous glucose analog named Alloxan selectively attacks and destroys beta cells which are the reservoirs for producing insulin in the pancreas. This leads to diabetes mellitus, which is insulin-dependent (also called "Alloxan diabetes") observed in animals, showing clinical symptomatology of diabetes (Type 1) in humans. The compound, Alloxan, is highly toxic to the pancreatic beta cells responsible for producing insulin, and its preferential uptake by the GLUT2 glucose transporter contributes to this. Furthermore, Alloxan induces the production of ROS (reactive oxygen species) molecules in the presence of intracellular Thiols via a cyclic process involving the reduction reaction producing dialuric acid molecules. As a result of the free radicals produced in such a redox reaction, Alloxan can be harmful to beta cells. Research indicates that Alloxan does not increase the risk of diabetes in humans [9]. While some studies failed to find any significant difference in plasma Alloxan levels between children with and without type 1 diabetes, others found a stark contrast [10].

Because of its toxic effects on the pancreatic beta cells that secrete insulin, Alloxan significantly induces diabetes in test animals [11, 13]. The compound's chemical similarity to glucose and the efficient uptake mechanism of the beta-extreme cell may be responsible for this mode of action (GLUT2). Furthermore, there are conditions wherein the glutathione levels are lower, which symbolizes that Alloxan shows a strong affinity for the thiol group-containing biological molecules. Also, the thiol group containing the enzyme glucokinase, which is essential for glucose-induced insulin synthesis, is inhibited by the Alloxan molecule [14].

Most research indicates that Alloxan is not harmful to human beta cells, even at very high doses. Humans and rats have different pathways for absorbing glucose [15, 17].

Single doses of 50–150 mg/kg, depending on administration and strain, are considered to induce persistent hyperglycemia in rats [18, 14]. The increase in

plasma insulin level generates a brief period of hypoglycemia before the onset of long-term hyperglycemia; Alloxan is administered and begins functioning within two minutes [21].
Diabetes mellitus, also known as hyperglycemic syndrome, can be induced by the alkylating anticancer drug streptozotocin, also known as streptozocin (INN, USP) (STZ). Animal studies have shown that this chemical compound harms pancreatic beta cells. Medically, it is used to treat islets of Langerhans tumors, and it is also utilized in varied doses to create an animal model of Alzheimer's disease, hyperglycemia, and diabetic (either Type 1/Type 2) symptoms in research [22].

Materials and Methods

Materials

This research used the following materials:
Blood Glucose Kits –Diabetes-Testing Kits containing 1 Glucometer, Blood Sugar Testing Strips -100 no.s, 1 Lancet Attaching Device, Lancets – 100 no.s, Rigid boxes for placing the Diabetic Supplies and Blood Glucose Meter during travel.
Soluble Insuline (Solusion in Vial).
AlIoxan (Solusion in Ampules)
Insulin Injection Needle (100 I.U.)
A rat-specific diet (sold under the Harlan Teklad and Mazuri brands) was developed and released to the public (it comprises fruits such as blackcurrant and apple proving their antioxidant potentialities and increased vitamin content, promoting better health). It is excellent for your heart and blood vessels since it contains many heart-healthy polyunsaturated fats and almost no saturated fats or cholesterol. Every ingredient in Selective was chosen for its beneficial effects on your pet's skin and coat.

Composition of the special diet
The unique diet consisted of bread, vegetables, fruits, and a few nuts, all readily accessible in the marketplace. (It comprises fruits such as blackcurrant and apple, proving their antioxidant potentialities and increased vitamin content, promoting better health). It is excellent for your heart and blood vessels since it contains many heart-healthy polyunsaturated fats and almost no saturated fats or cholesterol. Every ingredient in Selective was chosen for its beneficial effects on your pet's skin and coat.

