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Diuretic Activity of Gokshuradi Guggulu (A Multi-Herbal Formulation) In Rats

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Abstract
Gokshuradi guggulu (Gg) is multi-herbal formulation consisting of nine ingredients which is used in Ayurvedic, traditional and folkloric medicine to promote urinary out flow. However, the diuretic potential of Gg has not been validated or refuted. The aim of this study was to investigate the diuretic potential of Gg purchased from Sri Lankan open market using rat hydrated assay. Different doses of Gg (4000, 2000 and 1000 mg /kg) or distilled water (vehicle) or 13 mg/kg of furosemide, the reference drug, was orally administered to 18 h fasted (deprived of water but not food) rats and their cumulative urine output was determined at hourly intervals for 6h. The results raveled that Gg does not possess significant (P> 0.05) diuretic activity (both in term of hourly and cumulative urine output), at the doses tested. It is concluded that Gg purchased from Sri Lankan open market is devoid of any diuretic activity. This is a noval finding with therapeutic implications.

Keywords: *Gokshuradi guggulu, diuretic, Ayurveda medicine*

Introduction
Gokshuradi guggulu (Gg) is an Ayurvedic multi herbal formulation, consisting of nine ingredients which is used in the treatment of several disorders in male reproductive system and urinary system of both males and females (Jayasinghe 1976). In reproductive field, it is used in the treatment of spermatorrhoea, nocturnal eneuresis,premature ejaculation and loss of sexual desire (Jayasinghe 1976). Amoungst urinary disorders it is recommended for nephrities, albuminaria, urinary inspections, cystitis, uteric and bladder stones (Jayasinghe 1976). It is also recommended by Ayurvedic, traditional and folkloric medicine to be used as a diuretic. However, the diuretic potential of Gg has not been scientifically validated or refuted. The aim of this study was to investigate scientifically the diuretic potential of Gg using rat hydrated diuretic assay.

Materials and Methods

Test drug
Gg Tablets were purchased from registered Ayurvedic pharmacy at Rajagiriya, Colombo, Sri Lanka. This Gg is claimed to contained 9 ingredients: 48 grams of tubers of *Zingiber officinale*, fruits of *Piper nigrum*, *Piper longum*, *Terminalia chebula*, *Terminalia belerica*, *Emblica officinalis*, *Cyperus rotundus* and 336 grams of purified resinous gum of *Balsamodendron mukul* (Gugul) and *Tribulus terrestris* (as a bhāvana dravya).

Preparation of sample
Gg was dissolved in water and different doses (1000, 2000, 4000 mg/kg) of it or the vehicle or furosemide (the reference drug), was orally administered to rats deprived of water, but not food (18 h), and subsequently hydrated with 15 ml of isotonic saline (n=6/group). The cumulative urine output was monitored at hourly intervals for 6 h.

Experimental animals
Healthy adult cross bred male albino rats (200-225g) from our own colony were used. They were kept under standard environment condition (temperature: 28-31°C, photoperiod: approximately 12h natural light per day, relative humidity: 50-55%). The animals were fed with pelleted food (Ceylon Grain Elevators, Colombo, Sri Lanka) and clear drinking water ad labitum. All the experiments were

conducted in accordance with the internationally accepted laboratory animal use and care and the guidelines and rules of the Faculty of Science, University of Colombo,SriLanka.

Evaluation of Diuretic activity

Thirty rats were deprived of water but not food for 18h. Their urinary bladders were emptied by gentle compression of the pelvic area and by pull of their tails. Then, each rat was orally administered with 15ml of isotonic saline (NaCl 0.9%w/v) to impose a uniform water load. Forty five minutes later, these rats were randomly divided into 5 groups (n=6/per group) and treated orally in the following manner: Group 1:1ml of distilled water, group 2:1000 mg/kg of Gg, group 3: 2000 mg/kg of Gg, group 4: 4000mg/kg of Gg and group 5: 13mg/kg of furosemide (State Pharmaceutical Corporation, Colombo, Sri Lanka), the reference drug, (BNF 2001). Each of these rats was individually placed in metabolic cages and their cumulative urine output was determined at hourly intervals for 6 hours.

Statistical analysis

Data are given as mean ±SEM. Statistical comparisons were made by one-way ANOVA e) Statistical analysis: 2nd line, ANOVA using should be ANOVA followed by Turkey post hoc test using Minitab 13.0 version statistical package. Significance was set at $p<0.05$.

