

EFFECTS OF MULUNGU (*ERYTHRINA MULUNGU*) AND NRG® (HERBALIFE) IN THE BEHAVIORAL PROFILE AND WEIGHT OF WISTAR RATS

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ABSTRACT

Erythrina mulungu (EM) is a Southern Brazilian plant commonly used in folk medicine as sedative, hypnotic, hypotensive, analgesic and as anti-convulsivant. NRG® (HERBALIFE) is a commercial product that contains maltodextrin, black tea, guarana, and caffeine, and its use is to increase metabolism rate and caloric burns and thus helps to lose weight. The lifestyle of modern societies leads people to seek alternatives to weight loss and, on the other hand, lead to the need to consume products that reduce anxiety. For this reason, the aim of this study was to compare the effects of EM and NRG® on the behavior and nutritional status of Wistar rats. After approval by the Ethics Committee, thirty male Wistar rats were divided in G1 (Control group that received water and feed *ad libitum*), G2 (Group treated with *Erythrina mulungu* solution (1g of EM extract/200mL of water) and rat feed *ad libitum*), and G3 (Group treated with NRG® solution (1g of NRG® powder/200mL of water) and rat feed *ad libitum*). After forty days, animals performed the Elevated Plus Maze (EPM) to the evaluation of anxiety. Body weight was evaluated every 7 days. Our results showed no significant differences among the groups when performing the Elevated Plus Maze but G2 and G3 increased body weight at the end of the experimental protocol. Substances commonly used by the population for specific purposes does not always produce the expected results as they may not have the quality needed to present the effects shown in the literature. Our data show that the two products did not produce significantly different behavioral effects in the animals. In addition, substances that claim to reduce anxiety like EM or that are used as thermogenic should not increase weight gain in animals that received the same amount of food.

KEYWORDS: *Erythrina mulungu*; NRG®; behavior; weight, rats.

INTRODUCTION

Many drugs may be used for treating anxiety. Nevertheless, they are linked to a plethora of side effects such as addiction liability, potentiation of other central depressant drugs and psychomotor impairment. For these reasons, several plants have been studied in order to identify new possibilities to treat anxiety once they are easier to obtain, have substantially lower costs and are associated with fewer side effects.^[1,2]

Erythrina mulungu (EM) is a Southern Brazilian plant that belongs to the family Leguminosae, genus *Erythrina* that is commonly used in folk medicine as sedative, hypnotic, hypotensive, analgesic and as anti-convulsivant. This medium-sized tree is mainly found in

tropical regions, its effects may be promote by alkaloids, and steroids present in the seeds and barks.^[1,3,4]

Studies have shown that EM possesses anxiolytic effects in acute or chronic doses both in human and animal models. Interestingly is that these effects are not associated with motor abnormalities. Volunteers that participated in a study with EM did not present motor impairment, and the only side effects found by the authors was drowsiness. The maintenance of motor reflexes is an important advantage of substances with anxiolytic effects once benzodiazepines for example, may lead to motor disorders.^[1,5-7]

NRG® (HERBALIFE) is a commercial product that contains maltodextrin, black tea, guarana, caffeine,

flavoring and acidulant citric acid. The manufacturer of this product points out as advantages of its use the increase in the metabolism rate because it increases the caloric burning and thus helps to lose weight, stimulates the state of alertness and concentration, and it has antioxidants that diminish the oxidative stress. The product also aims to minimize motor and psychic fatigue through its components, such as caffeine. Caffeine acts directly on the central nervous system, altering the basal metabolism and stimulating the production of gastric juice. Tea is also source of catechins that belong to a family of chemically related compounds usually classified as antioxidant molecules.^[8-11]

The lifestyle of modern societies leads people to seek alternatives to weight loss and, on the other hand, lead to the need to consume products that reduce anxiety. For this reason, the aim of this study was to compare the effects of EM and NRG® on the behavior and nutritional status of Wistar rats.

METHODS

Ethical principles

This study was approved by the Animal Research Ethics Committee of the Medical School of Marília (UNIMAR), Marília – São Paulo, Brazil. Animals were cared for according to the recommendations of the Canadian Council's "Guide for the care and use of experimental animals".