Methods

Establishment of mice model:
Visualizing a model for inducing hyperglycemia in "Black rats" was feasible by intraperitoneal injection of ALLOXAN.
From the first to the thirty-first day, 150 mg/kg/kg/body weight of ALLOXAN is administered (Leatherdale, B. A. et al., 1981). The number of rats in each group was six. These particular dosages can induce hyperglycemia within one to two hours [24].
Additionally, Momordica charantia L was administered intraperitoneally as a solution for 30 days. The optimal dosage was determined to be 300 mg/kg body weight. In addition, no adverse effects were observed during a limited evaluation of MCP's toxicity in rats and mice (5). Insulin was delivered subcutaneously in a dose (4IU per gram body weight). The Injection group received injections of 4 I.U./200 g of body weight of 100 IU/ml of insulin in subcutaneous mode daily [25].

In vivo assays protocol for performing experiments on animals:

The experiments were conducted with "24 Black Rats" ". With body masses between "75-90 g - "These rats followed a specific diet [26].
These animals were separated into "four groups" of six individuals:
1-The first group consisted of healthy individuals. Following that, tap water was provided to the CONTROL group.
2- The second group was administered 250-300 mg/kg of Momordica charantia L body weight, but not Alloxan (Ray R. B. et al., 2010).
After each medicine was provided, the blood sugar levels of each animal were measured.
3-The third and fourth groups were administered 150 mg/kg body weight per 24 hours of ALLOXAN as follows: on the first, seventh, twenty-first, and twenty-eighth days [27].
After administering Alloxan, the blood sugar levels of all animals in this study were monitored.
The third group was treated with -300 mg/kg body weight/24 hours of Momordica charantia L on the first, seventh, twenty-first, and thirty-eighth days (Ray R. B. et al., 2010; [28]).
4- The fourth group was administered subcutaneous INSULIN at 2 international units per kilogram of body weight [28, 29].
The blood sugar level was routinely monitored after each drug was administered intravenously to the animals (fasting and postprandial).
Animal research conformed to the standards for the care and use of laboratory animals and was approved by the relevant animal care and use committees (Data Sciences International, Eli Lilly). A veterinary device (POCG A) and four instruments for human use (POCG B through E) (A* and B*) were among the POCG (point-of-care glucometers) evaluated, point-of-care glucose monitor [30, 31].

Results

Indications Of Momordica charantia L. In contrast to insulin in the management of type 1 diabetes mellitus in rats, the following was found:-
The average plus standard deviation on the 7th day (148.42 +/-3.65), 14th day (127.66 +/-2.520), 21st (95.78 +/-1.18), and 28th day (86.54 +/3.55), with a number of 6 animals (Black rats) for each group. These results are presented in Table 1 and statistical Figure 1.
This suggests that Momordica charantia L is highly effective at lowering Alloxan-induced hyperglycemia. While insulin's hypoglycemic impact is statistically significant (P0.0001), Momordica charantia L's is statistically identical (P0.0001).
Table 2 and Figure 2 display Momordica charantia L's substantial impact on lowering these animals' Blood Glucose content.
That median and S. D. of the hypoglycemic impact of both the Momordica charantia L-treated and the Insulin-treated groups compared to the Alloxan-treated group (producing severe hyperglycemia; P0.0001), which led to a highly significant increase in blood glucose level.
Table No.2 and Figure No.2 indicate the results obtained after treating Alloxan with the dramatic hypoglycemic impact of Momordica charantia L on black rats.
All animal experiments were conducted following institutional and national norms and approval from the appropriate institutional animal experimentation committees (Data Sciences International, Eli Lilly). One veterinary instrument (POCG A) and four instruments (POCG B–E) for human use (A* and B*) were among the POCGs put through their paces. Point-of-Care Glucometer (POCG) [30,31].