Results

The results obtained are depicted in Tables 1 and 2. As shown, none of the doses of Gg tested possessed significant ($P>0.05$) diuretic activity (both in terms of hourly and cumulative urine output). In contrast, furosemide the well-known diuretic drug markedly (108%) and significantly ($p<0.05$) increased the urine output. The urine of tested rats was colorless and not turbid as in control rats.

Table 1: Time course of diuresis in rats treated with different doses of Gg upto 6 hours (Mean±SEM), (n=6/group)

Dose mg/kg	Urine output (ml/100g/bw/h)					
	1h	2h	3h	4h	5h	6h
4000	1.27±0.44	1.42±0.50	1.64±0.70	1.72±0.68	2.025±0.71	2.45±0.72
2000	1.065±0.18	1.52±0.25	1.97±0.28	1.89±0.37	2.11±0.46	2.18±0.46
1000	1.324±0.43	1.564±0.43	1.82±0.58	1.82±0.60	2.13±0.68	2.32±0.73
Furosemide 13	1.86±0.11*	2.55±0.16*	3.16±0.15*	3.32±0.12	3.56±0.16	3.64±0.15
Water (1ml)	0.913±0.40	1.50±0.38	1.62±0.21	2.128±0.53	2.201±0.60	2.21±0.60

$p<0.05$ as compared with control ANOVA –followed by Turkeys post hoc test

Table 2.Cumulative urine output in rats over a six-hour period following oral administration of Gg in rats (Mean±SEM), (n=6/group)

Dose	Cumulative urine output (ml/100g/bw/h)
4000mg/kg	2.45±0.72
2000mg/kg	2.18±0.46
1000mg/kg	2.32±0.73
Furosemide13mg/kg	3.64±0.15*
Water (1ml)	2.21±0.61

$p<0.05$ as compared with control ANOVA –followed by Turkeys post hoc test

Discussion

This study examined the diuretic potential of Gg using rat hydrated diuretic assay (Ratnasooriya *et al*., 2004). This assay is validated, rapid, reliable, sensitive and a widely used method to assesses the potential of diuretic and antidiuretic drugs (Fernandopulle *et al*., 1999). The results showed that none of the doses of Gg tested increased the cumulative urine output at six hours or at hourly intervals of six hours. In contrast, the reference drug, furosemide increased the urine output with a rapid onset as is claimed in the Western medicine (BNF, 2001).

Inability of Gg to enhance urine output suggests that it does not acts as a diuretic (at least in the doses

tested) as is claimed in the Ayurvedic medicine. This is a novel, yet, an unexpected finding which may have therapeutic implications. The doses used were 1000 mg/kg: (50% lower than human equitant dose), 2000 mg/kg (human equivalent dose) and 4000 mg/kg (50% higher than human equitant dose). Thus, it is unlikely that, the lack of diuretic activity is due to insufficient dosage. Absence of diuretic activity of Gg, in rats, may be due to species specificity. For example, aqueous root extracts of *Withania somnifera* which is claimed to possess male aphrodisiac activity in traditional medicine has no such activity in rats (Illeperuma *et al*., 2002). On the other hand, several herbal drugs which are claimed to have diuretic actions in humans also exhibit promising diuretic activity in rats (Ratnasooriya *et al., 2004, Fernandopulle et al., 1999)*

Enhanced hepatic and/ or renal clearance of the bioactive constituent/s responsible for diuresis in Gg is a potential mechanism for the absence of diuresis in this study (Ratnasooriya *et al.*, 2013). Alternatively, production of a metabolite, in rats, which overrides the diuretic activity of Gg could also inhibit diuresis as observed in this study. Impairment or inability of absorption of active constituent/s in rats is yet another possibility. The Gg tablets was purchased from an Ayurvedic drug outlet but the expiry date was not mentioned in the packet. Further, the Gg was stored at ambient temperature (28-32^{0}C). Thus, possibility exists that degradation of active constituent/s could contribute to the lack of diuretic activity: it is well-known that claimed activities of herbal products deteriorate with improper storage (Martin 1995). Gg is a multiherbal formulation, as such, lack of diuretic activity could also results from using substitutes or inferior quality ingredients or even improper weights of ingredients. Lack of standardization is common problem seen in Ayurvedic and traditional medicine sold in Sri Lanka.

Conclusion

Tested Gg tablets purchased from the open market did not possess diuretic activity as claimed in Ayurvedic medicine.

"Cite this Article"

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