Research Article

Charantin: A Neglected Antidiabetic Compound from *Momordica charantia* L.

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ABSTRACT

The advancement of active and safe blood glucose lowering agent is yet a significant challenge for present day scientific research. Generally fruit juice of *Momordica charantia* has been utilized for the treatmet of diabetes for a considerable length of time. Charantin, a special steroidal glycoside, isolated from *Momordica charantia*, has been identified as a therapeutic agent with blood sugar lowering capacity. However, for treating diabetes, this compound was not clinically investigated. This survey compresses the science, mode of operation and revealed clear strategies for charantin.

Keywords: Charantin, *Momordica charantia*, Anti Diabetic, Pharmacology, Extraction, Analysis.

INTRODUCTION

Momordica charantia L. (Bitter Melon-MC), a tropical vegetable belonging to the family Cucurbitaceae is a typical vegetable in Indian diet, and it is widely consumed as raw juice and as cooked vegetable. It is one such medication which has been utilized since ages for its culinary purposes and additionally for therapeutic properties – mainly as hostile to a person with diabetes. MC is widely known as bittermelon, balsam pear or bitter cucumber in English.[1] Its vernacular names in India are Karela (Hindi) and Karvella (Sanskrit).

The examination of the products of MC expounds a gathering of more than 30 triterpenoids and more than ten steroids which have been discovered from leaves, organic products, seeds, roots, and stems.[3]

Various phytoconstituents are isolated from MC, such as, momordicins, momordin, charantin, cucurbitins, gentisic acid, erythrodiol, diosgenin, chorine, cryptoxantin, multiflorenol etc..[4-5] These are accounted for in every part of the MC plant.[6]

The seeds and fruits of MC are proved to have antioxidant, hepatoprotective, antiviral, anticancer, antiulcer, analgesic, anti-inflammatory, and antifertility activities.[5-6]

Charantin is one of the bioactive compound found in all parts of the plant especially in fruits. Charantin improves blood sugar levels by increasing glucose uptake and glycogen synthesis in the liver, muscles, and fat cells. It also enhances insulin release from pancreatic beta cells, and repair or promotes new growth of insulin-secreting beta cells. Alcoholic extract of charantin was found to be more effective antidiabteic agent than tolbutamide, sometimes used in treating diabetes.[7] Charantin is reported to be an Anti-HIV protein.[8]

Profile of Nutrients[9-10]

The examination of the products of Momordica Charantia portrayed the accompanying dietary certainties.

Moisture (83.2%), Protein (5.3g), Total Carbohydrate (3.3g), Phosphorous (99mg), Ascorbic acid (85mg), Calcium (84 mg), Iron (2.04 mg), Niacin (1.11 mg), Riboflavin (0.362 mg), Thiamin (0.181 mg), Folate (128 mcg), Nicotinic acid (0.5 mcg), Vitamin A (1734 IU), Total Omega 3 (omg), Total Omega 6 (omg).

Occurrence and Distribution

MC is a tropical plant broadly developed in Asia, East Africa, and South America for its effectively unsavory natural items that are commonly used as a piece of cooking and as a characteristic answer for treating diabetes.[11]

Plant Description[12-13]

It is a monoecious annual climber with a slender, branched, angled and grooved stem that grows up to 5 m. Its leaves are alternate, petiolate, orbicular, 5-7 lobed, 5-12 cm in diameter, both surfaces glabrous and prominently nerved. Tendrils are slender and straightforward. Flowers are pale yellow to orange, solitary and unisexual. Fruits are dark green to whitish pepo, 5-25 cm long, oblong, ribbed with many tubercles. Seeds are brownish, compressed, 12-16 mm long, embedded in bright red pulp. It is characteristic in odour and bitter in taste.

Antidiabetic activity of *M. charantia* extracts

The reported antidiabetic activity of extracts of *M. charantia* L. have been given in Table 1.

Table 1: Reported Antidiabetic activities corresponding to *M. charantia* L.

