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Research Article

INFLUENCE OF *NELUMBO NUCIFERA* EXTRACTS ON EXPLORATORY AND DESPAIR BEHAVIOR OF RATS

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ABSTRACT

The present study was aimed at the experimental research of the psychotropic action of the seeds, leaves, petals and fruit extracts of *Nelumbo nucifera* grown in Astrakhan. In the article we study general motor activity, exploratory behavior, anxiety and behavior of despair of adult rats after treatment with extracts of seeds, leaves, petals and fruits of *Nelumbo nucifera*. The animals of experimental groups received intra gastric *Nelumbo nucifera* extracts for 14 days. Exploratory behavior and anxiety of rats were studied using Suok-test. Despair behavior of rats was studied using Porsolt test. It was found that seeds, leaves, petals and fruits extracts of *Nelumbo nucifera* contributed to the activation of exploratory behavior patterns and to a decrease of anxiety in animals in the Suok-test. More significantly, the behavior of animals in the Suok test was altered by the action of extracts of petals and fruits of the *Nelumbo nucifera*. These extracts have shown antidepressant activity in Porsolt test. The fruit extract of *Nelumbo nucifera* showed the most vivid antidepressant properties.

Keywords: *Nelumbo nucifera*, extract, seed, leaf, petal, fruit, neuro-cognitive functions, exploratory behavior, despair behavior.

INTRODUCTION

Prevention of disorder of the higher integrative functions of the brain, learning and memory processes is an urgent problem of medicine and health care. Every year, there is an increase in mental and neurological disorders that arise as a result of a constant increase in the influence of stress factors[1]. In this regard, one of the tasks is the development and implementation of new preventive and therapeutic and recovery technologies with the initial forms of violations of higher brain functions.

Herbal substances have a wide spectrum of biological activity and low toxicity, so they are promising for pharmacological correction and prevention of functional disorders of the nervous system. It was interesting for us to research *Nelumbo nucifera*. *Nelumbo nucifera* Gaertn. Nymphaeaceae. This herb is also known as sacred lotus. It is a large aquatic plant with stout, creeping rhizome found throughout India. *Nelumbo nucifera* is also native in China and Japan. Almost all parts of the lotus plant are eatable. *Nelumbo nucifera* is a part of more than two hundred preparations of Chinese and Indian medicine. *Nelumbo nucifera* is reported to possess anti diarrhoeal, psychopharmacological, diuretic, antipyretic, antimicrobial, hypoglycemic qualities. Its biologically active substances have different effects: adaptogenic, antidepressant, sedative[2,3], lipid-lowering[4], anticarcinogenic[5,6] and others[2,7,8]. Antioxidant activity of various parts of *Nelumbo nucifera*is well determined, e.g. leaves[8-10], stamens[11] and rhizomes[3].

Large areas of the river Volga delta are occupied with *Nelumbo nucifera*, preserved from the pre glacial period. The *Nelumbo* has a scientific value as a relic of the Gondwana flora that existed more than 100 million years ago (Mesozoic, late Cretaceous)[12]. *Nelumbo nucifera* belongs to the Nelumbonaceae. The Astrakhan population of *Nelumbo* grows in shallow water areas of the Volga estuary along the banks of small rivers, in delta. It is gelofit, grassy long-rooting polycarpic, coastal-water hyper glykophyte, hydrophyte[13].

The major phytoconstituents provided by the *Nelumbo nucifera* are alkaloids like dauricine, lotusine, nuciferine, pronuciferine, liensinine, isoliensinine, roemerine, nelumbine and neferine. *Nelumbo nucifera* also contain flavonoids, saponins, phenolics and carbohydrates[14].

In this study we explored the psychotropic effects of the *Nelumbo nucifera* extracts, which were realized through cholinergic, dopaminergic, noradrenergic and serotonergic neurotransmitter systems by activating cAMP in the hippocampus and prefrontal cortex.

So, the purpose of this article was an experimental study of the psychotropic action of the seed, leaf, petal and fruit extracts of *Nelumbo nucifera* grown in Astrakhan region.

MATERIALS AND METHODS

Plant Material

Lotus seeds, leafs, petals and fruits were collected from natural resource in Astrakhan Nature Reserve (45°34′52″N, 47°54′59″E), Astrakhan Oblast, Russia. The specimens were identified by

scientific staff of the Astrakhan Nature Reserve, Astrakhan Oblast and Russia.

