ORIGINAL ARTICLE

Evaluation of hypoglycaemic and anti-hyperglycaemic activities of *Guduchi Ghana* in Swiss albino mice

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Background: Diabetes mellitus is a common endocrine disorder, characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. Ayurvedic herbs are relatively low cost, more suitable and have negligible side-effects than synthetic oral anti-hyperglycaemic agents. *Guduchi* is reported as highly potent anti-diabetic herb in Ayurveda and *Guduchi Ghanavati* is popularly known by the Ayurvedic fraternity for its therapeutic properties on *Madhumeha* represented as diabetes mellitus. **Aim:** The aim of this study is to evaluate hypoglycaemic and anti-hyperglycaemic activities of *Guduchi Ghana* (GG) in Swiss albino mice. **Materials and Methods:** Hypoglycaemic and anti-hyperglycaemic potential of GG was evaluated in normal mice using both 18 h fasted mice model and oral glucose tolerance test. GG was suspended in distilled water and administered to animals at the dose of 130 mg/kg. **Statistical Analysis:** The results were statistically interpreted using 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:** GG showed mild reduction in blood sugar level (BSL) at all the time intervals in normoglycaemic mice. In anti-hyperglycaemic activity, glibenclamide at a dose of 0.65 mg/kg studied as the reference standard to compare the potency of test drug. Administration of GG prior to glucose over load resulted significant attenuation in BSL at 60 min, 90 min and 120 min in comparison to glucose control group. **Conclusions:** GG has mild hypoglycaemic and significant anti-hyperglycaemic activity and can be used in the treatment of diabetes mellitus as well as a supportive drug without fear of producing hypoglycaemia.

Key words: Anti-hyperglycaemic, *Ghana*, glibenclamide, *Guduchi*, hypoglycaemic, tinospora cordifolia

INTRODUCTION

Diabetes mellitus is a metabolic disorder, characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action or both.[1] Hypoglycaemia is the major side-effect reported from synthetic anti-diabetic agents. Ayurvedic herbs are relatively low cost, significantly potent, more suitable and considered to have negligible side effects in comparison to synthetic oral anti-hyperglycaemic agents,[2] World Health Organization expert committee has listed in one of its recommendations that traditional methods of treatment for diabetes should further be investigated.[3]

Guduchi (*Tinospora cordifolia* Willd. Miers.) is reported as a renowned and highly potent anti-diabetic herb.[4-6] Its safety and non-toxic nature have been reported in experimental and clinical studies on various systems of the body.[7] Number of pharmacological studies have been carried out on different parts of *Guduchi* including exploring its anti-hyperglycaemic and hypoglycaemic potential. Aqueous root extract,[8,9] alcoholic root extract,[10-12] alcoholic stem extract,[13,14] ethyl acetate and hexane extracts of stem,[15] aqueous, alcoholic and chloroform extracts of leaves[16] and aqueous whole plant extracts[17] have been reported to have significant anti-hyperglycaemic activity.

Ghana Kalpana (preparation of solidified aqueous extract) is mentioned in Ayurvedic pharmaceutics as an *Upakalpa* (secondary derivative preparation) of *Kwatha Kalpana* (decoction). This modification of *Panchavidhakashaya Kalpana* is needed in the present era because of advantages such as lower dose, higher concentration and more potency. '*Guduchi Ghanavati*' is mentioned by the name *Sanshamani vati* in *Jvaradhikara* and is popularly known by the Ayurvedic fraternity for its therapeutic properties on *Madhumeha*.[18] However, no reference of pharmacological study on anti-diabetic activity of *Guduchi Ghana* (GG) has been found until date. Thus, the current study was undertaken to

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evaluate the hypoglycaemic and anti-hyperglycaemic potential of GG in experimental animals.

