Coccinia grandis Extract Exerts Antihyperglycemic Effect through its Antioxidant, α-Amylase and α-Glucosidase Inhibitory Activities: An in vitro Study

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ABSTRACT

An increasing demand for herbal medicines has shifted the attention from synthetic to natural antioxidants and antidiabetic agents. In this study, the edible plant Coccinia grandis fruits (CGF) were assessed for radical scavenging and antioxidant potentials based on NO (nitric oxide) radical scavenging activity, ABTS [(2,2'-Azino-bis(3-ethylbenzothiazoline- 6-sulfonic acid) diammonium salt] and FRAP- Ferric reducing antioxidant power. In vitro α-amylase and α-glucosidase inhibitory activities were evaluated by using porcine pancreatic α-amylase and yeast α-glucosidase, respectively. The results from free radical scavenging and antioxidant tests clearly indicated the concentration dependent free radical scavenging and antioxidant activities. The extract exhibited the best inhibitory activities against α-amylase and α-glucosidase with IC50 (half maximal inhibitory concentration) values of 117.64± 4.54 µg/mL and 81.6 ± 3.64 µg/mL, respectively. These data suggest that the possible mechanisms underlying antihyperglycemic activity of C. grandis extract, presumably by its radical scavenging/antioxidant activities and through inhibition of α-amylase and α-glucosidase. This study also provides scientific evidence to corroborate the efficacy of this plant as an alternative antidiabetic agent.

Key words: Diabetes mellitus, Coccinia grandis, Antioxidant, α-glucosidase, α-amylase.

INTRODUCTION

The total predicted increase in numbers of people with diabetes from 2012 to 2030 is about 180 million (371.33 million to 551.87 million, respectively), an astonishing increase of 48% from 2012 at an annual growth of 2.7%, which is twice the annual growth of the total world adult population. Forty-two percent of the anticipated absolute global increase of 180 million people with diabetes is projected to occur in India and China alone. According to International Diabetes Federation (IDF), nearly 5 million people died due to diabetes and its related complications, in 2012.[1] Therefore, new concepts in the management of diabetes have aroused a curiosity among researchers as well as among the patients throughout the world. In countries such as India and China, use of herbal medicines is a very common practice from ancient time, and herbal medicines are considered to be much safer and less expensive therapeutic strategies for the treatment of various diseases. A proper scientific investigation of traditional herbal remedies, in particular, can provide valuable leads for the development of alternative drugs and strategies for the management of diabetes.[2] Role of herbs in the management and control of diabetes has emerged fast over the years with the discovery
Meenatchi and Maneemegalai.: Antidiabetic Efficacy of Coccinia grandis (L.) Voigt

Kingdom: Plantae
Order : Cucurbitales
Family : Cucurbitaceae
Genus : Coccinia
Species: C. grandis (L.) J. Voigt

Figure 1: (A) Mature unripe whole fruits. (B) Small slices, air dried under shade and (C) Pulverized to fine powder of Coccinia grandis.

The search for new pharmacologically active agents obtained by screening natural sources, such as medicinal plants or their extracts can lead to potent and specific inhibitors for amylase and α-glucosidase. The use of α-glucosidase inhibitors, such as acarbose that can also inhibit pancreatic α-amylase revealed that the complications of DM, such as onset of renal, retinal and neurological changes and the development of ischemic diseases are prevented or delayed. Long-term day-to-day management of diabetes, with acarbose is well tolerated and can improve glycaemic control as monotherapy, as well as in combination therapy. Natural inhibitors of carbohydrate degrading enzymes (α-amylase and α-glucosidase) especially from plant sources offer an attractive strategy for the control of postprandial hyperglycemia.

