

## 13-Week Oral Toxicity of Guarana Extract in F344/DuCrj Rats

(Received April 1, 2005)

(Accepted June 3, 2005)

Seiko Tamano<sup>a)</sup>, Mayumi Kawabe<sup>a)</sup>, Yuriko Hatahara<sup>a)</sup>, Masashi Sano<sup>a)</sup>, Akihiro Hagiwara<sup>a)</sup>,  
Takayuki Fukumoto<sup>b)</sup>, Mikio Nakamura<sup>b)</sup> and Tomoyuki Shirai<sup>c)</sup>

a) DIMS Institute of Medical Science, Inc.

b) San-Ei Gen F.F.I., Inc.

c) Nagoya City University Graduate School of Medical Sciences

Department of Experimental Pathology and Tumor Biology

### Abstract

The potential toxicity of Guarana extract was investigated in groups of 10 F344 rats of each sex given solid diet containing the compound at 0.625, 1.25, 2.5 or 5.0% for 13 weeks. No toxicologically significant treatment-related effects were noted regarding clinical signs, survival rate, body weights, food consumption, food efficiency, urinalyses, hematology, blood biochemistry, ophthalmology and gross pathology.

Parameters that showed toxicologically significant alterations with Guarana extract treatment included the following: increased water consumption in the 2.5% or more females; increased salivary gland weights in the 5.0% males and females; increased incidences of an acinar cell hypertrophy in the submandibular and sublingual glands of the 2.5% or more males and females.

The present results indicated that the no observed adverse effect level for 13 weeks dietary treatment to be 1.25% (male: 940 mg/kg/day, female: 949 mg/kg/day) being in accord with 35 mg/kg/day of caffeine in both sexes.

**Key words:** Subchronic toxicity, Guarana extract, F344 rats

## I. Introduction

Guarana extract from the seed of *Paullinia Cupana* H.B.K. var. *sorbilis* (Mart.) Ducke, which grows in the Amazon region, is used as a supplement of a soft drink<sup>1-3)</sup>. The main constituents are caffeine, tunic acid, polyphenols and saponin and various physiological activities of Guarana extract have been reported, such as inhibition of obesity<sup>4, 5)</sup>, anti-stress effect<sup>6)</sup>, prevention of dementia<sup>7, 8)</sup>, inhibition of platelet aggregation<sup>9)</sup>, promotion of agglutinated platelet decomposition<sup>10)</sup> and inhibition of hypoglycemia<sup>11)</sup>. No adverse chronic toxicity was apparent in a study in mice<sup>12)</sup>, but genotoxic activity in aqueous extracts was found, related to the presence of a molecular complexes formed by caffeine and flavonoids (catechin or epicatechin) in the presence of potassium<sup>13)</sup>.

The toxicity of caffeine, a main constituent of Guarana extract, has been well documented and the acute oral LD<sub>50</sub> of caf-

feine is 200 mg/kg bw in rats<sup>14)</sup>. Caffeine has been shown to reduce food intake, body weight gain and thymus weights, and induce vacuolar degeneration of spermatogenic cells in male Sprague-Dawley rats given diet containing 0.5% (approximately 150 mg/kg bw) for 7 or 8 weeks<sup>15)</sup>. Increased salivary gland weights and acinar cell hypertrophy have been documented in rats given 110 mg/kg/day for 100 days<sup>14, 16)</sup>.

The present study was conducted to determine whether it might exert any toxicological effects in F344 rats in the 13-week oral toxicity study.

## II. Materials and methods

### 1. Test Chemical

Guarana extract was prepared by the following procedure. Grinded Guarana seed was extracted with acetone. After the ex-