Studying the efficacy of the plant extract of Tetracera scandens as an antidiabetic treatment

Dr. Louai alallan*
Dr. Mays Khazem**
Dr. Nasser Thallaj***

(Received 2 / 12 / 2022. Accepted 25 / 1 / 2023)

□ ABSTRACT □

In Southeast Asia, a metabolic disease with a high prevalence was known as diabetes mellitus. Diabetes mellitus was treated with traditional medicinal plants.Tetracera scandens (L.) Merr is one of them.The purpose of this study was to assess the homeostatic model of insulin resistance (HOMA-IR) and blood glucose levels in alloxan-induced rats in order to determine the ethanol extract of T.scandens strains' anti-diabetic activity.There were five groups of animals:normal group, a negative control, and extract dosages of 180, 355, and 710 mg/kg body weight, respectively.The animals were given 180 mg/kg body weight of alloxan to induce their behavior.The extract was taken orally for 21 days.Ethanol extract from T.scandens strains was found to significantly lower blood glucose levels, increase insulin levels, and reduce insulin resistance when administered (p 0.05).As a result, it is possible to draw the conclusion that the ethanol extract of T. scandens could be used to treat diabetes mellitus.

Keywords: Tetracera scandens, Ethanol extraction, alloxan, diabetes mellitus, blood glucose, insulin, insulin resistance.

*Doctor, Department of pharmacognosy, faculty of pharmacy, university of damascus , Damascus, Syria. Louy2.allan@damascusuniversity.edu.sy
**Assistant Professor Department of pharmacognosy, faculty of pharmacy, university of damascus , Damascus, syria . mays.khazem@damascusuniversity.edu.sy
***Professor, Pharmaceutical chemistry and drug quality control Department, Faculty of Pharmacy, Al-Rachid privet University, Damascus, Syria. profthallaj@gmail.com.

دراسة فعالية مستخلص نبات الملَّاح التائه (Tetracera scandens) كعلاج مضاد لمرض السكر

د. لؤي العلان*

د. ميس خازم**

د. ناصر ثلاج***

(تاريخ الإيداع 2 / 12 / 2022. قُبِل للنشر في 25 / 1 / 2023)

□ ملخّص □

في جنوب شرق اسيا، كان يُعرف أحد الأمراض الأيضية ذات الانتشار الواسع بمرض السكري، وقد تم علاج داء السكري بالنباتات الطبية التقليدية، وتعد تيتراسيرا سكاندينس (**Tetracera scandens** L) او الملاح التائه أحد هذه العلاجات، وكان الغرض من هذه الدراسة هو تقييم نموذج الأنسولين المتماثل. المقاومة (HOMA–IR) ومستويات الجلوكوز في الدم في الفئران التي يسببها الألوكسان من أجل تحديد نشاط مستخلص الإيثانول لسلالات T. scandens كمضاد لمرض السكري. تم إعطاء الفئران 180 و 355 و 710 ملغ / كغ من وزن الجسم على التوالي، وتم إعطاء الحيوانات 180 ملغ / كغ من وزن الجسم من الألوكسان لتحفيز سلوكها ، وتم تناول المستخلص عن طريق الفم لمدة 21 يومًا ، وتم العثور على مستخلص الإيثانول من سلالات T.scandens لخفض مستويات الجلوكوز في الدم بشكل ملحوظ ، وزيادة مستويات الأنسولين ، وتقليل مقاومة الأنسولين عند تناوله (p 0.05). ونتيجة لذلك، يمكن استنتاج أن مستخلص الإيثانول من T. scandens يمكن استخدامه لعلاج مرض السكري.

الكلمات المفتاحية : تتراسيرا سكاندينس ، استخلاص الإيثانول ، ألوكسان ، داء السكري ، جلوكوز الدم ، الأنسولين ، مقاومة الأنسولين.

* دكتور ، قسم العقاقير ، كلية الصيدلة ، جامعة دمشق ، دمشق ،سورية dr.loaiallan.la@gmail.com

** أستاذ مساعد، قسم العقاقير ، كلية الصيدلة ، جامعة دمشق ، دمشق ، سورية mays.khazem@damascusuniversity.edu.sy

*** أستاذ مساعد، قسم الكيمياء الصيدلانية والمراقبة الدوائية، كلية الصيدلة، جامعة الرشيد الخاصة للعلوم والتكنولوجيا، دمشق، سورية .profthallaj@gmail.com

Introduction

All parts of the world are affected by the disease, but the percentage of diabetics in the general population is particularly high in the countries of the eastern Mediterranean and the Middle East (9%), North America (8%), and Europe (7%).The World Diabetes Foundation (WDF) anticipates a 2.5% annual increase in the number of diabetics to approximately 380 million by 2025 [1].As a result, newer drug therapies must be developed to reduce the burden of disease-related complications.As a source of therapeutic agents, natural products and their derivatives have historically been valuable.Traditional medicines have always been proven to be a fruitful source of future drugs to combat any disease, including insulin resistance, consistent with a resurgence of interest in drug discovery from natural products [2-4]. The scientific community is now more interested in evaluating crude and isolated natural products in experimental studies.The picked plant given underneath could be an expected contender for this point.