Coccinia grandis (L.) Voigt, the ivy gourd, also known as baby watermelon. In traditional medicine, fruits have been used to treat leprosy, fever, asthma, bronchitis, and jaundice. The fruit possesses mast cell-stabilizing, antianaphylactic, and antihistaminic potential. In Bangladesh, the roots are used to treat osteoarthritis and joint pain. A paste made of leaves is applied to the skin to treat scabies. Scientific investigations have supported the efficacy of leaf extracts in amelioration of diabetic conditions. The juice of the roots and leaves is used to treat diabetes, and the aqueous and ethanolic extracts of the plant exhibit hypoglycemic action. The leaves of C. grandis have been shown to stimulate insulin secretion in diabetic rats. However, the scientific record on the antioxidant and antidiabetic efficacy of unripe mature fruits of C. grandis is very poor and scarce. Hence, the present study was aimed to evaluate the antioxidant effect and α-amylase and α-glucosidase inhibitory activities of its fruits in vitro, which has not been reported despite its traditional use in diabetes.

MATERIALS AND METHODS

Chemicals and reagents
Porcine pancreatic α-amylase was obtained from HiMedia Laboratories Mumbai, India. Acarbose was obtained from Bayer Pharmaceuticals Pvt. Ltd. (Mumbai, India). Yeast α-glucosidase, p-nitrophenyl α-D-glucopyranoside, ABTS-2,2’-Azino-bis-(3-Ethylbenzthiazoline-6-Sulfonate) as sulfonic acid, Trolox [(+/-)-6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid] and DNSA (dinitrosalicylic acid) were obtained from Sigma-Aldrich (Bangalore, Karnataka, India). All other chemicals and solvents were of analytical reagent grade. Water was purified by Milli Q Water Purification System, Millipore, USA.

Plant materials and extraction
Coccinia grandis (L.) Voigt mature unripe whole fruits were collected from the Kancheepuram District, Tamil Nadu State, India in the month of December 2019. The pharmacognostic authentication was done by Siddha Central Research Institute, Central Council for Research in Siddha, Department of AYUSH, Ministry of Health and Family Welfare, Government of India, Chennai-600 106. The fruits were cut into small slices, air dried under shade, pulverized to fine powder (shown in Figure 1) using a laboratory scale cutting mill and extracted with ethanol at 35°C for 24 hrs. The extract was filtered, centrifuged and the residue was subjected to subsequent extraction with the same solvent and stored at -20°C.

Nitric oxide (NO) radical scavenging activity
Nitric oxide (NO) generated from sodium nitroprusside was measured by the Griess reaction. Sodium nitroprusside (5 µM) in phosphate-buffered saline was mixed with 3 mL of different concentrations (12.5-250 µg/mL) of CGF extract and the mixture was incubated at 25°C for 150 min. The samples were then allowed to react with the Griess reagent (1% sulfanilamide and 0.1% naphthyl ethylenediamine dihydrochloride in 2% H₃PO₄). The absorbance of the chromophore during the diazotization of nitrite with sulfanilamide and subsequent coupling with naphthyl ethylenediamine was measured at 546 nm. A similar procedure was repeated with respective solvent instead of the extract, which served as the control; L-ascorbic acid (12.5-250 µg/mL) was used as the positive control. All the tests were performed in triplicate. The percentage of scavenging activity was measured using the formula:
Antioxidant assay using ABTS [(2,2’-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) diammonium salt]

In this method, the radical scavenging capacity was measured by using ABTS⁺ solution radical cation. The assay was performed according to the method described by Thaipong et al., (2006) and Gan et al., (2010). The stock solution of ABTS⁺ was prepared by mixing 7.4 mM ABTS solution and 2.6 mM potassium per sulfate solution in the ratio of 1:1 and allowed to react for 12 h at room temperature in the dark. The ABTS⁺ working solution was prepared by diluting the stock solution (3 mL stock solution in 100 mL volumetric flask, diluting it to the mark with methanol) to get the absorbance of 1.1±0.05 unit at 734 nm using a UV-visible spectrophotometer. A series of standard were prepared in the range of 0–250 µg/mL. Standard solutions (150 µL) and sample extract (150 µL) were placed in different test tubes then ABTS working solution (2850 µL) was added to each test tube. These tubes were kept in the dark for 30 min. After that their absorbance was taken at 734 nm. The % inhibition of both standard and samples were calculated and the concentration of ABTS content in the extract was reported as mg of trolox equivalent (TE)/g extract.