Animal Groups

Thirty Wistar rats, with a mean weight of 193.7g, were obtained from the Animal Experimentation Center (CEMA) / University of Marília (UNIMAR), Marília – São Paulo, Brazil. Prior to the experimental protocol, all animals were acclimated for seven days to laboratory conditions and divided into three groups (n=10) G1, G2 and G3. Rats were maintained in plastic boxes (40x30x17cm) in a room with temperature (20 ° C - 25 ° C) and light/dark cycle of 12 hours (5 animals/box). The treatment lasted 40 days and was performed according to the following:

- G1: Control group that received water and feed *ad libitum*;
- G2: Group treated with *Erythrina mulungu* solution (1g of EM extract/200mL of water) and rat feed *ad libitum*;
- G3: Group treated with NRG® solution (1g of NRG® powder/200mL of water) and rat feed *ad libitum*.

Both EM and NRG® were obtained from local markets in the city of Marília – São Paulo – Brazil.

The animals were weighed weekly and at the end of four weeks, the rats were submitted to the Elevated Plus Maze (EPM) test for evaluation of the behavior. In the 41^o day of the experimental protocol, the animals were euthanized with a lethal intraperitoneal injection of thiopental (200 mg/Kg).

Behavioral test

The Elevated Plus Maze was performed for behavioral assessment in order to evaluate the anxiety index in rats from the control group (G1) and treated groups according to Boerngen-Lacerda et al.^[12] and Blanchard et al.^[13] The structure of this apparatus is wood maden and stands 50 cm from the ground. It possesses two open and opposed arms (50x10 cm), two enclosed arms (50 x 10 x 40cm), platforms with the same extent of the open arms that cross them perpendicularly, enclosing a central area of 10 cm². The animals of the 3 groups (G1, G2 and G3) were placed in the apparatus for 5 minutes and frequency and time spent in the center, open and closed arms were evaluated.

Statistical analysis

For the Statistical analysis, Kruskal-Wallis and Dunn test were performed. Variables were presented as mean and standard deviation, adopting a 5% level of significance.

RESULTS

Our results show that there are not significant differences among the 3 groups (G1, G2 and G3) in the time and frequency spent in the EPM (Figure 1 and Figure 2).

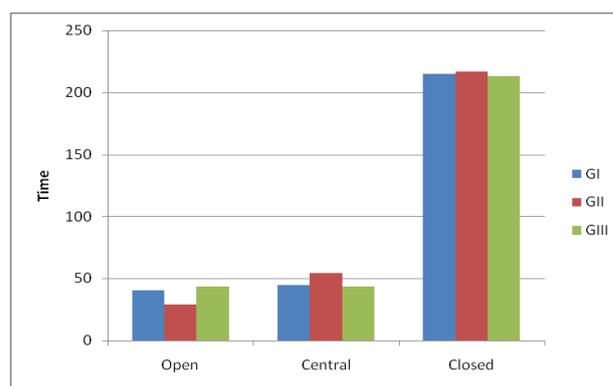


Figure 1: Time spent by the animals from G1 (control group), G2 (group treated with *Erythrina mulungu*) and G3 (group treated with NRG®) in the open, central and closed areas of the Elevated Plus Maze.

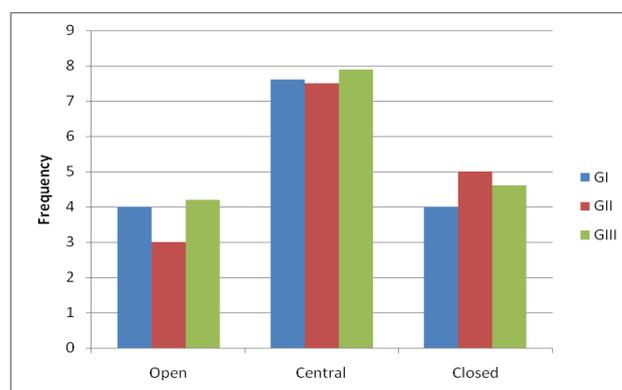


Figure 2: Frequency spent by the animals from G1 (control group), G2 (group treated with *Erythrina mulungu*) and G3 (group treated with NRG®) in the open, central and closed areas of the Elevated Plus Maze.

In Figure 3 it is possible to see that both treatments increased the body weight of the animals. This figure only shows the results of the weight obtained in the first day, after 20 days and at the end of the experimental protocol.