A metabolic disorder known as diabetes mellitus is characterized by hyperglycemia as a result of impaired insulin secretion, insulin action, and progressive changes in the structure of the pancreas [5].In Southeast Asia, diabetes mellitus is prevalent.However, the prevalence varies based on ethnicity and province [6].Metformin, sodium glucose transport protein-2 (SGLT-2) inhibitors, glucagon-like peptide-1 receptor agonist (GLP-1RA), dipeptidyl peptidase-4 (DPP-4) inhibitors, thiazolidinediones, and sulfonylureas are among the numerous synthetic drugs used to treat diabetes [7].However, many people treat diabetes with herbal medicine because it is safer, more effective, and less expensive [8]. This is because some drugs have side effects.

Merr. Tetracera scandens (L.)Linn., Tetracera scandensMerr. ((Family: T. scandens L.) Dilleniaceae), also known asTetracera monocarpa Blanco, Tragia scandens L., Delima sarmentosa L., and Tetracera hebecarpa (DC.)Boerl.) (nearby Malaysian names-mempelas kasar, palas, pampan, and stone leaf) is a climbing plant developing from 3 to 5 m or more long and fills broadly in India, southern China, Southeast Asia, Myanmar, Philippines, Thailand, Vietnam and Malaysia.Various parts (leaves, stems and underlying foundations) of T. scandens L. are utilized in society cures by different native individuals in various nations for the treatment of stiffness, bringing down hypertension, bringing down pulse, fiery illnesses, hepatitis, inside torments, urinary issues, looseness of the bowels, labor, sore throat, gout and diabetes ailments.The roots are traditionally used as an astringent in diarrhea and a traditional ingredient in a mixture against burns. Droplets of water/sap from freshly cut stems are used for eye irritation. Juice gathered by smashing the stem is taken to reduce body heat. The roots are ground and the juice of it is applied to mouth ulcers. The leaves of T. scandens L. are traditionally applied to boils to ripen them. The juice is typically taken to treat internal pains. A decoYoung shoots that have been finely crushed are used as a poultice to treat snake bites in Southeast Asia.The stem's sap is drank to treat coughs.In the Philippines, tuberculosis hemoptysis is treated with an infusion of the stem.It is gargled to combat thrush.Because of its high concentration of tannins, the infusion is applied externally to a sore throat.In hepatic and renal oedema, the stem is used in combination with other plants as a diuretic in Cambodia.In Vietnam, hepatitis, gout, and inflammation are treated with root and stem.In India, the juice of the aerial portion is taken orally once per day to alleviate the burning sensation experienced when urinating [9-13].

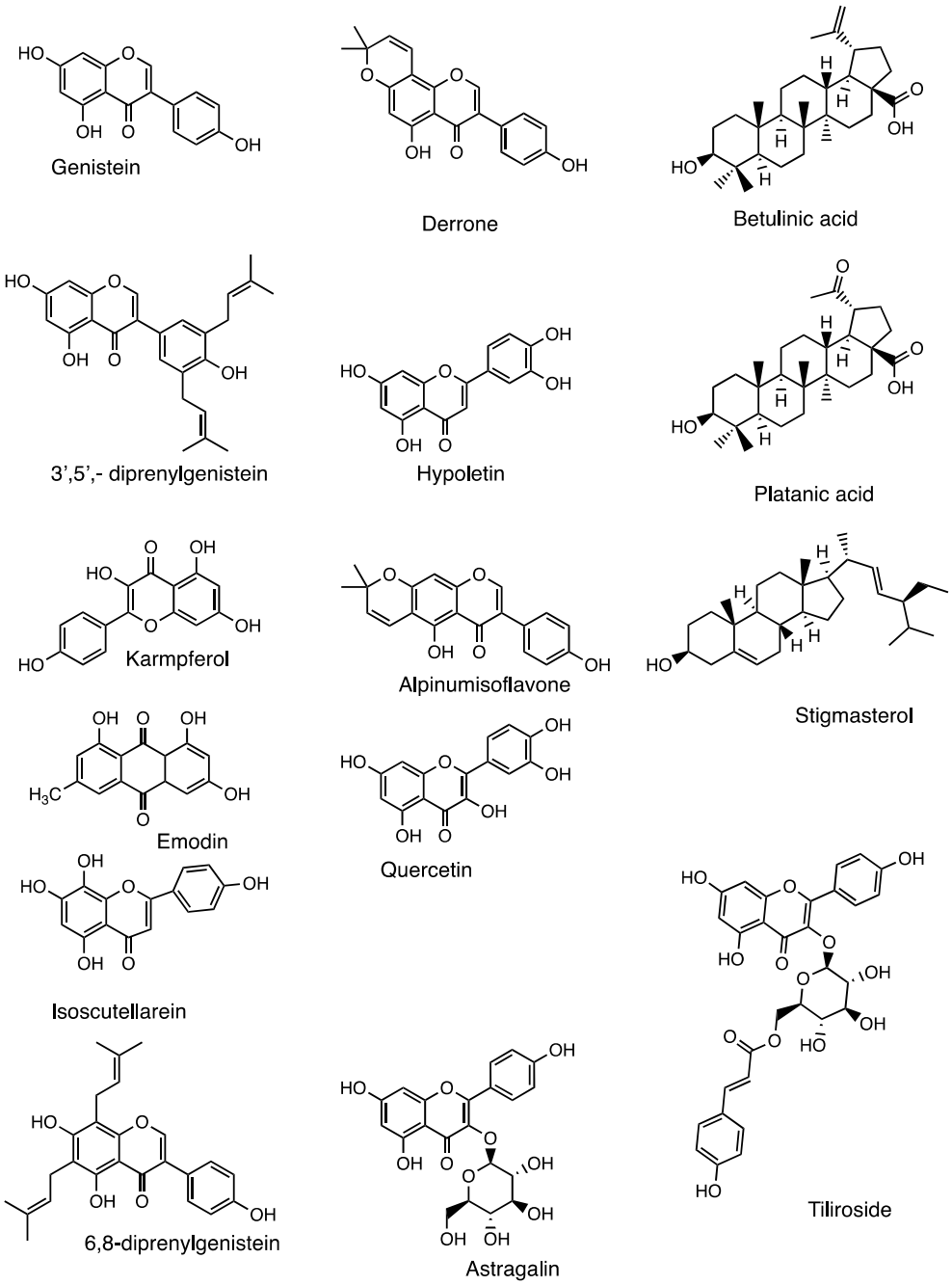
It has been demonstrated in vitro that the polar extracts of T. scandens L. have potential therapeutic Xanthine oxidase (XO) inhibitory activity in a concentration-dependent manner [14].There are five iso-flavonoids:It has been demonstrated that derrone, alpinum

