Asian Australas. J. Biosci. Biotechnol. 2018, 3 (2), 136-142

Asian-Australasian Journal of Bioscience and Biotechnology
ISSN 2414-1283 (Print) 2414-6293 (Online)
www.ebupress.com/journal/aajbb

Article

Anti-diabetogenic impact of bitter melon (*Momordica charantia*) and mahogany (*Swietenia macrophylla*) on alloxan induced diabetic rabbit model

Mahabuba Begum , Fahima Binthe Aziz , Rakibul Islam , Md. Mahmudul Hasan, Misrat Masuma Parvez and Sumon Sarkar*

Dept. of Physiology and Pharmacology, Hajee Mohammad Danesh Science and Technology University, Dinajpur-5200, Bangladesh

*Corresponding author: Sumon Sarkar, Dept. of Physiology and Pharmacology, Hajee Mohammad Danesh Science and Technology University, Dinajpur-5200, Bangladesh. Phone: +8801721545509; E-mail: sarkarsumon.setu@gmail.com

Received: 15 July 2018/Accepted: 12 August 2018/ Published: 30 August 2018

Abstract: The increasing prevalence of diabetes mellitus in recent years to the focus of public health interests in Bangladesh. Herbal medicinal plant such as mahogany and bitter melon can be used as alternative of synthetic drugs to avoid side effects and high cost. So the present study was undertaken to investigate the antidiabetogenic effect of bitter melon and mahogany on diabetic rabbits. Four months old rabbits were randomly assigned into five groups (T_1, T_2, T_3, T_4 and T_5) with 4 rabbits. Group T_1 was kept for negative (no alloxan) control, the rest of the group (T_2, T_3, T_4 and T_5) were injected with alloxan intramuscularly at a dose rate of 75mg /kg body weight. T_2 was positive control group. Group T_3, T_4 and T_5 was considered for bitter melon (150mg/kg b.w.), mahogany (50mg/kg b.w) and combined with previous dose respectively. Suspension of both fruit was tested for its efficacy in alloxan induced diabetic rabbit. Over the course of the trial, observations were recorded for induction of diabetics, blood glucose level, and body weight after 72 hours. Blood glucose level were increased significantly ($p<0.05$) in all treated groups compared to the control group and the highest induction was recorded in T_2 group treated with alloxan. Body weight was decreased significantly ($p<0.05$) in all alloxan treated groups and lowest was recorded in group T_2. There was significant decreased in blood glucose level in all bitter melon and mahogany treated group (T_3, T_4, T_5) compared to the T_2 group and lowest glucose level was recorded in T_5 group. The present study reveals that combined treatment with bitter melon and mahogany decreases blood glucose level without affecting health of rabbits. The results of this study show that chronic oral administration of a suspension of bitter melon fruits and mahogany seeds in appropriate dosage may be good alternative as anti-diabetic agent.

Keywords: diabetes; rabbit; alloxan; mahogany; bitter melon

1. Introduction

The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels (Kitabchi *et al.*, 2009). The therapeutic measures for the treatment of hyperglycemia include the use of insulin and other agents, such as amylin analogs, and alpha-glucosidase inhibitors such as acarbose and miglitol, voglibiose, sulfonylureas, and biguanides. These drugs have certain adverse effects, such as causing hypoglycemia at higher doses, liver problems, lactic acidosis, and diarrhea (Kenny, 2014). Therefore, there is a necessity to look for newer agents that meet the requirement of an ideal antidiabetic compound. Nature has been a source of medicinal substances for thousands of years, and plant-based systems continue to play an essential role in the primary health care of 80% of the world's underdeveloped and developing countries (ADA, 2013). There is an increasing demand for natural products with antidiabetic activity for use by diabetic patients. Ethnopharmacological surveys indicate that more

than 1200 plants are used worldwide in traditional medicine for their alleged hypoglycemic activity (Mallick *et al.*, 2009). The investigation of antidiabetic agents of plant origin, which are used in traditional medicine, is thus of great significance.

Bitter melon has been used as a folk remedy for treating cancer, aiding digestion, and fighting viral infections. The fruit has also been used medicinally in Asia, Africa, India, and South America to lower blood glucose levels. Experimental and clinical research conducted worldwide has established its blood glucose-lowering action.