Antioxidant assay using ferric reducing antioxidant power (FRAP)

For FRAP assay, Fresh FRAP reagent was prepared by mixing 300 mM acetate buffer (100 mL), 10 mM TPTZ (2,4,6-tri(2-pyridyl)-s-triazine) solution (10 mL) and 20 mM FeCl₃.6H₂O (10 mL) solution and kept warmed at 37°C until used in experiment. 300 mM acetate buffer pH 3.6 was prepared by dissolving sodium acetate trihydrate (3.1 g) in distilled water (500 mL) then glacial acetic acid (16 mL) was added and made up to the mark of 1 L with distilled water and checked for its pH. 10 mM TPTZ solution was prepared in 40 mM HCl and 20 mM FeCl₃.6H₂O was prepared in distilled water. Trolox was used as the standard and a calibration curve in the range of 0–250 µg/mL was prepared. Standard solution (150 µL) and sample extract (150 µL) were allowed to react with FRAP solution (2850 µL) in different test tubes for 30 min in the dark. Reading of the colored solution (ferrous tripyridyltriazine complex) of standard and sample was taken at 593 nm. The concentration of FRAP content in the extract was reported as mg trolox equivalent (TE)/g extract.

Porcine pancreatic amylase inhibition assay

Chromogenic 3,5-dinitrosalicylic acid (DNSA) assay was employed to assess the α-amylase activity as reported earlier. CGF Extract (25–200 µg/mL) was incubated with 50 µg/mL of porcine pancreatic α-amylase at 37°C for 10 min. One percent starch was used as a substrate. α-amylase without extract was used as control. Acarbose was used as a reference standard. Reducing sugar was estimated using DNSA assay at A 540 nm and the inhibitory activity was calculated by using the formula:

\[
%\text{Inhibition} = \frac{(A_{540\text{Control}} - A_{540\text{Test}})}{A_{540\text{Control}}} \times 100
\]

In vitro α-glucosidase inhibitory assay

α-glucosidase inhibitory activity was determined according to Kumar et al., (2010) and Gowri et al., (2007) with slight modifications. In brief, 50 µL of test sample (25-250 µg/mL in phosphate buffer, pH 6.8) was reconstituted in 100 µL of 100 mM phosphate buffer, pH 6.8 and incubated with 50 µL yeast α-glucosidase (0.25 U/mL in phosphate buffer) for 15 min at 37°C. The reaction was stopped by adding 1 mL of Na₂CO₃ (0.1 M). Release of p-nitrophenol was measured at 405 nm by spectrophotometer (T60U, PG Instruments Limited, United Kingdom). Individual blank for test sample was prepared by replacing substrate with 50 µL of the buffer. The control sample was prepared in similar manner but using 50 µL of buffer in place of test sample. Acarbose was used as a reference standard in all the experiments. All the tests were run in triplicate. The percentage of enzyme inhibition was calculated by using the formula:

\[
%\text{Inhibition} = \frac{(A_{405\text{Control}} - A_{405\text{Test}})}{A_{405\text{Control}}} \times 100
\]

The IC₅₀ (half maximal inhibitory concentration) values were determined by regression analysis of the data for at least five concentrations of sample.

Data analysis

All the results were expressed as mean ± standard deviation. Linear regression analysis was used to calculate the IC₅₀ values. Data were analyzed using one-way analysis of variance (ANOVA) followed by the Dunnett post hoc test using GraphPad Prism 5 (GraphPad Software, Inc., La Jolla, CA, USA). Differences were considered to be statistically different when p value was < 0.05.
RESULTS

Nitric oxide (NO) scavenging activity

Results related to the NO radical scavenging activity of CGF extracts and positive control showed significant NO radical scavenging activity in a concentration-dependent manner (Figure 2). In this assay, the ethanol extract caused a potential inhibition with IC$_{50}$ value of 0.15 mg/mL. The IC$_{50}$ value of positive control ascorbic acid was found to be 0.04 mg/mL.

