

Psychoactive effects of “Enoant” and “Resveratrol” in Wistar rats of both sexes

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Abstract. The effect of two supplements containing resveratrol ("Resveratrol" and "Enoant") on the psycho-emotional state of animals with an initial index of anxiety and depression above 0.5 was studied. For this, the "Elevated plus maze" (EPM) and "Forced swim test" (FST) were used. "Resveratrol" significantly reduces the index of depressivity (ID) in males on the 7th and 14th days of application, in females – only on the 14th day. No significant influence on the anxiety index (AI) was found in both sexes. "Enoant" significantly reduces the ID in males on the 7th day, but not on the 14th day, while no significant differences were observed in females. However, unlike "Resveratrol", "Enoant" significantly reduces the AI on the 14th day in rats of both sexes.

Keywords: *resveratrol, rats, "Enoant", grape polyphenols*

1 Introduction

Grape polyphenols are powerful antioxidants of natural origin with a wide spectrum of biological activity, including the normalization of the psycho-emotional state [1-3]. It is also known about their anxiolytic and stress-protective actions [2, 4]. "Resveratrol" is a widespread dry food supplement, mainly consisting of the substance of the same name. Along with this, the domestic Crimean product "Enoant" is being produced and is already being distributed – a liquid non-alcoholic food concentrate of total polyphenols of grapes "Cabernet Sauvignon", which has positively proved itself in practice [5-7], but has no comparative characteristics with its closest competitors. Therefore, the aim of the current study was to compare the psychoactive effects of "Enoant" and "Resveratrol".

2 Methods

For the study, an experimental sample of 60 male rats, 8 months old, of the Wistar line was formed. Initially, the animals were divided in such a way that for the study in the FST, 3 groups were formed: "control" (n=10), "Resveratrol" (n=10) and "Enoant" (n=10) with ID of more than 0.5. For the study of behavioral reactions in EPM – similar groups of male rats with an AI of more than 0.5. Animals of the "control" groups were not exposed to any influences and remained native throughout the experiment. Rats of the "Resveratrol" groups

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consumed a solution of "Resveratrol" orally for 14 days at a daily dose of 20 mg/kg, calculated as resveratrol; "Enoant" groups – "Enoant" solution at a dose of 20 mg/kg per day, in terms of the polyphenol fraction [2]. Testing was carried out on day 1 (background), on days 7 and 14 of taking food concentrates.

To study the behavioral reactions of female rats, an experimental sample of 60 individuals aged 8 months of the Wistar line was also formed and all actions were completely identical to those described for male rats. An important aspect was that females of all groups at the beginning of the study were in the "diestrus" phase, which was determined visually by vaginal smears.

ID was calculated by the formula $(t_{total} - t_{as}) / t_{total}$, where t_{total} is the total testing time (5 minutes), t_{as} is the active swimming time. AI was calculated using a similar formula: $(t_{total} - t_{oa}) / t_{total}$, where t_{oa} – time in open arms, other designations are the same as in the previous equation. Thus, these indices take on a value between 0 and 1 c.u. Statistical analysis of differences was performed using Tukey's test for multiple comparison.

3 Results

Analysis of ID in male rats showed that resveratrol by the 14th day of administration gradually decreases this index from 0.78 ± 0.05 c.u. in the background up to 0.43 ± 0.08 c.u. ($p \leq 0.05$). The effect of taking "Enoant" turned out to be unstable: on day 7, the ID significantly decreases from 0.79 ± 0.04 c.u. in the background up to 0.53 ± 0.08 c.u. ($p \leq 0.05$), and on the 14th day it does not differ from the background level (Fig. 1).

When analyzing AI in male rats, it was revealed that a 14-day intake of resveratrol does not cause noticeable changes in this index; "Enoant" – gradually reduces AI with the achievement of a reliable level of differences on day 14 from 0.76 ± 0.03 c.u. up to 0.4 ± 0.06 c.u. at $p \leq 0.05$ (Fig. 2).