Type of extract	Study design			Observation
	Type of Animal	Dose Administered	Duration	
Acetone extract	Albino rats of both sexes	25mg, 50mg & 75mg/100g	45 days	Decline in blood sugar level[14]
Fruit extracts	Male Thriller mice	4ml/kg	2 hours	Different time-dependent effects indicated for hypoglycaemic effect[15]
Aqueous extract	Charles foster rats of both sexes	4g in total	Three weeks	Significant reduction of blood sugar level[16]
Aqueous extract of pericarp	Male albino mice	0.5g/kg p.o	Eight days	Reduction in fasting glucose level[17]
Ether extract	Male albino rabbits	0.75g/kg body weight	3 hours	Reduced fasting blood glucose by 26%[18]
Alcohol extract of pulp	Male Wistar rats	500mg/kg	Seven days	Increased glucose utilization in the liver[7]
Fruit juice	Male Wistar rats	10ml/kg	One week	Renewal of β-cells[19]
Aqueous juice of Fruit	BALB/c Mice	10ml/kg body weight	Five days	Reduced plasma glucose[20]
Fruit powder	Male Sprague Dawley rats	0.5, 1 & 3 % included in diet	14 days	Consistent reduction in serum glucose[21]
Aqueous extract of fruit	Male ddy mice & male KKAY mice	100mg/kg	Three weeks	Consistent hypoglycemic effect[22]
Freeze dried juice	Female Sprague Dawley rats	1.5% & 0.75%	15 weeks	Improvement in insulin resistance in rats fed high-fat diet[23]
	Sprague Dawley rats	0.75%	11 weeks	
Water extract powder	Male Wistar rats	20mg/kg bodyweight	Four weeks	Reversal of induced hyperglycemia with no side effects[24]
Fruit juice	Male Wistar rats	10ml/kg	Ten weeks	Activity similar to insulin[25]
Aqueous extract of Seeds	Male Wistar rats	150mg/kg body weight /day	30 days	Normalize the impaired oxidative stress in STZ induced diabetes[26]
Aqueous extract if fruit	Male Sprague Dawley rats	NM	30 days	Hypoglycemic response[27]
Fruit extract	Wistar rats of both sexes	150 & 300mg/kg	30 days	Antidiabetic activity and amelioration of diabetes-associated complications[28]
Saponins fraction	Male Wistar rats	50 & 100 mg/kg body weight	1 hour	Inhibited disaccharide activity[29]
Methanolic extracts of fruit	Male Sprague Dawley rats	0.2,1g/(kg/day) of both fractions	Eight weeks	Improved insulin sensitivity & hyperglycemia[30]
Alcoholic fruit extract	Female wistar rats	100mg/kg & 200mg/kg	45 days	Antidiabetic activity[31]
Charantin rich extract	T1DMice & T2DMice	200mg/kg/day	Eight weeks	Improved insulin sensitivity[32]
Polysaccharide	Kumming mice of both sexes	100, 200 & 300mg/kg body weight per day	28 days	Dose-dependent Antidiabetic activity[33]
9:1 water-ethanol extract	Wistar rats of both sexes	200mg/kg	28 days	Decline in blood glucose level[34]
Methanolic fruit extract	Male Sprague Dawley rats	500mg/kg.p.o	75 days	Reduced diabetic complications[35]
Aqueous extract	Male wistar rats	100mg/kg & 200mg/kg	2 hours	Hypoglycemic activity[36]
Methanol extract	Swiss albino mice	200mg/kg & 400mg/kg body weight	2 hours	Enhanced antihyperglycemic activity when administered along with glibenclamide[37]
Fruit juice	Male Wistar rats	10ml/kg body weight/day	21 days	Improved glucose uptake by diaphragm in the absence and presence of insulin[38]

p.o.: per oral

Charantin

Charantin is acquired from the Asian bitter melon, responsible for the hypoglycemic activity of these plants. Charantin (Figure 1) is a equal mixture of two steroidal saponins, β-sitosteryl glucoside ($C_{35}H_{60}O_6$) and 5,25-stigmasteryl glucoside ($C_{35}H_{58}O_6$). Physically it is a white crystalline material, neutral and tasteless, melting at 266-

268°C, poorly soluble in water or then again other profoundly polar solvents, and also in apolar solvents like hexane, yet is dissolvable in the ether, ethanol, and methanol, and can be proficiently removed from the plant by pressurized ethanol or acetone at 100°C.