Antioxidant assays

The antioxidant ability of medicinal plants is associated with its medicinal values. In this study, the antioxidant activity of CGF was measured using two different assays, namely FRAP and ABTS. Ferric reducing antioxidant power (FRAP) assay depends on the reduction of ferric ion into ferrous ion.$^{[20]}$ ABTS assay depends on the antioxidant compound ability to scavenge ABTS radical. By this assay we can measure antioxidant capacity of lipophilic and hydrophilic compounds in the same sample. Both the assays are very simple, inexpensive and usually employed methods for the determination of antioxidant activity and can give reproducible results. In the present study, the antioxidant activity of CGF was found to be 53.67 ± 2.24 mg trolox equivalent (TE)/g extract using ABTS method and that of FRAP was found to be 48.25 ± 1.87 mg trolox equivalent (TE)/g extract (Table 1).

Porcine pancreatic amylase inhibition assay

The CGF extract was found to show maximum inhibition up to 62.21 ± 3.88% against porcine pancreatic a-amylase at the concentration of 250 µg/mL (Figure 3). The IC$_{50}$ values of CGF and acarbose (positive control) were found to be 117.64 ± 4.54 µg/mL and 63.82 ± 2.17 µg/mL, respectively.

In vitro α-Glucosidase inhibition assay

The CGF extract showed inhibitory activity against yeast α-glucosidase with the maximum inhibition of 67.64 ± 2.77% at the concentration of 250 µg/mL, compared to 87.34 ± 4.64% of acarbose at the same concentration. The IC$_{50}$ of CGF extract was found to be 81.6 ± 3.64 µg/mL, whereas that of acarbose was 44.5 ± 2.34 µg/mL (Figure 4).

DISCUSSION

Diets biased towards plant-based components are known to provide a high amount of antioxidant phytochemicals, which offer protection against reactive oxygen species (ROS)- induced cellular damage.$^{[21]}$ Oxidation of biomolecules such as DNA, lipids and proteins by ROS play an important role in diabetes, cardiovascular disease, cancer, immune and inflammatory disorders and many other diseases related to the aging process.$^{[22]}$ This study has focused on the free radical scavenging, antioxidant capacities of CGF.
In the present study, ability of CGF to scavenge NO was analysed. The reactive oxygen species NO has been implicated in diabetes, inflammation, cancer, and other pathological conditions. NO is a very unstable species under aerobic conditions. The plant products have the property to counteract the effect of NO formation and, in turn, may be of considerable interest in relation to preventing the ill effects of excessive NO generation in the human body. Several studies have evaluated the relationship between the antioxidant activity of plant products and their phenolic content. Substances that are able to perform these reactions can be considered as antioxidants and radical scavengers.

The trolox equivalent antioxidant capacity (TEAC) of CGF extract were measured using the ABTS and FRAP methods. The antioxidant activity of the extract was found to be 53.67±2.24 trolox equivalent (TE)/g for the ABTS method and 48.25±1.87 mg trolox equivalent (TE)/g for the FRAP method. Based on NO radical scavenging and antioxidant activities (ABTS and FRAP) results, it can be inferred that the C. grandis has promising antioxidant capacity and novel drug candidate for diabetes mellitus. The radical scavenging and antioxidant activities of the CGF extract might be attributed to the presence of phenolic compounds and flavonoids.

Potent inhibitors of mammalian α-amylase found in some vegetables and herbs have been known as effective antidiabetic treatment for diabetes. Therefore, this research investigated α-amylase inhibitory activity of CGF extract, since this enzyme is known as one of the key enzyme in human digestive system to degrade starch to monosaccharide’s and cause the rise in blood glucose. It is noteworthy that the selected plant with significant inhibitory activity (IC50 value 117.64 μg/mL) has been consistently used in traditional medicinal systems as antidiabetic treatments or consumed together with starch-based products as salads or incorporated into porridge. Uncontrolled hyperglycemia in diabetic patients is associated with profound complications, such as increased risk of coronary heart disease, peripheral vascular disease, and cerebrovascular disease. The reduction of postprandial hyperglycemia has been approached by suppression of carbohydrate absorption from gastrointestinal tract. Several plant extracts have been reported to exert antidiabetic property through α-glucosidase inhibition. It was found in the present study that CGF extract also inhibited α-glucosidase in vitro with the IC50 of 81.6 μg/ml, whereas the IC50 of acarbose, an antidiabetic drug known to inhibit intestinal α-glucosidase, was found to be 44.5 μg/ml (Figure 4). Thus, from the results it can be inferred that the α-amylase and α-glucosidase inhibitory activities might contribute to the anti-hyperglycemic effect of the extract. The result also suggests that the extract may be clinically useful for the control of postprandial hyperglycemia.

