AYU

Access this article online
Website: www.ayujournal.org
DOI: 10.4103/0974-8520.127726
Quick Response Code:

Pharmacological Study

Hypoglycemic and anti-hyperglycemic activity of *Guduchi Satva* in experimental animals

Rohit Sharma, Vijay Kumar[1], B. K. Ashok[2], Galib R.[3], Pradeep Kumar Prajapati[4], B. Ravishankar[5]

Ph.D. Scholar, Department of Rasashastra and Bhaishajya Kalpana, Institute for Post Graduate Teaching and Research in Ayurveda, Jamnagar, Gujarat, [1]Assistant Professor, Department of Pharmacology, Gurukul College of Pharmacy, Suratgarh, Rajasthan, [2]Discovery Scientist, Research and Development, The Himalaya Healthcare, Makali, Bangalore, Karnataka, [3]Assistant Professor, [4]Professor and Head, Department of Rasashastra and Bhaishajya Kalpana, Including Drug Research, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar, Gujarat, [5]Director, Research and Development, SDM Research Centre for Ayurveda and Allied Sciences, Udupi, Karnataka, India

Abstract

Over the centuries, herbs have served as a major source of medicines for prevention and treatment of diseases including diabetes mellitus. These herbs are getting more importance around the globe and many studies have provided safety and efficacy of such herbal drugs in different condition. *Guduchi* (*Tinospora cordifolia* [Willd.] Miers) is reported as highly potent *Pramehahara* (anti-diabetic) herb in Ayurveda and *Guduchi Satva* (GS) is popularly used to treat *Paittika* type of *Prameha*. In the present study, GS prepared from the stem of *T. cordifolia* was evaluated for hypoglycemic and anti-hyperglycemic activity in 18 h fasted mice. GS was suspended in distilled water and administered to animals at the dose of 130 mg/kg that showed the marginal reduction in blood sugar level (BSL) at all the time intervals in normoglycemic mice. In anti-hyperglycemic activity, administration of GS prior to glucose over load failed to attenuate BSL at all-time interval in comparison to glucose control group. The study concludes that mild hypoglycemic insignificant anti-hyperglycemic activities of GS.

Key words: *Guduchi Satva*, anti-hyperglycemic, hypoglycemic

Introduction

Diabetes mellitus is a chronic metabolic disorder, characterized by hyperglycemia resulting from a variable interactions of hereditary and environmental factors, defects in insulin secretion, insulin action or both.[1] Today, it is a vulnerable endemic problem all over the globe, affecting carbohydrate, protein, and fat metabolism in addition to damaging liver, kidney, and cells of pancreas.[2] Currently available oral anti-diabetic synthetic drugs in the management of diabetes partially can compensate metabolic derangements, but do not necessarily improve the elementary biochemical lesions,[3] moreover, they have accompanied side-effects.[4] Furthermore, insulin therapy in insulin dependent diabetes mellitus has several drawbacks such as insulin resistance,[5] develops anorexia nervosa, brain atrophy, and fatty liver[6] after chronic treatment.

Address for correspondence: Dr. Rohit Sharma, Department of Rasashastra and Bhaishajya Kalpana, Including Drug Research, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar, Gujarat, India.
E-mail: dhanvantari86@gmail.com

Thus, in modern medicine, no satisfactory effective therapy is still available to control this condition. Herbal medicines may prove to be safer and significantly effective than the synthetic anti-hyperglycemic agents.[7]

Researchers conducted during past few decades on about 45 plants or their products (active, natural principles, and crude extracts) have shown experimental or clinical anti-diabetic activity.[8] It is estimated that more than 800 species of plants exhibit hypoglycemic properties, and *Guduchi* is one among them.[9] *Guduchi* may have been favorably used for thousands of years; however, modern herbal pharmacology appears to have just begun to appreciate the tremendous therapeutic potential of it. *Guduchi* is incredibly versatile and safe [10-13] herbaceous vine in Ayurvedic system of medicine indicated to combat various diseases and is proved to be a highly potent anti-diabetic herb.[14-16]

The most common example of herbal *Satva*[17] is *Guduchi Satva* (GS), which is very commonly prescribed in Ayurveda.[18]

Ayurvedic classics emphasized using of GS in different stages of prameha.[19-21] However, no reports on anti-hyperglycemic activity of GS have been reported till date. Hence the present study was undertaken to evaluate hypoglycemic and anti-hyperglycemic activiies of GS in Swiss Albino mice.

