

E. G. Prokopchuk, A. I. Aleksandrova, I. A. Kravchenko

**Neurotropic properties of new complex compounds of SnCl<sub>4</sub> with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde***Odesa National polytechnic university*

*Key words: sedative effect, anti-anxiety drugs, salicyloyl hydrazone complexes*

Physicians often deal with symptoms that overlap with depression and anxiety in people, when they observe abnormal emotional behaviour [1]. This partly could be explained that many neuropsychic diseases, primarily anxiety disorders, practically do not appear in isolated form. Anxiety is usually characterized by a state of chronic fear, which persists in the absence of a direct threat [2]. In fact, signals from the environmental stress factors such as life-threatening hazards, social stressors and reaction to injury in the organism, firstly transmitted by the sensory nervous system and then this information are processed by the so-called emotional patterns in the brain [3, 4].

Existing data demonstrate that various medicines used for depressive disorders had a number of additional effects such as sedation [5] and mood improvement [6]. Treatment of various diseases that usually accompanied with neuropsychic disorders leads to «polypragmasia» – prescription of many medicines (5 and more) at the same time [7]. Therefore, there is a big of interest to develop complex medicine with broad spectrum of the pharmacological action for the treatment of depressive disorders.

Our previous research was focused on the anti-depressive [8], analgesic [9], anti-inflammatory [10, 11] properties of the complex compounds of SnCl<sub>4</sub> with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde [8] and their functional aspects.

*The aim of our research* is to determine anxiolytic and sedative activity of

new complex compounds of SnCl<sub>4</sub> with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde in: «Open-field test» and «Light-dark box».

**Materials and methods.** Investigated substances – complex substances of tin tetrachloride with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde (C-I and C-II) (synthesized in the laboratory at the Department of general chemistry and polymers, Odesa I. I. Mechnikov National University), salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde in comparison with reference medicine – amitriptyline and such compounds as benzaldehyde and 4-bromobenzaldehyde.

Experiments were conducted on 96 sexual mature mice (weight 18–22 g) of both sexes. The experimental animals were obtained from the vivarium of Odessa National Medical University, which were kept in standard vivarium conditions. All studies conformed to the rules of the national «General ethical principles of animal experiments» (Ukraine, 2001), consistent with the provisions of the «European Convention for the protection of vertebrate animals used for experimental and other research purposes» (Strasbourg, France, 1986) [12].

The data obtained were processed by means of statistical analysis using computer software; arithmetic mean determination (M), standard error (m), Student's t distribution (t-test) and statistical significance coefficient (p-value), analysis of variance (ANOVA) were used for comparison of three and more samples. The compounds were administered orally as a water-twin emulsion in doses calculated based on the equimolar ratio in terms of salicylic acid residue at a dose of 40 mg/kg. Amitriptyline

---

---

was used as reference medicine («Doslidnyy zavod "GNTSLS"», TOV, Kharkiv) – 20 mg/kg equivalently to oral clinical dose 150 mg/kg [13].

Behaviour was analysed by means of the test «light-dark box» (LDB-test). It was conducted during 5 min in 1h, 3 h, 5 and 24 h after the oral administration of substances, registering the following values: residence time in the light box and number of peeps from black to light box (when mouse cross the hole by the front paws) [14].

Study of anxiety was conducted by means of «open-field test» during the equal time (1 h, 3 h, 5 h and 24 h). Examination was conducted during 5 min, registering numbers of stands on the hind paws (vertical mobility), numbers of peeps into holes (exploratory activity) and numbers of crossings the boxes (locomotor activity) [15].

*Light-dark box testing (LDB-test).* Rodents prefer the dark fields to the light ones. However, when rodents are in the new environment, they tend to explore the new space. These two conflicting emotions arouse interest in studying the anxiety level as a symptom [16]. Rodents generally spend more time in the dark places of the box than in the light one. The percentage of residence time in the «light box» increases when mice are under the effect of anxiolytic drugs. Increase of numbers when mice stand on their hind paws is an exploratory trait and increase of locomotor activity is an action of anxiolytic drug. In a case when these characteristics decrease but animals are mostly in the «dark box» indicates sedative effect of drugs [17].

