

## EVALUATION OF ACUTE ADMINISTRATION OF NATURAL PRODUCTS WITH POTENTIAL DIURETIC EFFECTS, IN HUMANS

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*In order to evaluate the potential diuretic effect of two natural products, *Elephantopus scaber* and *Alpinia speciosa*, a trial administration was carried out in ten healthy volunteers and the effects compared to the those of a placebo. The substances were given on different days, with a seven day interval between doses. The amount of substance administered to the subjects was five times the usual dose i.e. 7.5 g/100 ml and 0.8 g/100 ml respectively.*

*The following parameters were measured: urinary and plasma sodium, potassium, uric acid, calcium, phosphate, urea, creatinine. The subjects were also examined clinically and total urinary volume was assessed.*

*The only significant finding ( $p < 0.05$ ) was a slight diuresis with *Alpinia speciosa*, which also lowered the diastolic ( $p < 0.05$ ) and systolic ( $p < 0.01$ ) blood pressures. No effect on electrolytes or renal function parameters was observed, and this probably excludes any renal tubular or glomerular effect from these substances.*

Key words: natural products – diuretics – *Elephantopus scaber* – *Alpinia speciosa*

As a result of the large size of Brazil, and many different types of soil, Brazilian flora is very diverse. Many plants have been used medicinally by the general population, especially in underdeveloped inland regions, where access to health care centres is difficult. In order to evaluate the clinical and pharmacological effects of these substances, the Brazilian Government committee on Drugs developed a program of research at various major centres.

In this project, two plants that are popularly used as diuretics, *Elephantopus scaber* ("língua de vaca") and *Alpinia speciosa* ("colônia"), were studied in the Dept. of Nephrology of the Escola Paulista de Medicina.

### MATERIALS AND METHODS

Ten healthy volunteers were used for the experiment; five men and five women aged between 20 and 32 years old. They were each given three types of tea: placebo (water & vanilla), *Elephantopus scaber* (7.5 g/100 ml) and *Alpinia speciosa* (0.8 g/100 ml) with a seven day interval between each dose. These doses are

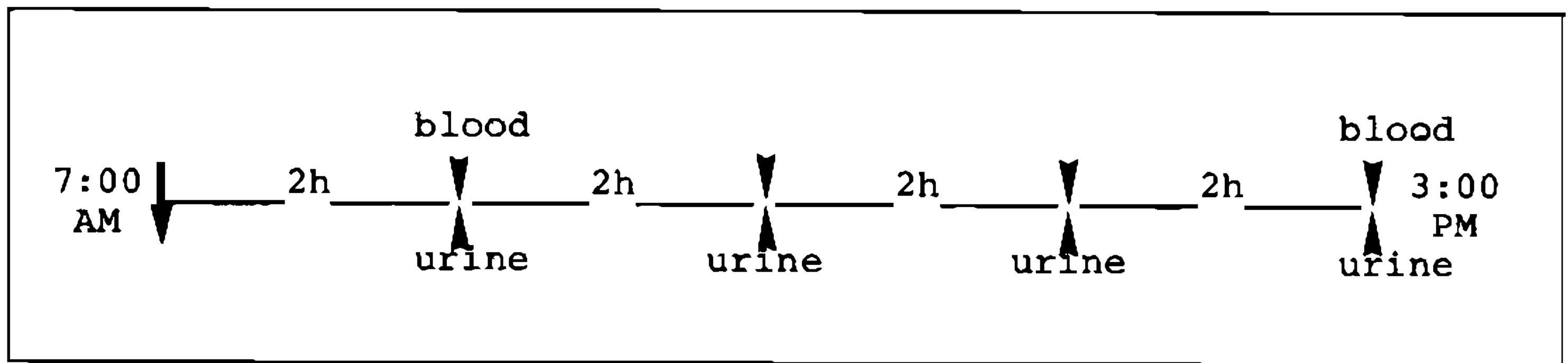
five times what is usually taken in general use. The subjects were not aware of which tea they were drinking.

*Volunteer exclusion criteria* – 1. The presence of chronic or acute diseases; 2. Use of drugs of medication; 3. Pregnancy or puerperium.

