

The effect of *Syzygium cumini* (L.) skeels on post-prandial blood glucose levels in non-diabetic rats and rats with streptozotocin-induced diabetes mellitus

Claudio Coimbra Teixeira ^{a,*}, Luciano Pilla Pinto ^a, Felix Henrique Paim Kessler ^a, Lia Knijnik ^a, Cristiano Pilla Pinto ^a, Glédison José Gastaldo ^b, Flávio Danni Fuchs ^a

^a Departamento de Farmacologia, Universidade Federal, Rio Grande do Sul, Brazil

^b Hospital de Clínicas de Porto Alegre, Universidade Federal, Rio Grande do Sul, Brazil

Received 28 February 1996; accepted 20 February 1997

Abstract

This study was undertaken to investigate whether a tea prepared from *Syzygium cumini*, reported to be used by diabetics in Porto Alegre, Brazil, might have an antihyperglycemic effect in experimental models. Teas prepared from leaves and seeds of *S. cumini*, in concentrations ranging from 2–64 g/l, were administered, as water substitute for 14–95 days, to 16 groups with 8–9 normal albino rats and to four groups with 10–12 rats with streptozotocin-induced diabetes mellitus. Post-prandial blood glucose levels were determined by the glucose oxidase method on blood samples obtained by decapitation. None of the tea concentration had any detectable antihyperglycemic effect either in normal or in diabetic rats, suggesting that this plant, prepared in a manner similar to that employed by humans, is destitute of an antihyperglycemic effect. © 1997 Elsevier Science Ireland Ltd.

Keywords: Diabetes; Treatment of diabetes; Streptozotocin

1. Introduction

Tea prepared from the leaves of *Syzygium cumini* (L.) skeels (synonym: *Eugenia jambolana*

Lam.) or *Syzygium jambos* (L.) Alst. (Myrtaceae) (common name for both plants is 'jambolão' in Brazil) has been reported to be used by diabetics in Porto Alegre, a southern city of Brazil (Teixeira et al., 1992), and by diabetics elsewhere (Sepaha and Bose, 1956; Steinmetz, 1960; Bramachari and Augusti, 1961; Shrotri et al., 1963; Sigogneau-Jagodzinski et al., 1967; Ratsimamanga et al., 1973; Bansal et al., 1981; Srivastava et al., 1983;

* Corresponding author. Present address: Departamento de Farmacologia, Instituto de Biociências, U.F.R.G.S. Rua Sarmiento Leite, 500 90.046-900, Porto Alegre, RS, Brazil; Fax: + 55 51 2267191.

Kedar and Chakrabarti, 1983; Krall, 1985; Kohli and Singh, 1985; Giri et al., 1985; Nair and Santhakumari, 1986; Jain and Shaw, 1987; Handa and Chawla Maninder, 1989; Rahman and Zaman, 1989; Ivorra et al., 1989). To determine whether such teas could really lower blood glucose levels, we tested them first in non-diabetic human volunteers (Teixeira et al., 1990). The results were negative, however this can not rule out the possibility that an effect could be seen in diabetic animals, patients or even, in non-diabetic rats using higher concentrations of the tea. The postulated antidiabetic efficacy could involve an action on the metabolic abnormalities seen in diabetes mellitus.

We therefore studied the effects of *S. cumini* on post-prandial blood glucose levels in non-diabetic and streptozotocin-induced diabetes mellitus rats.

2. Methodology

The leaves from *S. cumini* were collected in the spring by the researchers in the Experimental Agronomic Farm of the State Department of Agriculture. The leaves were dried at room temperature for 30 days. The leaves and flowers were identified in the Department of Botany at the University, and a voucher herbarium specimen has been deposited at the University Herbarium (acquisition number ICN-94670). The tea was prepared by decoction of dried leaves of 'jambolão' (*S. cumini*) and offered as a substitute of water for ad libitum ingestion.

Adult female albino rats, raised and maintained under standard conditions, and having an average body weight of 200 g, were used in the experiments.

