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Short communication

Antidiabetic activity of a standardized extract (Glucosol™) from *Lagerstroemia speciosa* leaves in Type II diabetics A dose-dependence study

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Abstract

The antidiabetic activity of an extract from the leaves of *Lagerstroemia speciosa* standardized to 1% corosolic acid (Glucosol™) has been demonstrated in a randomized clinical trial involving Type II diabetics (non-insulin-dependent diabetes mellitus, NIDDM). Subjects received a daily oral dose of Glucosol™ and blood glucose levels were measured. Glucosol™ at daily dosages of 32 and 48 mg for 2 weeks showed a significant reduction in the blood glucose levels. Glucosol™ in a soft gel capsule formulation showed a 30% decrease in blood glucose levels compared to a 20% drop seen with dry-powder filled hard gelatin capsule formulation ($P < 0.001$), suggesting that the soft gel formulation has a better bioavailability than a dry-powder formulation.

Keywords: Type II diabetes; Blood glucose; *Lagerstroemia speciosa*; Glucosol™

1. Introduction

Lagerstroemia speciosa L. (Lythraceae), commonly known as Crepe Myrtle, grows widely in tropical countries, including the Philippines, India, Malaysia, China, and Australia. *Lagerstroemia speciosa* is a popular folk medicine in Southeast Asia; in the Philippines, a tea from the leaves has been used for the treatment of diabetes mellitus (Quisumbing, 1978; Matsuyama, 2001). The leaves contain large amounts of corosolic acid, which has previously been shown to possess antidiabetic properties (Murakami et al., 1993) and significant amounts of tannins (Hayashi et al., 2002).

The hypoglycemic effect of *Lagerstroemia speciosa* has been demonstrated in animal and in vitro studies. When genetically diabetic mice (Type II) were fed a diet containing hot-water extract from *Lagerstroemia speciosa* for 5 weeks, their elevated blood glucose was significantly suppressed (Kakuda et al., 1996). In another study, when obese diabetic rats were fed a diet containing the same extract for 12 weeks, their blood glucose levels were not suppressed, but their body weights were lowered significantly (Suzuki et al., 1999).

In a recent study, both hot water and methanol extracts of the leaves of this plant were shown to stimulate glucose uptake in 3T3-L1 cells in a manner similar to insulin, and to inhibit adipocyte differentiation induced by insulin and isobutyl-methyl-xanthin and dexamethasone, suggesting that plant extract may be useful for prevention and treatment of hyperglycemia and obesity in Type II diabetics (Liu et al., 2001).

In a bioassay-guided fractionation, employing glucose transport activity in Ehrlich ascites tumor cells, researchers in Japan isolated corosolic acid (2α-hydroxyursoloic acid, $C_{30}H_{48}O_4$) from the methanol extract of *Lagerstroemia speciosa* leaf, which showed a significant glucose transport-stimulating activity at a concentration of 1 μM (Murakami et al., 1993). Accordingly, extracts from the leaves of the plant were standardized to corosolic acid, and one such extract is Glucosol™, which is standardized to contain 1% corosolic acid. In this paper, we report on the efficacy of this extract in balancing blood sugar in humans.

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2. Subjects and methods

2.1. Plant extract

The leaves of *Lagerstroemia speciosa* L. (Lythraceae) were harvested in March from Luzon Island in the Philippines. Permit to collect and export plant material was given by The Foreign Trade Statistics of the Philippines under Volume 2—Export Food and Live Animal No. 074.10 on 2 February 1999. The voucher specimen (#Lag-0037) is kept at the Department of Medicine, Hiroshima University, Japan. The leaves were dried, extracted with 80% (w/w) aqueous ethanol at 80 °C for 1.5 h, cooled to room temperature, then filtered. The extract was treated with activated carbon to remove chlorophyll, filtered and concentrated under reduced pressure to give a dry solid, which was shown by HPLC to contain 3% corosolic acid. The HPLC conditions: ODS C18 column (4.6 mm × 150 mm); 35:65 (v/v) water containing 0.1% trifluoroacetic acid:acetonitrile as a mobile phase; flow rate of 1.0 ml/min; and UV detection at 210 nm. The extract was standardized to contain 1.0% corosolic acid to give Glucosol™.

Glucosol™ was provided to subjects in either a soft gelatin capsule as a suspension in a vegetable oil-base or in a two-piece hard gelatin capsule as a powder in rice-bran base.

2.2. Subjects

Fifty-six Type II diabetic volunteers were recruited and screened by means of a physical examination and medical history. The inclusion criteria were such that the basal blood glucose levels were between 140 and 250 mg/dl. Of the 32 qualified subjects, 10 subjects aged 55–70 years old were selected and randomly divided into two groups, five each, for the dose–response study. The first group received Glucosol™ in a soft gel formulation and the second group received Glucosol™ in a two-piece hard gelatin capsule formulation.