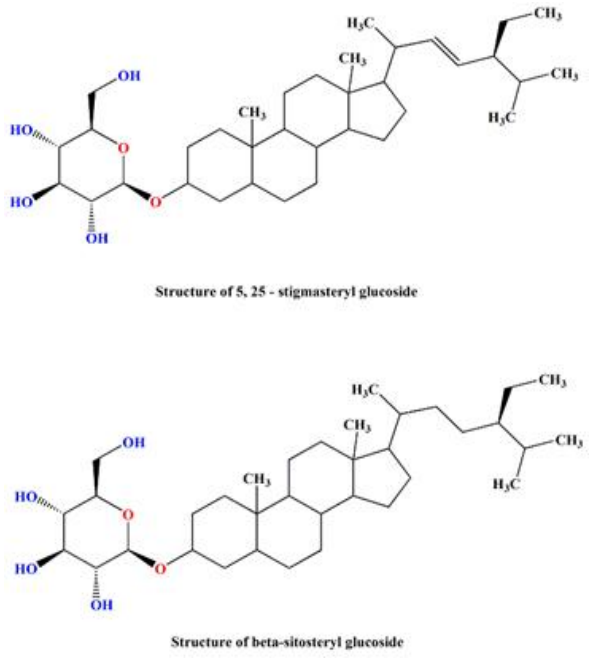

Figure 1: Steroidal saponin of Charantin

Lolitkar and Rao identified charantin in 1966[39]. Later, works were carried out to know the pharmacology of charantin. Some of the works include analysis of charantin.

Blood sugar lowering capacity of unripe fruits of bitter melon like that of insulin attributes to its antidiabetic property. The antidiabetic aggravate responsible for the reported activity is charantin, a blend of sitosteryl glucoside and stigmasteryl glucoside.[40-41] This mixture could be utilized to treat diabetes and can supplant treatment by infusion of insulin which has not been effective in animating the pancreas of the diabetic patients to bring down glucose to the coveted level.[42] At times, the injected subjects hints at symptoms. Ohytoconstituent that show antidiabetic propery, for instance, charantin and others are currently broadly acknowledged as an elective solution for diabetes mellitus, and they are free from adverse events.[43]

Blends of solvents like chloroform, dichloromethane, ethanol or methanol are conventionally used for isolating charantin. Though methods which were found to be successful in isolating charantin has devised, one crucial work in this particular area by J. Pitipanapong *et al.* was proposed to be a kinder option for the extraction of charantin from MC.[44] Employing pressurized liquid extraction technique as one of the approaches towards separation of charantin, revealed similar yields of charantin but with less extraction time and the dissolvable sum required when compared with conventional soxhlet method. This evidence suggests a fascinating new strategy for quick partition of charantin.[44] A work by D.M. Cuong *et al.* reported transcriptome investigation to recognize genes with the triterpenoid biosynthesis pathway in the seedlings of bittermelon. Also, the above said work reported build-up sequences of charantin and their coincidence with the expression pattern of *McSE and McCAS1* genes to demonstrate the importance of these genes in the biosynthesis of charantin in bitter melon.[45]

Extraction techniques

Extraction techniques for the extraction of Charantin have been given in Table 2.

Table 2: Reported Extraction Techniques for Charantin.

