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The influence of clathrate β -cyclodextrin with para-amino-benzoic acid and silyl group over behavioral performance of laboratory animals

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ABSTRACT

In this work the assessment of the neurotropic activity of clathrate β -cyclodextrin with para-amino-benzoic acid and silyl group (CD-PABA-CG) under the conditions of instrumental stress during self-defensive motivation in the universal problem-solving camera are shown. The testing was held in 30 days in the universal problem camera on 86 non-linear white male rats. When using the new synthesized compound CD-PABA-CG in the dosage 10 mg/kg it changes positively the indicators of motivational-energetic sphere in the instrumental defensive behavior's conditions, and it demonstrates actoprotecting feature. CD-PABA-CG have positive neurotropic effect by the example of cognitive indicate. The compound presented have a wide action spectrum and is perspective in the pharmacological area.

INTRODUCTION

Currently β -cyclodextrin and its numerous derivatives are widely used in physiology and pharmacology [1-6]. They are mainly used as the "containers" of medicinal drugs due to its natural ability to encapsulate different hydrophobic compounds with the formation of inclusion compounds of the type "quest – host" [5, 6]. Encapsulation defends the enclosed medicinal substance from bio-degradation, conduces the increase of its solubility and helps its selective delivery to the appropriated place during the required time period [6, 7]. In our previous research works the high bioactivity and pharmacological activity of alike compounds are presented in particular clathrate compounds and conjugates β -cyclodextrin with para-amino-benzoic acid in order to reveal its neurotropic activity [7]. For that matter, the definite interest presents the examination of the new similar complex compound, which differs with its composition containing the silyl group.

In our mind the strong component can exactly increase the possibly action of substance's complex compound, defending it additionally from the biodegradation. Herewith the changing of substance's structure can exclude the features, which these analogs have.

The purpose of the project is the assessment of the neurotropic activity in laboratory animals under the conditions of instrumental stress during self-defensive motivation in the universal problem-solving camera.

MATERIALS AND METHODS

Experiment was held on 86 non-linear white male rats with the weigh 150-200 g, kept in the standard conditions of the vivarium taking into consideration the principles of humanity, and the plan of the study met conditions of Helsinki declaration of World Medical Association (WMA) of the latest revision (Edinburg, 2000), with the account of explaining comment to the paragraph 29, which was added by General Assemblée of WMA (Washington, 2002). Before organizing the study all the animals was kept in the standard conditions. The rats was given a full food ration during 10 days before the beginning of the experiment according to the Rules of organizing works using experimental animals (1977).

All animals was previously selected to the behavioral types according to the methods.

The testing was held in 30 days in the universal problem camera [8]. The testing consisted of 2 stages: at the first stage the formation of an instrumental reflex of active avoidance behavior in the problem camera was held; at the second stage the registration of the behavior was taken twice under the conditions of self-defensive motivation in 24 and 48 hours after 10-days pause period. During the second stage the characteristics of the motivational-energetic (according to the indicants of search time (ST) and search intensity (SI)) and cognitive spheres (according to the cognitive indicant (CI)) according to the accepted methods [9].

The utilized substance (pic.1) represents the chemical synthesized compound.

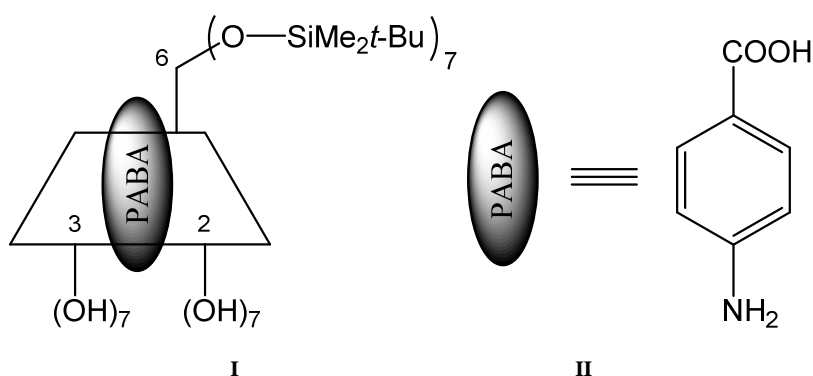


Fig.1 I – Structural formula of clathrate CD-PABA-CG, II – formula of paraminobenzoic acid, included in β-cyclodextrin

