Original Article

Behavior of rats treated with Rhus toxicodendron 200cH

Marcos Paulo da Silva Rocha[1] ; Fernanda Martins Soares[1] ; Lucienne Colombo Martini(PhD)[1]; Leoni Villano Bonamin(Vet MD DSc)[1,2]

[1]Universidade de Santo Amaro, SP, Brazil; [2]Universidade Paulista, SP, Brazil

ABSTRACT

One of the main pathogenetic characteristic of Rhus toxicodendron (Rhus-t) is the presence of articular pain and aggravation on standing, which improve only by motion. The present study proposes an experimental model to evaluate the action of Rhus-t 200cH. Rats were divided into 3 groups according to treatment received (Rhus-t, diazepam and water); each group was further divided into two sub-groups according to the initial pattern of behavior (hyperactive and hypoactive) as assessed by open-field procedure. A second evaluation of behavior performed 24 hours later pointed out to the effects of the medications under study. Results were analyzed through Kruskal-Wallis/Dunn's test, with a level of significance $p \leq 0,05$.

Keywords: Rhus toxicodendron; Animal behavior; Open-field; Idiosyncrasy

Introduction

Native to North America, Toxicodendron radicans (L) Kuntze (poison ivy) supplies one of the most valuable remedies employed by North-American Indians [1]. A climbing vine belongs to the Anacardiaceae, it may also be found in humid areas in the south of France. To prepare the mother tincture of the homeopathic remedy Rhus toxicodendron (Rhus-t) it is employed a brown-yellowish sap, of a sharp and caustic odor, distributed all through the plant. The leaves have a higher content of this sap and the optimal time to collect them is in May[2]). The main active principle is urushiol[3].

The homeopathic pathogenetic trial shows that Rhus-t has a inhibiting action, provoking prostration and stupor[2]. Furthermore, it has significant action on fibrous tissues: joints, tendons, aponeurosis[4]. It is indicated in patients presenting rheumatic symptoms, with pain arising from aponeurosis, especially when triggered by stress[2]. A peculiar trait is the amelioration of muscle and bone lesions by motion, a characteristic strongly associated to Rhus-t idiosyncrasy[1].

The aim of the present study was to evaluate the effects of Rhus-t 200cH on the general behavior of rats on open-field taking into account possible variations according to the idiosyncratic characteristics of the animals regarding ambulation, in accordance with the materia medica of the remedy.

The effects were compared to the ones elicited by diazepam, a benzodiazepine with anxiolytic effects well characterized in the open-field procedure[5].

Materials and methods

Male Wistar rats, mean age 8 weeks, supplied by Unitox-Royal were employed. Animals were lodged in polypropylene cages, kept in a room under controlled temperature (22±2 ºC) and humidity (50-70%) conditions. A 12-hour light cycle was kept (light was turned on at 6:00 am and turned off at 6:00 pm); water and food were supplied ad libitum all through the study.

Open-field as described by Broadhurst[6], is composed of a wooden circle divided into three colored concentric circles, divided by segments of line forming quadrants of equal area. Animals were individually exposed to the open-field and their behavior was observed for 5 minutes from the moment the animals were put at the center of the field. Analysis of behavior took into account the following parameters: 1) frequency of locomotion (ambulation) – number of squares penetrated by the experimental subject with all 4 legs; 2) grooming time – motions directed to the head or the body with the front legs; 3) rearing - number of times the experimental subject removes the front legs from

the open-field and stands exclusively on the rear legs; 4) immobility time – amount of time the experimental subject remains motionless; 5) defecation – number of fecal boli in the 5-minute observation period. Between individual tests, the open-field was cleaned with a piece of cloth imbibed in 20% alcohol and dried with a dry piece of cloth, allowing some minutes for air circulation.

After the evaluation of initial behavior, frequency of ambulation was employed as criterion to divide sub-groups. From each group of 16 animals, 8 rats that ambulated the largest number of quadrants was called "hyperactive", while the other 8 rats with the lowest number of quadrants was called "hypoactive". Thus, each experimental group was composed of 50% hyperactive and 50% hypoactive animals, and received a specific treatment: Rhus-t 200cH, diazepam (Hipolabor®) 2mg/kg or distilled water (control).

Rhus-t was prepared according to the Brazilian Homeopathic Pharmacopoeia, 2nd edition [7], prepared until 198cH in 70% alcohol. The last 2 dilutions (199cH and 200cH) were prepared on the day of the test, employing water as solvent. Rhus-t 200cH was added to the drinking water (1:500) for 23 hours before the second open-field observation. The remedy was given again 30 minutes before the test by oral gavage 0.1mL/100g. Diazepam was given oral gavage 2.0mg/kg/100g body weight 30 minutes before the test. Animals in the control group took distilled water oral gavage 0.1mL/100g 30 minutes before the test.

Kruskal-Wallis' method followed by Dunn's mean test was applied to each parameter. Experimental groups and sub-groups were compared. Significance was established at $p \leq 0,05$

The experimental protocol was approved by the committee of ethics in research of UNISA, No. 081/2007.

Results

Hyperactive animals treated with Rhus-t 200cH and diazepam showed a statistically significant reduction ($p=0.02$) in locomotion on the second open-field observation when compared to the initial behavior. The animals in the control group showed no difference. No difference was also shown by the hypoactive animals in any group. (Figure 1) None of the other open-field parameters showed any significant difference. (Table 1)

The comparison between locomotion and immobility showed complementary results in all groups and sub-groups, although the latter did not show statistically significant differences.