Method	Conditions			
	Solvent	Temperature (°C)	Time	Yield
Soxhlet extraction[18]	Petroleum ether and 80% EtOH	40-60	N.M.	N.M.
Pressurized liquid extraction (PLE)[44]	EtOH 60ml	100	1h	0.126± 0.018 mg/g dried fruit
Soxhlet extraction[44]	EtOH 200ml	78.5	150m	Comparable with yield obtained by PLE
Ultrasonication[44]	2ml n-Hexane & 100% MeOH 1ml	RT	1h	40.54 µg/g dry weight
Soxhlet extraction[45]	MeOH (4 × 50L)	70	N.M.	15 mg/ 35kg dried fruit
Soxhlet extraction[46]	95% EtOH	60-80	48h	0.091 % of dried fruit
Soxhlet extraction[47]	50% EtOH	70.24	60h	55.27 mg equiv./g dry fruit
Soxhlet extraction[47]	70% EtOH	80.34	70h	144.58 mg equiv./g dry leaves
Soxhlet extraction[48]	EtOH 200ml	B.P.	150m	N.M.
Hot Reflux[49]	50% EtOH 500ml	150	6h	10.23 mg/50g dried

				fruit
Ultrasound-assisted Extraction[50]	MeOH (80) : H2O (20) (v/v)	46	120m	3.12 ± 0.14 mg/g dried fruit
Soxhlet extraction[51]	Water/EtOH	30-80	1-72h	N.M.

N.M.: not mentioned, N.A.: not applicable, B.P.: boiling point, R.T.: room temperature, EtOH: ethanol, MeOH: methanol.

Pharmacology of Charantin

Pharmacological activities specific to charantin are less reported, whereas, most of the reported activities were based on extracts of bitter melon and expected to be charantin as a primary cause for the action.

Patel S *et al.* reported antibacterial activity of charantin in a specific gram-positive, gram-negative strains of bacteria and a fungal strain *using agar diffusion method.*[46] Also acknowledged the importance of understanding the mechanism of action and viability of charantin in relation to psoriasis like skin disorders. Another work by T.B. Ng *et al.*, designated charantin, isolated from a bitter gourd, as a peptide having a molecular mass of 9.7kDa. This work confirms the small ribosome inactivating capacity of charantin along with γ-momorcharin and luffin S. This work also reported the inhibitory activity of cell-free translation in a rabbit reticulocyte lysate system.[5]

Analysis of Charantin

Analytical methods for the identification and quantification of charantin have been given in Table 3.

Table 3: Reported Analytical methods for identification and quantification of Charantin

Technique	Stationary Phase	Mobile Phase	Wavelength Or R_f (TLC/HPTLC)
TLC[18]	Silica gel	Petroleum ether (3): diethyl ether (1)	N.M.
HPLC[41]	C-18 Hypersil Column (10µm × 3.9mm × 300mm)	MeOH (100) : H_2O (2) (% v/v)	204 nm
HPLC[44]	C-18 Intersil ODS-3-column (5µm × 4.6mm × 250mm)	MeOH (100) : H_2O (2) (% v/v)	204 nm
HPLC[52]	C-18 Hypersil column (10µm × 3.9 mm × 300mm)	MeOH (100) : H_2O (2) (% v/v)	204 nm
	C-18 Intersil ODS-3-column (5µm × 4.6mm × 250mm)	MeOH (100) : H_2O (2) (% v/v)	204 nm
TLC[46]	Silica gel	MeOH (2) : Benzene (8) (% v/v)	0.45
HPTLC[48]	Silica gel	Chloroform (1.5) : MeOH (6) : H_2O (2.5) (% v/v/v)	536 nm 0.40 ± 0.03
HPLC[49]	C-18 Waters symmetry column (5µm × 3.9mm × 150mm)	MeOH (100) : H_2O (2) (% v/v)	204 nm
HPTLC[53]	20 × 10 cm Aluminium backed plates coated with Silica gel $60F_{254}$	Toluene (68) : Ethyl Acetate (20) : MeOH (10) : Formic Acid (02) % (v/v/v/v)	525 nm 0.71
HPLC[54]	Optimapak (5µm × 4.6mm × 250m)	98% MeOH	204 nm
HPTLC[55]	Silica gel $60F_{254}$ TLC plates	MeOH (2) : Benzene (8) (v/v)	536 nm 0.31
HPLC[56]	Zorbax SB C-18 column (5µm × 4.6mm × 250mm)	Solvent A - H_2O Solvent B - Acetonitrile	205 nm
HPLC[44]	Optimapak C-18 Column(5µm × 4.6mm × 250mm)	MeOH (98) : H_2O (2) (% v/v)	204 nm

MeOH: Methanol, N.M.: Not mentioned.