Today, bitter melon remains a popular and frequently studied dietary botanical used for managing diabetes. But 60 years of research on this bitter-tasting plant as an adjunctive for diabetes management has yielded uncertain results. Vicine, charantin, and polypeptide-P are the three known compounds present in bitter melon that are responsible for its antidiabetic properties. Together they increase glucose uptake and glycogen synthesis in the liver, muscle, and adipose tissue and also improve glucose tolerance (Ooi *et al.*, 2012). Possible mechanisms include increased insulin secretion, tissue glucose uptake, liver muscle glycogen synthesis, glucose oxidation, and decreased hepatic gluconeogenesis (Qin *et al*., 2004).

Swietenia macrophylla is a beautiful, lofty, evergreen large tree, native to tropical America, Mexico and South America usually 30–40 m in height, and 3 m in girth (Li *et al.*, 2005). The seeds of *S. macrophylla* have been reported for their anti-inflammatory, anti-mutagenic, and anti-tumor activities (Lin *et al.*, 2009; Fuangchan *et al.*, 2011). The seeds of *S. macrophylla* are traditionally used by the local healers of Azhagar hills, Madurai, Tamil Nadu, India, for curing diabetes.

Hence, the present study was undertaken to evaluate the combined antidiabetic potential of the alcoholic seed extract of *S. macrophylla* and *M. charantia* experimentally in normal and alloxan-induced diabetic rabbit to prove its use by the tribes in folk medicine.

2. Materials and Methods

2.1. Selection of animal

Twenty white rabbit aged between 4 months and weighting between 1000 to1200 g were collected from rabbit farm under the department of Animal Genetics and Breeding, HSTU, Dinajpur. All the rabbit were housed at screen bottomed wire cages arranged in rows and kept in the departmental (Dairy & Poultry Science, HSTU) animal house. The animals were fed with pellet at a recommended dose of100 g/kg as advised by ICDDRB. Drinking water was supplied add libitum. The rabbit were maintained in this condition for a period of two weeks to acclimatize them prior to experimental uses.

2.2. Grouping of animal

Twenty rabbits were used to carry out this investigation. These rabbits were divided into five groups containing 4 rabbits in each group. The groups were designated as T_1, T_2, T_3, T_4 and T_5.

2.3. Chemicals

- Alloxan monohydrate – (NH-CO-NH-COCO.H2O). (Sigma Aldrich Chemical, Saint Louis, MO, USA), Dresden, Germany
- Blood Glucose determination Kit – Glucolab Active blood glucose system (strip method).

2.4. Induction of diabetics in rabbit

Alloxan was dissolved in normal saline .This solution was injected intravenously and intraperitoniously to rabbits and maintained fasting condition for 18 hours. After 18 hours diabetic condition could not found than this solution was injected intramuscularly to rabbits and maintained fasting condition for 18 hours. To induce diabetic condition in rabbits a dose of 75mg alloxan per kg of body weight was chosen following the recommendation of works done previously (Puri and Prabhu, 2002).

2.5. Preparation of seed extract

Fresh bitter melon and dried mahogany seed are purchased from the local market at a reasonable price then these are measured separately by electronic balance and grinded with mortar and pestle than blended with blender machine. Finally, the extracts are mixed with 100 ml distilled water separately and stirred to make homogenous mixture and then filtered through silk cloth. All above solution were preserved at 0°-4°c in Laboratory.

2.6. Animal treatment

From the entire animal group T_1 was kept as negative control group. Body weights and blood glucose level were measured at the time when that of other groups was measured. The rest of the group (T_2, T_3, T_4 and T_5) were injected with alloxan (75 mg/kg b.w.) and T_2 kept as (diabetic control) positive control group. T_3 was treated with bitter melon (150mg/kg b.w.) and T_4 was treated with mahogany (50mg/kg b.w.) seed extract. T_5 was treated with combined as the previous dose.