CONCLUSION

From the aforementioned results, it can be concluded that mature unripe fruits of Coccinia grandis extract exerts antihyperglycemic activity via its free radical scavenging, antioxidant activities and inhibition of the enzymes, such as α-amylase and α-glucosidase. Further studies are required to isolate the active components from the extract and in vivo oral rodent efficacy studies in a disease model.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.
ABBREVIATIONS
ABTS: [(2,2’-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt]; CGF: - "Coccinia grandis" fruits; FRAP: Ferric reducing antioxidant power; IC_{50}: half maximal inhibitory concentration.

SUMMARY
This study reports the antidiabetic efficacy of mature unripe fruits of an indigenous medicinal plant Coccinia grandis. The data suggest that the possible mechanisms underlying antihyperglycemic activity of C. grandis extract, presumably by its radical scavenging / antioxidant activities and through inhibition of α- amylase and α-glucosidase. Present findings provide experimental evidence that the fruits of C. grandis have potential antidiabetic activity which might be used as a functional food and safe remedy for the management and treatment of diabetes and associated complications. This study also revealed that the plant can be a promising source for development of natural novel antidiabetic drugs.

Authors’ contributions
PM performed the experiments, analyzed/interpreted data and wrote the manuscript.
SM contributed to the concept, designed experiments, analyzed/interpreted data and finalized the manuscript.