BLOOD GLUCOSE LEVEL(mg/kg)					
Treatment	Dose (mg/kg)	7th day	14th day	21st day	28th day
Control group	----	93.59 +/-1.32	97.53 +/-1.58	97.11 +/-1.04	98.10 +/-0.52
Diabetic group by **ALLOX-AN**	**150mg/kg Intra-personally**	284.83 +/-5.37	285.58 +/-4.22	288.64 +/-3.56	294.32 +/-4.16
Group treated with **Momor-di-ca *charantia***	**0.5 g/kg* Intra-personally**	148.42 +/-3.65	127.66 +/-2.52	95.78 +/- 1.18	86.54 +/-3.55
Group treated with **INSU-LIN**	**2U/Kg Subcuta-neously**	138.91 +/-3.61	122.88 +/-3.18	92.25 +/-2.60	84.75 +/-3.09
	X±SD	166.43+/-3.48	158.41 +/- 2.87	143.44 +/-2.10	140.92 +/-2.83

Table 1: The efficacy of Momordica *charantia* L. in the treatment of Type 1 Diabetes Mellitus in Comparison to Insulin in Rats.

GROUP	1st day	7th day	14th day	28th day
Normal Group	81.64 +/-1.06	79.94 +/-1.50	81.75 +/-1.52	82.63 +/-1.32
Control group	324.32 +/-1.12	308.70 +/2.14	332.5 +/-2.71*****	340.2 +/-2.07*****
Standard group (on **ALLOXAN)**	268.40 +/-0.96	311.70 +/-1.03	193.12****** +/1.99	150.05 +/-1.06*******
Group treated with **MCL**	298.22 +/-0.52	310.02 +/-1.07	236.1 +/-1.62*****	170.2 +/-1.09******
Group treated with **In-sulin**	282.4 +/-2.16	316.30 +/-1.28	189.9 +/-2.12******	134.01 +/-1.64*******
X±SD	250.98 +/-1.164	**265.32** +/-1.40	206.67+/-1.99	175.42+/-1.43

Table 2: The significant effects of Momordica *charantia* L. in the treatment of Type 1 Diabetes Mellitus in Comparison to Insulin in Rats.

M N1: Normal control group

N2; standard D.M.

N3 and N4 were treated with Momordica *charantia* in a dose of 0.5mgkg and 2U insulin.

No. of each group was 6 RATS.

Discussion

Bitter melon (Momordica charantia) is a plant frequently used in traditional medicine to treat the hyperglycemic disease known as diabetes mellitus (D.M.). Human and animal research has demonstrated that Momordica charantia (Mc) boosts blood sugar levels. We do not know, however, if the stems and leaves of plants or if this action persists in the chronic state might influence the anti-hyperglycemic effect. [32]

Alloxan, or Alloxan hydrate, is a pyrimidine derivative with the formula O.C. (N(H) C.O.)2C(OH)2 and the chemical formula O.C. (N(H) C.O.)2C(OH)2. Alloxan is used to create diabetes in experimental animals because it eliminates insulin-producing beta cells in the pancreas [33, 34].

Lantus® (insulin glargine injection) is an insulin analog used to treat diabetes (type 2) in adults and children over the age of 6 with diabetes (type 1). This type of insulin is utilized in this study, which is why this type of insulin was used in this study [36].

By Danilova I. G., Sarapultsev P. A., Medvedeva S.U. The preferential uptake of this chemical is likely due to its structural resemblance to glucose and the beta-efficient cell absorption mechanism (GLUT2). Alloxan's strong affinity for SH-containing biological compounds significantly decreases glutathione concentrations. Additionally, it inhibits the function of glucokinase and thiol (S.H.)-containing enzymes required for glucose-induced insulin secretion. [34, 33, and 20].

The remaining 12 rats with Alloxan-induced hyperglycemia were later treated with either Momordica Charantia L or insulin. The Momordica charantia (bitter melon) is a plant widely accepted for treating diabetes mellitus in traditional ways, as mentioned by Wang, Limei, Waltenberger et al. (D.M.). In addition, Momordica charantia (Mc) has been shown to boost human and animal blood sugar levels. However, the author does not know if this rapid action is maintained in the chronic state or if extract derived from the plant's stems and leaves influences the anti-hyperglycemic effect. [37].

Based on these findings, it appears that Momordica charantia L.'s hyperglycemic condition generated by Alloxan in Black Rats has an effect identical to that of insulin. This agrees with the research done by Parker Nelson M Edmond K. Farhad, 2019 who found that insulin stimulates pancreatic beta-cells, lowering the hyperglycemic effects of drugs like Alloxan and Streptozotocin [38].