Extracts Preparation

Seeds, leaves, fruits and petals alone removed from the flower of *Nelumbo nucifera* were separately ground to powder in mortar. Then, 20 g of powder was placed into 500 ml of 60% ethanol and placed for 3 hours at 60 °C in the thermostat. After it, the alcohol was distilled off in a rotary evaporator[15]. The extract solutions were administered to the animal's intra gastric by means of a probe for 14 days at a dose of 200 mg /kg.

Chemical Analysis of Extracts

In the received aqueous-alcoholic *Nelumbo nucifera* extracts, the total content of flavonoids was determined by thin layer chromatography with chromate densitometry.

For quantitative processing of the chromatogram, a CAMAG TLC Scanner 3 scanning densitometer at a wavelength of 410 nm and a slit size of 2.00 x 0.2 mm was used.

Data reception and quantitative processing of the obtained results was performed on a computer using the Win CATS program (plotting the area calibration and calculating the amount of quercetin in the samples).

The concentration of quercetin in the analyzed samples was calculated by the formula:

$$C\ (mg/tab) = Ctlc\ (mg/l) \times P \times V\ (ml) \times Mt\ (mg) \times 0.001 / Mn\ (mg)$$
$$C\% = Ctlc\ (mg/l) \times P \times V\ (ml) \times 0.1 / Mn\ (mg),$$

where Cmg/tab –the concentration of quercetin in the sample, mg/tablet; C% - the concentration of quercetin in the sample,%; Ctlc – the concentration of quercetin in the sample, calculated by TLC calibration, mg/l; P – the dilution factor (used only in case of dilution of the extract); V – the volume of methanol in which the sample was extracted, ml; Mt – the mass of the tablet, mg; Mn – the sample weight for extraction, mg; 0.001 – is the conversion factor of l to ml; 0.1 – conversion factor to%.

The obtained solutions of extracts with the precipitate were divided into two fractions: 1 - liquid (G); 2 – sediment. The flavonoids were extracted from the precipitate with methanol for 30 minutes, centrifuged for 2 minutes at 16000 rpm, and the resulting methanol extracts were used for analysis (MeOH).

Experimental protocol

Animal care procedures were conducted in accordance with the guidelines set by the European Community Council Directives. The procedures used in this study stand in strict accordance with the European legislation and the guidelines of the National Institutes of Health on the use and care of laboratory animals, the Order of the Ministry of Health of the Russian Federation No. 199n of April 1, 2016 "On Approval of Laboratory Practice Rules" and the protocol of Ethical Committee of the FSBEI of HE "Astrakhan State Medical University" of the Ministry of Health of Russia No. 8 of November 24, 2015

To prove our hypotheses, we tested rats in the Suok and Porsolt tests. We studied general motor activity, exploratory behavior, anxiety and behavior of despair in adult rats after treatment with extracts of *Nelumbo nucifera*.

Experiments were carried out on 50 adult male rats (weighing about 200 g; n = 10 in each group). All the animals used in this study were experimentally naive, housed 6-8 per cage with free access to food. The animals were maintained on a 12:12 h light/dark cycle. Behavioral testing was always conducted between 10.00 and 12.00 o'clock.

The animals were divided into 5 equal groups randomly as follows:

Group I, Control: only saline solution treated;
Group II, Test group I: received seeds extract of *Nelumbo nucifera*, 200 mg/kg BW, p. o. for 14 days;
Group III, Test group II: received leaves extract of *Nelumbo nucifera*, 200 mg/kg BW, p. o. for 14 days;
Group IV, Test group III: received petals extract of *Nelumbo nucifera*, 200 mg/kg BW, p. o. for 14 days;
Group V, Test group IV: received fruits extract of *Nelumbo nucifera*, 200 mg/kg BW, p. o. for 14 days.

Porsolt Test

The behavioral despair test (Porsolt forced swimming test) is a test, centered on a rodent's response to the threat of drowning, whose result has been interpreted as measuring susceptibility to negative mood[16,17]. It is commonly used to measure the effectiveness of antidepressants. In the forced swim test rats are placed in a small, confined space, such as a large graduated cylinder filled halfway with water. In our experiments we used a cylindrical plastic tank with a height of 50 cm, with an internal diameter of 38 cm, filled with water to a height of 38 cm, and a water temperature of 22 ± 1 °C. During the first period of vigorous activity the animal tries to escape. After it, the animal ends vigorous activity and shows a characteristic immobility in which it only moves to keep its head above water. This physical immobility is considered as indicator of behavioral despair. Researchers measure the amount of time between the moment when the animal is placed in the chamber and the beginning of immobility. Testing time was 3 minutes. In the experiments were recorded the latency time to the first movement, the latent period to the first immobility, the time of active and passive swimming, the refusal of active swimming- immobilization or "freezing" (considered as an experimental model of behavior depression or "despair behavior"), number of diving.