**Results and discussion.** Thus, an hour after the experiment start both complexes were more effective comparing not only with the control group, but also with the reference medicine – amitriptyline. Hence, the sharp increase of the residence time in the «light box» has been evaluated for complex C-II 1 h after the LDB-test had started, i. e. by 81,6 % accordingly to the control and by 52,8 % for the complex C-I respectively. Three hours after the experiment start both complexes demonstrated lower anxiolytic

activity than reference medicine, but they remained at an adequately high level compared to the control.

Animals were in the «light box» and demonstrated no high anxiety level that indicated anxiolytic action of studied substances. Animals preferred «dark box» and almost did not visit the «light box» 5 h after administration of studied complexes. Such a reaction might be associated with combination of effects from the studied complexes, i. e., sedation that could be observed in animals. Absence of anxiolytic activity of reference medicine was observed in 24 h after the experiment start that could be associated with its elimination and duration of pharmacological activity. At the same time both complexes demonstrated the high anxiolytic effect, data were exceeded the control values by 46,7 % and 109,6 % for C-I and C-II respectively that probably indicated decrease of substance concentration in the organism by elimination and action prolongation of these complexes.

To determine whether the complexes and functional groups that contained in C-I and C-II demonstrate anxiolytic effect, the anxiolytic action of benzaldehyde (BA), 4-bromobenzaldehyde (4-BrBA), salicyloyl hydrazone of benzaldehyde (SHBA), salicyloyl hydrazone of 4-bromobenzaldehyde (SHBrBA) have been tested.

The data showed the pronounced anxiolytic action of SHBrBA that has statistically significant difference compared with reference medicine (Tabl. 1). Thus, 1 h after the oral administration the values exceed results from the group that received amitriptyline by 278 %. Next 3 h and 5 h after the SHBrBA administration the anxiolytic effect remained at the high level and even after 24 h it indicates the significant contribution into the anxiolytic effect of the studied complexes. Unlike SHBrBA, SHBA demonstrated sedation in animals after the oral administration and data were lower by 42,2–67,8 % according to the control. The results obtained from the animal group with administration of BA had no statistical difference as to the control.

Furthermore, the exploratory activity

Table 1

**Anxiolytic activity of studied substances during the LDB-test  
(residence time in the «light box», % to the control), (M ± m, n = 6)**

№	Substance	Anxiolytic activity, % to the control			
		1 hour	3 hours	5 hours	24 hours
1	Control	100,0 ± 12,1	100,0 ± 12,1	100,0 ± 12,1	100,0 ± 12,1
2	Amitripyline	2,0 ± 1,0**	279,0 ± 12,6**	150,4 ± 11,4**	23,1 ± 76,0
3	Complex I	152,8 ± 5,9**	123,9 ± 14,0**	36,6 ± 9,5*·	146,7 ± 7,2*·
4	Complex II	181,6 ± 28,5**·	172,5 ± 29,2*·	45,2 ± 6,4·	209,6 ± 9,4**·
5	BA	81,0 ± 4,0*	40,6 ± 6,9·	123,0 ± 11,2	128,0 ± 8,0·
6	4-BrBA	160,7 ± 7,0**	116,0 ± 1,3*·	116,0 ± 1,3*·	268,4 ± 9,0**·
7	SHBA	67,8 ± 12,7	32,2 ± 1,0**·	44,2 ± 8,2	43,9 ± 6,2
8	SHBrBA	278,5 ± 9,7**·	227,0 ± 9,6**	222,0 ± 8,8**·	229,5 ± 9,6**·

Note. Here and in Tabl. 2-5: \*p < 0,05 compared to the control, \*\*p < 0,01 compared to the control, ·p < 0,05 compared to the reference medicine, ··p < 0,01 compared to the reference medicine.

of mice have been investigated after the administration of studied compounds using the behavioral «LDB-test».

It should be emphasized that after the experiment start the data for both complexes were lower than control (Tabl. 2) that could be related to the effect overlapping, i. e., sedation. Thus, in 3 h after the administration of complexes C-I and C-II the number of peeps into the «light box» was drastically decreased, essentially to «zero».

