

Acute effects of the Paulinia Cupana, "Guaraná" on the cognition of normal volunteers

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The authors studied the acute effects of "Guaraná", when compared to caffeine and placebo, (double blind study) on cognition, anxiety and sleep in 30 normal volunteers. Although results were negative it cannot be concluded that "Guaraná" is harmless. Other studies shall be undertaken, administering "Guaraná" on a long term basis, as popularly proclaimed.

UNITERMS: "Guaraná" (*Paulinia cupana*), cognition, sleep, anxiety.

"Guaraná" (*Paulinia cupana*) is a typical Brazilian plant, very common in the Amazon river basin, Brazilian popular medicine attributes to the "Guaraná" preventive and healing powers

According to Nazario, 1989 (16):

"The long list of qualities (with no scientific evidence) includes contradictory virtues: it is proposed to control diarrhea and dysenteries as well as for constipation. Moreover, popular medicine propounds it for neuralgia, migraine, poor digestion, arteriosclerosis, hemorrhage, muscular pains, menstrual cramps, as sudorific, dietary, diuretic, cerebral stimulant, etc."

"Should all these physical effects not be sufficient, "Guaraná" is apparently also effective to reduce nervous depressions, recover optimism, develop greater mental fitness and avoid or retard fatigue".

"One more (questionable) virtue, highly praised by fans of the little fruit is its powerful aphrodisiac quality".

The anthropologist A. Henman, 1986 (13), in his paper on "Guaraná", describes how this plant used by the SATERÉ-MAUÉ Indians, presently living near the Marau and Urupadi rivers, in the Amazon, has had, for centuries, the repute of being stimulant, prophylactic, useful to treat some of their ailments; to be useful against headaches, fevers, cramps, reduce the effects of long fasting, and rendering the body light.

It is said that "Guaraná" enhances brain functions, increasing intellectual capacity. Many students take it in the form of pills, teas or syrups to remain awake longer when preparing for tests.

Regarding botanical classification, Pio Correa, 1984 (17), as well as Henman, 1986 (13) describe the "Guaraná" as pertaining to the Sapindaceae family, with two sub species: *Paulinia cupana* var. *sorhilis* and *Paulinia cupana* var. *typica*.

Chemically, "Guaraná" is characterized by its high content of the xanthic caffeine base, containing also, though in smaller quantities the bases theophylline and theobromine. It is known that these substances do not have a pharmacological action, which could explain all of the popularly alleged therapeutic effects. Indeed, the central stimulating effect of caffeine would not explain the majority of such effects (3). It further contains, high concentrations of polyphenols (tannins) ranging from 4 to 16%.

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In Brazil, until now, the scientific community does not seem to have focused on investigating our rich flora to confirm or not popular information.

The current study intended to verify the eventual acute effects of the "Guaraná" (*Paulinia cupana*) on cognition, anxiety and sleep of normal volunteers.

INDIVIDUALS AND METHODS

Ethics and criteria for inclusion

In order to avoid biased results, the following requisites were established as criteria for inclusion in this study:

- age ranging from 20 to 35 years;
- volunteers should not be under any kind of medication;
- minimum schooling : pre university graduates;
- not presenting any significant physical or psychic disorders.

The project was approved by the Commission for Ethics in Anima Nobili of the "Escola Paulista de Medicina" (São Paulo School of Medicine). All volunteers were aware of the study and signed a "Written Consent of Participation".

Details on the experimental groups

Three experimental groups were formed, each composed of 10 volunteers:

- Group I – Placebo
- Group II – Caffeine

A quantity of caffeine corresponding to the administered dose of "Guaraná". This group was needed to differentiate the effects on cognition, on anxiety and on sleep produced by "Guaraná" and by caffeine, should there be any.

- Group III – "Guaraná"

The utilized sample of "Guaraná" analyzed by "EMBRAPA- Empresa Brasileira de Pesquisa Agropecuária" (Brazilian Agency for Agricultural and Cattle Research) exhibited the following values:

Humidity	8.80%
Ashes	1.51%
Caffeine	2.10%
Tannin	16.00%

Volunteers of each experimental group under study took 2 capsules/day (in the morning and after lunch) for three consecutive days.

Each "Guaraná" capsule contained 500 mg of the substance in powder; capsules had 12.5 mg of caffeine,

corresponding approximately to the dosage of the same quantity of "Guaraná". The amount of caffeine ingested by the volunteers was monitored for three days before and during the testing period. Brown sugar was the placebo used as its color is similar to that of the "Guaraná" (500 mg/capsule).

The dosage of one gram per day of "Guaraná" was decided upon survey at the various laboratories that suggest an average of such dose/day.

Capsules were identical, as this was a "double blind" study, and the allocation of volunteers to each group under study was at random.