isoflavone, 3,5-diprenylgenistein, 6,8-diprenylgenistein, and genistein, all of which were isolated from the leaves of T. scandens L., have a significant effect on glucose uptake in basal and insulin-stimulated L6 Myotubes in vitro, indicating that genistein has great potential for diabetes management [15].Although the leaves of T. scandens L. are utilized in herbal medicine preparations for diabetics, no scientific report of this plant in vivo has ever been recorded or mentioned in the literature to confirm its utility in folkloric medicine by the local herbalists in Malaysia.Our current research interest is in evaluating the efficacy of the leaves of T. scandens L. in the management of diabetes mellitus using an animal model to confirm its effectiveness. This is due to the significant glucose uptake activity of the polyphenolic (iso-flavonoids) compounds of T. scandens L. in basal and insulin-stimulated L6 Myotubes in vitro and its use by local traditional practitioners in various formulations to treat various ailments, including diabetes-related complications
(Figure.1) is one of the traditional medicinal plants that the community uses to treat fever, the flu, tuberculosis, snakebite, hepatitis, rheumatism, gout, inflammation, diarrhea, ulcers, burns, cough, canker sores, diabetes mellitus, hypertension, urinary tract diseases, internal pain, and edema [16]. Other traditional uses include postnatal tonic, snakebite, hepatitis, rThe secretory structures of the strain of T. scandens are idioblast cells and unicellular glandular trichomes.The phytochemical reaction revealed that cat sandpaper idioblast cells primarily secrete alkaloids, terpenoids, and phenols in their substances.Only flavonoids are found in trichomes from the T. scandens gland [17].Flavonoids are regarded as an antihyperglycemic agent and are known to regenerate damaged cells [18,19].

Figure 1: *Tetracera scandens* (L.) Merr.

T. scandens' potential as an anti-diabetic traditional medicine has been the subject of numerous studies.Derrone and alpinum isoflavone, as well as genistein and its derivatives 3,5-diprenyl-genistein and 6,8-diprenyl-genistein, were found to be isolated from the leaves of T Schema1 Phytochemicals.L6 myotube glucose uptake, AMPK phosphorylation, GLUT4 and GLUT1 mRNA expression, and PTP1B inhibition are all significantly affected by scandens [20].In alloxan-induced diabetic rats without

hypoglycemia, an aqueous and methanolic extract of T. scandens leaves had a significant antihyperglycemic effect [21].



Schema1: Phytochemicals isolated from Tetracera scandens

Activity Hypoletin, derived from the methanol extract of T. scandens leaves, also demonstrated anti-diabetic activity in vitro by, like insulin action, increasing glucose absorption in adipocytes.By reducing adipogenesis and improving blood sugar absorption, the leaves of T. scandens were found to have anti-diabetic and anti-obesity properties [22].The -glucosidase enzyme can also be inhibited by T. scandens leaves [23].An investigation into the effects of ethanol extract from T. scandens stems on glucose, insulin, and insulin resistance in diabetic white rats was carried out in light of this description.

MATERIALS AND METHODS

Tetracera scandens (L.) Merr. was used as the materials.(PT.) 90% ethanol Hi-Pro-Vite 511 pellet food (PT.Charoen Indonesia), Na CMC (Sodium Carboxy Methyl Cellulose) (PT.Brataco), sugar (PT.Brataco), Aldrich's alloxan monohydrate, and the reagent for the blood glucose test (PT.Rajawali Nusindo), and the reagent for the insulin ELISA kit (PT.Scientific Gamma).

Plant sample Preparation

Fresh T. scandens L. leaves weighing 1 kilogram were used in the sample, which was taken in October 2021 from Taman Pertanian, Kuantan, Indera Mahkota, 25200 Kuantan, Pahang Darul Makmur, Malaysia.