Materials and Methods

Animals

Swiss Albino mice of either sex weighing 30 ± 04 g were obtained from animal house attached to Pharmacology Laboratory, IPGT and RA, Gujarat Ayurved University, Jamnagar. Six animals were housed in each cage made of poly-propylene with stainless steel top grill. The dry wheat (post-hulled) waste was used as bedding material, and was changed every morning. The animals were exposed to 12 h light, and 12 h dark cycle with the relative humidity of 50-70% Ambient temperature during the period of experimentation was 22 ± 03°C. Animals were fed with Amrut brand rat pellet feed supplied by Pranav Agro Mills Pvt. Limited, Vadodara and for their drinking purpose tap water *ad libitum* was used. The experiments were carried out after obtaining permission from Institutional Animal Ethics Committee (IAEC/9/11/22/MD).

Test drug

Plant, which grows encircling the *Neem* (*Azadirachta indica*) tree is said to be the best for the therapeutic purposes. Considering this, the stem of the plant spreading over *Neem* tree was procured from the campus of Gujarat Ayurved University, Jamnagar, and authenticated at Pharmacognosy Laboratory. The stem was cleaned to remove the physical impurities and washed thoroughly with water. The stem was crushed thoroughly to convert into coarse slimy mass and soaked in quantity sufficient water for overnight. The contents were macerated thoroughly on the next day for about 1 h, and filtered through four folded cloth carefully into another sterile container. The container was kept aside undisturbed for four hours and the supernatant liquid was decanted to collect smooth, white colored *Satva* that was scrapped from the bottom and then packed in an air tight sterile container.

Dose selection and schedule

The clinical dose of GS was considered taken from current available texts as 1 g/day.[22] The dose for the mouse was calculated by extrapolating the human dose to animals (130 mg/kg) based on the body surface area ratio by referring to the standard tables.[23] Glibenclamide (GB) at the dose of 0.65 mg/kg, was used as the reference standard control. The distilled water was used as the vehicle and test drug was suspended in it with suitable concentration depending on body weight of the animal prior to administration (2.6 mg GS and 0.013 mg GB/0.1 ml distilled water/20 g body weight). The test drugs were administered to animals orally with the help of gastric catheter sleeved to syringe. The drugs were administered to overnight fasted animals.

Experimental study

The hypoglycemic activity and anti-hyperglycemic activity were carried out by modified method.[24] Total 42 mice were selected and divided randomly into relevant groups of six each. The first group served as vehicle control (VC) and administered with distilled water. The second group was administered with test drug GS in the dose of 130 mg/kg, whereas, third group was served as standard control group with administration of GB. The fourth group was kept in anti-hyperglycemic activity with high glucose given but without treatment.

Hypoglycemic activity

The selected animals were acclimatized for 7 days prior to experiment and divided randomly irrespective of sex in three groups *viz*: VC, GS control, and GB control. They were fasted overnight and in the next morning. Initial fasting blood sugar level (BSL) was measured with the help of One Touch EzSmart CE0537 Glucometer Lifeline Surgicals, New Delhi, India, by using One Touch EzGluco test strips as per user's guideline after anaesthetizing the animals with diethyl ether. One drop of blood was collected by puncturing tail vein under aseptic conditions. Then the test drugs suspended in the vehicle were administered to the respective groups. The BSL was recorded after 1 h, 2 h, 3 h, and 5 h of the test drug administration for assessing the hypoglycemic effect of the test drug.