Diabetes was induced by 65 mg/kg of streptozotocin administered I.P. in saline, with the pH having been adjusted to 4.5 with 0.05 M citric acid (Palanichamy et al., 1988). After four days, glucose was measured by dextrostix in blood samples taken by cutting the tip of the tail. This method permits the measurement of blood glucose levels with a minimal injury to the rat. It was validated, through the comparison with the

glucose oxidase method in a previous experiment (Teixeira et al., 1990). Rats with glucose levels above 200 mg (%) were included in the experiment.

Two subacute (14 days) and two chronic (72 and 95 days) experiments were performed with non-diabetic rats. In the first subacute experiment, each group of eight rats were administered teas of 2, 8, or 32 g/l, or water. The second subacute experiment was composed with five groups: water, tea with 16, 32, and 64 g/l, and a tea prepared by decoction of 'jambolão' seeds, dried, pulverized and devoid of pericarps, with a concentration of 32 g/l. The first chronic experiment had two groups of rats, which consumed either water or a tea with 32 g of dried leaves per liter. The last experiment investigated the effect of the following tea concentrations: 8, 16, 32 and 64 g/l.

The groups of diabetic rats were maintained in cages with different concentrations of tea (8, 16 or 32 g of dried *S. cumini* leaves in 1 l of water prepared daily by decocting) or water as the only drink for 14 days.

The average daily volume consumed was calculated dividing the total amount of liquid by the number of animals. It ranged from 26.0–32.0 ml per rat.

To insure a uniform food intake on the day of experiment (fourteenth day), the rats were fasted at 22:00 h and fed ad libitum from 04:00–08:00 h (Kettelhut et al., 1980; Schmid et al., 1984), when they were killed by decapitation without anesthesia and with minimal handling. Blood glucose was determined by the glucose oxidase method in samples collected on decapitation (Trinder, 1969).

Each experimental group consisted of at least eight rats, which conferred a statistical power of 90% to detect a difference of 15% for post-prandial blood glucose levels among the four groups, for a $P\alpha$ of 5%. The results were analyzed by analysis of variance.

The comparison of blood glucose levels obtained in the confirmation of induced diabetes and on the day of the experiment was done, separately, through a one-way ANOVA (Armitage and Berry, 1987).

Table 1
The effect of tea prepared from dried leaves of 'jambolão' on the post-prandial blood glucose of non-diabetic rats

Duration of experiment (days)	Groups	N	Intervention (g/l)	Post-prandial blood glucose (S.E.)	F	P
14	I	8	2	123, 7 (3,4)	0.92	0.44
	II	8	8	125, 1 (3,4)		
	III	8	32	119, 2 (3,7)		
	IV	8	water	126, 9 (3,0)		
14	I	8	16	134, 6 (3,7)	0.11	0.98
	II	8	32	133, 9 (4,4)		
	III	8	64	136, 1 (4,5)		
	IV	8	32 ^a	133, 6 (2,7)		
	V	8	water	132, 6 (4,2)		
72	I	8	32	146, 6 (5,5)	1.43	0.07
	II	8	water	129, 9 (6,5)		
95	I	8	8	146, 9 (4,0)	1.12	0.36
	II	8	16	151, 4 (5,8)		
	III	9	32	154, 2 (2,9)		
	IV	9	64	158, 1 (4,8)		
	V	8	water	148, 7 (3,0)		

^a Prepared with seeds.

3. Results

Mean values of post-prandial blood glucose of the several experiments with non-diabetic rats are presented in Table 1. None of the different concentrations or periods of administration of tea produced an antihyperglycemic effect.

All groups of diabetic rats had similar mean baseline blood glucose ($P = 0.477$) (Table 2). After 14 days of tea or water consumption, the average blood glucose levels were still not different between the four groups ($P = 0.964$). The increase of glucose levels from the baseline to the post-treatment evaluation might be secondary to a deterioration in the metabolic control or to the different methods of glucose determination. Lack of any differences among the four groups indicates that none of the tea concentrations used had any effect on mean blood glucose concentrations of streptozotocin-induced diabetic rats.

4. Discussion and conclusions

The experiments did not show, in non-diabetic rats, a post-prandial antihyperglycemic effect of

teas prepared from leaves of 'jambolão', tested in subacute or chronic fashions. This is in accordance with the results of trials with nondiabetic volunteers, which failed to demonstrate an antihyperglycemic effect of both plant species (Teixeira et al., 1988; 1990).