CONCLUSION

Amidst of all reported activities for *M. Charantia* L., studies specific to charantin are less. Minimal efforts had not been taken to develop charantin as an alternative for treating diabetes. However, the importance of quantification of charantin in MC fruit extracts and formulations containing MC as a primary ingredient is gaining day by day. Problems existing with solvents like chloroform and dichloromethane were chronic to the health of human beings or animals involved and a necessity to create a benign environment by selecting solvents that possess less harm to humans and environment is inevitable. The achievement without bounds utilization of this compound got by pressurized liquid extraction would, consequently, rely on the advancement of a chromatographic procedure that is independent of the utilization of harmful solvents. There is also a dire need in considering wild species of *Momordica* as a potent nutraceutical for the treatment of diabetes. The importances of the antidiabetic property and a profile of unknown saponins and other compounds have to be acknowledged for further research.

LIST OF ABBREVIATIONS

p.o.: per oral

N.M.: not mentioned

N.A.: not applicable

B.P.: boiling point

R.T.: room temperature

EtOH: ethanol

MeOH: methanol

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Guest or honorary authorship based solely on position (e.g. research supervisor, departmental head) is discouraged.

SUPPLEMENTARY MATERIAL

Supportive/Supplementary material intended for publication must be numbered and referred to in the manuscript but should not be a part of the submitted paper. List all Supportive/Supplementary Material and include a brief caption line for each file describing its contents.