*Laboratory measurements* – 1. Plasma and urine creatinine using the alkaline picrate method by Jaffe's reaction (Mofate et al., 1954); 2. Plasma and urine calcium using a Perkin Elmer spectrophotometer model 290-B; 3. Plasma and urine phosphate by using Fisk & Sulbarow's methods (Fisk & Sulbarow, 1925); 4. Plasma and urine uric acid using Folin & Denis' methods as modified by Eichorn (Eichorn et al., 1967); 5. Plasma and urine sodium and potassium using a flame spectrophotometer model Pegasus II, Tecnow; 6. Urine sediment: red blood cells, leucocytes, casts, proteinuria and glycosuria.

Samples of blood were taken at the beginning and the end of the experiment and urine was collected at two hourly intervals according to the protocol (Fig.). Total urine volume was measured for each period.

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Protocol

The subjects arrived at the laboratory at 7.00 am where they remained, at rest, throughout the experiment. Fasting blood and urine samples were taken. Diet and water intake were standardized.

Two hour creatinine clearance was measured after ingestion of 300 ml of water. Following this, 300 ml of the 'tea' was given and the subject then had breakfast. This consisted of 200 ml of orange juice and a roll with unsalted butter. Lunch was rice, 2 g of salt, a 150 g steak, a portion of french fries, 200 ml of water and 50 g of chocolate.

#### RESULTS AND DISCUSSION

Diuretics are substances that increase the excretion of water and/or electrolytes. Thus, in order to study the diuretic effect of a substance, it is necessary to measure both the diuresis and the amount of sodium excreted.

Table I shows that the mean diuresis increased with the administration of *Elephantopus scaber* in the second period, but this increase was not statistically significant ( $p > 0.05$ ). However, the increase observed with the administration of *Alpinia speciosa* was significant ( $p < 0.05$ ). Moreover, the values return to control levels in the third period indicating a rapid but brief action with both species.

Table II shows the average plasma concentrations of sodium and potassium with their fractional excretions. No significant alterations in either Na or K levels were observed with the two substances.

Table III shows that no significant variation occurred in either plasma and urine calcium and uric acid levels, or in the fractional excretion of either substance. From this information we can discard the possibility of either of these having

a therapeutic effect in nephrolithiasis. Mean phosphate concentration and its fractional excretion did not change.

TABLE I

Diuresis (ml) in placebo, *Elephantopus scaber* (Es) and *Alpinia speciosa* (As) groups

Periods	Placebo	Es	As
1st	221 <sup>a</sup> ±40	211 32	255 40
2nd	340 36	435 33	462 <sup>b</sup> 47
3rd	167 26	157 24	132 16
4th	154 18	160 22	171 29
Total	882	963	1020

a:  $X \pm SE$ ; b:  $p < 0.05$ .

TABLE II

Plasma, Sodium and Potassium excretion and fractional excretions (FE) in the groups

	Placebo		Es		As	
	Pre	Post	Pre	Post	Pre	Post
Na <sub>p</sub>	142 <sup>a</sup> ±1	142 1	142 1	142 1	144 1	143 1
FE <sub>Na</sub>	.77 .14	.90 .10	1.05 .10	1.14 .10	.91 .14	1.11 .18
K <sub>p</sub>	4.1 0.1	3.9 0.1	4.1 0.1	3.8 0.1	4.0 0.1	3.9 0.1
FE <sub>K</sub>	16.0 6.8	9.4 0.8	7.8 1.5	9.9 1.3	7.6 2.0	10.6 1.7

a:  $X \pm SE$ ; Es: *Elephantopus scaber*; As: *Alpinia speciosa*.