2.7. Observation of rabbits

Body weight and fasting blood glucose level of each rabbits were measured after 18 hours of fasting before alloxan injection. Body weight and fasting blood glucose level of each rabbits were measured on 15th day of alloxan injection. Body weight and fasting blood glucose level of each rabbit were measured on Day 0 (Pre-treatment) and Day 7 & 14 & 21 (during treatment) of different treatment.

2.8. Hematological test

Blood samples were collected from ear vein of rabbit of both control and treated groups to study the effect of the serum extract of bitter melon and mahogany seed on diabetic rabbit and the following parameters were observed:

(a) Hemoglobin estimation (Hb)
(b) Packed Cell Volume (PCV)
(c) Erythrocyte Sedimentation Rate (ESR)

a. Determination of Hemoglobin Concentrations (Hb):

The N/10 hydrochloric acid was taken in a graduated tube up to 2 marks with the help of a dropper. Well-homogenized blood sample was then drawn into the Sahli pipette up to 20 cm. mark. The tip of the pipette was wiped with sterile cotton and the blood of the pipette was immediately transferred into the graduated tube containing hydrochloric acid. This blood and acid were thoroughly mixed by stirring with a glass stirrer. There was a formation of acid hematinic mixture in the tube by hemolysing red blood cells by the action of hydrochloric acid (HCL). The tube containing acid hematin mixture was kept standing in the comparator for 5 minutes. After that distilled water was added drop by drop. The solution was mixed well with a glass stirrer until the color of the mixture resembled to the standard color of the comparator. The result was read in daylight by observing the height of the liquid in the tube considering the lower meniscus of the liquid column. The result was then expressed in gm %.

b. Determination of Packed Cell Volume (PCV):

The citrated well mixed blood sample was drawn into special loading pipette (Wintrobe pipette). The tip of the pipette was inserted up to the bottom of a clean, dry Wintrobe hematocrit tube. Then the Wintrobe tube was filled from the bottom by pressing the rubber bulb of the pipette. As blood came out, the pipette was slowly withdrawn but pressure was continued on the rubber bulb of the pipette so as to exclude air bubbles. The tip of the pipette was tried to keep under the rising column of blood to avoid foaming and the tube was filled exactly to the 10 cm mark. Then the Wintrobe hematocrit tube was placed in the centrifuge machine and was centrifuged for 30 minutes at 3000 rpm. Then, the hematocrit or PCV was recorded by reading the graduation mark; the percent volume occupied by the hematocrit was calculated by using the following formula as described by Lamberg and Rothstein (1977).

$$PCV\% = \frac{\text{Height of the red cell volume in cm}}{\text{Height of total blood in cm}} \text{ X } 100$$

c. Determination of Erythrocyte Sedimentation Rate (ESR):

The fresh anticoagulant blood was taken into the Wintrobe hematocrit tube by using special loading pipette exactly up to 0 marks. Excess blood above the mark was wiped away by sterile cotton. The filled tube was placed vertically undisturbed on the wooden rack for one hour. After one hour the ESR was recorded from the top of the pipette. The result was expressed in mm in 1st hour.

2.9. Data and Statistical analysis

Data were analyzed using SPSS v.11 for Windows (SPSS Inc., Chicago, IL, USA). Statistically significant differences between group means were determined by analysis of variance (ANOVA). Mean values were considered significantly different at $P<0.05$. Data are expressed as mean ± SEM.

3. Results and Discussion

The experiment was conducted to determine the efficacy of alloxan to induce diabetics in rabbit. Attempts were also made to study the efficacy of bitter melon fruit and mahogany seed on blood glucose level and body weight in alloxan induced diabetic rabbit. And also compare the combined effect of bitter melon fruit and mahogany seed on blood glucose level and body weight in alloxan induced diabetic rabbit.

