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Research Article

Scientific Note on the Effect of Nutraceutical Containing Resveratrol Derived from *Polygonum Cuspidatum* on Male Wistar Rat: Behavioral and Immunological Aspects

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ABSTARCT

The use of nutraceutical based polyphenols showed an increase demands in consumers due to its health benefits. However, the side effects of these products are not overall known. In this work, males wistar rats were exposed to resveol, european nutraceutical containing resveratrol, at dose 30mg/kg for ten consecutive days showed antidepressant behavior and dysregulation in immune cell count. These results ensure behaviorally the positive impact of this nutraceutical on emotional state, on the other hand, the perturbation of immune count implies to do more studies in order to ensure its safety on immune response.

Keywords: Nutraceutical, resveol, resveratrol, behavior, immunity, rat

INTRODUCTION

Recently, Epidemiological studies determined a close link between plant derived food and health benefits, these benefits are mainly related to their containing on polyphenols compounds such as quercetin and resveratrol. Generally, Foods enriched with these molecules such as fruits and legumes are thought to improve status human health and delay the development of many diseases. However, their ingestion regularly and in significant amount plays an important role to exert noticeable physiological effects. In this respect and in addition to the increase of consumers demands, pharmaceutical industries opted to commercialized these health promoted food on galenic forms (solutions, softgels, pills,…etc) named nutraceuticals[1]. Resveratrol is among the bioactive molecules used in the industries and its content in nutraceuticals can be based exclusively on pure resveratrol such as resveol (www.nutrixeal.fr) or also combined with other polyphenols such as longevinex[2].

Resveratrol (RSV; trans-3,5,40-trihydroxystilbene) is a polyphenolic compound occurring naturally in various plants, including grapes, berries, and peanuts. It is produced in response to biotic stress and against damage from exposure to ultraviolet radiation[3]. A remarkable range of biological functions has been ascribed to this molecule. It acts as a cancer chemopreventive agent and as an antioxidant [4.5]. It also has been shown to be a powerful anti-inflammatory molecule in several inflammation models including arthritis, asthma, encephalomyelitis, atherosclerosis, and intestinal inflammatory diseases, among others[6.7]. Although current studies indicate that resveratrol produces neuroprotection against ischemia, seizure, Alzheimer's disease, Parkinson's disease, and Huntington's disease, the precise mechanisms for its beneficial effects are still not fully understood[8].

Besides the beneficial effects of resveratrol, its side effects are still unclear regarding the risk of high dose and the quality of the product. Furthermore, international regulations relating to human health require that all new pharmaceutical and nutraceutical products are tested for their safety [9]. With this respect, we attempted to examine the effect of european nutraceutical based resveratrol derived from *Polygonum cuspidatum*, resveol, on male wistar rat and whether the outcomes are similar to those know with resveratrol.

MATERIAL AND METHODS

Experimental protocol

Fourteen male Wistar rats obtained from Pasteur Institute (Algiers, Algeria) were housed in transparent cages at a constant temperature (23±1 °C) with a 12 h/12 h light/dark cycle (lights on at 07:30 a.m.). Rats had access to standard rodents chow and tap water ad libitum and weighing 250 ±10 g at the beginning of the experiment.

Resveol was purchased from Nutrixeal (Lyon, France). According to the bottle, recommended dose ranged from 100mg to 200mg per day. According to the translating dosing [10], this approximates from 10.24 to 20.54mg/kg in conditions when human weight corresponds to 60 kg and the rat weight corresponds to 150g. In our work conditions the rat of 250g implies 34,23 mg/kg of resveol for 200mg. In our experiment, 30mg/kg diluted in 1ml/kg of corn oil was tested and administered orally for 10 consecutive days, and then behavior testing was carried out, finally decapitation of the rat.

Behavioral test

Open field test

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The open field (OF) can be considered as a non-conditioned anxiety test based on the creation of a conflict between the exploratory drive of the rat and its innate fear of exposure to an open area[11]. The OF test was performed to measure changes in exploratory behavior and emotionality. Briefly, the apparatus consist of a gray square (70 cm x 70 cm x 40 cm) divided into 16 equal squares that had been drawn in the floor of the arena. Each rat was placed in the arena individually, and allowed to freely explore it for 5 min. Upon completing the task, the rat was removed from the arena by the experimenter and returned to the home cage. After each test, the apparatus was cleaned with an alcoholic solution followed by wet and dry paper towels to avoid transfer of olfactory cues between animals. Traveled distance was measured.

Table 1: Details of materials used

Name	Resveol
Source	Nuttrixeal,Lyon, France
Colour	Straw yellow
State	Softgel
Purity	100% extracted from
Ingredients	*Polygonum cuspidatum Each Softgel contains 100mg of transresveatrol,* extra virgin olive oil, glycerin, beeswax, purified water, non-GMO soy lecithin.

