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Research Paper

About the nootropic properties of donsumine

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ABSTRACT

Background: Donsumine shows a kinda clear dose dependent impact on motor activity, also on the exploratory part which lets you look at its nootropic value. In this context, adrenergic receptors (α1) and dopaminergic receptors are often thought of as the main mediators behind nootropic drug effects.
Objective: The goal was to describe the nootropic profile of Donsumine, using behavioral pharmacology models, and also to spell out what's going on at the receptor level, mechanism wise.
Methods: Motor activity (MA) and verticalization were tracked across doses from 3–100 mg/kg, like repeatedly and in a controlled way. Then, the phenamine induced MA boost was checked at 3 and 30 mg/kg. As for exploratory behavior, they used the open field test (Hall paradigm) at 1, 10, and 100 mg/kg. Nootropic performance was assessed through conditioned reflex passive avoidance (CRPA), plus a classical maze, specifically the esophageal reflex acquisition, and finally the Morris water maze for spatial memory. To check the cholinergic side, scopolamine induced amnesia was used, and then there was a competitive interaction analysis, to see how it lines up.
Results: Donsumine had dose dependent biphasic effects on MA, like it initially ramps up at 3, 5, and 10 mg/kg, and then at 100 mg/kg it drops it by about 60%. It also strengthened phenamine induced MA, and verticalization at 3 and 30 mg/kg, with the effects that lasted through the whole observation window and then returned back to usual after discontinuation. In the open field test, the treated groups showed enhanced searching and more exploratory activity at all doses tested. In the nootropic models, Donsumine sped up CRPA acquisition, helped the esophageal reflex develop in the classical maze, and improved spatial memory in the Morris water maze too. Finally, Donsumine showed competitive antagonism against scopolamine induced amnesia across all cognitive tests, if you look at the pattern as a whole.
Conclusions: Donsumine shows a pretty broad nootropic profile, like it helps with learning, memory consolidation, and spatial cognition at the same time. When it is given against scopolamine, the effects look like competitive antagonism, so it seems to involve muscarinic cholinergic pathways, plus α1-adrenergic and

dopaminergic mechanisms too. In other words it kinda points to a mix of systems, not just one.

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1. INTRODUCTION

Arundo (reed) or Arundo donax L. for many years it has been used not only for agricultural or household needs, but also for preparation of tincture from its leaves [1], [2], [3], [4], is used in oriental folk medicine as a diuretic, for the treatment of sexual diseases, as well as for diseases such as ascites, candidiasis, stomatitis, decoctions of dried crushed parts. This type of plant is much more often cultivated in countries such as Romania, Italy, France, it is widely distributed in the Bukhara, Kashkadarya and Ferghana regions of our country scattered. In our country, as well as all over the world, academicians A.P. Orekhov and S.Yu Yunusov's have been for many years continuation of scientific research, Arundo Donax L. A number of scientific research works are carried out on the basis of the plant [5], [6]

The forage plant reed (Arundo donax L) is a source of indole alkaloids of the tryptamine series [3] and, first of all, donaxin, in which selectivity to 5HT2A receptors of the serotonin receptor subtype has been revealed [4]. According to T. Mestre [7], 5HT2A are a source of psychotropic drugs, including nootropic ones. In particular, at the Institute of Chemistry of Plant Substances, academician named after S.Yu. Yunusov of the Academy of Sciences of Uzbekistan Arundo Donaks L. in continuation of a series of research works based on the plant for many years, the nootropic effect of the amount of alkaloids on the surface of this plant was studied [5]. Thus, the comparison of anticonvulsant, antidepressant and anxiolytic activity of recently synthesized tabium and synthetic structured substances with some drugs that are widely used in practice under experimental conditions is being studied. As a direct continuation of this research work, screening studies study the biological activity of substances isolated from plants, with their large-scale distribution in our country and Asia [8], [9]. In this regard, our studies of Donsumin, in addition to the psychostimulating effect, also revealed the anxiolytic, as well as the described nootropic effect.

2. METHODOLOGY

All studies to determine nootropic activity were conducted on mongrel laboratory white mice with a body weight of 20-22 g and on mongrel laboratory white rats with a body weight of 180-220 g, which were cared for and kept in standard quarantine conditions for 14 days [10].