3.1. Alloxan induced diabetes and comparison with control

Blood glucose level of different groups of rabbits is presented in Table 1.The study was revealed that glucose level was the highest in group T_2, which was treated with alloxan compare to the T_1 group. This treatment significantly ($p \leq .0.05$) increases the blood glucose level in treated rabbits. The present results are agreed with other results. Sharma *et al*. (2009); Yakaiah *et al.* (2013); Puri and Prabhu (2002**)** suggested that alloxan treatment increased the blood glucose level in treated birds compared to the control rabbits. Alloxan induced experimental diabetes is also associated with marked reduction of anti-oxidant enzyme superoxide dismutase activity in islets cells. In antioxidant enzyme superoxide dismutase activity (Rao *et al.,* 2003). Alloxan induced diabetes is also suggested to result from initial islet cell inflammation followed by activation of macrophages and lymphocytes might be the source of cytotoxic oxygen radicals (Ying *et al.,* 2012). Alloxan has been shown to inactivate a calcium and calmodulin dependent protein kinase which reduces insulin secretion (Verrotti *et al*., 2012). (Gillman *et al.,* 2003) claim that structural similarity between alloxan and glucose may be responsible for its affinity with the B receptor on the B cell. Alloxan binds almost instantly to islets cell membranes and causes rapid in vitro or in vivo inhibition of the insulin secretory mechanism. According to Epand *et al.* (1985) zinc removal from insulin in chelate form may be the reason for its diabetogenic effect.

3.2. Alloxan induced diabetes and comparison with bitter melon fruit

Blood glucose level of different groups of rabbits are presented in Table 1.The study was revealed that glucose level was the lowest in group T_3 which was treated with bitter melon compare to the T_4 group. The effect of fruit suspension at a dose of 150gm/kg body weight in lowering blood sugar level showed statistically significant Comparison with T_2 group. We have evaluated the suspension of the unripe fruit of the *Momordica charantia* (Bitter gourd) was assessed for its anti diabetic activity in alloxan-induced diabetic rabbits. The blood sugar levels were highly decreased of a treatment with high dose of extract. The blood sugar levels are almost comes to the normal levels. The present results are agreed with Ying *et al.* (2012); Yakaiah *et al.* (2013) and Lin *et al.* (2009)

Yakaiah *et al.* (2013) suggested that results of this study show that chronic oral administration of an extract of Momordica charantia fruit at an appropriate dosage may be good alternative anti diabetic agent in alloxan induced diabetics.

3.3. Alloxan induced diabetes and comparison with mahogany seed

Blood glucose level of different groups of rabbits are presented in Table 1.The study was revealed that glucose level was the low in group T_4, which was treated with mahogany seed compare to the T_2 group. The effect of seed suspension at a dose of 50mg/kg body weight in lowering blood sugar level showed statistically significant Comparison with T_2 group. We have evaluated the suspension of the seed of the *switaneia macrophylla* (mahogany) was assessed for its anti diabetic activity in Alloxan-induced diabetic rabbits. The blood sugar levels were highly decreased of a treatment with high dose of extract. The blood sugar levels are almost comes to the Normal levels. The present results are agreed with results of Naveen, *et al*. (2014); the results of this study also agreed with Panda, *et al.,* (2010). The result of this study indicates that a dose of 50 mg/kg body weight of *Swietenia macrophylla* (mahogany seed) might be a beneficial adjuvant to oral hypoglycemic agents in Alloxan induced diabetics.

3.4. Alloxan induced diabetes and comparison among different groups of rabbits

The fall in the blood sugar was compared among the groups of animals.

The study was reveled that blood glucose level was the lowest in group T_5 compare to the T_3 and T_4 group, which was treated with bitter melon fruit and mahogany seed. The effect of this combined treatment significantly ($p \leq .0.05$) affects the blood glucose level.

Table 1. Effects of bitter melon fruit and mahogany seed suspension and combined treatment on blood glucose (m mol/L, mean±SE) concentration in Alloxan induced diabetic rabbits (n=4).

Group	Day 0 (Mean ± SE) mmol/L	Day 7 (Mean ± SE) mmol/L	Day 14 (Mean ± SE) mmol/L	Day 21 (Mean ± SE) mmol/L
T_1	7.550 ^{b} ± 0.44	7.725 ^{c} ± 0.37	7.425 ^{d} ± 0.24	7.875 ^{d} ± 0.13
T_2	28.33 ^{a} ± 0.69	27.00 ^{a} ± 1.15	24.23 ^{a} ± 0 .60	19.02 ^{a} ± 0 .70
T_3	27.95 ^{a} ± 0.72	23.45 ^{b} ± 0.76	18.27 ^{b} ± 0 .71	12.98 ^{b} ± 0 .45
T_4	28.42 ^{a} ± 0.82	21.13 ^{b} ± 0.48	14.52 ^{c} ± 0.48	10.93 ^{c} ± 0.15
T_5	29.05 ^{a} ± 0.44	21.58 ^{b} ± 0.92	14.52 ^{c} ± 1.41	10.15 ^{c} ± 1.06