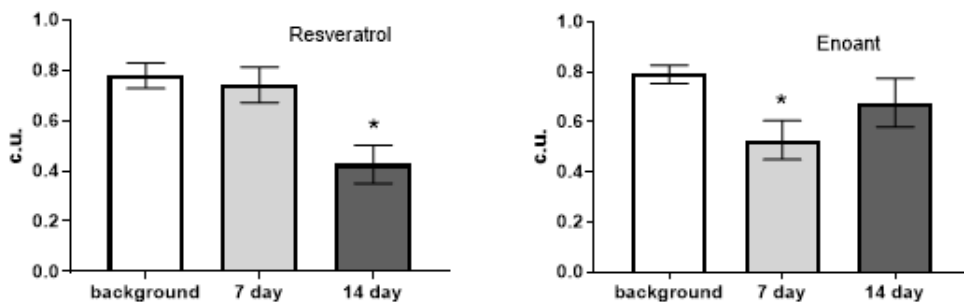


Fig. 1. ID dynamics in male rats after oral administration of resveratrol and "Enoant". The mean value and standard error are given, * - differences from the background level at $p \leq 0.05$.

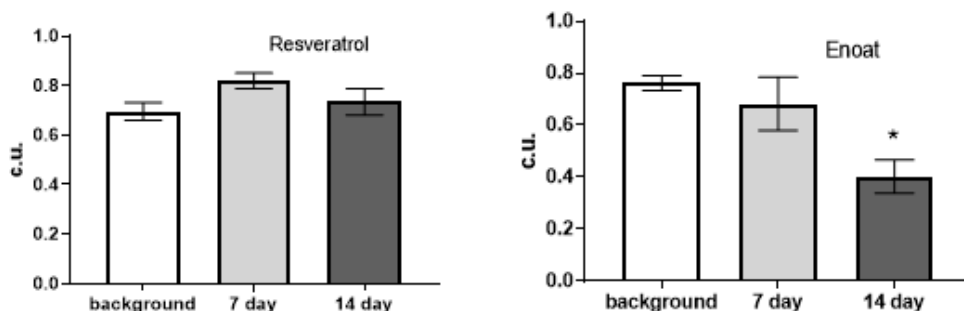


Fig. 2. AI dynamics in male rats after oral administration of resveratrol and "Enoant". Designations are the same as in Fig. 1.

Consequently, in male rats, resveratrol induces a gradual decrease in ID with the achievement of significance of differences by the fourteenth day of oral administration. "Enoant" has an unstable antidepressant effect, or an effect with a pronounced cyclicality, which requires further experimental verification.

In general, the behavioral responses in female rats corresponded in direction to those of male rats, but there were some differences. Thus, by the 14th day of taking resveratrol, the ID of females significantly decreased from 0.81 ± 0.3 c.u. up to 0.7 ± 0.04 c.u. ($p \leq 0.05$), as in males. But when taking "Enoant", no noticeable changes were observed at all. When analyzing AI, it was revealed that a 14-day intake of resveratrol did not cause noticeable changes in female rats, as well as in male rats. A 14-day intake of "Enoant", on the contrary, leads to a significant decrease in AI by the 14th day of intake from 0.76 ± 0.03 c.u. up to 0.59 ± 0.05 c.u. ($p \leq 0.05$).

Thus, the effects of resveratrol in female rats completely coincided with those in male rats, and "Enoant" did not demonstrate antidepressant activity.

Further, we compared the ID dynamics in rats of the respective sexes when taking resveratrol and "Enoant" with each other and with the control group of animals.

As can be seen from Fig. 3, on the 7th day of the study, the ID value in male rats that orally consumed "Enoant" significantly decreased to 0.53 ± 0.08 c.u. ($p \leq 0.05$) compared to the control values and the "Resveratrol" group, but on the 14th day, the ID level is equalized with the value in the control group. Male rats that consumed resveratrol showed a decrease in the ID on the 14th day of the experiment to 0.43 ± 0.08 c.u. with a level of significant differences from the control group and the "Enoant" group at $p \leq 0.05$.