Regarding the number of fecal boli after each open-field session, animals treated with diazepam presented a light increase in the second observation (after treatment) independently from the sub-group they belonged to, (Table 1) confirming thus data reported in literature[8].

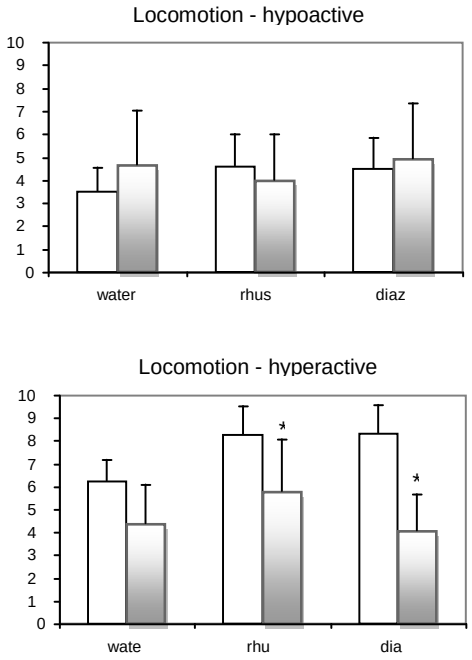

Figure 1: Total locomotion open-field observation (in numbers of squares) of subjects classified as hypoactive and hyperactive according to initial observation (first observation: white columns). Total locomotion after treatment (color columns). rhus: Rhus-t 200cH; diaz: diazepam. *p=0.02 regarding first observation.

Discussion

Controlled experimental trials conducted with Rhus-t are the subject of recent studies, however reports on experimental models focused on the behavioral aspects of this remedy are few[9,10].

The evaluation of motor behavior in open-field is widely employed by physiologists, pharmacologists and psychologists to assess the effects of pshychotropic or drugs acting on the nervous system[8]. The choice of a classic method to observe the effects of Rhus-t 200cH was grounded on the need to employ well defined and well known parameters in order to consolidate the construction of a new experimental model.

On the basis of the materia medica of Rhus-t, animals in the hyperactive group – i.e. those that showed higher spontaneous agitation on the initial open-field session – would supposedly be more responsive to a treatment with this remedy, when compared to the hypoactive group. Homeopathic remedies are known to act through similarity, depending on the idiosyncrasy of both remedy and experimental subject[11]. The results seen in the

parameter locomotion in this study agree with this hypothesis.

Table 1: Measurement of open-field parameters (rearing, grooming, immobility and defecation) in the different groups and sub-groups before and after treatment. Values expressed in mean and standard deviation. Kruskall-Wallis.

Rearing	Before		After	
	mean	SD	mean	SD
Hypoactive				
Control	9.25	3.73	8.62	5.44
Diazepam	15.37	11.07	10.62	9.27
Rhus-t 200cH	10.87	5.74	15.37	13.97
Hyperactive				
Control	14.50	6.48	7.75	6.84
Diazepam	21.00	6.04	14.62	15.62
Rhus-t 200cH	24.75	15.33	18.75	7.92

Grooming	Before		After	
	mean	SD	mean	SD
Hypoactive				
Control	7.77	8.34	9.53	9.50
Diazepam	8.85	16.62	9.99	5.44
Rhus-t 200cH	8.43	23.66	4.22	5.86
Hyperactive				
Control	6.90	8.59	13.38	12.67
Diazepam	9.53	7.89	11.79	12.67
Rhus-t 200cH	5.87	10.74	6.01	6.85

Immobility	Before		After	
	mean	SD	mean	SD
Hypoactive				
Control	28.86	32.15	28.62	20.38
Diazepam	30.65	37.40	16.33	1.28
Rhus-t 200cH	23.08	27.99	51.76	56.01
Hyperactives				
Control	18.05	19.45	46.76	44.24
Diazepam	2.24	4.19	58.36	50.08
Rhus-t 200cH	3.25	4.68	21.99	18.90

Defecation	Before		After	
	mean	SD	mean	SD
Hypoactive				
Control	3.00	2.50	0.87	1.24
Diazepam	1.87	3.56	2.75	3.15
Rhus-t 200cH	1.75	3.01	2.50	2.13
Hyperactive				
Control	3.25	2.49	1.25	2.37
Diazepam	1.25	1.83	2.75	3.69
Rhus-t 200cH	4.62	3.02	4.12	4.05

On the other hand, the discrete action of diazepam in this study might have been caused by a limited absorption in the digestive tract. As it is known[12], diazepam is highly liposoluble and tends to accumulate in the adipose tissue which, by its turn, has an influence on its elimination half-life. However, the high liposolubility contributes to the drug lack of spontaneous solubilization in polar solvents[13]. Future studies employing other forms of solubilization may elicit more remarkable effects.

It is concluded that the proposed experimental design might be a useful tool in the evaluation of the effects of homeopathic remedies regarding changes in behavior and it shows the need to select subjects compatible to the principle of similarity for an adequate observation of the phenomena under study. Non compliance with this conceptual requirement might result in false negative outcomes[14].

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Correspondence author: Leoni Villano Bonamin; Universidade Paulista, Brazil; leonibonamin@gmail.com
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