MATERIALS AND METHODS

Animals

Swiss albino mice (*Mus musculus*) of either sex weighing 28 ± 02 g were obtained from animal house attached to Pharmacology Laboratory of I.P.G.T. and R.A., 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% and the 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 and for their drinking purpose tap water *ad libitum* was used. The experiments were carried out after obtaining permission from Institutional Animal Ethics Committee (Approval number: IAEC/09/11/22MD).

Test Formulation

Fresh *Guduchi* stem spreading over Neem (*Azadirachta indica*) tree was collected from the campus of Gujarat Ayurved University, Jamnagar and authenticated at Pharmacognosy Laboratory of the institute. *Guduchi* plant, which grows on Neem tree is said to be the best as the synergy between these plants enhance its efficacy.[19] The physical impurities were removed and washed thoroughly with water. The stem was crushed thoroughly to convert into coarse slimy mass. Decoction was prepared by following the classical method.[20] It was then filtered and further heated until it become into a concentrated form (*Ghana*). The *Ghana* was compressed into tablets each of 500 mg.

Dose Selection and Schedule

The dose of GG for adult is 1 g/day.[21] The dose for 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 table of Paget and Barnes (1964).[22] Distilled water was used as a vehicle. Fresh test drug solutions were prepared in distilled water with suitable concentration depending upon body weight of animals just prior to administration and were administered to animals orally with the help of gastric catheter sleeved to syringe.

Experimental Study

The hypoglycaemic activity and anti-hyperglycaemic activities were carried out by modifying previously described method.[23] The mice were selected instead of rats as per their availability. A total of 42 mice were selected and divided randomly into relevant groups of six each after 7 days of acclimatization. Both activities were then evaluated in the test drug as per the following protocols.

Hypoglycaemic activity

Swiss albino mice of either sex were randomly divided into three groups of six each. The first group served as vehicle control (VC) and given distilled water. Test drug GG was administered to the second group in the dose of 130 mg/kg and the third group served as standard control group to which glibenclamide (0.65 mg/kg) was administered. The animals were fasted overnight prior to experiment and in the morning the initial fasting blood sugar level (BSL) was measured with the help of One Touch Ez Smart CE0537 Glucometer (Lifeline Surgicals, New Delhi, India), by using One Touch Ez Gluco test strips as per user guideline after anaesthetizing the animals with ether and collecting the blood sample from the tail vein following aseptic conditions. Then, vehicle, test drug and standard drug were administered to respective groups. The BSL was recorded after 1 h, 2 h, 3 h and 5 h of the test drug administration for assessing the hypoglycaemic effect after drug administration.[23]

Anti-hyperglycaemic activity

Swiss albino mice of either sex were randomly divided into four groups of six each. VC, test drug control (GG) and standard drug control groups (GL) maintained as per protocol mentioned in the above experiment. The only second group served as glucose control (GC) to which glucose (5 g/kg) solution alone was administered without any treatment. The animals were fasted overnight prior to experiment and fasting initial BSL was measured as mentioned in hypoglycaemic activity. Vehicle, test drug and reference standard drug were given to the respective group of animals as per the body weight. After 1 h of drug administration glucose (5 g/kg) 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-hyperglycaemic activity since glucose solution was given.[23]

Statistical Analysis

The results are presented as mean ± standard error of the mean. 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 occurred in VC group at 1 h, 3 h and 5 h and significant decrease was observed at 2 h in comparison to its initial BSL [Table 1]. GG treated group also showed apparent decrease in BSL in comparison to its initial values; however,

the observed decrease is non-significant in comparison to control group. Administration of glibenclamide to overnight fasted mice leads to a significant decrease in blood glucose level at almost all the time intervals.