Anti-hyperglycemic activity

Mice were randomly divided in to four groups of six each after 7 days of acclimatization. The animals were fasted overnight prior to the experiment and in the morning the fasting initial BSL was measured as mentioned in hypoglycemic activity. First group administered with distilled water, served as VC, second group served as glucose control (GC) to which glucose solution alone was administered. Third and fourth groups were administered with GS and GB were administered respectively. After 1 h of drug administration, glucose (5 g/kg body weight) solution was administered to second, third and fourth groups orally by dissolving it in distilled water. Thereafter, BSL was recorded at 30 min, 60 min, 90 min, and 120 min of post-glucose overload for accessing the anti-hyperglycemic activity of the test drug.[24]

Statistical analysis

The results are presented as mean ± SEM. The data generated during the study were subjected to Student's *t*-test for paired and unpaired data to assess the statistical significance and the significant level was set at $P < 0.05$.

Results

A marginal and statistically non-significant decrease in BSL was occurred in the control group at 1 h, 3 h, and 5 h, but significant decrease was observed at 2 h in comparison to its initial BSL [Table 1]. In GS treated group also a marginal and statistically non-significant decrease in BSL occurred at all the time intervals in comparison to its initial BSL. Administration of GB to overnight fasted mice leads to a significant decrease in the blood glucose level at almost all the time intervals progressively to the end of the study.

Glucose overload to overnight fasted mice leads to significant increase in BSL in GC group at all the time intervals [Table 2]. Administration of GS prior to glucose overload failed to attenuate BSL at an all-time interval in comparison to GC group. Administration of GB significantly attenuated the BSL at all the time intervals.

Discussion

It is essential to prove all the Ayurvedic principles and drug efficacy scientifically by modern parameters, through which

Table 1: Effect of GS on BSL in normal overnight fasted Swiss Albino mice at various time intervals

Groups	Initial (mg/dl)	1 h (mg/dl)	2 h (mg/dl)	3 h (mg/dl)	5 h (mg/dl)
VC	76.17±5.25	72.83±6.19	68.00±6.00$^{\#}$	71.83±5.38	65.50±5.66
GS	87.33±7.96	71.00±4.19	74.50±4.57	68.83±6.10	61.33±4.27
GB	86.64±4.02	75.50±3.32$^{\#}$	71.17±4.25$^{\#\#}$	66.67±3.26$^{\#\#*}$	61.33±3.84$^{\#\#\#}$

Data: Mean±SEM, $^{\#}P<0.05$, $^{\#\#}P<0.01$, $^{\#\#\#}P<0.001$ (compared with initial BSL), $^{*}P<0.05$ (compared with VC group). BSL: Blood sugar level, VC: vehicle control, GS: Guduchi Satva, GB: Glibenclamide

Table 2: Effect of GS on BSL in glucose overloaded Swiss Albino mice at various time intervals

Groups	Initial (mg/dl)	30 min (mg/dl)	60 min (mg/dl)	90 min (mg/dl)	120 min (mg/dl)
VC	95.67±4.80	90.83±5.56$^{\#}$	90.83±5.83	84.83±4.21$^{\#}$	72.83±4.53$^{\#}$
GC	98.83±3.37	134.50±15.15$^{\#*}$	120.17±6.43$^{\#\#**}$	116.50±2.96$^{\#\#***}$	116.50±4.67$^{\#***}$
GS	113.00±6.80	147.25±3.90$^{\#}$	143.75±17.39	130.50±12.44	113.75±3.90
GB	87.00±3.13	82.33±1.89$^{\alpha}$	75.33±2.04$^{\alpha}$	66.33±1.75$^{\alpha\alpha}$	62.67±2.04$^{\alpha}$

Data: Mean±SEM, $^{\#}P<0.05$, $^{\#\#}P<0.01$ (compared with initial BSL), $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$ (compared with VC group), $^{\alpha}P<0.05$, $^{\alpha\alpha}P<0.01$, $^{\alpha\alpha\alpha}P<0.001$ (compared with GC group). BSL: Blood sugar level, GC: Glucose control, VC: vehicle control, GS: *Guduchi Satva*, GB: Glibenclamide

Ayurveda can excel in the current era as "evidence based, well-documented system of medicine.