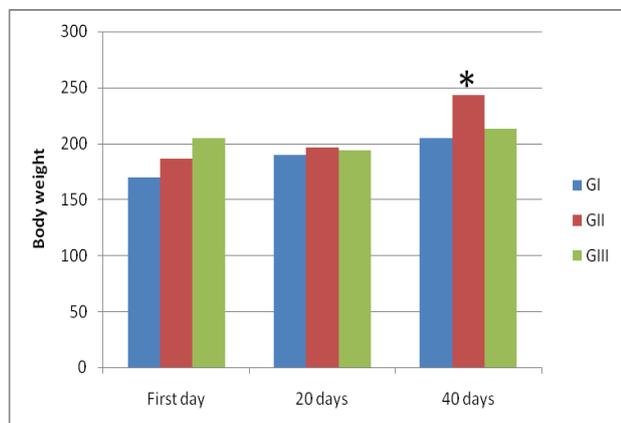


Figure 3: Body weight of the animals from G1 (control group), G2 (group treated with *Erythrina mulungu*) and G3 (group treated with NRG®) obtained on the first day, after 20 days and at the end of the experimental protocol.

DISCUSSION

The root of anxiety comes from a reaction of defense of the animals in response to the dangers found in their environment when there is a threat to their well-being, physical integrity, or survival. Due to this, the animal may exhibit a series of behavioral and neuro-vegetative responses, which are characterized by fear reaction. The EPM is a model widely used in the study of anxiety and to evaluate psychomotor performance and emotional aspects of rats. The behavioral profile that animals present in the EPM depends on several factors to which these animals are submitted but normally the rat without treatment remains longer time in the closed arms because it represents an exposition to natural threatening situation what makes them to avoid exploring open areas. Closed areas work as a safe place to the animal for example, to avoid the presence of predators. The use of substances that diminish anxiety patterns makes the animal feel calmer and consider the environment less threatening.^[14-17] However, our results with the use of EM did not significantly differ from the control group.

Anxiety is a common pathology that can affect millions of people around the world. It possesses neurobiological, cognitive, and behavioral aspects, and is considered as a negative emotion that may appear as a result to perceived threats deriving from internal or external sources. Many authors have shown that EM anxiolytic effect without significant changes in physiological parameters and point it may be used to control the anxiety in adult patients and animals.^[1,2,18-20]

The effects of EM in the anxiety are probably due to the presence of alkaloids (+)-alpha-hydroxy-erysotrine,

erythravine and (+)-11alpha-hydroxy-erythravine that were isolated from the flowers. These substances also promote an antagonist effect of $\alpha 4\beta 2$ nicotinic receptors.^[21-23] Santos-Rosa *et al*^[24] isolated the alkaloid erysotrine from the hydroalcoholic extract of EM flowers and found that the administration of this compound inhibited seizures evoked by bicuculline and kainic acid. This compound also lead to the increase in the frequency but not in the time spent in the open arms of the EPM. These authors did not find modifications in the GABA or glutamate synaptosomal uptake and binding and concluded that this alkaloid may have induced to a mild anxiolytic effect that does not modify the general behavior of the animals.

Despite possessing caffeine, the use of NRG® did not interfere in the pattern of anxiety of the studied animals probably due to the amount of this compound in the product. This substance is the most consumed psychostimulant in the world. Anxiogenic effects of caffeine is shown by several studies with human and animal models.^[25-27]

Literature also shows many studies showing that caffeine may be effective in reducing and maintain body weight. It may be an adjuvant in the weight loss because it can interfere with the energy balance because it has a potential in increasing the energy expenditure. Caffeine also may increase the thermogenesis and fat oxidation.^[28-30] We did not find studies showing the effects of EM on the body composition of Wistar rats.

Our results show that although several products are sold in Brazilian markets, consumer should be aware of the quality and ANVISA (National Health Surveillance Agency) approval once these products may not lead to the desired effects due to the presence of undeclared pharmaceutical drugs that can be harmful for the health in a short or long period of use.

CONCLUSION

Substances commonly used by the population for specific purposes does not always produce the expected results as they may not have the quality needed to produce the effects shown in the literature. Our data show that the two substances did not produce significantly different behavioral effects in the animals. In addition, substances that claim to reduce anxiety like EM or that are used as thermogenic should not increase weight gain in animals that received the same amount of food.

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