This isclathrate para-amino-benzoic acid with β-cyclodextrin having the silyl group with the degree of substitution in 7 in the ratio 1:1 (CD-PABA-CG (short abbreviated name of the compound)), which was administered per os once in the dosage of 10mg/kg of the animal's weight.

RESULTS AND DISCUSSION

The usage of this modified method of formation and simultaneous measurement of characteristics of behavioural indicants under the conditions of permanent value of the nutritional motivation in the first set of experiments revealed the tendency to the improvement of characteristics of the energetical sphere of behavioural performance (BP).

The average search time (pic.2) of the animals from the first type of behavior during the first testing (in 24 hours) decreased from 448±42,4 to 360±31,3 s. without the significant difference. While the second testing (in 48 hours) it decreased from 323±24s. to 234±17,8 s. The difference was 89s (p<0,01). The difference of search time between the primary and secondary testing is significant (p<0,001). The energetical characteristics of BP according to this data are more preferable during the re-testing.

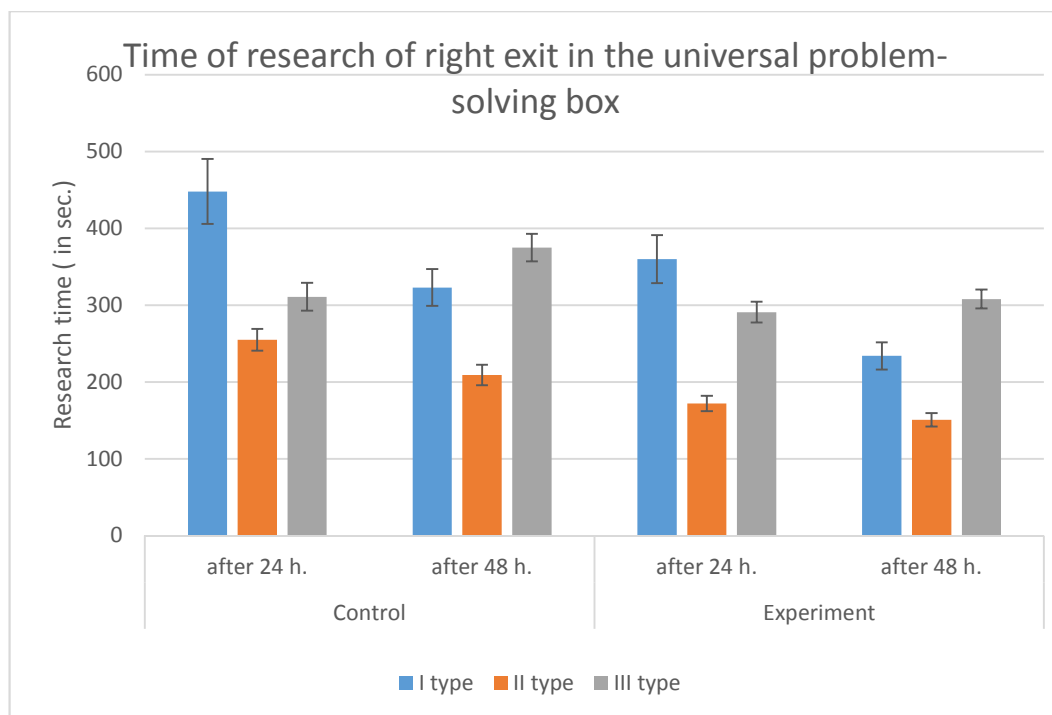


Fig. 2. Time features of taking decision in the problem-solving box by the influence of CD-PABA-CG (experiment)

It was found the most optimal results in the group of II behavioral type. By the first testing (after 24 h.) searching time reduced almost on the 1,5 times ($p < 0,05$) by the influence of CD-PABA-CG, and by the second testing this indicate reduced on the 1,4 times ($p < 0,05$).