The effect of Donsumine on D2 of the stimulating effect of phenamine. It is known that phenamine stimulates D2 dopamine receptors, which are involved in the process of cognitive functions of animals and humans. [11], [12] is mediated with the participation of DA2 α_1 adreno receptors in the form of verticalization (strut) and enhancement of MA.In this experiment, the effect of Donsumine on the sensitivity of DA 2 receptors was studied. The experiments were carried out on 3 groups of mice using the I. P. Lapin technique [13].

The experience consisted of: the number of verticalization and intersection of the lines of MA mice in the control was calculated. against the background of D2 stimulating effect of phenamine from a dose of 5 mg / kg n / a and the same experience on the background of Donsumine administered 2 hours before

administration of phenamine. At the same time, the effect of the drug on the severity of verticalization was determined. Study of search and research activities in the open field by Hall. The mice landed on an open area divided into 5x5 squares and drilled holes D = 15 mm. The number of contacts of mice with squares was estimated as the search activity of mice, and the contacts of mice with minks (peeping) were taken as research activity.

The effect of Donsumine on the development of the conditioned reflex of passive avoidance (CRPA) was evaluated in a 2-chamber block, of which one chamber was light and had an entrance to a dark chamber with an electrode floor. Which was connected to the electrical stimulator ESU 01-1. In the experiment, mice landed one animal at a time in a light compartment with their tail pointing towards a dark compartment, from where they, as a rule, moved into a dark compartment with an electrode floor. After 5 seconds, an alternating electric discharge (50 volts, 0.5 mA, 20 Hz) was applied to the floor electrodes.

The influence of Donsumine on the speed of the conditional motor reflex was determined in a classic maze with 2 chambers. The experiments were carried out for 3 days. In the evening, the rats were deprived of food with access to water. In the morning, an experiment began on finding a compartment with food by rats, sweetened milk with bread in a 100 ml Petri dish. On the first day, the rats were trained three times to find food, while the time of finding the final compartment with food was recorded.

The effect of (E) on the spatial memory of mice was studied in a water maze using the Morris method. The water maze consisted of a galvanized tank D = 40cm and 30 cm high. At the opposite end of the tank there is a wooden platform D = 5 cm, immersed in water with a temperature of 27-29 C at 0.5-0.7 cm below the water surface. To ensure the opacity of the water, milk with a volume of 300 ml of 3.2% fat content was poured.

The time of the platform 's location was recorded Effect of Donsumine on the amnesia of mice caused by the administration of scopolamine 1 mg/kg s/c. The discussion of the results obtained on the basis of the conducted studies was carried out in comparison with the control group and statistical processing of the results was performed using the methods presented in [14].

3. RESULTS AND DISCUSSION

The effect of Donsumin on MA. Previous studies have shown that Donsumine starting with a dose of 1 mg/ kg, the behavior of verticalization also increases. At a dose of 3 mg/kg, these effects increased 2-3 times. At a dose of 10 mg/kg, they were additionally increased by 45%, i.e. relatively less than from a dose of 3 mg/kg. It must be assumed that Donsumine in these doses enhanced MA and verticalization due to the activation of DA2 dopamine a1 receptors [11], [12] which participate in the manifestation of the nootropic effect of Ginko Biloba, Piracetam and others [15], [16], [17], [18], [5].

The above data were confirmed in experiments on the influence of Donsumine on search and research activity in experiments in an open field by Hall. The following studies are designed to confirm the participation of Donsumine nootropic action.

The effect of donsumine on the development of the conditioned reflex of passive avoidance of punishment (CRPA). The experiments were carried out on 2 groups of mice with 6 animals in a 2-chamber block with dark and light compartments. It was found that in the control group of mice, when re-placed in a light chamber, out of 6 mice, only 2 did not enter the dark chamber, i.e. they developed an avoidance reflex (33%) [19]. In the second experimental group of mice that were previously injected with Donsumine at a dose of 5 mg/kg 24 and 2 hours before the start of the experiment, none entered, i.e. the avoidance reflex was developed in all mice [20].

The effect of Donsumine on the latent period of the food-motor reflex in experiments on rats in a maze. On the first day of the experiment, each rat was trained to run through the maze 3 times. The next day, each rat was passed through the maze and the duration of the run was used as control data.

The 2nd and 3rd runs were carried out 2 and 4 hours after administration of Donsumine 3 and 10 mg/kg. It was found that the latency period in three groups of rats averaged 15, 17, 18 seconds. After 2 hours, the runs were repeated, and the latent periods were from a dose of 3 mg/kg-8 seconds, from a dose of 10 mg/kg-10 seconds, and in controls-14 seconds [21].