Extraction

By macerating the stems of T. scandens in 90 percent ethanol, the ethanol extract was made.At a ratio of 1:10, 1 kilogram of sticks were placed in the macerator;For the first six hours, add 10 liters of submersible solvent and stir occasionally. Allow to stand at room temperature for 18 hours.To separate the macerate, use a flannel to filter it.Using the same solvent type and concentration, repeat the filtration twice.Utilize a rotary evaporator (Heidolph) to collect and concentrate all of the macerates until a thick extract is produced.

Secondary Metabolite Screening.

The T. scandens extract's secondary metabolite content was determined.Alkaloids, flavonoids, phenolics, terpenoids, and steroids were all tested in the assay [24].

Animals

Twenty white male rats weighing 20-30 grams and aged 2 to 3 months.The rats were fed and watered adequately for seven days prior to the treatment.The rats used are healthy male rats with normal behavior, no noticeable abnormalities, and a weight deviation of no more than 10% from normal during maintenance.The animals were sorted into five groups of four rats at random.The Research Ethics Commission has approved the pharmacological activity assay's ethical review.

Dosage

The dose of T. scandens stem ethanol remove given to exploratory creatures was 180, 355, and 710 mg/kg BW given orally.Alloxan at a dose of 180 mg/kg BW was used to induce hyperglycemia in rats.

Pharmacological Activity Test

Five treatment groups were divided among the rats in this study.Alloxan at a dose of 180 mg/kg BW was administered subcutaneously to four groups (the negative control group, extract doses of 180, 355, and 710 mg/kg BW), and 10% glucose was administered for two days.Na CMC was only given to the normal group.For 21 days, the extracts were administered.The animal's blood was taken from it after 21 days.Before receiving the blood, the animal fasted for eight hours.Rats's sinus orbital blood was taken in one milliliter, placed in a vacuum tube, and centrifuged for twenty minutes at 3000 RPM.The serum was isolated.A blood glucose test reagent (PT) was used to measure the patient's glucose levels.Rajawali Nusindo), and the clinical photometer 5010 v5+ (Riele) was used to measure it.Insulin level was broke down with an insulin ELISA unit reagent (PT.Gamma Scientific) and measured at 450 nm with an ELISA reader from RayBio.

Calculation of HOMA-IR Value

Insulin obstruction was evaluated in view of the homeostasis model appraisal of insulin opposition (HOMA-IR).The following formula is used in this method to determine insulin resistance in animals and humans:HOMA-IR is equal to 405 [25,70-74]: fasting insulin x fasting blood glucose.

Statistical Analysis

Using parametric (ANOVA 1-way) and non-parametric (Kruskal-Wallis) statistical tests, the data were analyzed in SPSS 24.

RESULTS

Tetracera scandens (L.) Merr was identified as the plant used in the experiment.and the Dilleniaceae family.

The maceration method was used to extract stems from T. scandens.Because it does not require any special equipment or heating, this method can prevent compounds from decomposing or evaporating due to heating.Since ethanol is a universal solvent that dissolves polar, semi-polar, and non-polar compounds, it was utilized.

About 1 kg is macerated by T. Scandens.Three times, the sample was immersed for 24 hours with occasional stirring for the first six hours.It aims to attract the effective active ingredients it contains.Additionally, a rotary evaporator was used to concentrate the collected macerate, evaporating the remaining solvent and water to produce a 77.4856-gram thick extract.The extract was characterized to determine its quality after obtaining a thick extract.The organoleptic analysis revealed that the extract was tasteless, odorless, thick, and reddish-black in color.One of the five senses' specific parameters is this organoleptic determination, which aims for a straightforward and subjective initial recognition.In addition, the components of the compounds in the extract were identified through a phytochemical search test.Alkaloids, phenols, terpenoids, and flavonoids were found in the T. scandens strain ethanol extract during the phytochemical screening test.