In the group which belongs to the III type it was marked the time features of taking decisions by the defensive behavior only after 48 hours during the second testing, and this indicate reduced on the 1,2 times ($p < 0,05$).

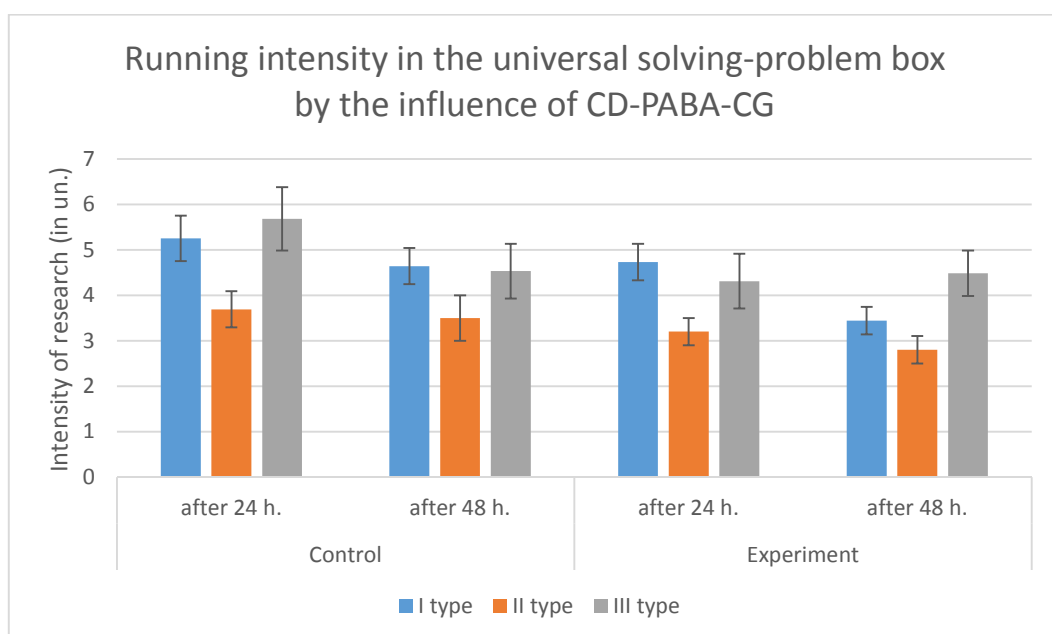


Fig. 3. Intensity of running research by the defensive behavior in the universal problem-solving box by the influence of CD-PABA-CG (experiment)

Intensity of searching (fig.3) as the second energetic indicate had also changes for the improving of its characteristics. This indicate reduced in the group of animals of II behavior type on the 1,4 times ($p < 0,01$) according the results of the test after 24 hours and on the 1,3 times ($p < 0,05$) according the results of the test after 48 hours

from the moment of injection. In the other cases it preserved the dynamic of running intensity changing for the reducing in all subgroups despite of having no significant difference.

Intensity of researching, expressing in the periodicity of animal's actions in the universal problem-solving box, shows increasingly the time of brain's analysis the changes of the actual situation in the universal problem-solving box. The situation is under the control of the experimenter. The brain's analysis can be connected with the parts of afferent synthesis in the taking decision process. The data received demonstrates optimizing affect of CD-PABA-CG.

Percent of wrong actions (fig. 4) as the indicate of cognitive sphere, reduced on the 1,4 times ($p < 0,01$) after 24 hours and 1,3 times ($p < 0,05$) after 48 hours from the moment of injection by the influence of CD-PABA-CG of the animal from the II typological group.