REFERENCES

1. Dasgupta AA, Mukherjee AA, Mitra A, Phyto-pharmacology of *Momordica charantia* linn. A review, Journal of Global Pharmaceutical Technology, 3, 2009, 7-14.
2. Taylor T. Technical data for bitter melon (Momordica charantia), herbal secrets of the rainforest. 2nd ed. Austin, USA: Sage Press Inc.2002.
3. Rastogi RP and Mehrotra BN, Compendium of Indian Medicinal Plants. 1, 2, 4, 5, CDRI, Lucknow & NISCAIR, New Delhi. 2008, 278, 430, 480, 549.
4. Yuan YR, He YN, Xiong JP, Xia ZX, Three-dimensional structure of beta-momorcharin at 2.55 A resolution. Acta Crystallographica Sec D-Biol Crystallo. 55, 1999, 1144-1151.
5. Parkash A, Ng TB, Tso WW, Purification and characterization of charantin, a napin-like ribosome-inactivating peptide from bitter gourd (Momordica charantia) seeds. Journal of Peptide Research. 59, 2002, 197-202.
6. Murakami T, Emoto A, Matsuda H, Yoshikawa M, Medicinal Foodstuffs, XXI, Structures of New Cucurbitaceae-Type Triterpene Glycosides, Chemical Pharmaceutical Bulletin, 49, 2001, 54-63.
7. Sarkar S, Pranava M, Marita R, Demonstration of the hypoglycemic action of Momordica charantia in a validated animal model of diabetes. Pharmacology Research. 33(1), 1996, 1-4.
8. Sathish Kumar D, Vamshi Sharathnath K, Yogeswaran P, Harani A, Sudhakar K, Sudha P, David Banji, A Medicinal Potency of Momordica Charantia Linn, International Journal of Pharmaceutical Sciences Review and Research. 1(2), 2010, 95-100.
9. Joseph B, Jini D, Antidiabetic effects of *Momordica charantia* (bitter melon) and its medicinal potency. Asian Pacific Journal of Tropical Disease, 3(2), 2013, 93-102.
10. Bakare R, Magbagbeola O J, Nutritional and chemical evaluation of Momordica charantia. Medicinal Plants Research, 4(21), 2010, 2189-2193.
11. Kathy Abascal, Eric Yarnell, Using Bitter Melon to Treat Diabetes. Alternative and Complementary Therapies, 11(4), 2005, 179-184.
12. Kumar S, Ashish J, Satish N, Momordica charantia Linn. : A mini review, International Journal of Biomedical Research, 2(11), 2011, 579-587.
13. Leung L, Birtwhistle R, Kotecha J, Hannah S, Cuthbertson S, Anti-diabetic and hypoglycemic effects of Momordica charantia (bitter melon): a mini review. British Journal of Nutrition and Dietetics, 102(12), 2009, 1703-1708.
14. Neera Singh SD, Tyagi, Agarwal SC, Effects Of Long Term Feeding Of Acetone Extract Of *Momordica Charantia* (Whole Fruit Powder) On Alloxan Diabetic Albino Rats. Indian Journal of Physiology and Pharmacology, 33(2), 1989, 97-100.
15. Day C, Cartwright T, Provost J, Bailey CJ, Hypoglycaemic Effect of Momordica charantia Extracts. Planta Medica, 56, 1990, 426-429.
16. Srivastava Y, Venkatakrishna Bhatt H, Verma. Y, Venkaiah K, Raval BH, Antidiabetic and Adaptogenic Properties of *Momordica charantia* Extract: An Experimental and Clinical Evaluation. Phytotherapy Research, 7, 1993, 285-289.
17. Caklcl I, Hurmoglu C, Tunctan B, Abacioglu N, Kanzlk I, Sener B, Hypoglycaemic effect of *Momordica charantia* extracts in normoglycaemic or cyproheptadine-induced hyperglycaemic mice. Journal of Ethnopharmacolology, 44, 1994, 117-21.
18. Subbiah Pugazhenthi, Suryanarayana Murthy P. Partial Purification of A Hypoglycemic Fraction From The Unripe Fruits Of *Momordica Charantia* Mnn (Bitter Gourd). Indian Journal of Clinical Biochemistry. 10(1), 1995, 19-22.
19. Ahmed I, Adeghate E, Sharma AK, Pallot DJ, Singh J. Effects of *Momordica charantia* fruit juice on islet morphology in the pancreas of the streptozotocin-diabetic rat. Diabetes Research and Clinical Practice, 40, 1998, 145-151.
20. Sitasawad SL, Shewade Y, Bhonde R, Role of bitter gourd fruit juice in stz-induced diabetic state *in vivo* and *in vitro*. Journal of Ethnopharmacolology, 73, 2000, 71-79.
21. Jayasooriya AP, Sakono M, Yukizaki C, Kawano M, Yamamoto K, Fukuda N, Effects of *Momordica charantia* powder on serum glucose levels and various lipid parameters in rats fed with cholesterol-free and cholesterol-enriched diets. Journal of Ethnopharmacolology, 72, 2000, 331-336.
22. Miura T, Itoh Y, Iwamoto N, Kato M, Ishida T, Hypoglycemic Activity of the Fruit of the Momordica charantia in Type 2 Diabetic Mice, Biological and Pharmaceutical Bulletin, 47, 2001, 340-4.
23. Chen Q, Chan LL, Li ET, Bitter Melon (*Momordica charantia*) Reduces Adiposity, Lowers Serum Insulin and Normalizes Glucose Tolerance in Rats Fed a High Fat Diet, Jounral of Nutrition, 133, 2003, 1088-1093.
24. Virdi J, Sivakami S, Shahani S, Suthar AC, Banavalikar MM, Byanim MK, Antihyperglycemic effects of three extracts from *Momordica charantia*. Journal of Ethnopharmacology, 88, 2003, 107-11.
25. Ahmed I, Adeghate E, Cummings E, Sharma AK, Singh J, Beneficial effects and mechanism of action of Momordica charantia juice in the treatment of streptozotocin-induced diabetes mellitus in rat. Molecular and Cellular Biochemistry, 261(1-2), 2004, 63-70.
26. Sathishsekar D, Subramanian S, Beneficial Effects of *Momordica charantia* Seeds in the Treatment of STZ-Induced Diabetes in Experimental Rats. Biological and Pharmaceutical Bulletin, 28(6), 2005, 978-983.