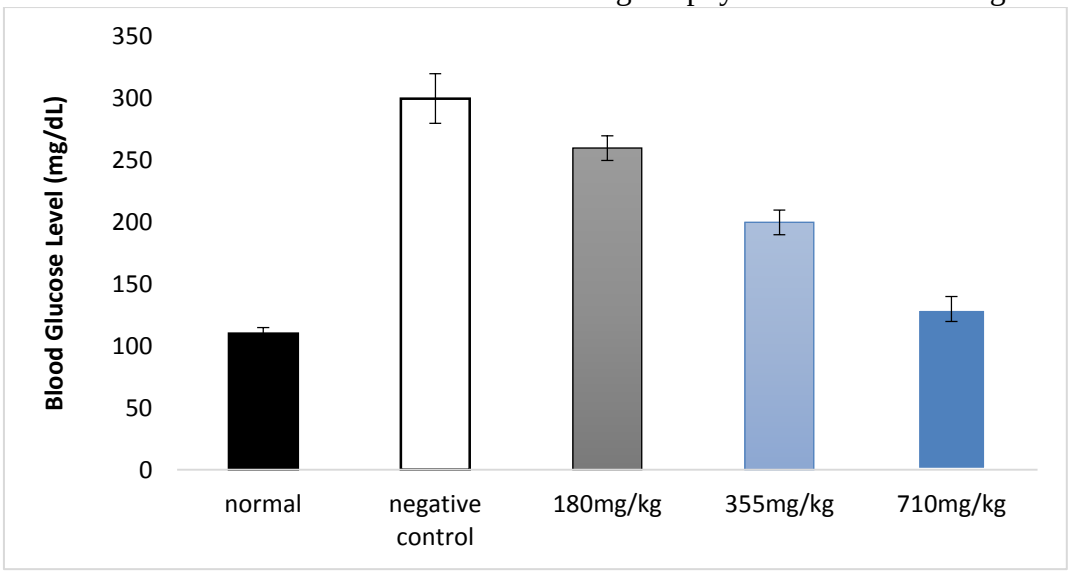


Figure 2. Blood Glucose Level

In addition, experimental animals were used to test the pharmacological activity of the drug against diabetes.According to Figure 2, the study found that the three doses (180, 355, and 710 mg/kg body weight) significantly reduced the alloxan-induced blood glucose

levels in rats (p 0.05), with 710 mg/kg body weight having the greatest impact on this reduction.The extract's administration also significantly raises insulin levels (p 0.05). (Figure. 3).

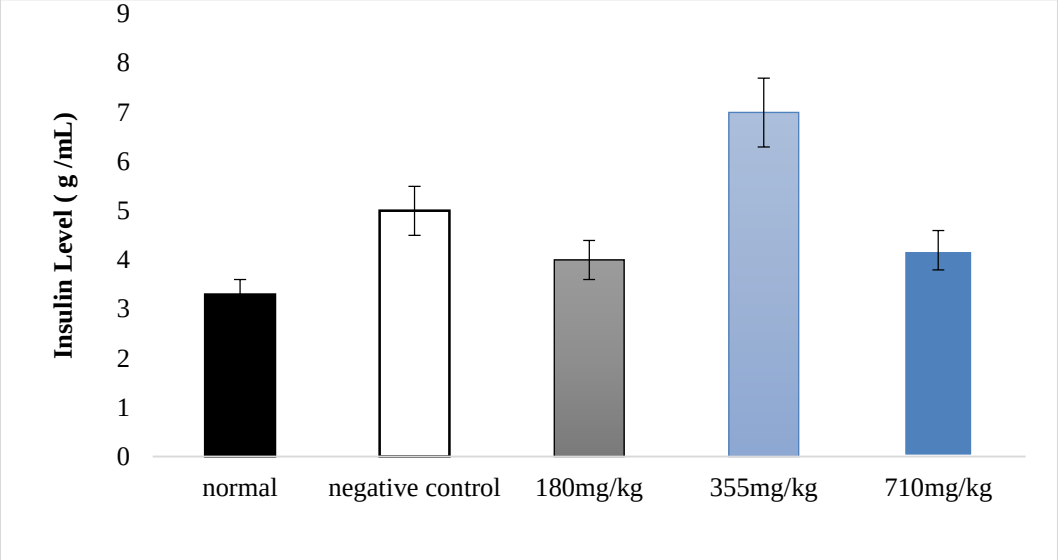


Figure 3. Insulin Level

The HOMA-IR value can be determined after blood glucose and insulin levels have been measured.A method that is both practical and simple to use is the HOMA IR measurement.The extract's administration was found to significantly lower the HOMA-IR value, according to the findings of the study.This indicates that there was an increase in insulin sensitivity or a decrease in insulin resistance following the administration of T. scandens strain ethanol extract (p 0.05), with a dose of 710 mg/kg BW having the most significant effect on reducing shown insulin resistance. (Figure 4).