Values with the different superscripts in the same column are statistically significant ($P<0.05$). T_1, Control (without treatment); T_2 Alloxan induction (75 mg); T_3, Bitter melon treatment (150 gm); T_4, mahogany seed treatment (50 mg); T_5, Bitter melon and Mahogany seed treatment.

3.5. Body weight (gm)

The percent increased in body weight gain in normal control rabbits (Group T_1, n=4) was 1133 gm as shown in Table 2. On the contrary, in diabetic positive group (Group T_2, n=4), the percentage of body weight loss was 1000gm. The percent increased in body weight gain over 21 days in. Group T_3 (n=4), following oral administration of suspension of bitter melon @ 150 gm/kg was 1080 gm. In Group T_4 (n=4), following administration of mahogany seeds @ 50 mg/kg for 21 days the percentage of body weight gain was 1113 gm. In Group T_5 (n=4), following administration of bitter melon and mahogany seeds @ previous doses for 21 days the percentage of body weight gain was 1083 gm comparison with T_2 group which is treated with alloxan.

Table 2. Effects of bitter melon fruit and mahogany seed suspension and combined treatment on body weight (gm) in alloxan induced diabetic rabbits (n=4).

Group	Day 0 (Mean ± SE) gm	Day 7 (Mean ± SE) gm	Day 14 (Mean ± SE) gm	Day 21 (Mean ± SE) gm
T_1	1056.0 ^{a} ± 21.34	1078.0 ^{a} ± 21.75	1108.0 ^{a} ± 21.75	1133.0 ^{a} ± 20.56
T_2	1025.0 ^{a} ± 32.27	1020.0 ^{a} ± 31.09	1010.0 ^{b} ± 29.72	1000.0 ^{b} ± 32.40
T_3	1056.0 ^{a} ± 21.35	1048.0 ^{a} ± 20.56	1065.0 ^{ab} ± 21.06	1080.0 ^{a} ± 20.82
T_4	1069.0 ^{a} ± 11.97	1073.0 ^{a} ± 11.09	1083.0 ^{a} ± 14.36	1113.0 ^{a} ± 21.75
T_5	1044.0 ^{a} ± 15.73	1053.0 ^{a} ± 18.87	1065.0 ^{ab} ± 16.58	1083.0 ^{a} ± 16.52

Values with the different superscripts in the same column are statistically significant ($P<0.05$). T_1, Control (without treatment); T_2, Alloxan induction (75 mg); T_3, Bitter melon treatment (150 gm); T_4, mahogany seed treatment (50 mg); T_5, Bitter melon and mahogany seed treatment.

3.6. Hematological parameter

3.6.1. Hb (Hemoglobin) g/dl

Hemoglobin content is presented in Table 3.1. The values of Hb in all treated groups and control group were almost similar and the values were within the normal range. These values show a little fluctuation they were not statistically significant ($p>0.05$).

Table 3.1. Hemoglobin content.

Group	Day 0 (Mean ± SE)g/dl	Day 7 (Mean ± SE) g/dl	Day 14 (Mean ± SE) g/dl	Day 21 (Mean ± SE) g/dl
T_1	11.90 ^{a} ± 0.54	12.10 ^{a} ± 0.60	12.43 ^{a} ± 0.55	12.60 ^{a} ± 0.64
T_2	12.15 ^{a} ± 0.57	12.10 ^{a} ± 0.43	11.82 ^{a} ± 0.48	12.15 ^{a} ± 0.25
T_3	12.20 ^{a} ± 0.63	12.07 ^{a} ± 0.65	12.55 ^{a} ± 0.68	12.43 ^{a} ± 0.62
T_4	11.25 ^{a} ± 0.45	11.45 ^{a} ± 0.49	11.27 ^{a} ± 0.58	11.70 ^{a} ± 0.47
T_5	11.75 ^{a} ± 0.71	11.38 ^{a} ± 0.73	11.95 ^{a} ± 0.60	11.98 ^{a} ± 0.60

* = Significant at the 0.05% level

3.6.2. Packed cell volume (%)

Packed cell volume is presented in Table 3.2. The values of PCV in all treated groups and control group were almost similar and the values were within the normal range. These values show a little fluctuation they were not statistically significant ($p>0.05$).