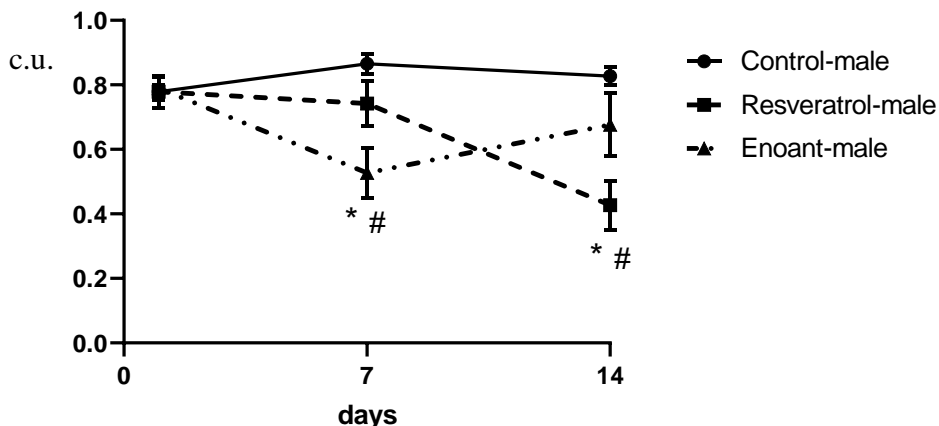


Fig. 3. Comparison of the ID dynamics in male rats of the control and experimental groups. The mean and error of the mean are given, * - differences between the control and experimental groups at $p \leq 0.05$, # - differences between the two experimental groups at $p \leq 0.05$.

When comparing the ID dynamics of female rats, it can be stated that significant differences were observed only between control animals and rats of the "Resveratrol" group on the 14th day of the study ($p \leq 0.05$, Fig. 4). In the "Enoant" group, there were no differences either from the values in the control group, or from the "Resveratrol" group.

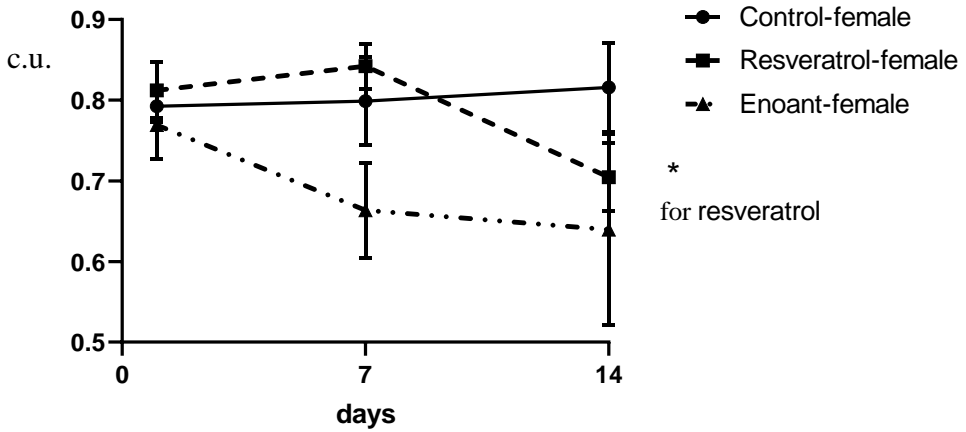


Fig. 4. Comparison of the ID dynamics in female rats of the control and experimental groups. Designations as in fig. 3.

Let us turn to the analysis of the dynamics of AI in male rats of three groups. It is clearly seen that the 14-day dynamics of AI in animals of the control group and male rats of the "Resveratrol" group completely coincide and do not show any noticeable differences (Fig. 5). In the "Enoant" group, there is a linear decrease in this index (up to 0.4 ± 0.06 c.u.), which reaches a significant level ($p \leq 0.05$) by the 14th day. Moreover, the differences are recorded both in relation to the control values and the "Resveratrol" group.