Evaluation Implements

1.Cognitive Evaluation

A simplified set of neuropsychological tests was applied to evaluate which cognitive aspects might change with the acute utilization of the substances being tested. Among these tests, the "Digit Span" was applied to evaluate immediate memory (21); "Free Recall" to measure short term memory (1); "Digit Symbol" to evaluate psychomotor performance and attention (8,11); "Cancellation Tests" to observe the pattern of awareness-attention (7) ; and the "Mosaic" test to assess visual-space organization (15).

2. Scale to evaluate sleep

A questionnaire was submitted to the volunteers to verify the eventual interference of the tested substance upon their sleep (4).

3. Scale to evaluate anxiety

The "State - Trait Anxiety Inventory " was applied (STAI) (20).

All evaluations are routine procedures at our Research Center (18,19).

Details on the experimental procedure

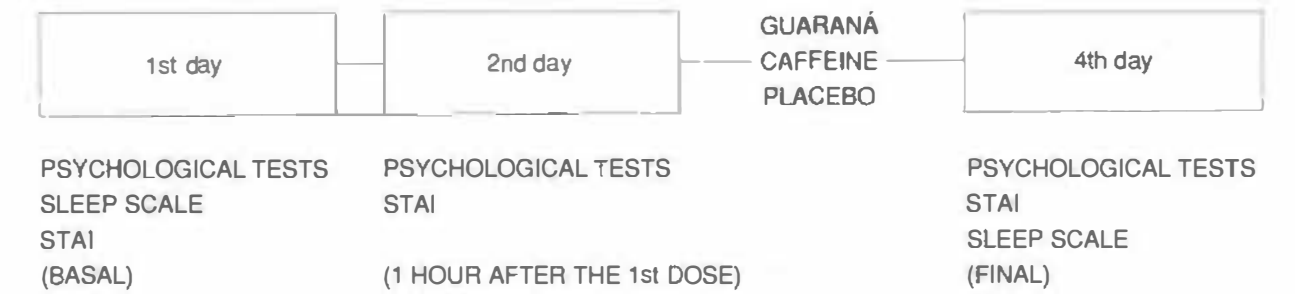
Each volunteer underwent a clinical evaluation, followed by the application of neuropsychological tests to determine the basal cognitive condition, therefore exempt from the action of any substance. Scales to measure anxiety and the sleeping pattern were also utilized.

On the following day, the volunteer ingested one of the three substances ("Guaraná", caffeine or placebo) and after one hour was submitted to the same array of tests, to evaluate the eventual immediate effects of "Guaraná".

On the fourth day of usage, they were submitted to a final re-test, following the same scheme as that of the second day (see Table 1).

Table 1
Scheme of the experimental procedure

Clinical Evaluation



STATISTICAL ANALYSIS

Non parametric analysis was used for the obtained data.

For independent samples the Kruskal-Wallis test was used and for the dependent ones the Friedman's test.

The adopted level of significance was $p < 0.05$.

The study was undertaken at the Clinical Psychobiology Research Center of the "Escola Paulista de Medicina" from April to August of 1991.

RESULTS

The selected sample presented the following demographic characteristics: median age of 28 years (24-35 years); 24 female volunteers (80%) and 6 males (20%); concerning schooling, 22 individuals (73%) were university graduates and 8 were not graduated; and finally 24 were single (80%) and six married.

Table 2 presents a synthesis of the obtained results.

Table 2
Synthesis of the cognitive evaluation of the 30 volunteers at the 3 stages of test applications

Results are presented as means of positive marks \pm standard deviation)

Cognitive tests / Stai	P ₁	P ₂	P ₃	C ₁	C ₂	C ₃	G ₁	G ₂	G ₃	Highest possible ranking for each test
Digit span	9.0 \pm 1	9.1 \pm 1.3	9.4 \pm 0.9	8.3 \pm 0.4	8.2 \pm 0.8	8.1 \pm 0.9	8.8 \pm 1	8.9 \pm 1	9.0 \pm 1	
Free recall	42.9 \pm 9	39.5 \pm 8	38.1 \pm 8	40 \pm 9	36.3 \pm 8	35.4 \pm 8	40.2 \pm 5	38.8 \pm 4	38.1 \pm 5	90
Digit symbol	57.4 \pm 9	60.0 \pm 6	62.0 \pm 4	55.5 \pm 5	61.3 \pm 5	63.0 \pm 4	50.9 \pm 9	56.0 \pm 9	60.1 \pm 6	67
Cancellation tests	57.6 \pm 11	62.0 \pm 12	63.7 \pm 14	56.0 \pm 10	58.6 \pm 8	63.8 \pm 9	58.0 \pm 6	56.9 \pm 6	61 \pm 6	112
Mosaic	46.5 \pm 5	48.6 \pm 1	48.1 \pm 1	47.8 \pm 3	48.3 \pm 3	49.5 \pm 1	42.3 \pm 7	44.1 \pm 5	47.4 \pm 3	50
Stai state	34.3 \pm 6	33.5 \pm 4	33.3 \pm 4	32.7 \pm 5	34.0 \pm 7	34.2 \pm 7	38.4 \pm 6	36.8 \pm 5	36.4 \pm 6	< 30 Low state of anxiety 30 - 40 Medium low 41 - 50 Medium high > 50 High state of anxiety