Informed consent was obtained from each subject, and the study protocol was approved by the Sarasota Memorial Hospital review board for human research. Subjects were refrained from taking oral hypoglycemic medication on the average of 45 days prior to the clinical trial. All subjects were requested to maintain their normal diets during the study.

2.3. Antidiabetic activity

Five subjects in each group received a daily oral dose for 15 days of either a soft gelatin or hard gelatin formulation of 16, 32 and 48 mg Glucosol™ sequentially with a 10-day wash-out period in between the doses.

Each volunteer provided a blood sample in the morning, after an overnight fast, seven days before the start of the study (−7 day) and on the day of the study (0 day) to evaluate the basal blood glucose level (control). Capillary bloods from finger-pricks were collected and blood glucose level was determined using a Precision Glucose Monitor. For each subject and at each time point, three capillary blood samples were taken and an average of three readings was recorded. The basal blood glucose for each subject was determined from a blood sample in the morning after an overnight fast a week before the treatment with Glucosol™.

2.4. Data analysis

Statistical means and standard deviations were calculated for each continuous variable. A paired *t*-test was used to evaluate significant differences among study groups. A *P*-value of 0.05 was considered as a significant difference in the analysis of the data.

3. Results and discussion

Compared to the control blood glucose levels, both soft gel and hard gel formulations of Glucosol™ showed a drop over the dose range of 16–48 mg per day. This translates to a daily dose of 0.16–0.48 mg of corosolic acid, the putative ingredient (Table 1 and Figs. 1 and 2). A statistically significant reduction in blood glucose level was observed at the 48 mg per day dose in both formulations.

Subjects received Glucosol™ in the soft gel form showed a 30% decrease in their blood glucose, while those received

Table 1
Percent reduction in basal blood glucose levels in Type II diabetics after 15 days of treatment with different doses of Glucosol™ in soft gel or hard gelatin capsule formulations

Dosage form	Dose (mg/person per day)	Percent reduction in blood glucose levels (±S.D.)	*P*-value[a]
Soft gel	16	4.9 ± 0.71	≤1.85
	32	10.7 ± 1.4	≤0.01
	48	30.0 ± 3.4	≤0.002
Hard gel	16	3.18 ± 0.39	≤0.37
	32	6.5 ± 1.13	≤0.09
	48	20.2 ± 1.29	≤0.001

[a] *P*-values are based on the difference in blood glucose levels after an overnight fasting, 1 week before treatment, and after 15 days of treatment with Glucosol™.

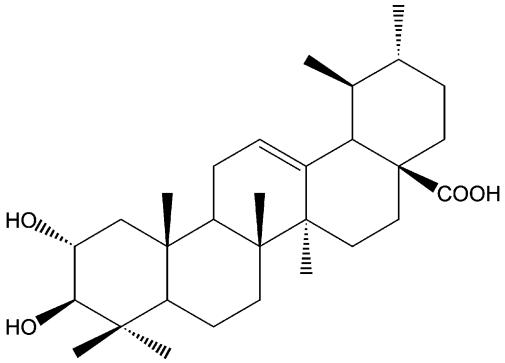

Fig. 1. Corosolic acid.

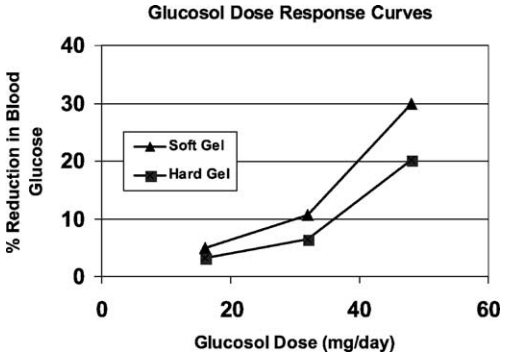

Fig. 2. Effects after 15 days of treatment with Glucosol™ (a *Lagerstroemia speciosa* extract standardized to 1% corosolic acid) on reducing basel blood glucose levels in humans. Two different dosage forms were evaluated.

Glucosol™ in the hard gel form had 20% reduction in the blood glucose level. The difference in blood glucose reduction at 32 and 48 mg per day dose of Glucosol™ between the soft gel and hard gel formulations was significant ($P < 0.001$), and thus, the soft gel is more effective compared to the hard gel dry-powder formulation.

These results clearly show that oral formulations of an extract from the leaves of *Lagerstroemia speciosa* standardized to 1% corosolic acid (Glucosol™) exert a marked lowering of blood sugar in Type II diabetics, and that Glucosol™ formulated in a soft gelatin capsule demonstrated a significant improvement in blood sugar lowering compared to Glucosol™ formulated in a dry-powder hard gelatin capsule. This suggests that the active triterpene ingredient in Glucosol™ is lipophilic and better absorbed in an oil-based soft gelatin capsule formulation.

4. Conclusion

Although Glucosol™ shows a significant dose–response relationship over the range of 16–48 mg per day, we do not believe that we reached the top of the dose–response curve and further studies are needed to evaluate the maximum dose before observing a leveling-off in the response.

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