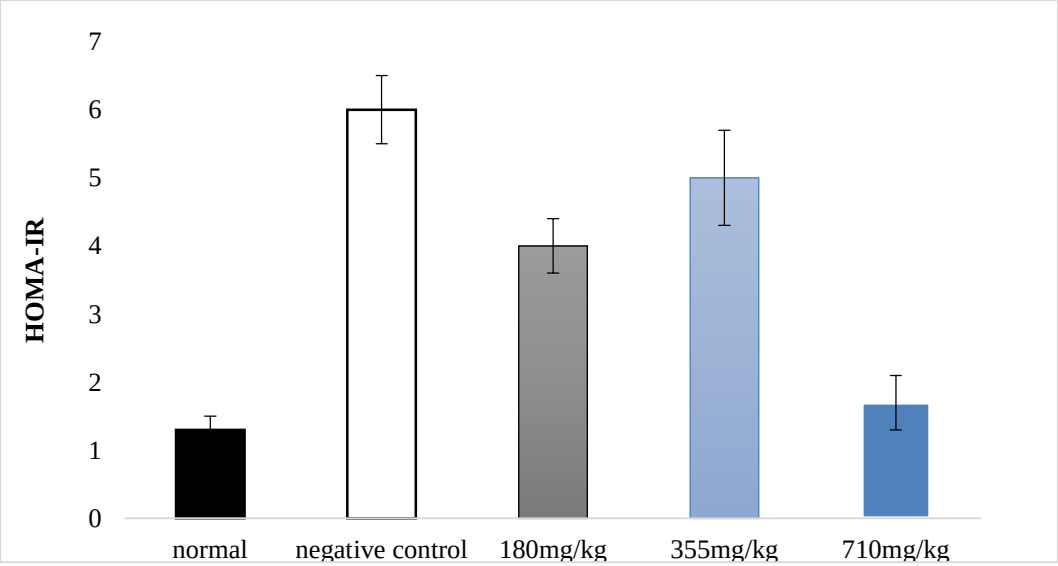


Figure 4. HOMA-IR value

DISCUSSION

Insulin opposition hinders the usage of glucose in fringe tissues by insulin.It may be due to glucose oxidation, which prevents glucose from entering cells, failed phosphorylation of the insulin receptor substrate (IRS) complex, a decrease in GLUT-2 translocation, or both;it causes high blood sugar.The amount of glucose absorbed and utilized by body cells increased with the HOMA-IR value;Sugar levels in the blood rise as a result [26,51-70-75]. The researchers hypothesized that the presence of secondary metabolites like flavonoids, which have been shown to have an anti-hyperglycemic effect, was the cause of the rats's lower blood glucose levels.Due to their ability to repair damaged cells in alloxan-induced diabetes, flavonoids were previously thought to be an effective antihyperglycemic [27-38,71-73].Flavonoids are anti-inflammatory and have the potential to increase insulin sensitivity in insulin-producing pancreatic cells.Flavonoids can also increase the insulin-secreting capacity of cells.By suppressing NF-B signaling, activating the PI3K/Akt pathway, inhibiting nitric oxide generation, and decreasing reactive oxygen species (ROS), flavonoids shield cells from cytokines, glucotoxicity, and lipotoxicity.Through PLC/PKC or cAMP/PKA signaling, increased insulin secretory capability boosts insulin secretion and mitochondrial activity [28, 39-50,74-79].

CONCLUSION

At the moment, various synthetic drugs, such as,In addition to insulin, many people worldwide use biguanides, thiazolidinediones, sulphonylureas, diphenylalanine derivatives, meglitinides, and -glucosidase inhibitors for diabetes management.However, the efficacy of these medications is highly contentious due to undesirable side effects, and there is a strong demand for new, safe medications that effectively treat diabetes.Tetracera scandens (L.) Merr ethanol extract was administered to alloxan-induced rats.stems from decreased insulin resistance or increased insulin sensitivity, increased insulin levels, and decreased glucose levels.

References

1. 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), pp.1047-1053.
2. Koehn, F.E. and Carter, G.T., 2005. The evolving role of natural products in drug discovery. Nature reviews Drug discovery, 4(3), pp.206-220.
3. Bnouham, M., Ziyyat, A., Mekhfi, H., Tahri, A. and Legssyer, A., 2006. Medicinal plants with potential antidiabetic activity-A review of ten years of herbal medicine research (1990-2000). International Journal of Diabetes and Metabolism, 14(1), p.1.
4. Fröde, T.S. and Medeiros, Y.S., 2008. Animal models to test drugs with potential antidiabetic activity. Journal of ethnopharmacology, 115(2), pp.173-183.
5. American Diabetes Association. Introduction : Standards of medical care in diabetes 2019. Diabetes Care. 2019;43(Suppl. 1):S1–S2.
6. Herningtyas EH, Ng TS. Prevalence and distribution of metabolic syndrome and its components among provinces and ethnic groups in Indonesia. BMC Public Health. 2019; 19(1):377. https://doi.org/10.1186/s12889-019-6711-7.
7. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of medical care in diabetes-2020. Diabetes Care. 2020;43(Suppl. 1):S98–110. https://doi.org/10.2337/dc20-S009.
8. Kim DH, Lee S, Chung YW, Kim BM, Kim H, Kim K, Yang KM. Antiobesity and antidiabetes effects of a Cudrania tricuspidata hydrophilic extract presenting PTP1B inhibitory potential. Biomed Res Int. 2016. https://doi.org/10.1155/2016/8462759.

