Contraceptive Properties of Stevia rebaudiana

Abstract. *A water decoction of the plant* Stevia rebaudiana *Bertoni reduces fertility in adult female rats of proven fertility. The decoction continues to decrease fertility for at least 50 to 60 days after intake is stopped. The decoction did not affect appetite and apparently did not affect the health of adult rats.*

Stevia rebaudiana Bertoni (Compositae) is a Paraguayan weed which contains a surprisingly sweet principle called stevioside (*1*). It is prescribed by some Paraguayan physicians as a hypoglycemic drug (*2*), although the hypoglycemic effect has not been confirmed. Paraguayan Matto Grosso Indian tribes use *Stevia rebaudiana* as an oral contraceptive. Women daily drink a decoction in water from dry, powdered leaves and stems.

Virgin females and females of proven fertility (one litter) all belonging to the Dispert colony of albino rats were used to investigate the effect of a decoction of *Stevia rebaudiana* on fertility. This is a strain of rats derived from 28 years of inbreeding the descendents of one pair. At the start of the experiments the age of the rats ranged from 90 to 152 days and their average body weight was 250 g. In experiment 1 virgin females (age 90 to 100 days), were divided into two groups of 14 rats each. One group drank 10 ml of a 5-percent decoction daily and the other group served as the control. All of the rats received the same commercial poultry feed, and were housed individually in similar cages. To determine if the animals were experiencing regular estrous cycles, vaginal smears were taken daily in all experiments for 1 week before treatment started. After 12 days, the 28 females were mated with males of proven fertility. The decoction was continued daily throughout the 6-day mating period, but it was not available to the male rats. After a recovery period of 50 to 60 days during which rats did not receive the decoction, females of the experimental group were mated again under normal conditions.

In experiment 2, 14 female rats (age 140 to 152 days) were allowed to bear one litter. A week after the litter was weaned the females received the same dose of decoction for the same period of time as in experiment 1. They were then mated at random with males of proven fertility under the same conditions as above. Each female rat served as its own control. After a recovery period of 50 to 60 days without decoction, females of the experimental group were again mated.

In experiment 3, 14 female rats (age 102 to 114 days) were allowed to mate with males of similar age under normal conditions. A week after the litter was weaned (28 days after birth), the females were started with the same treatment as in experiments 1 and 2. After drinking the decoction for 12 days, they were mated under the same conditions as in experiments 1 and 2 with the same male that fathered their first litter.

Table 1. Fertility of female albino rats after drinking an aqueous extract of *Stevia rebaudiana*. Each group consisted of 14 animals. Those in experiments 2 and 3 were of proven fertility.

Group	Average age (days)	Pregnant rats (No.)	Total offspring (No.)	Fertility (%)
	Experiment 1			
Control	96	11	65	78
Experimental	98	3	17	21
Recovery mating*	153	4	21†	28
	Experiment 2			
Control	101	14	91	100
Experimental	146	4	22	28
Recovery mating*	196	6	32	43
	Experiment 3			
Control	108	14	86	100
Experimental	148	3	21	21

* Of experimental group. † One pup died, age 3 days; no abnormalities were observed.

Because of the lack of information concerning the amount of decoction that the Indians take, the calculations were made on the basis of our own experience acquired in northern Argentina with different weeds used as medicinals by the Indians. The Indians make a decoction with dry weeds (about 15 g) in water (about 300 ml)—or approximately 5 percent in weight of dry weed. If we consider that adult human females have an average body weight of 60 kg and drink daily a cup of decoction, a female rat weighing 0.250 kg should drink 1.25 ml (5 ml/kg) daily. We raised the dosage to eight times that quantity, or 10 ml per individual rat per day. The decoction was prepared daily by boiling the dry, powdered weed in water for 10 minutes and filtering after cooling. The decoction was administered orally by replacing the water bottles with small bottles containing 10 ml of the decoction. As fast as each rat finished the decoction (usually in about 20 minutes), the normal water bottle was replaced.

Data are presented in Table 1. Fertility percentages were calculated on the basis of the number of litters as compared to the total females in each group. Fertility was reduced 57 to 79 percent in female rats drinking the decoction as compared to rats drinking water. A reduction of 50 to 57 percent in fertility was still evident 50 to 60 days after intake of the decoction had ceased. In experiment 1, eleven of the young belonging to two different litters of the experimental group lost their tails between the 12th and the 15th day of life as if they suffered a dry gangrene without visible cause. This abnormality was not observed in subsequent experiments.

GLADYS MAZZEI PLANAS
Faculty of Chemistry, University of the Republic, Montevideo, Uruguay
JOSEPH KUĆ
Department of Biochemistry, Purdue University, Lafayette, Indiana 47907

References and Notes

1. M. Bridel and R. Lavieille, *Bull. Soc. Chim. Biol.* **13**, 636 (1931); *ibid.*, p. 781; H. B. Wood, R. Allerton, H. W. Diehl, H. G. Fletcher, *J. Org. Chem.* **20**, 875 (1955); E. Mossetig, U. Begliner, F. Dolder, H. Lichti, P. Quitt, J. A. Waters, *J. Amer. Chem. Soc.* **85**, 2305 (1963).
2. J. B. Aranda, Conferencia sobre el Caa Hee, Asuncion (1945); O. Miquel, *Rev. Fac. Agr. Vet. Asuncion* **9**, 9 (1964).
3. Supported in part by Purdue Agricultural Experiment Station grant 1246, Faculty of Chemistry (Uruguay), Fulbright Commission, and AID (Uruguay). Journal paper 3394, Purdue Agricultural Experiment Station.

16 August 1968; revised 24 September 1968

Activation of Hageman Factor by L-Homocystine

Abstract. L-*Homocystine activates Hageman factor, as demonstrated by its capacity to initiate clotting and to induce the evolution of plasma kinins. Perhaps, strategically located deposits of this amino acid are responsible for the unusual frequency of thrombosis in patients with homocystinuria.*

Homocystinuria is a rare metabolic disorder inherited as an autosomal recessive trait (*1, 2*) in which cystathione synthetase, an enzyme needed to convert homocysteine to cystathione, is lacking (*3*). As a result, homocysteine cannot be metabolized, and is excreted in the urine in the form of homocystine (*4*).