Table 2. Behavioral parameters

Behavioral parameters	Control	Resveol
Immobility time (s)	185,5±6.7	105,23±5.92 a***
Time spent in open arms (s)	55,14±3.02	55,26±.67
Time spent in closed arms(s)	204,14±12.13	200,22±9.3
Traveled distance (cm)	1148,8 ± 70	1120±20.3

(n=07, a: compared to control, *p<0.05, **p<0.01, ***p<0.001).

Elevated plus-maze test

The elevated plus-maze (EPM) test is a widely used paradigm to investigate anxiety-related behavior in rats[12].The EPM was made of painted wood cross (arms 50 cm long x 10 cm wide) elevated 50 cm above the floor. Two opposite arms were enclosed by walls (10 cm x 50 cm x 45 cm high) and two arms were open. The arms extended from a central platform (10 x 10 cm). The open arms in the maze that we use do not have a railing, but addition of a 3–5 mm high railing on the open arms of the plus maze has been used with success to increase open arm exploration. The rat was placed in the center of the apparatus facing one of the open arms, for a free exploration of 5 min. Entry into an arm was defined as the animal placing all four paws on the arm. After each test, the rat was returned to its home cage and the maze was cleaned with an alcoholic solution followed by wet and dry paper towels, prior to the next trial. Time spent in open and closed arm was measured.

Table 3. Immune cells count

Parameters	Control	Resveol
WBC (x10^3/ul)	7,495±0.29	12,265±1.84 a**
Lym (%)	69,45±0.79	63,97±2.26 a**
Neut (%)	24,92±1.36	30,55±5.38 a**
Mono (%)	3,75±0.2	7,15±0.12 a**
Eosino (%)	1,85±0.20	0,8±0.18 a**

(n=07, a: compared to control, *p<0.05, **p<0.01, ***p<0.001).

Forced swimming test

Forced swimming test was performed according to the protocol of Porsolt et al [13] .The rats were placed individually in glass aquarium (height: 54.0 cm; length: 34.0 cm; width: 30.0 cm) filled with water to a depth of 40.0 cm (24.0±1 C°). The procedure consists of a pre-swimming test and swimming test separated by 24h. During the pre-swimming procedure, rats were placed in the aquarium for 15 min and then were removed from the aquarium, dried with towels, and placed in a warmer enclosure then returned back to their home cages. The aquarium was emptied and cleaned after every two testing sessions. Twenty-four hours later, rats were retested for 5 min (300 s) under identical conditions. Immobility time was measured during the 5 min test period. Rats were considered to be immobile when floating motionless or making only the movements necessary to keep their heads above the water surface.

Hematological analysis

After behavior testing, the rats were decapitated and blood samples for white blood cells counting were collected into (EDTA) tubes. Selected hematological parameters (WBC — total white blood cell count, LYM — Lymphocytes, MON — Monocytes and EOS —Eosinophiles) were measured using a full automated blood cell counter (PCE-210 model 2009, Japan).

Statistical Analysis

Results are expressed as mean ± SD and the statistical analysis of data was done using the student test.

Probability level less of 0.05 was considered statistically significant.

RESULTS

Behavioral analysis in table 2. Showed a significant decrease (p<0.001) in immobility time for resveol group as compared to control group. However, no difference was noted between groups regarding the other parameters.For the table 3. Total leucocytes, neutrophiles and monocytes showed significant increase as compared to control. However, lymphocytes and eosinophils showed a significant (p<0.01) decrease as compared to control.

DISCUSSION

Our study showed that administration of resveol at 30mg/kg in male wistar rat induced antidepressant-like behavior revealed by the decrease in the immobility time. However, no significant difference was observed for the traveled distance and the time spent in arms. The responses of antidepressant-like corroborate the well known effect of resveratrol and ensure the positive response of resveratrol. Ying et al[14] reported the antidepressant-effect of trans-resveratraol. These effects were related to the serotoninrergic and noradrenergic activation. Moreover, immune cells count showed a significant increase in leucocytes count, this leucocytosis was associated with increase in neutrophils and decrease in lymphocytes. This increase in WBC may indicate an activation of the animal's defense mechanisms and immune system. Furthermore, lymphopenia can expose the animal to the infection. With shift to other study, Sangeetha et al [15] didn't show any change in immune count in plain resveratrol or in modified form (longevinex). Nurgul et al[16] reported that resveratrol induced leucopenia. Considering the anti-inflammatory characteristic of resveratrol[17], the observed decrease in WBC was expected. Hismiogulları [18] also reported that WBC count was decreased in rats given resveratrol. Our work doesn't corroborate the previous study, this may due to the difference in the experimental conditions or of the quality of product.

CONCLUSION

Our work showed that exposure to resveol during ten consecutive days exerted antidepressant effect and leucocytosis associated with lymphopenia. This neuro-immuno-pharmacological link needs to be exploring to discover the underlying pathways and the risk of this immunological response at short and long term on animal organism.

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