9. Ipor, I., Sani, H. and Tawan, C., 2001. Floristic composition of forest formation at Mahua, Crocker range national park, Sabah. A scientific journey through Borneo: The Crocker Range National Park Sabah, 1, pp.21-31.
10. Vidal, G. and Werner, R.F., 2002. Computable measure of entanglement. Physical Review A, 65(3), p.032314.
11. Degryse, H. and Nguyen, G., 2004. Interbank exposure: An empirical examination of systemic risk in the belgian banking system.
12. Von Roon, A.C., Karamountzos, L., Purkayastha, S., Reese, G.E., Darzi, A.W., Teare, J.P., Paraskeva, P. and Tekkis, P.P., 2007. Diagnostic precision of fecal calprotectin for inflammatory bowel disease and colorectal malignancy. Official journal of the American College of Gastroenterology| ACG, 102(4), pp.803-813.
13. Sun, Y.K., Myung, S.T., Park, B.C., Prakash, J., Belharouak, I. and Amine, K., 2009. High-energy cathode material for long-life and safe lithium batteries. Nature materials, 8(4), pp.320-324.
14. Degryse, H. and Nguyen, G., 2004. Interbank exposure: An empirical examination of systemic risk in the belgian banking system.
15. Sun, Y.K., Myung, S.T., Park, B.C., Prakash, J., Belharouak, I. and Amine, K., 2009. High-energy cathode material for long-life and safe lithium batteries. Nature materials, 8(4), pp.320-324.
16. Nokhala A and, Siddiqui MJ. Phytochemicals and biological activity of Tetracera scandens Linn. Merr (Dilleniaceae): A short review. J Pharm Bioallied Sci. 2020;12(3):217–22. https://doi.org/10.4103/jpbs.JPBS_192_19.
17. Muliyah E, Sulistijorini S, Sulistyaningsih Y, Rafi M. Tetracera scandens as a medicinal plant: Secretory structures, histochemistry, and antibacterial activity. J Trop Life Sci. 2018;8(1):68–74. https://doi.org/10.11594/jtls.09.01.12.
18. Zhang CH, Xu GL, Liu YH, Rao Y, Yu RY, Zhang ZW, Wang YS, Tao L. Anti-diabetic activities of Gegen Qinlian decoction in high-fat diet combined with streptozotocin-induced diabetic rats and in 3T3-L1 adipocytes. Phytomedicine. 2013;20(3–4):221–9. https://doi.org/10.1016/j.phymed.2012.11.002
19. Ghorbani A, Rashidi R, Shafiee-Nick R. Flavonoids for preserving pancreatic beta cell survival and function: A mechanistic review. Biomed Pharmacother. 2019;111:947–57. https://doi.org/10.1016/j.biopha.2018.12.127.
20. Lee MS, Kim CH, Hoang DM, Kim BY, Sohn CB, Kim MR, Ahn JS. Genistein-derivatives from Tetracera scandens stimulate glucose-uptake in L6 myotubes. Biol Pharm Bull. 2009;32(3):504–8. https://doi.org/10.1248/bpb.32.504.
21. Umar A, Ahmed QU, Muhammad BY, Dogarai BBS, Soad SZBM. Anti-hyperglycemic activity of the leaves of Tetracera scandens Linn. Merr. (Dilleniaceae) in alloxan induced diabetic rats. J Ethnopharmacol. 2010;131(1):140–5. https:// doi.org/10.1016/j.jep.2010.06.016
22. Ahmed D, Kumar V, Sharma M, Verma A. Target guided isolation, in-vitro antidiabetic, antioxidant activity and molecular docking studies of some flavonoids from Albizzia Lebbeck Benth. bark. BMC Complement Altern Med. 2014;14:155. https://doi.org/10.1186/1472-6882-14-155.
23. Banu KS, Cathrine L. General techniques involved in phytochemical analysis. Int J Adv Res Chem Sci. 2015;2(4):25–32.
24. Amini L, Mojab F, Jahanfar S, Sepidarkish M, Raoofi Z, Maleki-Hajiagha A. Efficacy of Salvia officinalis extract on the prevention of insulin resistance in euglycemic patients with polycystic ovary syndrome: A double-blinded placebo-controlled clinical trial. Complement Ther Med. 2020;48. https://doi.org/10.1016/j.ctim.2019.102245.
25. Lee JM, Okumura MJ, Davis MM, Herman WH, Gurney JG. Prevalence and determinants of insulin resistance among U.S. adolescents: A population-based study. Diabetes Care. 2006;29(11):2427–32. https://doi.org/10.2337/dc06-0709.
26. Kameswara Rao B, Renuka Sudarshan P, Rajasekhar MD, Nagaraju N, Appa Rao C. Antidiabetic activity of Terminalia pallida fruit in alloxan induced diabetic rats. J Ethnopharmacol. 2003;85(1):169–72. https://doi.org/10.1016/s0378-8741(02)00396-3.