Conclusion

This study revealed that Momordica charantia L is effective against diabetes (type 1) in rats and concludes that insulin and extracts of Momordica charantia L could significantly lower the level of blood glucose.

Conflict of Interest

None.

Declarations

Study Limitations

The study is limited to the sample analyzed; no additional limitations were known at the time of the study.

Acknowledgements

I want to acknowledge all who helped me buy and prepare the animals, for those who took care of animals during this study who work in Thi-Qar University animal house.

Funding source

The authors funded this research

Competing Interests

There were no competing interests in this study.

References:

1. Palamthodi S., Lele S. S. Nutraceutical applications of gourd family vegetables: benincasa hispida, Lagenaria siceraria and Momordica *charantia*. *Biomedicine & Preventive Nutrition.* 2014;4(1):15–21. DOI: 10.1016/j.bionut.**2013**.03.004.
2. McCreight, J.D., Staub, J.E., Wehner, T.C. & Dhillon, N.P.S. Gone global: Familiar and exotic cucurbits have Asian origins *HortScience* 48 1078 1089. **2013** .
3. F. J. Breteler, G. H. de Bruijn, Goya Bitter melon (*Momordica charantia*) extract inhibits breast cancer cell proliferation by modulating cell cycle regulatory genes and promotes apoptosis. *Cancer Res.* Mar 1 **2010**; 70(5):1925-1931.
4. Bachok, M. F.; Yusof, B. N.; Ismail, A; Hamid, A. A. Effectiveness of traditional Malaysian vegeTable s (ulam) in modulating blood glucose levels. Asia Pacific Journal of *Clinical Nutrition.* **2014***; 23 (3)*: 369–76.
5. Cukierman T., Gerstein H.C., Williamson J. Cognitive decline and dementia in diabetes— systematic overview of prospective observational studies. *Diabetologia.* **2005** *Dec 8; 48(12*):2460–9.
6. Banerjee S, Sinharoy K, Singh AK. Oral hypoglycemic agent failure. *J Indian Med Assoc.* **2002** *Jul; 100(7):*452–6.
7. ALSHAYBAN, D., JOSEPH, R. The impact of medication adherence on health-related quality of life of diabetic patients in the Kingdom of Saudi Arabia: Findings from a cross-sectional study. Periódico Tchê Química, **2020**; 17(34), 867–873. DOI: https://doi.org/10.52571/ptq.v17.n34. 2020.891_p34_pgs_867_873.pdf
8. Chawla R, Thakur P, Chowdhry A, Jaiswal S, Sharma A, Goel R, Evidence-based herbal drug standardization approach in coping with challenges of holistic management of diabetes : A dreadful J Diabetes and Metabolic Disord. **2013**; 12(35):116.
9. Surathat Pongnikorn, Duriya Fongmoon, Watchara Kasinrerk, Porn-Ngam Limtrakul. Effect of bitter melon (*Momordica charantia Linn*) on level and function of natural killer cells in cervical cancer patients with radiotherapy. *J Med Assoc Thai.* Jan **2003**; 86(1):61-68.
10. Mrozikiewicz, A.; Kielstrokczewska-Mrozikiewicz, D.; Lstrokowicki, Z.; Chmara, E.; Korzeniowska, K.; Mrozikiewicz, P. M. "Blood Levels of Alloxan in Children with Insulin-dependent Diabetes Mellitus". *Acta Diabetologica.* **1994**; *31 (4):* 236–237. doi:10.1007/bf00571958. PMID 7888696.
11. Danilova I. G., Sarapultsev P. A., Medvedeva S. U., Gette I. F., Bulavintceva T. S., Sarapultsev A. P. "Morphological Restructuring of Myocardium during the Early Phase of Experimental Diabetes Mellitus". *Anat. Rec.* **2014**; *298 (2):* 396–407. doi:10.1002/ar.23052. hdl:10995/73117.
12. Pisoschi, C., Darie, V., Serban, M. Study Of Renal Sorbitoldehydrogenase In Experimental Diabetic Nephropathy. *Southern Brazilian Journal Of Chemistry*, **1998**; *6(7),* 77–82. Doi: Https://Doi.Org/10.48141/Sbjchem.V6.N7.1998.76_1998_2.Pdf
13. Loreto D., Elina V. Experimental surgical models in the laboratory rat. Boca Raton: CRC Press. **2009**.
14. Szkudelski T. "The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas". Physiol Res. 50: 536–546. **2001**.
15. Tyrberg, B.; Andersson, A.; Borg, L. A. "Species Differences in Susceptibility of Transplanted and Cultured Pancreatic Islets to the β-Cell Toxin Alloxan". General and Comparative Endocrinology. 122 (3): 238–251. DOI: 10.1006/gcen.2001.7638. PMID 11356036. **2001**.
16. Qasim, M. J., Falih, I. Q. Review About Diabetes Mellitus And Urinary Tract Infections. *Southern Brazilian Journal Of Chemistry,* **2020**; *28(29),* 07–16. Doi: Https://Doi.Org/10.48141/Sbjchem. V28.N29.2020.02_Qasim_ Pgs_07_16.Pdf
17. Eizirik, D. L.; Pipeleers, D. G.; Ling, Z.; Welsh, N.; Hellerström, C.; Andersson, A. "Major Species Differences between Humans and Rodents in the Susceptibility to Pancreatic β-Cell Injury. *Proceedings of the National Academy of Sciences of the United States of America.* **1994**;*91 (20):* 9253–9256.
18. Leiter and Schile
19. , "The Main action and toxic effect of alloxan and streptozotocin action in B cells of the rat pancreas". Physiol Res. 50: 536–546. **2013**
20. Szkudelski T "Susceptible dose effect the beta-cell of pancresae to induce publication years hypoglycemia" General and Comparative Endocrinology, **2001**; 122 (3): 238-251. Dio:10.1006/gcen.2001.