Suok-test

The light-dark modification of Suok test (ST) was constructed in accordance with the specifications published in Nature Protocols[18,19] and consisted of an aluminum rod, 2,4-m in length by 2 mm in diameter with four 60-W bulbs 40 cm above the rod (directed light) to illuminate the light part of the test, providing the only lighting in the experimental room. The rod was separated into two lengths of several 15-cm long segments on either side of a 30-cm long central zone and elevated to a height of 20 cm from the cushioned floor by two vertical stands. The experimental room was dimly lit during all tests. In all ST experiments, the rats were placed individually in the middle part of the test (snout facing either end) and their behaviors were observed for 5 min by an experienced observer, scoring the number (frequency) of anxiety and motor-related behaviors. The Suok test measures exploration, risk assessment behaviors, and sensorimotor integration; it was developed to target behavioral abnormalities that arise from pathways mediating anxiety and vestibular function.

We recorded the latent period (LP) of leaving the center; horizontal activity; vertical activity, orientation, the number of head dips, the number of missteps, the number of stops, the number of transitions and time spent in the dark and light

compartments of Suok-test. Each group of animals was tested in ST once, 30 minutes after the last feeding by extracts' solutions.

Statistics

All results are shown as mean ± SEM. Data were analyzed by Student test for comparisons between experimental groups. A probability of less than 0.05 is considered as statistically significant.

RESULT AND DISCUSSION

A chemical analysis was performed to determine the concentration of the main biologically active substances in *Nelumbo nucifera* extracts' samples obtained. Analysis of flavonoids content showed that extracts obtained from different parts of plants differed in the concentration of rutin and quercetin (Table 1 and 3). The concentration of flavonoids was studied in two fractions: in the liquid phase and in the MeOH precipitate. In the liquid phase, a small concentration of rutin was characteristic of the extract from the petals, the extracts were arranged in the following order: leaves - fruits. In the liquid phase of the *Nelumbo nucifera* seed extract rutin was not detected. The concentration of quercetin in the liquid phase was approximately the same in extracts of fruits, leaves and petals, whereas in the seed extract its concentration was slightly lower. In the MeOH precipitate, rutin was found only in the petals' extract. The content of quercetin was maximal in the extract of the leaves of the *Nelumbo nucifera*, and then it was decreasing in the extracts of petals, fruits and seeds.

In this study, we explored behavioral and psycho physiological effects of *Nelumbo nucifera* extracts. Control and experimental rats were exposed to Suok and Porsolt tests to assess exploratory behavior, anxiety and behavior of despair.

In the Porsolt test rats after treatment to *Nelumbo nucifera* seeds'extract showed a decrease of latent period before the first movement, significant increase of the time of active swimming in the test ($p \leq 0,05$) and simultaneously reduction of immobilization time ($p \leq 0,01$), while the remaining parameters varied less significantly in comparison with control animals (Table 2).

Rats after treatment to *Nelumbo nucifera* leaves' extract displayed similar changes in behavior in the Porsolt test. The extract treatment decreased the despair behavior in the Porsolt test, while the immobilization time significantly decreased ($p \leq 0,05$).

Rats after *Nelumbo nucifera* fruits' extract treatment showed the most significant changes in the behavior of despair in the Porsolt test. Under the influence of the extract, there was a significant decrease in desperation patterns in the test. The time of active swimming significantly increased in test, while the time spent by the animals for immobilization and the time before the first immobilization reduced (Table 2).

The petals' extract of *Nelumbo nucifera* also changed the behavior of the animals in the Porsolt test, but these changes were less significant.

Thus, the fruits' extract of *Nelumbo nucifera* had the most obvious antidepressant properties. Extracts of *Nelumbo nucifera* seeds, leaves and petals also had antidepressant properties, but they were less evident. So, we can rank the influence of *Nelumbo nucifera* extracts on rats in Porsolt test as follow: fruits > seeds > petals > leaves.

Patterns of behavior of female rats in the Suok-test varied depending on the type of the extract. All of they caused an increase in the patterns of exploratory behavior and a decrease in the anxiety of female rats.

In the light part of the light-dark test, rats after treatment by *Nelumbo nucifera* seeds' extract displayed an increased number of head dips and time spent compared to controls. No significant differences in number of segments which travelled, vertical rears, orientation, defecation boli were detected between controls and rats with treatment to *Nelumbo nucifera* seeds extract (Table 3).