27. Machkour A, Thallaj NK, Benhamou L, Lachkar M, Mandon D.Chemistry. 2006 Aug 25;12(25):6660-8.P 6660-6661-6662-6663.
28. Thallaj, N., Machkour, A., Mandon, D., Welter, R., New. J. Chem., 2005, 29, 1555 – 1558.
29. Thallaj, N. K. Damascus University Journal for Basic Sciences. 34 (1) 2018.
30. Thallaj. N. K. Journal of AlBaath University (39) 2017.
31. Thallaj. N. K. Tishreen University Journal for Research and Scientific Studies 38 (6) 2016.
32. Thallaj NK, Rotthaus O, Benhamou L, Humbert N, Elhabiri M, Lachkar M, Welter R, Albrecht-Gary AM, Mandon D. Chemistry. 2008;14(22):6742-53.P6745-6746-6747..
34. Wane A, Thallaj NK, Mandon D. Chemistry. 2009 Oct 12;15(40):10593-602. P10594-10595-10595.
35. Thallaj NK, Orain PY, Thibon A, Sandroni M, Welter R, Mandon D. Inorg Chem. 2014 Aug 4;53(15):7824-36. P7826-7827-7828.
36. N. K. Thallaj, J. Przybilla, R. Welter and D. Mandon, J. Am. Chem. Soc. 2008, 130, 2414-2415.
37. N. K. Thallaj, D. Mandon and K. A. White, Eur. J. of Inorg. Chem., 2007, 44–47.
38. N. K. Thallaj, A. Machkour, D. Mandon and R. Welter, New J. Chem., 2005, 29, 1555–1558.
39. Thallaj, N.; International journal of applied chemistry and biological sciences 2021, 2 (4), 65-77.
40. Thallaj, N.; Indian Journal of Advanced Chemistry (IJAC)2021, 1 (2), .
41. Thallaj, N.; International Journal of Research Publication and Reviews (IJRPR)2021, 2, 10, 951-959
42. L. Labban, N. Thallaj, Z. Malek; International Journal of Medical Studies, 2020, 5, No 12, 23-36.
43. L. Labban, M. Kudsi, Z. Malek, N. Thallaj; Advances in Medical, Dental and Health Sciences, 2020,3, 3,45-48.
45. L. Labban, N. Thallaj, M. Al Masri; Journal of Advanced Research in Food Science and Nutrition, 2020,3,1,34-41.
46. Thallaj, N; agha, M. I ,H;, nattouf; A.H; katib, CH; karaali, A; Moustapha, A; Labban L;open access library journal, 2020,7,5,1-21.
47. L. labban; N. thallaj; A. labban; archives of medicine, 2020, 12, 2:8, 1-5.
48. L. labban; N. thallaj; international journal of herbal medicine,2020, 8, 2, 33-37.
49. L. Labban, N. Thallaj, Z. Malek; Journal of Medical Research and Health Sciences, 2019, 2, 11, 784-787.
50. L. labban N. Thallaj; acta scientific nutritional health, 2019, 3,10, 7-12.
51, Malek, Z.S.; Sage D.; Pevet, P.; Raison, S.; Endocrinology 2007, 148 (11), 5165-5173.
52. Malek, Z.S.; Dardente, H.; Pevet, P.; Raison, S.; European Journal of Neuroscience 2005, 22 (4), 895-901.
53. Malek, Z.S.; Pevet, P.; Raison, S.; Neuroscience 2004, 125 (3), 749-758.
54. Malek, Z.S.; Labban, L.; The International Journal of Neuroscience, 2020, 1-7.
55. Malek, Z.S.; Labban, L.; European Journal of Pharmaceutical and Medical Research 2019, 6 (11), 527-532.
56. Malek, Z.S.; Journal of AlBaath University 2018, 40 (4), 39-62.
57. Malek, Z.S.; Tishreen University Journal for Research and Scientific Studies, 2018, 40.
58. ZS Malek, LM Labban; International Journal of Neuroscience, 2021,131 (12), 1155-1161.
59. ZS Malek, LM Labban; Journal of current research in physiology and pharmacology, 2020, 4, (1),1-5.
60. L.M. Labban, M. M. Alshishkli, A. Alkhalaf, Z. Malek; J. Adv. Res. Dent. Oral Health, 2017, 2(3&4), 1-4.
61. L Labban, ZS Malek, Open Access Library Journal, 2018, 5 (07), 1-11.
62. L Labban, ZS Malek, Ann Food Nutr Res J, 2019,1 ,1
63. Labban, L. and N. Thallaj, 2019. Acta Scient. Nutr. Health, 3: 7-12.

64. A Abbood, C Smadja, C Herrenknecht, Y Alahmad, A Tchapla, M Taverna Journal of Chromatography A 1216 (15), 3244-3251
65. A Abbood, C Smadja, M Taverna, C Herrenknecht Journal of Chromatography A 1217 (4), 450-458
66. A Abbood, C Herrenknecht, G Proczek, S Descroix, J Rodrigo, M Taverna,Analytical and bioanalytical chemistry 400 (2), 459-468
67. A Abbood, C Smadja, M Taverna, C Herrenknecht Journal of Chromatography A 1498, 155-162.
68. Y. alhomush, Z. malek, A. Abboud, N.Thallaj, Research Journal of Pharmacy and Technology, 2022, 15, 10.
69. N.Thallaj, Tishreen university journal,2022,44, 1, 59-77.
70. N.Thallaj, Tishreen university journal,2022,44,2, 87-105.
71. Z. Malek, H. Dardente, S. Raison, P. Pevet, Mesocricetus auratus neuronal tryptophan hydroxylase mRNA, partial cds, 2003, GenBank, AY345967.1.
72. N.Thallaj. Indian journal of advanced chemistry, 1, 3, 2022. 10-14.
73. N.Thallaj.Xi'an ShiyouDaxueXuebao (ZiranKexue Ban)/ Journal of Xi'an Shiyou University, Natural Sciences Edition.2022.65, 06. 289-301.
74. N.Thallaj.Xi'an ShiyouDaxueXuebao (ZiranKexue Ban)/ Journal of Xi'an Shiyou University, Natural Sciences Edition.2022.65, 06. 313-328.
75. Z. MALEK, A. ABBOOD, N.THALLAJ. Xi'an ShiyouDaxueXuebao (ZiranKexue Ban)/ Journal of Xi'an Shiyou University, Natural Sciences Edition.2022.65, 06. 302-312.
76. A. Abbood, N Thallaj, (2023). 44,(6), Arab Journal of Pharmaceutical Sciences.
77. N Thallaj, (2023). 44,(6),. Tishreen University Journal-Medical Sciences Series.
*78. A.Abbood, Z.Malek, **N.Thallaj**. 2022 15, 11, 4935-4939. Research Journal of Pharmacy and Technology.*
*79. A.Abbood, Z.Malek2, Y.Al-Homsh**, N.Thallaj**. 2022 15, 10, 4727-4732. Research Journal of Pharmacy and Technology.*
79. r.hallak, Z.malek, *(2022). 44,(5), 103-114, Tishreen University Journal-Medical Sciences Series.*