An overall view of these experiments and trials which do not exclude an antihyperglycemic effect in patients, suggests that the claimed effect is unlikely to be of a significant magnitude. All known hypoglycaemic drugs have effect in nondiabetic animals (Gerich, 1985), which is detectable by experimental protocol similar to the one used in this study. Even an effect on carbohydrate absorption can be ruled out, since the rats drank the teas while on experimental feeding.

Previously we reported that tea prepared from *S. cumini* did not lower blood glucose levels in glucose-loaded non-diabetic humans (Teixeira et al., 1988). We have also shown its lack of efficacy in lowering blood glucose levels in streptozotocin-induced diabetic rats. Nevertheless, even though streptozotocin has been reported (Ollin, 1990) to induce, in animals, a diabetes that resembles human nonketotic diabetes mellitus, our results do not necessarily rule out the possibility that it might have efficacy in human diabetics.

Table 2

The effect of tea prepared from dried leaves of 'jambolão' on the post-prandial blood glucose of streptozotocin-induced diabetic albino rats

Groups	N	Intervention(g/l)	Blood glucose levels (mg%, S.D.)	
			Pre-treatment	Post-treatment
I	12	water	334.7 (61.4)	525.7 (100.2)
II	10	8	365.4 (32.5)	521.6 (66.7)
III	11	16	355.5 (46.1)	519.9 (93.5)
IV	11	32	344.6 (44.4)	507.6 (77.9)

ANOVA Pre-treatment: $F = 0.84$, $P = 0.477$. ANOVA Post-treatment: $F = 0.09$, $P = 0.964$.

Experiments with spontaneously diabetic rats and non-insulin dependent diabetics individuals should be carried out. For a while, the tea prepared from these plants should not be considered as substitute or adjunct to the conventional treatment of diabetes.

Acknowledgements

Research supported, in part, by CNPq and FAPERGS.