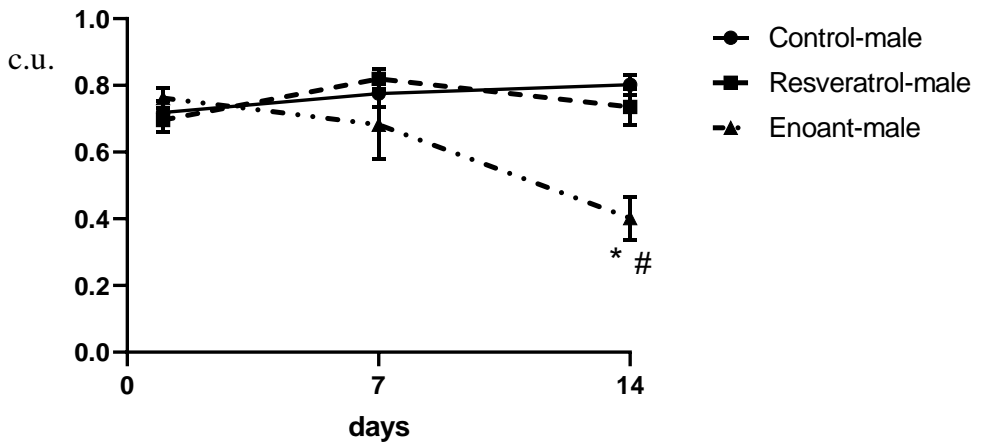


Fig. 5. Comparison of the AI dynamics of male rats in the control and experimental groups. Designations as in fig. 3.

Similar changes are observed in female rats. When taking resveratrol, no noticeable differences from the control group were observed (Fig. 6). When "Enoant" was taken by the 14th day, the AI of female rats significantly decreased to 0.6 ± 0.05 c.u. ($p \leq 0.05$) in comparison with the control and the "Resveratrol" group.

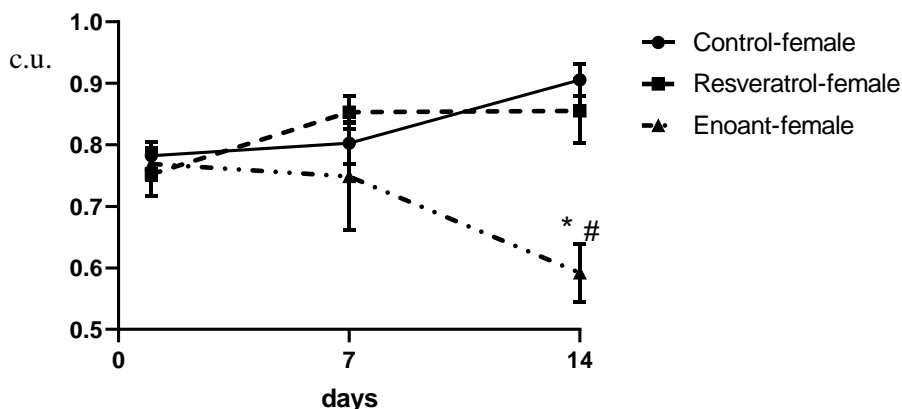


Fig. 6. Comparison of the AI dynamics of male rats in the control and experimental groups. Designations as in fig. 3

The psychoactive effects of resveratrol in male and female rats are very similar, however, when using "Enoant", this pattern is not traced. In males, "Enoant" on the 7th day caused a significant decrease in ID, while in females no significant effects were observed after a 14-day intake. We believe that the noted difference is due to a number of reasons:

1. As a result of the presence of the menstrual cycle in female rats, the hormonal background of the body changes, which entails behavioral and reactive changes;
2. The antidepressant effect of "Enoant" is weaker than that of resveratrol, and does not manifest itself in females due to biorhythmological characteristics (see paragraph 1).

Thus, resveratrol demonstrated antidepressant potential in both sexes of rats within fourteen days, but did not change the AI dynamics. The use of "Enoant" had an unstable, possibly cyclic, antidepressant effect, but caused a noticeable decrease in AI by the 14th day of administration in both sexes. In general, the Crimean product "Enoant" may be a stronger anxiolytic than "Resveratrol".

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