

Herb Extract Ephedra Sinica Effect on Dipsogenesis is Dose-Dependent in Rats

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Abstract. Currently, many herbal compounds have been evaluated for use in weight loss diets. However is necessary to establish a link between the substance, regulation of nutrient metabolism and thirst mechanism by disease treatment. Analysis shows that significant decrease in food intake and body weight in animals treated with herb extract Ma Huang (*Ephedra sinica*) in 25-mg and 50-mg concentration per 100-g body weight per day. But the fluid intake is increased, even above the levels of control animals and tests, in treated groups in Ma Huang 100-mg per 100-g body weight per day, indicating that Ma Huang effects on dipsogenesis are dose-dependent. Ma Huang can change the thirst mechanism in rats. In herb extract Ma Huang concentration 100-mg per 100-g body weight per day can signal their toxic effects. Further studies are need for obesity on treatment with Ma Huang.

Keywords: *Ephedra sinica*, Thirst mechanism, Rat

INTRODUCTION - Many nutraceuticals and herbal compounds have been evaluated for use in weight loss diets in humans. Herb Ma Huang (*Ephedra sinica*) contains ephedrine alkaloids which, although not as potent as a central nervous system stimulant as the pharmaceutical products, is a useful herb for treating asthma, cough and wheezing and the misuse of this herb in dietary supplements for weight loss [5]. However, water is a vital nutrient in for body because it helps to keep the body temperature down, reducing sweating and dehydration, and

serves as a transport mechanism in the body by carrying nutrients. Thus, there is a need to establish a link between the regulation of nutrient metabolism [2] and water ingestion for obesity treatment. And in contrast to the numerous studies of meals, investigations of the control of fluid consumption in drinking bouts have been relatively sparse. Thus, in view of the complexity of the study of dipsogenesis, the objective of this work was to determine the possible alterations in dipsogenic responses associated with herb extract Ma Huang (curve dose-response), food intake and efficacy in weight loss in rats.

MATERIAL AND METHODS - The study was approved by institutional ethical committee (CEUA 2649). The experiments were carried out in groups of male Wistar Hannover rats with eight weeks of age (CEMIB-UNICAMP). The rats were housed under controlled climatic conditions, in accordance with current international bioethics and biosafety norms for animal experimentation and with the guidelines of the Brazilian College of Animal Experimentation (COBEA). By 5 days, at 9:00 a.m., each rat received by gavage with 3-ml vehicle (filtered water) in control group (n=10) vs. 25-mg, 50-mg or 100-mg herb extract Ma Huang (Pharma Nostra) per 100-g body weight per day [1] (dose-response curve) diluted in 3-ml vehicle (filtered water) in test groups (n=10). Were allowed free access to tap water and standard rat chow (Nuvilab Radiated - Nuvital Nutrientes S/A, Brazil) in assessment period.

RESULTS - In Ma Huang treated groups, the signs (is concentration independent) observed were increase in locomotor activity, piloerection, tachycardia and exophthalmia. But some of these signals are reported in the literature in humans [6] and the intake is associated with an increased risk of psychiatric, autonomic or gastrointestinal symptoms and heart palpitations. The Figure1 show water and food intake and body weight per 100-g body weight rats and curve dose-response. Mean \pm SD (ANOVA and t-test Bonferroni $*p \leq 0,05$):

- **Pellet earned in g**: - Control (9,1 \pm 0,7 in 24-h); (9,7 \pm 0,9 \pm in 48-h), (8,3 \pm 0,6 in 72-h), (8,5 \pm 0,8 in 96-h). - 25mg (5,4 \pm 0,3 in 24-h); (6,3 \pm 0,3 in 48-h), (6,4 \pm 0,3 in 72-h), (6,2 \pm 0,4in 96-h). -50mg (5,8 \pm 0,5 in 24-h); (4,9 \pm 0,8 in 48-h), (4,8 \pm 0,9 in 72-h), (5,6 \pm 0,9 in 96-h). -100mg (5,7 \pm 0,5 in 24-h); (5,4 \pm 0,4 in 48-h), (5,6 \pm 0,5 in 72-h), (6,3 \pm 0,9 in 96-h).