According to the demonstrated data (Tabl. 2), it is obviously visible that animals spent more time in the «light box», hence, the number of «peeps» has been decreased. The data obtained (Tabl. 2) showed that C I and C-II essentially decreasing the number of «peeps» from the light to the dark space by animal after their administration in 3 h and 5 h. This behaviour indicated the significant seda-

tion and stress reduction against the exploring of new space rather than action of the reference medicine – amitripyline.

The animal behaviour has changed after 24 h probably by elimination and, respectively, by reducing concentration of the substance in the organism. It is possible to evaluate the increase of interest to the new space in animals that occurred in the increased numbers of «peeps» after the administration of substance C-I. The values in animals that received substance C-II substantially has not changed. According to data obtained it has showed the pronounced increase of «peeps» during the whole experiment by animals that received BA. The group that received SHBA showed decrease of «peeps» into the «light box» supported the sedative effect.

*Open-field test (OF-test).* OF-test is used both for evaluation of anxiolytic

Table 2

**Anxiolytic activity of studied substances during the LDB-test  
(number of «peeps» into the «light box», % to the control), (M ± m, n = 6)**

№	Substance	Anxiolytic activity, % to the control			
		1 hour	3 hours	5 hours	24 hours
1	Control	100,0 ± 10,6	100,0 ± 10,6	100,0 ± 10,6	100,0 ± 10,6
2	Amitripyline	68,8 ± 5,1**	79,2 ± 11,0**	87,5 ± 9,1**	108,3 ± 8,3
3	Complex I	57,0 ± 15,0**·	11,4 ± 6,0**·	6,8 ± 2*·	79,5 ± 15,0
4	Complex II	52,3 ± 1,0**·	28,4 ± 5,6**·	45,5 ± 9,3**·	34,1 ± 7,6**·
5	BA	220,1 ± 20,0·	166,7 ± 6,0**	159,0 ± 1,2	148,0 ± 4,0·
6	4-BrBA	50,0 ± 12,5**	122,3 ± 8,2*·	87,2 ± 4,2	42,6 ± 9,4**·
7	SHBA	63,5 ± 3,2**·	34,9 ± 3,2**	42,1 ± 8,3**	54,0 ± 1,4**·
8	SHBrBA	185,2 ± 42,8	61,7 ± 12,3**·	72,6 ± 9,4	86,4 ± 2,7

and sedative effects among studied substances as well as their impact on locomotor activity in the test animals. Sedation appeared in decrease of psychomotor agitation and daytime activity, decrease of mental alertness and reaction rate etc. [18]. Reduction of locomotor activity might indicate the stressing in animals [19].

According to the data on Tabl. 3 it is obviously visible that behavior of animals with administration of C-I and C-II had no statistical difference between both complexes and control 1 h after the experiment start, may be due to the partial admission into the systemic blood flow. In 3 h and 5 h the significant inhibition of locomotor activity have been observed by amitriptyline as well as by action of complex compounds through the increase of substance concentration which entered the systemic circulation. In 3 h and 5 h the significant inhibition of locomotor activity have been observed by amitriptyline as well as by action of complex compounds through the increase of substance concentration which entered the systemic circulation. In 3 h after experiment start the locomotor activity has been lower than controls by 80 % for both complexes, and in 5 h it has been 8,0 % and 27,3 % respectively for C-I and C-II comparing with control. 24 h after administration the animal locomotor activity increased under action of complexes, but did not reach the control values that indicated prolonged action – it was by 54 % and 42 %, lower comparing with control for the C-I and C-II respectively. It comes

to conclusion that pronounced anxiolytic activity of both complexes C-I and C-II had the same effect as reference medicine – amitriptyline.

According to the demonstrated data (Tabl. 3) in is visible that administration of SHBrBA, SHBA and 4-BrBA in 1 h after the oral administration increased locomotor activity at the level of amitriptyline. During next 24 h of experiment the gradual reduce of locomotor activity have been observed that indicated the increase of anxiolytic action of such substances. The most pronounced anxiolytic effect of substances has been observed in 5 h after administration, but their efficacy has not been permanent and in 24 h they decreased to the control level.