References

- Armitage, P. and Berry, G. (1987) *Statistical methods in medical research*. 2nd ed. Blackwell Scientific Publications, Oxford, pp. 186–196.
- Bansal, R., Ahmad, N., and Kidwai, J.R. (1981) Effects of oral administration of *Eugenia jambolana* seeds and chloropropamide on blood glucose level and pancreatic cathepsin B in rat. *Indian J. Biochem. Biophysics* 18, 377.
- Bramachari, H.D. and Augusti, K.T. (1961) Hypoglycaemic agents from Indian indigenous plants. *J. Pharm. Pharmacol.* 13, 381–382.
- Gerich, J.E. (1985) Sulfonylureas in the treatment of diabetes mellitus—1985. *Mayo Clin Proc.* 60, 439–443.
- Giri, J., Sakthidevi, T.K. and Dushyanthy, N. (1985) Effect of jamun seed extract on alloxan induced diabetes in rats. *J. Diab. Assoc. India* 25, 115–119.
- Handa, S.S. and Chawla Maninder, A.S. (1989) Hypoglycaemic plants—A review. *Fitoterapia* LX 3, 195–225.
- Ivorra, M.D., Payá, M. and Villar, A. (1989) A review of natural products and plants as potential antidiabetic drugs. *J. Ethnopharmacol.* 27, 243–275.
- Jain, A.K. and Shaw, B.P. (1987) Effect of herbal compound on maturity onset diabetes. *Ancient Sci. Life* VII 1, 12–16.
- Kedar, P. and Chakrabarti, C.H. (1983) Effects of jambolan seed treatment on blood sugar lipids and urea in streptozotocin induced diabetes in rabbits. *Indian J. Physiol. Pharmacol.* 27, 135–140.
- Kettelhut, I.C., Foss, M.C. and Migliorini, R.H. (1980) Glucose homeostasis in a carnivorous animal (cat) and in rats fed high-protein diet. *Am. J. Physiol.* 239, R437–R444.
- Kohli, K.R. and Singh, R.H. (1985) *Eugenia jambolana*: a plant drug with potential antidiabetic property (a review). *J. Sci. Res. Pl. Med.* VI, 21–28.
- Krall, L.P. (1985) Oral hypoglycemic agents. In: A. Marble, et al. (Eds.), *Joslin's Diabetes Mellitus*. Lea and Febiger, Philadelphia, p. 413.
- Nair, R.B. and Santhakumari, G. (1986) Anti-diabetic activity of the seed kernel of *Syzygium cumini* Linn. *Ancient Sci. Life* VI 2, 80–84.
- Ollin, B.R. (1990) *Facts and Comparisons*. J.B. Lipincott, St. Louis, p. 649.
- Palanichamy, S., Nagarajan, S. and Devasagayam, M. (1988) Effect of *Cassia alata* leaf extract on hyperglycemic rats. *J. Ethnopharmacol.* 22, 81–90.
- Rahman, A.U. and Zaman, K. (1989) Medicinal Plants with hypoglycemic activity. *J. Ethnopharmacol.* 26, 1–56.
- Ratsimamanga, A.R., Loiseau, A., Ratsimamanga-Urverg, S. and Bibal-Prot, P. (1973) Nouvelle contribution à l'étude de l'action d'un principe hypoglycémiant mis en évidence dans l'écorce jeune de *Eugenia jambolana* (Myrtacées) sur l'hyperglycémie provoquée du lapin normal et poursuite de sa purification. *C.R. Acad. Sc. Paris* 277 (20), 2219–2222.
- Schmid, H., Kettelhut, I.C. and Migliorini, R.H. (1984) Reduced lipogenesis in rats fed a high-protein carbohydrate-free diet. *Metabolism* 33, 219–223.
- Sepaha, G.C. and Bose, S.N. (1956) Clinical observations on the antidiabetic properties of *Pterocarpus marsupium* and *Eugenia jambolana*. *J. Indian Med. Ass.* 27, 388–391.
- Shrotri, D.S., Kelkar, M., Deshmukh, V.K. and Aiman, R. (1963) Investigation of the hypoglycemic properties of *Vinca rosea*, *Cassia auriculata* and *Eugenia Jambolana*. *Indian J. Med. Res.* 51, 464–467.
- Sigogneau-Jagodzinski, M., Bilbal-Prot, P., Chanez, M., Boiteau, P. and Ratsimamanga, A.R. (1967) Contribution à l'étude de l'activité hypoglycémiant et antidiabétique

- d'un principe extrait du Roitra de Madagascar (*Eugenia jambolana* Lamarck). *C.R. Acad. Sc. Paris* 264, 1119–1123.
- Srivastava, Y., Venkatakrishna-Bhatt, H., Gupta O.P., and Gupta, P.S. (1983) Hypoglycemia induced by *Syzygium cumini* Linn. seeds in diabetes mellitus. *Asian Med. J.* 26 (7), 489–491.
- Steinmetz, E.F. (1960) A botanical drug from the tropics used in the treatment of the diabetes mellitus. *Acta Phytotherapeutica* 7, 23–25.
- Teixeira, C.C., Blotta, R.M., Costa, A.P., Müssnich, D.G., Ranquetat, G.G. and Fuchs, F.D. (1992) Plants employed in the treatment of diabetes mellitus: results of an ethnopharmacological survey in Porto Alegre, Brazil. *Fitoterapia* LXIII (4), 320–322.
- Teixeira, C.C., Fuchs, F.D., Blotta, R.M., Knijnik, J., Delgado, I.C., Neto, M.S., Ferreira, E.M., Costa, A.P., Müssnich, D.G., Ranquetat, G.G. and Gastaldo, G.J. (1990) Effect of tea prepared from leaves of *Syzygium jambos* on glucose tolerance in nondiabetic subjects. *Diabetes Care* 13, 907–908.
- Teixeira, C.C., Fuchs, F.D., Ferreira, E.M., Lança, E.A. and Hassegawa, C.Y. (1988) Avaliação de efeito do chá de jambolão (*Syzygium cumini*) sobre a curva de tolerância à glicose em voluntários normoglicêmicos. *Proc. X Simpósio de Plantas Mediciniais do Brasil*, São Paulo, 40.
- Trinder, P. (1969) Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Ann. Clin. Biochem.* 6, 24–27.