Table 3.2. Packed cell volume (%).

Treatment group	Day 0 (Mean ± SE) %	Day 7 (Mean ± SE) %	Day 14 (Mean ± SE) %	Day 21 (Mean ± SE) %
T_1	40.47 ^{a} ± 0.78	40.08 ^{ab} ± 0.37	40.70 ^{ab} ± 0.39	41.14 ^{bc} ± 0.37
T_2	38.97 ^{a} ± 1.058	37.83 ^{c} ± 0.82	37.00 ^{c} ± 0.78	35.82 ^{d} ± 0.47
T_3	38.17 ^{a} ± 0.81	38.75 ^{bc} ± 0.52	40.33 ^{b} ± 0.60	40.72 ^{c} ± 0.55
T_4	39.83 ^{a} ± 0.55	40.60 ^{ab} ± 0.57	41.65 ^{ab} ± 0.46	42.67 ^{ab} ± 0.49
T_5	39.65 ^{a} ± 0.95	41.03 ^{a} ± 0.62	42.38 ^{a} ± 0.44	43.0 ^{a} ± 0.70

3.6.3. Erythrocyte sedimentation rate (mm/1st hour)

Erythrocyte sedimentation rate content is presented in Table 3.3. The values of ESR in all treated groups and control group were almost similar and the values were within the normal range. The highest ESR was recorded in Group T4 and lowest in Group T1. Although these values show a little fluctuation they were not statistically significant ($p>0.05$).

Table 3.3. Erythrocyte sedimentation rate (mm/1st hour).

Treatment group	Day 0 (Mean ± SE) mm/1st hour	Day 7 (Mean ± SE) mm/1st hour	Day 14 (Mean ± SE) mm/1st hour	Day 21 (Mean ± SE) mm/1st hour
T_1	1.875 ^{b} ± 0.27	1.700 ^{a} ± 0.22	1.900 ^{b} ± 0.23	1.950 ^{b} ± 0.22
T_2	1.850 ^{b} ± 0.07	2.200 ^{a} ± 0.11	2.750 ^{a} ± 0.17	3.525 ^{a} ± 0.10
T_3	2.550 ^{a} ± 0.32	2.300 ^{a} ± 0.19	2.075 ^{b} ± 0 .08	2.150 ^{b} ± 0.08
T_4	2.250 ^{ab} ± 0.14	2.275 ^{a} ± 0.13	1.925 ^{b} ± 0.11	1.850 ^{bc} ± 0.06
T_5	2.150 ^{ab} ± 0.06	1.925 ^{a} ± 0.29	1.625 ^{b} ± 0.24	1.450^{c} ± 0.20

4. Conclusions

In conclusion, it may be stated that the aqueous-methanolic extract of mahogani seed and bitter melon may provide a new therapeutic avenue against diabetes mellitus. Further work is necessary to search out the active ingredients present in this extract having antidiabetic efficacy. Extensive research is currently taking place in India, China, and Korea and in other countries in order to develop potential herbal medicine to prevent metabolic diseases including diabetes and its related complications.

Conflict of interest

None to declare.

References

American Diabetes Association (ADA), 2013. Economic costs of diabetes in the U.S. in 2012. Diabetes Care, 36: 1033–1046.

Epand RM, AR Stafford, M Tyers and E Nieboer, 1985. Mechanism of action of diabetogenic zinc-chelating agents. Model system studies. Mol. Pharmacol., 27: 366-374.

Fuangchan A, P Sonthisombat, T Seubnukarn, R Chanouan, P Chotchaisuwat and Sirigulsati, 2011. Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes patients. J. Ethnopharmacol., 134: 422–428.