- **Water intake in ml** : - Control (9,1 \pm 0,7 in 24-h); (10,7 \pm 0,7 in 48-h), (9,7 \pm 0,3 in 72-h), (10,2 \pm 0,6 in 96-h). - 25mg (7,6 \pm 0,4 in 24-h); (8,4 \pm 0,5 in 48-h), (8,4 \pm 0,3 in 72-h), (8,8 \pm 0,2 in 96-h). -50mg (6,0 \pm 0,6 in 24-h); (6,3 \pm 0,9 in 48-h), (6,6 \pm 0,4 in 72-h), (6,8 \pm 0,4 in 96-h). -100mg (12,6 \pm 0,8 in 24-h); (12,9 \pm 0,9 in 48-h), (12,0 \pm 0,7 in 72-h), (12,7 \pm 0,9 in 96-h).

- **Body weight per 100-g**: - Control (1,9 \pm 0,5 in 24-h); (1,7 \pm 0,4 in 48-h), (1,8 \pm 0,3 in 72-h), (1,9 \pm 0,5 in 96-h). - 25mg (0,9 \pm 0,1 in 24-h); (0,8 \pm 0,0 in 48-h), (1,0 \pm 0,1 in 72-h), (1,0 \pm 0,0in 96-h). -50mg (-2,1 \pm 0,7 in 24-h); (-0,2 \pm 0,2 in 48-h), (-0,9 \pm 0,7 in 72-h), (-0,5 \pm 0,3 in 96-h). -100mg (-2,4 \pm 0,8 in 24-h); (-1,9 \pm 0,1in 48-h), (-2,1 \pm 0,4 in 72-h), (-1,0 \pm 0,4 in 96-h).

DISCUSSION - Analysis shows that significant decrease in food intake in animals with herb extract Ma Huang treated and promote a small short-term weight loss is proportional to the increase of the concentration (mg) herb extract Ma Huang ingested, as literature reported [4]. The biological effect promoted by administration of herb extract Ma Huang can involve the leptin that reduces the ingestion for the reduction of others orexins peptides or to increase thermogenesis and quench appetite [3]. What should be considered, the effective concentration when combined with thirst mechanism results in rats. Because the decrease in water intake accompanies the food behavior in concentration 25-mg and/or 50-mg per 100-g body weight per day; but, surprisingly, the fluid intake is significantly increased, even above the levels of control animals and tests, in treated groups in herb extract Ma Huang 100-mg per 100-g body weight per day. Herb extract Ephedra sinica is adrenergic stimulants that may have three modes of action: direct interaction with specific receptors, and/or indirect action by stimulating release of neurotransmitters, and/or a mixed action involving both. Still, for thirst, the excitatory signals that initiate a drinking bout are established: increased systemic plasma osmolality, decreased plasma volume, and increased blood levels of angiotensin II (Ang II), or some combination of the three. Initially, the Ma Huang can stimulates the central nervous system including hypothalamus and cell bodies in area express high concentrations of Ang II receptor type 1 (AT₁), which respond rapidly to an AngII stimulus and enhanced dipsogenic effect [9] by in 100-mg concentration herb extract Ephedra sinica. The paraventricular and the supraoptic nucleus are considered osmoregulatory centers and the vasopressin sends signals (V1 receptors) to hypothalamus directly or indirectly to stimulate the production of corticotropin-releasing hormone for the hypothalamic neurons [7]. In any case, herb extract Ephedra sinica can activate the hypothalamic-pituitary-adrenal axis through primarily central mechanisms, i.e. those that involve the paraventricular nucleus and/or its afferents, as also for other brain areas potentially involved in a variety of neuronal responses and behaviors [8]. The increase or the decrease of the water ingestion can suggest that the interaction of herb extract Ma Huang with the osmoreceptors is dose-dependent. Thus, herb extract Ephedra sinica can change the thirst mechanism in rats and, on the other hand, in 100-mg per 100-g body weight per day can signal their toxic effects [1].

CONCLUSION - Further investigations on association on cell signaling pathway relating leptin and Ang II hypothalamic receptors and toxicology and pharmacophysiology studies are need for herb extract Ma Huang use obesity treatment.