Rats after treatment to *Nelumbo nucifera* leaves' extract displayed an increased number of orientations, head dips, number of stops and latency to leave compared to controls. No significant differences in number of segments which travelled and missteps between controls and rats that got treatment to *Nelumbo nucifera* leaves extract were detected (Table 3).

Extract of *Nelumbo nucifera* fruits led to similar but more prominent changes. In the light part of the light-dark test, rats after treatment to *Nelumbo nucifera* fruits extract displayed a significant increase of number of orientations, head dips, stops and time spent compared to controls. No significant differences in number of vertical rears and missteps between controls and rats after treatment to *Nelumbo nucifera* fruits' extract were detected (Table 3).

After treatment to *Nelumbo nucifera* petals' extract rats displayed an increased number of sectors visited, orientation, head dips, number of stops and time spent compared to controls (Table 3).

In the dark compartment of the Suok-test, there was a similar effect of all studied *Nelumbo nucifera* extracts on rats' behavior (Table 4).

In the dark part of the light-dark Suok-test, rats after treatment to *Nelumbo nucifera* seeds extract, as well as in the control group, showed an increase in the number of stops, head dips, orientation and the time spent in the compartment. Also these rats showed significant increase in the number of transitions, and a decrease in displacement activity to zero compared to control values.

Rats after treatment to *Nelumbo nucifera* petals' extract displayed an increase in horizontal activity, the number of stops and the number of head dips, orientation and the number of transitions between compartments in comparison with the control group.

In the dark compartment of the Suok-test, rats after treatment to *Nelumbo nucifera* leaves extract displayed an increase in horizontal activity, the number of stops and the number of head dips, orientation and the time spent in the dark compartment of the test in comparison with control animals.

It is interesting to note the difference between the content of Rutin and Quercetin in plant parts studied and the influence of their extracts on Porsolt test's results. One can see that if maximal Rutin and Quercetin content was found in leafs and petals, the most pronounced *Nelumbo nucifera* effect in Porsolt test was detected for fruits and seeds. So, we can suppose that the main influence on Porsolt test's results have not rutin and querticin, but other biologically active substances of studied parts of *Nelumbo nucifera,* such as flavonoids, alkaloids, etc.

Table 1: Concentration of quercetin and rutin in extracts; mg / l

Nelumbo nucifera extracts	flavonoid	Rf	X (average)
Fruits G	rutin	0.33	4.89 mg
	quercetin	0.77	27.26 mg
Leaves G	rutin	0.30	16.63 mg
	quercetin	0.77	25.64 mg
Petals G	rutin	0.28	29.50 mg
	quercetin	0.76	29.28 mg
Seeds G	rutin	-	-
	quercetin	0.77	15.01 mg
Fruits MeOH	rutin	-	-
	quercetin	0.78	14.85 mg
Leaves MeOH	rutin	-	-
	quercetin	0.78	43.12 mg
Petals MeOH	rutin	0.36	14.55 mg
	quercetin	0.77	16.64 mg
Seeds MeOH	rutin	-	-
	quercetin	0.78	12.21 mg

Table 2: The influence of *Nelumbo nucifera* extracts on the behavior of despair in the Porsolt test

Parameter	Control	*Nelumbo nucifera* extracts			
		seeds	leaves	fruits	petals
Latency period (sec)	1, 3 ± 0, 28	1, 0 ± 0	1, 4 ± 0, 16	3, 0 ± 1, 21	0, 7 ± 0, 18
The time of active swimming (sec)	63, 1 ± 16, 7	136, 6 ± 19, 96 *	64, 6 ± 17, 71	156, 5 ± 6, 62*	68, 0 ± 23, 80
The time of passive swimming (sec)	16, 9 ± 2, 10	13, 6 ± 2, 26	11, 6 ± 2, 17	14, 4 ± 2, 60	9, 3 ± 2, 51 *
The time of immobilization (sec)	4, 8 ± 1, 13	0,5 ± 0, 32 *	2, 0 ± 0, 47 *	0, 7 ± 0, 67*	2, 0 ± 0, 86
Time before 1-st immobilization (sec)	87, 0 ± 15, 41	38, 8 ± 25, 46	60, 1 ± 16, 60	12, 7 ± 12, 66*	54, 7 ± 21, 48

*P < 0.05 vs. experimental groups

Table 3: The Influence of *Nelumbo nucifera* extracts on the parameters of behavior in the light part of the Suok Test