Gillman MW, S Rifas-Shiman, CS Berkey, AE Field and GA Colditz, 2003. Maternal gestational diabetes, birth weight, and adolescent obesity. Pediatrics, 111: 221-226.

Kenny C, 2014. When hypoglycemia is not obvious: diagnosing and treating under-recognized and undisclosed hypoglycemia. Primary Care Diabetes, 8: 3–11.

Kitabchi AE, GE Umpierrez, JM Miles and JN Fisher, 2009. Hyperglycemic crises in adult patients with diabetes. Diabetes Care, 32: 1335–1343.

Lamberg SL and R Rothstein, 1977. Laboratory Manual of Hematology and Urinalysis, West Port Connecticut, USA.: Avi. Publishing Company, Inc.

Li DD, JH Chen and Q Chen, 2005. Swietenia mahagony extract shows agonistic activity to PPARγ and gives ameliorative effects on diabetic db/db mice. Acta Pharmacol. Sin., 26: 220–222.

Lin BD, T Yuan, CR Zhang, L Dong, B Zhang, Y Wu and JM Yue, 2009. Structurally diverse limonoids from the fruits of Swietenia mahagoni. J. Nat. Prod., 72: 2084-2090.

Mallick C, R Maiti and D Ghosh, 2006. Antidiabetogenic effects of separate and composite extract of seed of Jamun (*Eugenia jambolana*) and root of Kadali (*Musa paradisiaca*) in streptozotocin-induced diabetic male albino rat: a comparative study. International Journal of Pharmacology, 2: 492–503.

Naveen YP, G Divya Rupini, F Ahmed, A Urooj, 2014. Pharmacological effects and active phytoconstituents of Swietenia mahagoni: a review. J. Integr. Med., 12: 86-93.

Ooi CP, Z Yassin and TA Hamid, 2012. Momordica charantia for type 2 diabetes mellitus. Cochrane Database Syst. Rev., 15: CD007845.

Panda SP, PK Haldar, S Bera, S Adhikary, CC Kandar, 2010. Antidiabetic and antioxidant activity of Swietenia mahagoni in streptozotocin-induced diabetic rats. Pharm. Biol., 48: 974-979.

Puri D, KM Prabhu, PS Murthy, 2002. Mechanism of action of a hypoglycemic principle isolated from fenugreek seeds. Indian J. Physiol. Pharmacol., 46: 457-462.

Qin B, M Nagasaki, M Ren, G Bajotto, Y Oshida and Y Sato, 2004. Gosha-jinki-gan (a Herbal Complex) corrects abnormal insulin signaling. Evidence-Based Complementary and Alternative Medicine, 1: 269–276.

Rao BK, PR Sudarshan, MD Rajasekhar, N Nagaraju and CA Rao, 2003. Antidiabetic activity of Terminalia pallida fruit in alloxan induced diabetic rats. J.of Ethnopharmacol., 85: 169–172.

Sharma A, M Vijayakumar, CV Rao, MK Unnikrishnan and GD Reddy, 2009. Action of Portulaca oleracea against streptozotocin-induced oxidative stress in experimental diabetic rats. J. Complement. Integr. Med., 6: 1-10.

Shibib BA, LA Khan and R Rahman, 1993. Hypoglycaemic activity of Coccinia indica and Momordica charantia in diabetic rats: depression of the hepatic gluconeogenic enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase and elevation of both liver and red-cell shunt enzyme glucose-6-phosphate dehydrogenase. Biochem. J., 292: 267–270.

Verrotti A, A Scaparrotta, C Olivieri and F Chiarelli, 2012. Seizures and type 1 diabetes mellitus: current state of knowledge. Eur. J. Endocrinol., 167: 749–58.

Yakaiah V, SS Mishra, B Ambudas, P Ramesh, G Meghavani, K Deepika and A Prathibha, 2013. Anti-diabetic effect of *Momordica charantia* (bitter melone) on alloxan induced diabetic rabbits. Int. J. Med. Res. Health Sciences, 2:137-142.

Ying ZD, Q Xiwen, C Fengjie, G Qin, Z Xinghua, Yun Wang, 2012. Effect of superfine grinding on antidiabetic activity of bitter melon powder. Int. J. Mol. Sci., 13: 14203-14218.