P₁ = Placebo
 C₁ = Caffeine
 G₁ = Guarana

P₂ = Placebo
 C₂ = Caffeine
 G₂ = Guarana

2nd evaluation
 (1 hour after ingesting the substance)

P₃ = Placebo
 C₃ = Caffeine
 G₃ = Guarana

None of the tests utilized to evaluate cognition showed a significant modification during the experiment, when matching the basal stage (exempt from substances) to the two following stages of re-testing. The same can be stated about the level of anxiety measured by the STAI State.

As for the STAI Trait no major differences were observed among the three groups (placebo $X = 34.9 \pm 7$; Caffeine $X = 36.2 \pm 8$ and "Guaraná" $X = 38 \pm 6$). Furthermore in none of the volunteers did the sleeping patterns suffer any changes during the days of the experiment, even though sleep induction (time to fall asleep), overall sleeping hours, night insomnia, presence of dreams and nightmares, morning sleepiness, etc. were also evaluated.

The spontaneous reports of three volunteers led to the observation of some curious aspects. One of the volunteers stated that the substance had produced a "greater fitness" and "well-being": he was given placebo.

Another female volunteer stated that diuresis had greatly increased, and afterwards it was observed that as she had great difficulty to swallow the capsules, she had ingested larger quantities of liquid: she was given caffeine.

And, finally, one volunteer reported on an "exceptional" sexual performance, during the days of the experiment: he was given placebo.

It is noteworthy that none of the participants mentioned any other effect.

DISCUSSION

Although results of the current study were negative some significant aspects are to be noted.

The first obvious question to be formulated is whether the utilized psychological tests could detect changes brought about by "Guaraná". It can be stated that these tests are widely employed in a great number of works, when studying the interference of drugs on cognition (14,19).

Another valid speculation is that: as all volunteers were young it would not be possible to further enhance their cognitive capacity as it was at its maximum. Indeed, the average performance at each test was near to the highest limit, however, none of the volunteers reached the peak in any of the tests, therefore, it can be stated that "they could still do much better and none of them reached the apex", about 50% as shown on Table 2. As a matter of fact, the answer to such question can only be found when the same experimental procedure will be utilized on normal elderly, who have a normal cognitive drop (6,12).

Another argument for the lack of positive results that might be used by the "Guaraná" defendants is that the dosage and the time period were insufficient. As for the chosen dose, it was based upon recommendations of several laboratories and also upon another pilot study undertaken in this department, where many people exhibited strong tachycardia after of 2 grams of "Guaraná" doses (unpublished data).

The short administration period of "Guaraná" might justify the lack of positive results, asserted by popular medicine. As such, it is an open issue and deserves further studies.

In the last 20-30 years the concept of adaptagenous or resistagenous" drugs has gained momentum, because of the extensive researches of Soviet, Japanese and other scientists, with different plants, especially, specimens of the Araliacal family. At first it was difficult to conciliate folklore information on the use of these vegetals with the observations of little or no effect, for studies were limited to the acute administration, conversely to the popular sayings (9,10), permitting to apply here the same reasoning for the "Guaraná"(5).

Only, since research has started to follow a different route, that is, not search for the acute effects in normal animals or in isolated functions, but prove the protection against aggressive agents, after long chronic or constant use, was it possible to record the typical effects of such plants and to separate a variety of their active principles (2).

Therefore to investigate if the "Guaraná" performs as an "adaptagenous" plant seems an urgent requirement, a question which could be answered some months from now. Such a research is being undertaken in this department.

Finally, we must never forget the "placebo effect", always quite important and often overlooked. In the current study, two volunteers (7%) reported propitious results, which at an early stage thrilled these researchers.

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RESUMO

A *Paulinia Cupana* (guaraná), é uma planta da flora brasileira que goza de grande prestígio na medicina popular. Dentre as características popularmente atribuídas a ela, citamos, a de ser potente estimulante das funções cerebrais.

Os autores avaliaram os efeitos da administração crônica da guaraná sobre a cognição de voluntários idosos normais.

Foram estudados 45 voluntários, sendo distribuídos aleatoriamente para um dos três grupos experimentais: Placebo (n=15), Cafeína (n=15) e Guaraná (n=15), em estudo duplo-cego.

Não se obteve nenhuma mudança significativa na cognição desses voluntários.