TABLE III

Mean plasma Ca, P and uric acid measurements and fractional excretion (FE) in the groups

	Placebo		Es		As	
	Pre	Post	Pre	Post	Pre	Post
Cap	9.0 <sup>a</sup> ±0.1	9.1 0.1	10.0 0.1	8.9 0.1	8.9 0.1	8.9 0.1
FE <sub>Ca</sub>	0.43 0.06	0.82 0.14	0.59 0.10	0.96 0.16	0.73 0.12	1.04 0.18
P <sub>p</sub>	3.6 0.1	3.5 0.2	3.5 0.1	3.5 0.1	3.6 0.1	3.8 0.1
FE <sub>P</sub>	8.0 1.2	9.5 0.8	8.8 0.7	9.0 0.9	8.2 0.6	7.9 0.6
AcU <sub>rP</sub>	4.1 0.3	4.3 0.3	4.3 0.2	4.2 0.3	4.4 0.2	4.4 0.2
FE <sub>AcUr</sub>	7.0 0.9	9.8 1.1	7.7 0.8	10.2 0.5	9.2 1.0	9.6 1.0

a: X ± SE; Es: *Elephantopus scaber*; As: *Alpinia speciosa*.

Table IV shows the fall in systolic blood pressure from 105 mmHg to 97 mmHg that occurred with *Alpinia speciosa* (p < 0.05). A corresponding fall in diastolic BP of 10 mmHg was observed (74 mmHg to 64 mmHg) (p < 0.05). No significant change in cardiac rate was observed.

TABLE IV

Systolic and diastolic mean arterial pressure and heart rate (HR) in the groups

	Placebo		Es		As	
	Pre	Post	Pre	Post	Pre	Post
PA <sub>syst</sub> (mmHg)	102 <sup>a</sup> ±4	103 3	102 4	106 4	105 4	97 <sup>b</sup> 5
PA <sub>diast</sub> (mmHg)	77 3	74 2	75 3	70 2	74 <sup>b</sup> 3	64 <sup>b</sup> 4
HR (bet/min)	65 2	63 3	67 3	71 4	71 4	70 3

a: X ± SE; Es: *Elephantopus scaber*; As: *Alpinia speciosa*; b: p < 0.01, n = 10.

We also observed a tendency to drowse of the treated volunteers. This may be due to some depressor effect on the central nervous

system which may also be responsible for a slight decrease of the mean BP. However since it was not our objective to study this effect, we sent the species to the hypertension section of our division.

Mild wheezing was observed in one volunteer with *Elephantopus scaber*. This did not manifest itself clinically, but was observed on physical examination. The wheezing disappeared at the end of the experimental period without needing treatment.

Table V shows mean plasma urea and creatinine concentrations, creatinine clearance, and diuresis. No changes were observed in plasma urea, creatinine or creatinine clearance and hence no change in glomerular function occurred.

TABLE V

Mean plasma, creatinine and urea, creatinine clearance and diuresis (V') in the groups

	Placebo		Es		As	
	Pre	Post	Pre	Post	Pre	Post
Creat. Plasma (mg/dl)	0.75 <sup>a</sup> ±0.04	0.80 0.04	0.84 0.06	0.83 0.04	0.91 0.05	0.92 0.04
Cl <sub>creat</sub>	155 11	129 6	132 4	129 4	136 10	114 5
V' (ml/min)	1,8 0,3	1,8 0,2	1,8 0,3	2,0 0,2	2,1 0,3	2,1 0,2
Urea Plasma (mg/dl)	32 2	28 1	35 2	29 2	36 2	31 2

a: X ± SE; Es: *Elephantopus scaber*; As: *Alpinia speciosa*.

In summary, changes were observed with *Alpinia speciosa* which had a mild lowering effect on systolic, diastolic and mean blood pressure. We also detected a slight and momentary increase in diuresis with this substance. We did not observe any effect on electrolytes with either 'tea', excluding therefore, any tubular or glomerular effect.

REFERENCES

EICHORN, F.; ZILMANOUSKI, S.; PAUL, E.; RUTEMBERG, A. & FARRAS, B., 1967. Improvement

- of the uric acid determination by the carbonate method for serum and urine. *J. Clin. Pathol.*, 14: 450-460.
- FISKE, C. H. & SULBAROW, Y., 1925. Inorganic phosphate. *J. Biol. Chem.*, 63: 375-400.
- MOFATE, R. P.; COHN, C.; EICHEBBERGETR, L.; & COOPER, J. A. D., 1954. Symposium on azotemia. *Am. J. Clin. Pathol.*, 24: 511-571.