Glucose overload to overnight fasted mice leads to significant increase in BSL in GC group at all-time intervals [Table 2]. In VC group a marginal fall in BSL was observed with reference to the initial values, the decrease was found to be statistically significant with respect to the 90 min and 120 min readings. In glucose overload group (GC) significant elevation in BSL was observed by 30th min and continued until 120 min though at a reduced level. The BSL at 30 min, 60 min, 90 min and 120 min was found to be significantly high in comparison to initial values as well as the corresponding values of the control group. Administration of GG prior to glucose over load resulted in significant attenuation in BSL at post-glucose 60 min, 90 min and 120 min in comparison to GC group. At 30 min, the BSL was found to slightly higher even than the GC group, but there after significant decrease was observed with reference to the corresponding values of the GC group. In GL group glucose over load failed to elevate the BSL during the entire observation period starting from 30 min post-glucose to 120 min.

DISCUSSION

A good anti-diabetic agent is that which would not lower the blood glucose level below the normal level in normoglycaemics and should have a good blood glucose lowering effect in hyperglycaemic subjects. Hypoglycaemia is an abnormally diminished content of glucose in the blood.[24]

The most common forms of hypoglycaemia occur as a complication of treatment of diabetes mellitus with insulin or oral medications. Hypoglycaemia can be a fatal medical emergency, which require immediate therapeutic intervention to cover up the glucose deficiency in the blood. Thus, hypoglycaemic potential of GG was compared with the standard reference drug, glibenclamide in which hypoglycaemia like side-effects are not uncommon. The results of this study show that GG treated group showed only a marginal decrease in BSL in normoglycaemic mice.

Glucose overloading to overnight fasted mice leads to significant increase in BSL in GC group at all-time intervals up to 2 h. GG significantly attenuated it at almost all time intervals, which indicate the presence of anti-hyperglycaemic activity in this formulation. It has been established that the anti-diabetic activity of this plant is not through the insulin secretion by pancreatic beta cells and may be due to the increased entry of glucose into the peripheral tissues and organs like the liver and also decreased the activity of phosphorylase in the liver, thereby it may prevent the release of glucose into the blood.[25] Further, it has been reported that 1, 2-substituted pyrolidines isolated from the stem is responsible for anti-diabetic activity of *Guduchi*.[26] The same component as well as mechanism may be involved in the observed activity profile; however, further detailed studies are needed to establish exact mechanism involved.

CONCLUSION

GG has mild hypoglycaemic and significant anti-hyperglycaemic activity. This study indicates that GG can be used in the treatment of diabetes mellitus alone. It is further suggested that it can also be used as a supportive drug with other Ayurvedic drugs giving it as a sahapana after doing its experimental study.

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Table 1: Effect of *Guduchi Ghana* on blood sugar level 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
GG	93.00±6.63	74.33±4.33$^{\#}$	75.67±3.99$^{\#}$	73.83±5.64$^{\#}$	80.00±4.21
GL	86.64±4.02	75.50±3.32$^{\#}$	71.17±4.25$^{\#\#}$	66.67±3.26$^{\#\#*}$	61.33±3.84$^{\#\#\#}$

Data: Mean±SEM; VC – Vehicle control; GG – *Guduchi Ghana* control; GL – Standard drug control; SEM – Standard error of mean; $^{\#}P$<0.05; $^{\#\#}P$<0.01; $^{\#\#\#}P$<0.001 (compared with initial BSL); $^{*}P$<0.05 (compared with normal control group)

Table 2: Effect of *Guduchi Ghana* on blood sugar level 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$^{\#\#**}$
GG	88.67±6.55	142.67±17.24$^{\alpha\alpha}$	106.50±7.68$^{\alpha\alpha\alpha}$	95.67±5.33$^{\alpha\alpha}$	89.67±7.17$^{\alpha}$
GL	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; VC – Vehicle control; GC – Glucose control; GG – *Guduchi Ghana* control; GL – Standard drug control; SEM – Standard error of mean; $^{\#}P$<0.05; $^{\#\#}P$<0.01 (compared with initial blood sugar level); $^{*}P$<0.05; $^{**}P$<0.01; $^{***}P$<0.001 (compared with normal control group); $^{\alpha}P$<0.05; $^{\alpha\alpha}P$<0.01; $^{\alpha\alpha\alpha}P$<0.001 (compared with glucose control group)

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