REFERENCES
1. Kaplan W. Priority medicines for Europe and the world ‘A public health approach to innovation’. Update on 2004 background. 2013;6(4):8-10:Paper BP 6.4 Diabetes.
2. Amardy R, Chamukuttan S. Early diagnosis and prevention of diabetes in developing countries. Rev Endocr Metab Disord. 2008;9(3):193-201. doi: 10.1007/s11154-008-9079-z, PMID 18604667.
3. Welthinda J, Karunanyake EH, Sheriff MH, Jayasinghe KS. Effect of Momordica charantia on the glucose tolerance in maturity onset diabetes. J Ethnopharmacol. 1986;17(3):277-82. doi: 10.1016/0378-8741(86)90116-9, PMID 3807390.
4. Ali L, Khan AK, Mamun MI, Moshijuzzaman M, Nahar N, Nur-e-Alam M, et al. Studies on hypoglycemic effects of fruit pulp, seed, and whole plant of Momordica charantia on normal and diabetic model rats. Planta Med. 1993;59(5):408-12. doi: 10.1055/s-2006-959720, PMID 8255932.
5. Tarling CA, Woods K, Zhang R, Brastianos HC, Brayer GD, Andersen RJ, et al. The search for novel human pancreatic α-amylase inhibitors: high-throughput screening of terrestrial and marine natural product extracts. Chembiochem. 2008;9(3):433-8. doi: 10.1002/cbic.200700470, PMID 18214874.
6. Creutzfeldt W. Effects of the α-glucosidase Inhibitor acarbose on the Development of Long-term Complications in Diabetic Animals: Pathophysiological and Therapeutic Implications. Diabetes Metab Res Rev. 1999;15(4):289-96. doi: 10.1002/sdr.327, PMID 10550607.
7. Mertes G. Safety and efficacy of acarbose in the treatment of Type 2 diabetes: Data from a 5-year surveillance study. Diabetes Res Clin Pract. 2001;52(3):193-204. doi: 10.1016/S0168-8227(01)00221-2, PMID 11323089.
8. Taur DJ, Patil RY. Mast cell stabilizing, anti-anaphylactic and antihistaminic activity of Coccinia grandis fruits in asthma. Chin J Nat Med. 2011;9:359-62. doi: 10.3724/SP.J.1091.2011.00359.
9. Zakaria DM, Islam M, Sharif Anisuzzaman MD, Kundu SK, Khan MS, et al. Ethnomedical survey of medicinal plants used by folk medical practitioners in four different villages of Gazipur District, Bangladesh. Adv Nat Appl Sci. 2011;5(4):392-9.
10. Venkateswaran S, Pari L. Effect of Coccinia indica leaf extract on plasma antioxidants in streptozotocin-induced experimental diabetes in rats. Phytother Res. 2003;17(6):605-8. doi: 10.1002/trp.1195, PMID 12820225.
11. Akhtar MA, Rashid M, Wahed M, Islam R. Comparison of longterm antihyperglycemic and hypolipidemic effects between Coccinia cordifolia (Linn.) and Calycanthus roseus (Linn.) in alloxan-induced diabetic rats. Res J Med Sci. 2007;2:29-34.
12. Kumar GP, Sudheesh S, Vijayalakshmi NR. Hypoglycaemic effect of Coccinia indica: Mechanism of action. Planta Med. 1993;59(4):330-2. doi: 10.1055/s-2006-959693, PMID 8372150.
13. Govindarajan R, Rastogi S, Vijayakumar M, Shrirao A, Rawat AK, Mehrotra S, et al. Studies on the antioxidant activities of Desmodium gangeticum. Biomed Pharmacother. 2003;6(10):1424-7. doi: 10.1248/bbp.26.1424, PMID 14519948.
14. Thaipong K, Boonprakob U, Crosby K, Cisneros-Zevallos L, Hawkins Byrne DH. Comparison of ABTS, DPPH, FRAP, and ORAC assays for estimating antioxidant activity from guava fruit extracts. J Food Compos Analysis. 2006;19(8-9):669-75. doi: 10.1016/j.jfca.2006.01.003.
15. Gan GY, Xu XR, Song FL, Kuang L, Li HB. Antioxidant activity and total phenolic content of medicinal plants associated with prevention and treatment of cardiovascular and cerebrovascular diseases. J Med Plants Res. 2010;4:2348-44. doi: 10.5987/JMPR10.581.
16. Mane RS, Ghosh S, Singh S, Chopade BA, Dhavalae DB. Synthesis of anomic 1,5-anhydro sugars as conformationally locked selective α-mannosidase inhibitors. Biomed Chem. 2011;19(22):6720-5. doi: 10.1016/j.bmc.2011.09.046, PMID 22001328.
17. Sanap SP, Ghosh S, Jagabande AM, Pinjari RV, Gejji SP, Singh S, et al. Synthesis, computational study and glycosidase inhibitory activity of polyhydroxylated conidine alkaloids—a bicyclic iminosugar. Org Biomol Chem. 2010;8(14):3307-15. doi: 10.1039/c004690f, PMID 20517582.
18. Kumar JA, Tiwari AK, Ali AZ, Madhusudhana K, Reddy BS, Ramakrishna S, et al. New antihyperglycemic, alpha-glucosidase inhibitory, and cytotoxic derivatives of benzenemiazoles. J Enzyme Inhib Med Chem. 2010;25(1):80-8. doi: 10.3109/14756360903017122, PMID 2030512.
19. Gowri PM, Tiwari AK, Ali AZ, Rao JM. Inhibition of α-glucosidase and amylase by bertorganic acid isolated from Barringtonia racemosa Roxb. seeds. Phytother Res. 2007;21(8):796-9. doi: 10.1002/ptr.2176, PMID 17536368.
20. Benzke IF, Strain JJ. The ferric reducing ability of plasma (FRAP) as a measure of “antioxidant power”: the FRAP assay. Anal Biochem. 1996;239(1):70-6. doi: 10.1016/0003-2687(96)00070-4, PMID 8660267.
21. Shi J, Ho CT, Shahidi F. Asian functional foods. Boca Raton, FL: CRC Press: 2005.
22. Rother KI. Diabetes treatment–bridging the divide. N Engl J Med. 2007;356(15):1499-501. doi: 10.1056/NEJM200705243561506, PMID 17429082.
23. Moncada S, Palmer RM, Higgs EA. Nitric oxide: Physiology, pathophysiology, and pharmacology. Pharmacol Rev. 1991;43(2):109-42. PMID 1652778.
24. Shrirao A, Prabhu KS, Punitha IS. In vitro antioxidant studies of Sphaeranthus indicus (Linn). Indian J Exp Biol. 2006;44(12):993-6. PMID 1718673.
25. Purushothaman A, Nandhakumar E, Sachidanandam P. Modulation of lipid peroxidation and antioxidant status upon administration of ’Shemamrutha’ in 7,12-dimethylbenz[a]anthracene induced mammary carcinoma bearing rats. Asian Pac J Trop Biomed. 2012;2(2):S765-71. doi: 10.1016/S2221-1691(12)60311-6.
26. Meenatchi P, Purushothaman A, Maneemegalai S. Antioxidant, antiglycation and insulinotropic properties of Coccinia grandis (L.) in vitro: Possible role in prevention of diabetic complications. J Tradit Complement Med. 2017;7(1):54-64. doi: 10.1016/j.jtcm.2016.01.002, PMID 28053889.
27. Hirsh AJ, Yao SYM, Young JD, Cheeseman CI. Inhibition of glucose absorption in the rat jejunum: A novel action of α-D-glucosidase inhibitors.