Parameter	Control	*Nelumbo nucifera* extracts			
		seeds	leaves	fruits	petals
Latency to leave, sec	13, 4 ± 4, 03	13, 8 ± 3, 73	22, 3 ± 7, 01	13, 1 ± 3, 05	11, 7 ± 4, 21
Horizontal activity (number of sectors visited)	4, 5 ± 1, 76	3, 8 ± 1, 38	4, 8 ± 1, 26	6, 0 ± 1, 87	11, 8 ± 3, 11*
Vertical activity (number of vertical rears)	0, 2 ± 0, 22	0, 1 ± 0, 11	0	0, 1 ± 0, 11	0
Orientation (side-directed exploration)	0, 7 ± 0, 27	1, 5 ± 0, 54	2, 2 ± 0, 47*	3, 1 ± 1, 03*	2, 8 ± 0, 71
Head dips (number of exploratory looks down)	1, 7 ± 0, 75	2, 8 ± 0, 91	4, 0 ± 1, 48	7, 0 ± 2, 21*	5, 3 ± 0, 82*
Time spent, sec	72, 1 ± 15, 79	90, 1 ± 21, 29	73, 5 ± 24, 57	132, 7 ± 20, 38*	148, 2 ± 22, 59*
Number of missteps	1, 4 ± 0, 24	0, 5 ± 0, 14*	0, 7 ± 0, 46	2, 5 ± 0, 72	1, 8 ± 0, 51
Stopping activity (number of stops)	1, 4 ± 0, 46	1, 6 ± 0, 58	4, 0 ± 1, 06*	3, 4 ± 0, 94*	2, 6 ± 0, 83

*P < 0.05 vs. experimental groups

Table 4: The Influence of *Nelumbo nucifera* extracts on the parameters of behavior in the dark part of the Suok Test

Parameter	Control	*Nelumbo nucifera* extracts			
		seeds	leaves	fruits	petals
Horizontal activity (number of sectors visited)	4, 7 ± 0, 73	9, 2 ± 2, 02	6, 1 ± 1, 29	4, 5 ± 1, 41	9, 1 ± 1, 29
Vertical activity (number of vertical rears)	0, 5 ± 0, 29	0, 2 ± 0, 22	0, 1 ± 0, 11	0, 1 ± 0, 11	0
Orientation (side-directed exploration)	1, 5 ± 0, 32	2, 7 ± 0, 71	3, 5 ± 0, 61	1, 7 ± 0, 68	3, 7 ± 1, 04*
Head dips (number of exploratory looks down)	3, 3 ± 1, 08	5, 6 ± 1, 41	6, 3 ± 1, 33	3, 5 ± 0, 99	6, 6 ± 1, 94
Time spent, sec	109, 3 ± 22, 35	166, 9 ± 27, 27	202, 9 ± 33, 71*	117, 6 ± 24, 14	153, 3 ± 29, 46
Number of missteps	1, 7 ± 0, 36	1, 8 ± 0, 27	1, 8 ± 0, 42	1, 8 ± 0, 53	2, 3 ± 0, 84
Stopping activity (number of stops)	1, 8 ± 0, 53	2, 6 ± 0, 60	4, 6 ± 0, 84*	2, 8 ± 0, 9	3, 6 ± 0, 83
Transitions	1, 0 ± 0, 27	2, 7 ± 0, 76*	1, 3 ± 0, 28	1, 1 ± 0, 35	1, 8 ± 0, 11

It is known that fruits, seeds, petals and leaves *Nelumbo nucifera* differs in the content of these biologically active substances[20,21]. Some of them, especially in fruits[22,23] and, were shown to have strong antidepressant effects. So, we can suppose that strong effect of fruit's and seed's extracts on Porsolt test's results deal with such biologically active substances as alkaloid Neferine[24], which was shown to possess psychotropic activity[16] and Liensinine and isoliensinine from which were shown to elicit antidepressant-like effects in mice[25]. So, our experiments not only further confirm the effects of *Nelumbo nucifera* different parts extracts in Porsolt and Suok tests, but also allows us to suggest their main active ingredients for future investigations.

CONCLUSION

Biologically active substances of fruits, petals, leaves and seeds of *Nelumbo nucifera* had a similar influence on the behavior of animals in the Suok-test. Their orientation-exploratory behavior was activated, while the emotionality and anxiety level of the rats under the influence of the biological active substances of *Nelumbo nucifera* was decreased, but the degree of these changes depends on the type of the extract.

The most prominent effect on psycho-physiological indicators was typical for petals and fruits *Nelumbo nucifera* extracts, and the highest content of rutin and quercetin according to the results of chemical analysis was detected in them.

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