21. Szkudelski T., The effect of Alloxan on blood sugar level, *Proceedings of the National Academy of Sciences of the United States of America. 65 (15): 7253–7256)* **1998**.
22. Brentjens R., Saltz L. Islet cell tumors of the pancreas: the medical oncologist's perspective. *Surg Clin North Am*. **2001**;81 (3): 527–42.
23. Leatherdale, B. A.; Panesar, R. K.; Singh, G.; Atkins, T. W.; Bailey, C. T.; Bignell, A. H. C. Improvement in glucose tolerance due to Momordica *charantia* (karela). *Br. Med. J. (Clin. Res. Ed.)* **1981**, *282*, 1823–1824.
24. Zhao, G. T.; Liu, J. Q.; Deng, Y. Y.; Li, H. Z.; Chen, J. C.; Zhang, Z. R.; Qiu, M. H. Cucurbitane-type triterpenoids from the stems and leaves of Momordica *charantia*. Fitoterapia **2014**, 95, 75–82.
25. Chang, C. I.; Chen, C. R.; Liao, Y. W.; Cheng, H. L.; Chen, Y. C.; Chou, C. H. Cucurbitane-type triterpenoids from the stems of Momordica *charantia. J. Nat. Prod.* **2008**, *71*, 1327–1330.
26. Ojewole, J.A.; Adewole, S.O.; Olayiwola, G. Hypoglycaemic and hypotensive e_ects of Momordica *charantia* Linn. (Cucurbitaceae) whole-plant aqueous extract in rats. *Cardiovasc. J. Afr.* **2006**, *17*, 227–232.
27. Peter, E.; Kasali, F.; Deyno, S.; Mtewa, A.; Nagendrappa, P.; Tolo, C.; Ogwang, P.; Sesaazi, D. *Of Momordica charantia L.* lowers elevated glycaemia in type 2 diabetes mellitus patients: Systematic review and meta-analysis. *J. Ethnopharmacol.* **2019**, *231*, 311–324.
28. Nuckols, T.; Keeler, E.; Anderson, L.; Green, J.; Morton, S.; Doyle, B.; Shetty, K.; Arifkhanova, A.; Booth, M.; Shanman, R.; *et al*. Economic evaluation of quality improvement interventions designed to improve glycemic control in diabetes: A systematic review and weighted regression analysis. *Diabetes Care* **2018**, *41*, 985–993.
29. Jia, S.; Shen, M.; Zhang, F.; Xie, J. Recent advances in Momordica *charantia*: Functional components and biological activities. *Int. J. Mol. Sci.* **2017**, *18*, 2555.
30. Cohn LA, McCaw DL, Tate DJ, Johnson JC. Assessment of 5 porTable blood glucose meters, a point-of-care analyzer, and color test strips for measuring blood glucose concentration in dogs. *J Am Vet Med Assoc.* **2000**; 216:198–202.