Asian Journal of Biological and Life Sciences, Vol 10, Issue 3, Sep-Dec, 2021
Meenatchi and Maneemegalai: Antidiabetic Efficacy of Coccinia grandis (L.) Voigt

Gastroenterology. 1997;113(1):205-11. doi: 10.1016/S0016-5085(97)70096-9, PMID 9207279.

28. Samad A, Shams MS, Ullah Z, Wais M, Nazish I, Sultana Y, et al. Status of herbal medicines in the treatment of diabetes: A review [review]. Curr Diabetes Rev. 2009;5(2):102-11. doi: 10.2174/157339909788166837, PMID 19442095.

29. Patel DK, Kumar R, Laloo D, Hemalatha S. Natural medicines from plant source used for therapy of diabetes mellitus: An overview of its pharmacological aspects. Asian Pac J Trop Dis. 2012;2(3):239-50. doi: 10.1016/S2222-1808(12)60054-1.

30. Schlienger JL. Type 2 diabetes complications [Type 2 diabetes complications]. Presse Med. 2013;42(5):839-48. doi: 10.1016/j.pmcj.2013.02.313, PMID 23528336.

31. Si MM, Lou JS, Zhou CX, Shen JN, Wu HH, Yang B, et al. Insulin releasing and alpha-glucosidase inhibitory activity of ethyl acetate fraction of Acorus calamus in vitro and in vivo. J Ethnopharmacol. 2010;128(1):154-9. doi: 10.1016/j.jep.2009.12.044, PMID 20051258.

32. Lee YH, Choo C, Watawana MI, Jayawardena N, Waisundara VY. An appraisal of eighteen commonly consumed edible plants as functional food based on their antioxidant and starch hydrolase inhibitory activities. J Sci Food Agric. 2015;95(14):2956-64. doi: 10.1002/jsfa.7039, PMID 25491037.

33. Olakun OO, McGaw LJ, Eloff JN, Naidoo V. Evaluation of the inhibition of carbohydrate hydrolysing enzymes, antioxidant activity and polyphenolic content of extracts of ten African Ficus species (Moraceae) used traditionally to treat diabetes. BMC Complement Altern Med. 2013;13:94. doi: 10.1186/1472-6882-13-94, PMID 23641947.

34. Bothon FT, Debiton E, Avlessi F, Forestier C, Teulade JC, Sohounhloue DK. In vitro biological effects of two anti-diabetic medicinal plants used in Benin as folk medicine. BMC Complement Altern Med. 2013;13:51. doi: 10.1186/1472-6882-13-51, PMID 23452899.

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