**TIME-RESPONSE CURVES FOR DIFFERENT DOSES OF EPHEDRA SINICA
IN REGARD TO WATER AND FOOD INTAKE AND BODY WEIGHT IN RATS**

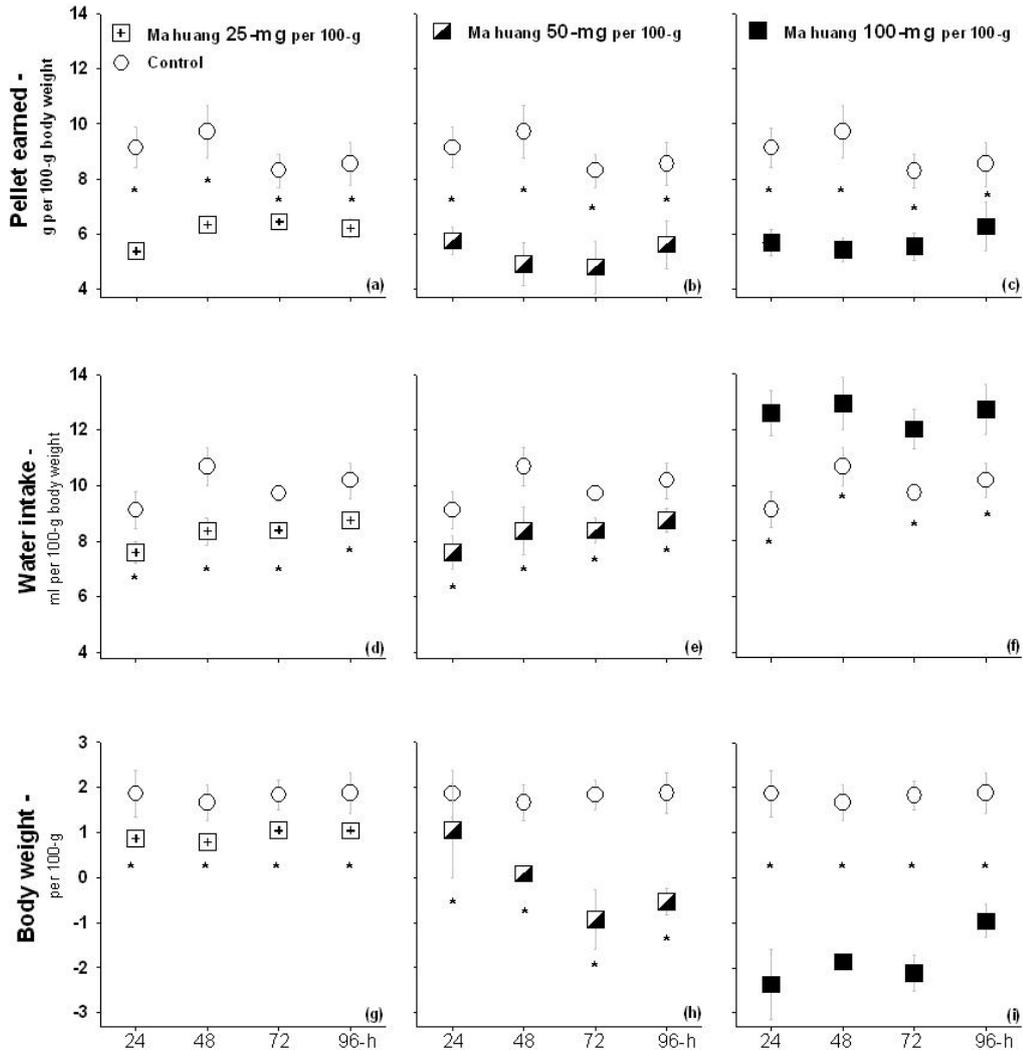


FIGURE 1 – TIME-RESPONSE CURVES FOR DIFFERENT DOSES OF EPHEDRA SINICA IN REGARD TO WATER AND FOOD INTAKE AND BODY WEIGHT IN RATS. Comparisons were made between vehicle in control group (n=10) vs. 25 mg, 50 mg or 100 mg Ma Huang herb extract in test groups (n=10), with measurements recorded at 24 h, 48 h, 72 h, and 96 h, and expressed in milliliters and/or grams per 100 grams body weight of rats. Statistical analysis of the data was performed using one-way analysis of variance (ANOVA) for repeated measures and Bonferroni's *t-test* to determine differences between the groups of animals. A *p* value ≤ 0.05 (*) was considered to indicate significance.

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Received: March, 2012