The results of the experiments indicate that the duration of the run in the control group did not change much, from a dose of 3 mg/kg, the latency period decreased from 17 to 8% or by 53%; from a dose of 10 mg/kg, it changed from 18 seconds to 44%.

The experiments confirmed the nootropic effect of Donsumine was confirmed, and the dose of 3 mg/kg was the most active [22].

The effect of Donsumine on the amnesic effect of scopolamine. On the third day, the experiment was repeated, but the second group after Donsumine 3 mg/kg after 1 hour was injected with scopolamine 1 mg/kg s/c., the third group was still 10 mg/kg s/c. As a result, in the 1st group of mice, the latency period decreased from 15 seconds to 14 seconds, i.e. practically unchanged; in the second group, against the background of Donsumine 3 mg/kg + scopolamine 1 mg/kg, there was a less pronounced shortening of the latency period. i.e., in the second group, the latency period after scopolamine and Donsumine in the indicated the dose was from 18sec, i.e. decreased to 14 seconds, i.e. the latency period was longer than in the second experiment, which proved the mutual antagonism of Donsumine and scopolamine. In group 3, the latency period from Donsumine 10 mg/kg remained the same, i.e. did not change, was the same as in the previous experiment. The data provided indicate that the latency period has remained the same.
The results of the experiment indicate the competitive antagonism of scopolamine and Donsumine.

The effect of Donsumine on the latent period of the platform in the water maze in Morris experiments on mice.

In these experiments, the effect of substances on spatial memory is studied. It was found that the average latency period of the platform in the control 6 mice was 126 seconds. In the groups of mice with the introduction of Donsumine 3 and 10 mg/kg inside, the time of finding the maze was 56, 65 seconds, i.e. about 2 times faster.

In experiments with a water maze, in a group of mice with the introduction of Donsumine 3 mg /kg, scopolamine 1 mg/kg was additionally injected, and in a group with the introduction of Donsumine 10 mg/kg, distilled water 0.2 ml/kg was injected. The speed of finding the platform in control mice was 114 seconds, against the background of Donsumine + scopolamine, the time of finding the platform was 86 seconds, and in the 3rd group against the background of Donsumine 10 mg/kg was 110 seconds. Thus, in this experiment, the 2nd group of mice in which Donsumine and scopolamine were injected extended the time of finding the maze from 56% to 114%, thus scopolamine and Donsumine counteracted each other, i.e. showed mutual antagonism. In group 3, the shortening of the latency period was almost no different from the results of the previous experiment.

From the data presented, it can be seen that scopolamine lengthened the latency period by 2.5 times, and the preliminary administration of Donsumine the latency period approached the control level. It can be seen from the experimental data that Donsumine has an antiamnestic or nootropic effect.

3.1. Discussion

Thus Donsumine, which is a fraction of indole alkaloids of the tryptamine series isolated from reed reed, is a new original nootropic agent whose mechanism is the activation of α1 adreno and D2 dopamine receptors plus, presumably, the blockade of 5HT2A serotonin receptors. Nootropic effect manifested in a test to accelerate the production of CRPA in mice, to accelerate the food-motor reflex in a classic maze, in a test for finding a water maze by Morris. The nootropic effect of Donsumine, was antagonized by the amnesic effect of scopolamine in the last two tests. The nootropic effect of Donsumine was manifested in doses of 3-10 mg/kg of 1/300 – 1/100 of LD_{50}. Doses up to 100 mg/kg orally also had a nootropic effect, but it was combined with muscle relaxation from large doses of Donsumine. -100 mg/ kg. Donsumine is a representative of a new chemical class of new nootropic drugs.

4. CONCLUSION

- Donsumine is a fundamentally new nootropic agent.
- Fractions of indole alkaloids of the tryptamine series are Donsumine, consisting of Donaxin (60-80%), Ardine, Donaxamine, Arundine. Donsumine consisting of these alkaloids has a nootropic effect.

- The mechanism of nootropic action of Donsumine involves α_1 adreno- DA2 dopamine receptors involved in the mechanism of action of Ginko, Piracetam.
- Donsumine and scopolamine showed antagonism to each other's effects by competitive type.

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Author Contributions Statement

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
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R. A. Botirov		✓	✓	✓			✓	✓	✓		✓	✓	✓	
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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

Conflict of Interest Statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Informed Consent

All participants were informed about the purpose of the study, and their voluntary consent was obtained prior to data collection.

Ethical Approval

Not Applicable.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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