The other typological groups had no significant difference despite of influence of CD-PABA-CG and we suggest that the reason of it is genetic individual features of these animals.

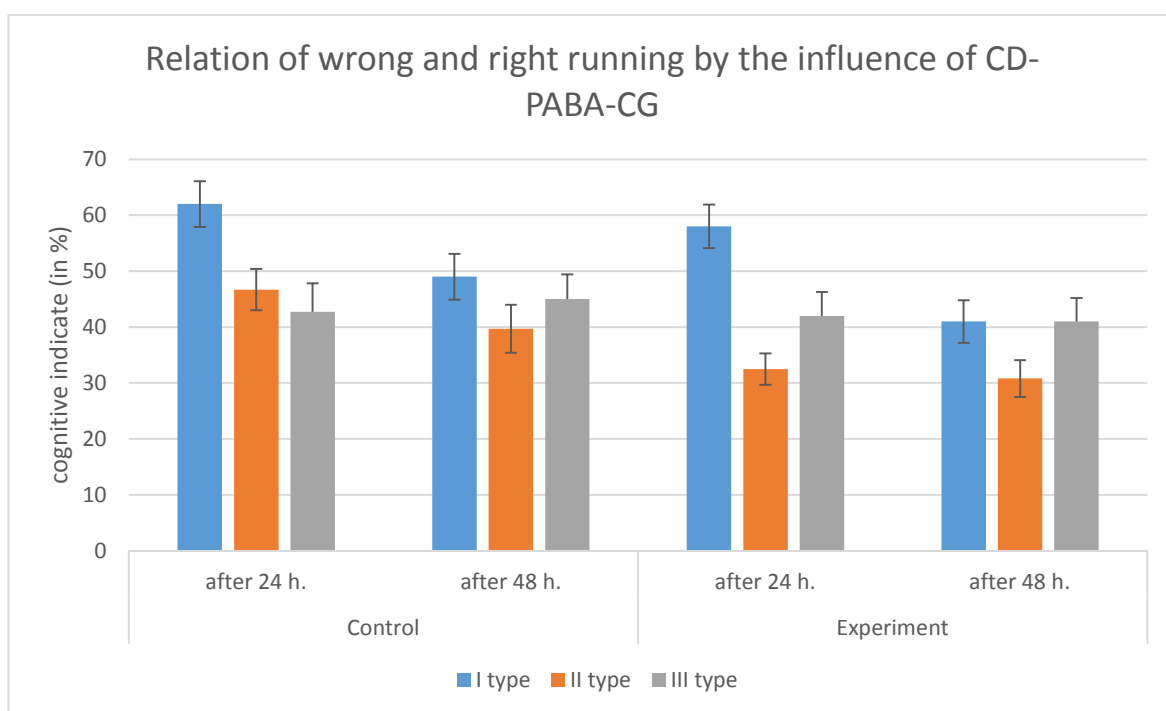


Fig.4. Changing of cognitive indicate in the different typological groups by the influence of CD-PABA-CG (experiment)

Percent of wrong active is an indicate of cognitive-informative sphere of instrumental behavior in the any moment of time. Positive dynamic of this parameter demonstrates about including the cognitive sphere in the researching processes, and increasing of wrong actions percent shows its disorganization and regress in the experimental conditions. Only this indicate demonstrate the process of learning in the cognitive way "know how". Energetic parameters of behavior is responsible for dynamic characteristics and can coincide or not. In our case when using CD-PABA-CG it was identical the tendency of indicates of these different spheres of behavior activity, and it confirms the highly effectivity of derivative of β -cyclodextrin in the form presented.

CONCLUSION

When using the new synthesized compound CD-PABA-CG in the dosage 10 mg/kg it changes positively the indicates of motivational-energetic sphere in the instrumental defensive behavior's conditions, and it demonstrates actoprotecting feature. CD-PABA-CG have positive neurotropic effect by the example of cognitive indicate.

The compound presented have a wide action spectrum and is perspective in the pharmacological area.

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