27. Chandra A, Mahdia AA, Ahmad S, Singh RK, Indian herbs result in hypoglycemic responses in streptozotocin-induced diabetic rats. Nutrition Research, 27, 2007, 161-168.
28. Fernandes NPC, Lagishetty CV, Panda VS, Naik SR, An experimental evaluation of the antidiabetic and antilipidemic properties of a standardized Momordica charantia fruit extract. BMC Complementary and Alternative Medicine, 7(29), 2007, 1-8.
29. Oishi Y, Sakamoto T, Udagawa H, Taniguchi H, Kobayashi-Hattori K, Ozawa,Y, Takita T, An experimental evaluation of the antidiabetic and antilipidemic properties of a standardized Momordica charantia fruit extract, Bioscience, Biotechnology and Biochemistry, 71(3), 2007, 735-740.
30. Shih CC, Lin CH, Lin WL, Wu JB, *Momordica charantia* extract on insulin resistance and the skeletal muscle GLUT4 protein in fructose-fed rats. Journal of Ethnopharmacology, 123, 2009, 82-90.
31. Syed Mudasir Ayoub, Suguna Rao, Sonnahallipura Munivenkatappa Byregowda, Mayasandra Laxmikanth Satyanarayana, Narayana Bhat, Narayan Bhat Shridhar, Pragathi Belagola Shridhar. Evaluation of Hypoglycemic Effect of Momordica charantia Extract in Distilled Water in Streptozotocin-Diabetic Rats. Brazilian Journal of Veterinary Pathology, 6(2), 2013, 56-64.
32. Wang HY, Kan WC, Cheng TJ, Yu SH, Chang LH, Chuu JJ. Differential anti-diabetic effects and mechanism of action of charantin-rich extract of Taiwanese Momordica charantia between type 1 and type 2 diabetic mice. Food Chemistry and Toxicology, 69, 2014, 347-356.
33. Xin Xu, Bin Shan, Cai-Hu Liao, Jian-Hua Xie, Ping-Wei Wen, Jia-Yi Shi, Anti-diabetic properties of Momordica charantia L. polysaccharide in alloxan-induced diabetic mice. International Journal of Biological Macromolecules, 81, 2015, 538-543.
34. Tripathi Nagja, Kumar Vimal, Acharya Sanjeev. Anti-Diabetic Activity of a Polyherbal Formulation in Streptozotocin Induced Type 2 Diabetic Rats. Journal of Natural Remedies, 16(4), 2016, 148-152.
35. Himanshu Rai, Sushma Attuluri, Nuzhath Irfana, Haritha P, Sandhya R, Seema Farheen, Pharmacodynamic Interaction of Momordica Charantia with Oral Hypoglycemic Agents in Diabetes Induced Gastropathy. World Journal of Pharmacy and Pharmaceutical Sciences, 6(8), 2017, 1388-1423.
36. Kalakotla Shanker, Jayarambabu Naradala G, Krishna Mohan G S Kumar, Pravallika PL, A sub-acute oral toxicity analysis and comparative in vivo anti-diabetic activity of zinc oxide, cerium oxide, silver nanoparticles, and Momordica charantia in streptozotocin-induced diabetic Wistar rats. RSC Advances, 7, 2017, 37158-37167.
37. Khosnur Jannat, Nurullah N, Mohammed Rahmatullah. Enhanced Antihyperglycemic Activity With A Combination Of Glibenclamide And Fruits of *Momordica Charantia* L. World Journal Of Pharmacy And Pharmaceutical Sciences, 6(10), 2017, 134-142.
38. Mona F Mahmoud, Fatma El Zahraa Z El Ashry, Nabila N El Maraghy, Ahmed Fahmy, Studies on the antidiabetic activities of Momordica charantia fruit juice in streptozotocin-induced diabetic rats. Pharmaceutical Biology, 55(1), 2017, 758-765.
39. Lotlikar MM, Raharama Rao MR, Note on a hypoglycemic principle isolated from the fruits of *Momordica charantia.* Journal of the University of Bombay, 29, 1962, 223-224.