Hypoglycemia is an abnormally diminished content of glucose in the blood.[25] A better and safer anti-diabetic agent is the one which have a good blood glucose lowering effect in hyperglycemia and maintain it to normal without lowering its level up to hypoglycemic stage, which may prove fatal. Prolonged hyperglycemic or hypoglycemic state can produce serious long-term complications. Thus, hypoglycemic potential of GS was compared with the standard reference drug, GB of which hypoglycemia like side-effects are not uncommon. The results of this study show that GS treated group showed only a marginal decrease in BSL in normoglycemic mice.

It has been reported that 1,2-substituted pyrolidines isolated from the stem is responsible for anti-diabetic activity of *Guduchi*.[26] Contrary to the expectations, in the present study GS did not produce significant anti-hyperglycemic activity, it may be due to the absence of sufficient quantity of 1,2-substituted pyrolidines in *Satva* samples. However, to explore exact reason behind this, detailed comparative phytochemical evaluation of stem and *Satva* samples are necessary.

Conclusion

GS is having mild hypoglycemic activity while it does not have a significant anti-hyperglycemic activity against glucose overload. Further, researches of this formulation on diabetic animals are needed to draw proper conclusions.

References

1. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;26:S5-20.
2. Baynes JW. Role of oxidative stress in development of complications in diabetes. Diabetes 1991;40:405-12.
3. Taylor R, Agius L. The biochemistry of diabetes. Biochem J 1988;250:625-40.
4. Bailey CJ, Flatt PR, Marks V. Drugs inducing hypoglycemia. Pharmacol Ther 1989;42:361-84.
5. Piédrola G, Novo E, Escobar F, García-Robles R. White blood cell count and insulin resistance in patients with coronary artery disease. Ann Endocrinol (Paris) 2001;62:7-10.
6. Yaryura-Tobias JA, Pinto A, Neziroglu F. Anorexia nervosa, diabetes mellitus, brain atrophy, and fatty liver. Int J Eat Disord 2001;30:350-3.
7. Pavana P, Sethupathy S, Manoharan S. Antihyperglycemic and antilipidperoxidative effects of *Tephrosia purpurea* seed extract in streptozotocin induced diabetic rats. Indian J Clin Biochem 2007;22:77-83.
8. Grover JK, Yadav S, Vats V. Medicinal plants of India with anti-diabetic potential. J Ethnopharmacol 2002;81:81-100.
9. Alarcon-Aguilara FJ, Roman-Ramos R, Perez-Gutierrez S, Aguilar-Contreras A, Contreras-Weber CC, Flores-Saenz JL. Study of the anti-hyperglycemic effect of plants used as antidiabetics. J Ethnopharmacol 1998;61:101-10.
10. Anonymous. Quality Standards of Indian Medicinal Plants. Vol. 1. New Delhi: Indian Council of Medical Research; 2003. p. 212.
11. Dhar ML, Dhar MM, Dhawan BN, Mehrotra BN, Ray C. Screening of Indian plants for biological activity: I. Indian J Exp Biol 1968;6:232-47.
12. Singh KP, Gupta AS, Pendse VK, Mahatma CP, Bhandari DS, Mahawar MM. Experimental and clinical studies on *Tinospora cordifolia*. J Res Indian Med 1975;10:9-14.
13. Kundnani KM, Mahajan VR, Jolly CI. A new hypoglycaemic agent from *Tinospora cordifolia*: Miers. Indian Drugs 1985;23:119-20.
14. Goel HC, Prem Kumar I, Rana SV. Free radical scavenging and metal chelation by *Tinospora cordifolia*, a possible role in radioprotection. Indian J Exp Biol 2002;40:727-34.
15. Subramanian M, Chintalwar GJ, Chattopadhyay S. Antioxidant properties of a *Tinospora cordifolia* polysaccharide against iron-mediated lipid damage and gamma-ray induced protein damage. Redox Rep 2002;7:137-43.
16. Gupta SS, Verma SC, Garg VP, Rai M. Anti-diabetic effects of *Tinospora cardifolia*. I. Effect on fasting blood sugar level, glucose tolerance and adrenaline induced hyperglycaemia. Indian J Med Res 1967;55:733-45.
17. Anonymous. The Ayurvedic Formulary of India. 2nd ed., Part 1. New Delhi: Ministry of Health and Family Welfare, Govt. of India; 2003. p. 560.
18. Namjoshi AN. Studies in the Pharmacognosy of Ayurvedic Drugs.: Gomantak Press; 1960. p. 6.
19. Ratnakar Nighantu by Panashikar VL, Somana KV, Navare K, editor. 1st ed. Delhi: Choukhambha Sanskrit Sansthan; 2011. Part 2. p. 579.
20. Yoga Ratnakar, with Vidyotini Hindi Commentary by Lakshmipati Shastri. In: Shastri B, editor. 7th ed. Varanasi: Choukhambha Sanskrit Sansthan; 2002. p. 118.
21. Bhaishjya Ratnavali, with Vidyotini Hindi Commentary by Ambikadatta Shastri. 16th ed., 37/9. Varanasi: Choukhambha Sanskrit Sansthan; 2002. p. 118.
22. Mishra SK. Bhaishajya Kalpana Vijnana. 1st ed., Ch. 16. Varanasi: Chaukhamba Orientalia; 2004. p. 376.

