Hypoglycaemic and antihyperglycaemic effects of *Aegle marmelos* leaves in rabbits

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Hypoglycaemic and antihyperglycaemic effects of an aqueous extract of *A. marmelos* leaves were studied in normal and alloxanized-rabbits respectively. In normal rabbits, the highest decrease (35.3%) in blood glucose level was recorded with 1 g equivalent dose after 4 h of administration. The hypoglycaemic effect at 12 h was moderate but no effect was observed at 24 h of drug administration. In diabetic rabbits, the extract produced significant ($P < 0.01$) antihyperglycaemic effect within 3 days when given at the dose equivalent to 1 g powder/kg/day.

AEGLE marmelos Linn. (Rutaceae; Bael) is a widely distributed plant in India and the leaf juice of this plant is used orally by Indian Ayurvedic practitioners for the management of diabetes mellitus[1,2]. However, scanty scientific information is available on the hypoglycaemic activity of *A. marmelos* leaves. We report here the role of an aqueous extract of *A. marmelos* leaves as a hypoglycaemic agent in normal and alloxan diabetic rabbits.

Fresh green leaves of *A. marmelos* procured locally were dried in the shade, powdered and boiled with distilled water. After filtration through Whatman filter paper No. 40, the extract was dried by slow heating and continuous stirring. The yield of the extract was 32%.

Adult albino rabbits of either sex and weighing 1.5–2 kg were used in these experiments. The animals were maintained on standard feeding and managemental condition[3].

Hypoglycaemic effect of the extract was evaluated in 24 fasted albino rabbits divided into four groups of 6. The animals of group-I received 20 ml of distilled water *per os*, while the other three were treated orally with an aqueous extract equivalent to 0.5, 1.0 and 1.5 g powder/kg respectively. Blood glucose was estimated[4] at 0, 4, 12 and 24 h following administration of the test drug and the percentage glycaemia variation was calculated for each group. A comparison was also made between 0, 4, 12 and 24 h values of different groups.

Antihyperglycaemic effect was evaluated in alloxan-diabetic rabbits[5] divided into three groups of 6. Group-I received extract equivalent to 1 g powder/kg/day, group-II was given reference drug (Phenformin @ 125 mg/rabbit) while group-III (untreated control) received 20 ml of distilled water. Treatment schedule was continued for 10 consecutive days. The diabetic blood glucose value (day 0) was compared with post-treatment values on days 3, 5 and 10 in all the groups. Comparison was also made between glucose values of different groups at different time intervals. The data were analysed statistically using analysis of variance and paired '*t*' test[6].

Result of the effect of aqueous extract of *A. marmelos* leaves on blood glucose level of normal rabbits is presented in Table 1. The test drug in all the three doses produced significant ($P < 0.01$) hypoglycaemic effect after 4 h of administration. However, it was more marked in animals receiving aqueous extract equivalent to 1 g powdered leaves (group-III). The hypoglycaemic effect was moderate with all the three doses at 12 h

Table 1. Effect of an aqueous extract of *A marmelos* leaves on blood glucose level of normal rabbits (mean ± SE)

Treatment	Dose equivalent to g powder/kg	Blood glucose levels (mg/100 ml)			
		0	Post-treatment (h) 4	12	24
Distilled water	20 ml	97.1 ± 0 8^{A}	96 0 ± 0.9^{A} (1.1)	93.3 ± 0 7^{A} (3.9)	89.7 ± 0 6^{A} (7.6)
Extract	0.5	95 8 ± 1.0^{A}	74 3 ± 1.2^{B} (22.4)	85 5 ± 1.0^{B} (10 7)	89 8 ± 0 4^{A} (6 2)
Extract	1	96.2 ± 1.3^{A}	62.2 ± 0 8^{C} (35 3)	81 4 ± 0.7^{C} (15 4)	88 0 ± 1 5^{A} (6 2)
Extract	1 5	94.4 ± 1 2^{A}	73 1 ± 1 4^{B} (22 6)	78 8 ± 0 8^{C} (16.5)	86 4 ± 1 6^{A} (8 4)

Figures in parentheses indicate % reduction in glucose levels over 0 h
Capital letters indicate between group comparison
Means having different letters are significant ($P < 0.01$) but same letters are non-significant

Table 2. Effect of an aqueous extract of *A. marmelos* leaves and phenformin on blood glucose levels of diabetic rabbits (mean ± SE)

		Blood glucose levels (mg/100 ml)			
		Diabetic level	Post-treatment (days)		
Treatment	Dose	0	3	5	10
Extract	Equivalent to 1 g powder/kg	263 1 ± 4 7^{A}	201.6* ± 5.3^{C} (–23 4)	184 7* ± 5 9^{B} (–29 8)	129 4* ± 3.4^{C} (–50 8)
Phenformin	@ 125 mg per rabbit	278.7 ± 6 0^{A}	239 9* ± 8 2^{B} (–13 9)	186.1* ± 5 5^{B} (–33 2)	114 6* ± 2 1^{B} (–58.9)
Distilled water (untreated control)	20 ml	276 1 ± 4 8^{A}	292 7* ± 4 0^{A} (+ 6.0)	314 2* ± 4 2^{A} (+ 13 8)	333 8* ± 4 0^{A} (+ 20.2)

Figures in parentheses indicate % reduction (–), or increase (+) over diabetic level
*Significantly different from diabetic level ($P < 0$ 01).
Capital letters indicate between group comparison
Means having different letters are significant ($P < 0$ 01) but same letters are non-significant.

and no significant difference in blood glucose level between treated and control group was observed at 24 h.

Table 2 summarizes the effect of an aqueous extract of *A. marmelos* and phenformin on blood glucose level of diabetic rabbits. Both phenformin and aqueous extract of *A. marmelos* were found to have significant ($P < 0.01$) antihyperglycaemic effect after day 3 of treatment. It is interesting to note that on day 3, aqueous extract of *A. marmelos* had comparatively higher antihyperglycaemic effect, while phenoformin was found more effective in reducing blood glucose level on day 10. In untreated diabetic rabbits there was a significant ($P < 0.01$) rise in blood glucose levels from day 3 onward.

These findings indicated that an aqueous extract of *A. marmelos* had a significant hypoglycaemic effect in normal rabbits which lasted for 12 h and the effect was dose-dependent up to 1 g equivalent of powder. However, the response decreased at 1.5 g/kg dose. Such a phenomenon of less hypoglycaemic response at higher doses is not uncommon with indigenous plants and has been observed with *Vinca rosea*[7] and *Cinnamomum tamala*[8]. The extract also produced marked decrease in blood glucose level in diabetic animals. The possible mechanism of the hypoglycaemic effect of *A. marmelos* in normal and diabetic rabbits is not clear. It may be supposed that in normoglycaemic rabbits, the extract exerted hypoglycaemic effect similar to phenformin by stimulating β-cells to release insulin. However, in diabetic rabbits the extract could not have acted by stimulating the β-cells as the alloxan treatment causes permanent destruction of the β-cells. *Ocimum sanctum* leaves[9] and seeds of *Cajanus cajan*[10] have been reported to produce an antidiabetic effect by inhibiting absorption of glucose from the intestine. The possibility of reduced absorption of glucose from the intestine after *A. marmelos* administration cannot be ruled out. A similar explanation has been put forward for antidiabetic activity of *Musa sapientum*[3] and *Caesalpinia bonducella*[5]. Aqueous extract of *A. marmelos* was, therefore, found to have antihyperglycaemic activity in normal as well as alloxanized rabbits, but the precise mechanism whereby this effect is mediated warranted further investigations.

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