40. Marderosiam AD, The review of Natural Products, USA. 2001; 71.
41. M. Chanchai. M.S. Thesis in Pharmacy. Bangkok: Faculty of Graduate Studies, Mahidol University. 2003.
42. Belinda OC, Herbal Supplements in Diabetes Management. 2000.
43. Sharma SR, Dwivedi SK, Vershney VP, Antihyper glycaemic and Insulin Release Effects of *Aegle marmelos* Leaves in Streptozotocin–Diabetic Rats. Phytotherapy Research, 10, 1996, 426-428.
44. Pitipanapong J, Chitpraset S, Goto M, Jiratchariyakul W, Sasaki M, Shotipruk A, J. Agric. Food Chem., (Just Accepted Manuscript). 2017. DOI: 10.1021/acs.jafc.7b01948.
45. Liu JQ, Chen JC, Wang CF, Qiu MH, New Cucurbitane Triterpenoids and Steroidal Glycoside from *Momordica charantia*. Molecules, 14, 2009, 4804-4813.
46. Subhashchandra Patel, Tushar Patel, Kaushal Parmara, Yagnesh Bhatta, Yogesh Patel, Patel NM, Isolation, Characterization And Antimicrobial Activity Of Charantin from *Momordica Charantia* Linn. Fruit. International Journal of Drug Development & Research, 2(3), 2010, 629-634.
47. Saad Mohamed El-Said, Ali Al-Barak S. Extraction of Insulin like Compounds from Bitter Melon Plants. American Journal of Drug Discovery and Development, 1, 2011, 1-7.
48. Chungath Telny Thomas, Y Padmanabha Reddy, Devanna N. Extraction of Insulin like Compounds from Bitter Melon Plants. International research journal of pharmacy, 3(6), 2012, 149-154.
49. Ee Shian Tan, Aminah Abdullah, Nur Kartinee Kassim. Extraction of steroidal glycoside from small-typed bitter gourd (*Momordica charantia* L.). Journal of Chemical and Pharmaceutical Research, 7(3), 2015, 870-878.
50. Javed Ahamad, Saima Amin, Showkat R Mir, Optimization of ultrasound-assisted extraction of charantin from *Momordica charantia* fruits using response surface methodology Journal of Pharmacy and Bioallied Sciences, 7(4), 2015, 304-307.
51. Mohini Mendiratta, Sarika Gupta. Exploring the Role of Phytochemicals and Antioxidants on Antihyperglycemic Potentials of Indian Medicinal Plants. International Journal of General Medicine and Pharmacy, 6(4), 2017, 21-32.
52. Alam S, Asad M, Asdaq SMB, Prasad VS. Antiulcer activity of methanolic extract of Momordica charantia L. in rats. Journal of Ethnopharmacology, 123(3), 2009, 464-469.
53. Ahamad J, Amin S, Mir SR. Development and validation of HPTLC densitometric method for estimation of charantin in Momordica charantia fruits and herbal formulation. Journal Pharmacognosy and Phytochemistry, 2(5), 2014, 172-176.
54. Yong Kyoung Kim, Woo Tae Park, Md Romij Uddin, Yeon Bok Kim, Hanhong Bae, Haeng Hoon Kim, Kee Woong Park, Sang Un Park. Variation of Charantin Content in Different Bitter Melon Cultivars. Asian Journal of Chemistry, 26(1), 2014, 309-310.
55. Shanmugapriya R, Poornima S. Detection of Charantin in the leaves and fruits of Momoridca tuberosa (Cogn) Roxb and Momordica dioica (Roxb Ex Wild) by Analytical HPTLC. International Journal of Scientific and Research Publications, 4(6), 2014, 1-8.
56. Kang Sung Goo, Sumeru Ashari, Nur Basuki, Arifin Noor Sugiharto. The Bitter Gourd *Momordica charantia* L.: Morphological Aspects, Charantin and Vitamin C Contents. IOSR Journal of Agriculture and Veterinary Science, 9(10), 2016, 76-81.

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