23. Paget GE, Barnes JM. Evaluation of drug activities. In: Lawrence DR and Bacharach AL, editors. Pharmacometrics. New York: Academic Press; 1964. p. 161.
24. Sah SP, Sah ML, Juyal V, Pandey S. Hypoglycemic activity of aqueous extract of *Urtica parviflora* roxb in normoglycemic rats. Int J Phytomedicine 2010;2:47-51.
25. Stedman TL. Stedman's Medical Dictionary. 28th ed. Baltimore: Lippincott Williams and Wilkins; 2005 [1911]. p. 2100.
26. Wadkar KA, Magdum CS, Patil SS, Naikwade NS. Anti-diabetic potential and Indian medicinal plants. J Herbal Med Toxicol 2008;2:45-50.

हिन्दी सारांश

गुडूची सत्त्व की हाइपोग्लासेमिक और ऐन्टिहाइपरग्लाइसेमिक प्रभाव का प्रायोगिक अध्ययन

रोहित शर्मा, विजय कुमार, बी. के. अशोक, गालिब आर., प्रदीपकुमार प्रजापती, बी. रविशंकर

सदियों से आयुर्वेदिक वनस्पतियाँ मधुमेह जैसे रोगो की रोकथाम एवं चिकित्सा के लिये औषधियो का एक प्रमुख स्त्रोत रही है और आज वनस्पतियाँ संपूर्ण विश्व में वैज्ञानिक एवं वैद्यकीय अन्वेषणो के आधार पर श्रेष्ठ व सुरक्षित सिद्ध हुई है । गुडूची की मधुमेहहर औषधि के रूप मे उत्तम कार्यकारी क्षमता सिद्ध है और गुडूची सत्त्व का प्रयोग पैत्तिक प्रमेह चिकित्सा मे किया जाता है । प्रस्तुत अध्ययन मे गुडूची काण्ड से निर्मित सत्त्व का हाइपोग्लासेमिक एवं ऐन्टिहाइपरग्लाइसेमिक कर्म का १८ घंटे भूखे रखे हुए चूहों में ओरल ग्लुकोज टोलेरन्स परीक्षण द्वारा अध्ययन किया गया । गुडूची सत्त्व को जल मे घोल कर १३० मिलिग्राम वजन की मात्रा मे चूहों को दिया गया । विभिन्न समय के अन्तराल पर किये गये अध्ययन से प्राप्त परिणामों के आधार पर गुडूची सत्त्व का नोर्मोग्लाइसेमिक चूहों मे हाइपोग्लाइसेमिक प्रभाव मन्द देखा गया एवं ग्लुकोज ओवरलोड चूहों पर ऐन्टिहाइपरग्लाइसेमिक प्रभाव नही पाया गया ।