31. Cengiz E, Tamborlane WV. A tale of two compartments: interstitial versus blood glucose monitoring. *Diabetes Technol Ther*. 2009; 11(suppl 1):S11-S16. doi:10.1089/dia.**2009**.0002.
32. Botanical Society of Britain and Ireland. Archived from the original (xls) on **2014**-10-23. Retrieved 2014-10-17.
33. Danilova I. G., Sarapultsev P. A., Medvedeva S. U., Gette I. F., Bulavintceva T.S., Sarapultsev A.P. "Morphological Restructuring of Myocardium during the Early Phase of Experimental Diabetes Mellitus". *Anat. Rec*. **2014**;*298 (2):* 396–407.
34. Mrozikiewicz, A.; Kielstrokczewska-Mrozikiewicz, D.; Lstrokowicki, Z.; Chmara, E.; Korzeniowska, K.; Mrozikiewicz, P. M. "Blood Levels of Alloxan in Children with Insulin-dependent Diabetes Mellitus". *Acta Diabetologica*. **1994**; *31 (4)*: 236–237
35. YUMASHEV, A., MATVEEVA, E., TAMBOVTSEVA, N., LI, J., YANG, B. Therapeutic and prophylactic application of mesodiencephalic modulation during dental implantation in patients with type 2 diabetes mellitus. Periódico Tchê Química, **2019**; 16(33), 82–93. DOI: https://doi.org/10.52571/ptq.v16.n33. 2019.97_periodico33_pgs_82_93.pdf
36. N. A. Calcutt, M. E. Cooper, T. S. Kern, and A. M. Schmidt, "Therapies for hyperglycaemia-induced diabetic complications: From animal models to clinical trials," *Nature Reviews Drug Discovery*, vol. 8, no. 5, pp. 417–429, **2009**.
37. Wang, Limei; Waltenberger, Birgit; Pferschy-Wenzig, Eva-Maria; Blunder, Martina; Liu, Xin; Malainer, Clemens; Blazevic, Tina; Schwaiger, Stefan; Rollinger, Judith M.; Heiss, Elke H.; Schuster, Daniela; Kopp, Brigitte; Bauer, Rudolf; Stuppner, Hermann; Dirsch, Verena M.; Atanasov, Atanas G. (**2014**).
38. Parket Nelson M, Admond K. Farhad, Steven F. Warefoo, "The role of Insulin on Beta-cells of injured pancreas *J. Mol. Sci.* **2019**, *17*, 1644.
39. Dry by Helios brewery of Okinawa, Department of Plant Taxonomy, Agricultural University, Wageningen (**1984**).
40. Lim, T. K. Edible medicinal and non-medicinal plants. Dordrecht: Springer. pp. 331–332. ISBN 9789400717640. **2013**.

Received: May 15, 2023/ Accepted: June 10, 2023 / Published: June 15, 2023
Citation: Al-Musawi J. F. H.. Evaluation of some Herbal Agents in the treatment of Diabetes in Comparison to Insulin. Revis Bionatura 2023;8 (3) 49. http://dx.doi.org/10.21931/RB/CSS/2023.08.03.49