This should be emphasized that BA had pronounced anxiolytic activity right in an hour after the experiment start and during 5 h its efficacy has persisted under sufficient level.

The decrease of the vertical activity has been observed (Tabl. 4). The vertical activity, i. e. the posture of animals characterises the interest to explore new places, to dominate in the population and to show the aggressive behaviour [20].

The oral administration of C-II has induced significant anxiolytic effect. During the 1<sup>st</sup> hour of the experiment the data have been lower than control by 49,4 %, the anxiolytic effect of the complex has been increased next 3 h and 5 h of the experiment.

Anxiolytic activity of C-I has been observed on 3<sup>rd</sup> h of the experiment and

Table 3

*Locomotor activity of studied substances during the OF-test (% to the control), (M ± m, n = 6)*

№	Substance	Locomotor activity, % to the control			
		1 hour	3 hours	5 hours	24 hours
1	Control	100,0 ± 5,2	100,0 ± 5,2	100,0 ± 5,2	100,0 ± 5,2
2	Amitriptyline	138,9 ± 2,4	58,4 ± 3,0**	50,4 ± 4,2**	66,2 ± 3,4*
3	Complex I	112,4 ± 10,0**	21,6 ± 6,9**, **	8,0 ± 0,7**, **	46,1 ± 4,1**, **
4	Complex II	89,7 ± 6,3**	22,0 ± 6,6**, **	27,3 ± 8,2**, **	58,1 ± 8,2**
5	BA	67,0 ± 4,0**	70,0 ± 14,2	95,0 ± 1,2**	99,0 ± 11,0
6	4-BrBA	156,9 ± 9,6**	77,7 ± 16,8	59,4 ± 2,2**	101,4 ± 25,1*
7	SHBA	131,9 ± 32,0	102,2 ± 19,2**	76,4 ± 2,6	110,3 ± 3,6
8	SHBrBA	149,0 ± 9,4*	110,4 ± 7,5**	59,4 ± 1,0**	91,7 ± 6,3

Table 4

*Vertical activity of the studied substances during the OF-test (% to the control),  
(M ± m, n = 6)*

№	Substance	Vertical activity, % to the control			
		1 hour	3 hours	5 hours	24 hours
1	Control	100,0 ± 10,9	100,0 ± 10,9	100,0 ± 10,9	100,0 ± 10,9
2	Amitripyline	263,6 ± 10,3**	72,4 ± 2,8	41,4 ± 6,9	89,7 ± 11,3
3	Complex I	104,1 ± 7,2**	39,0 ± 6,3**	4,2 ± 1,7**	44,3 ± 7,2*
4	Complex II	50,6 ± 20,3*..	45,1 ± 6,0**	19,0 ± 5,6**	78,1 ± 9,4
5	BA	101,0 ± 17,0**	86,0 ± 11,6	62,0 ± 6,0	45,0 ± 11,0*
6	4-BrBA	175,0 ± 11,7**..	92,4 ± 12,5	124,2 ± 4,2	111,3 ± 9,8
7	SHBA	257,1 ± 14,3**	64,3 ± 21,4*	58,6 ± 11,5	128,6 ± 11,5**..
8	SHBrBA	175,0 ± 21,7**..	106,3 ± 8,8	68,8 ± 11,3**	200,0 ± 12,5**..

Table 5

*Exploratory activity of studied substances during the OF-test (% to the control),  
(M ± m, n = 6)*

№	Substance	Exploratory activity, % to the control			
		1 hour	3 hours	5 hours	24 hours
1	Control	100,0 ± 11,9	100,0 ± 11,9	100,0 ± 11,9	100,0 ± 11,9
2	Amitripyline	210,5 ± 10,5**	47,4 ± 5,3	78,9 ± 10,5	78,9 ± 4,3
3	Complex I	87,7 ± 5,6**	21,7 ± 7,1**	18,9 ± 6,2**..	66,0 ± 7,6
4	Complex II	136,8 ± 9,1*..	78,3 ± 6,7	21,7 ± 3,5**..	31,1 ± 9,8*
5	BA	154,0 ± 8,0**..	132,0 ± 5,0**	118,0 ± 7,0*	114,0 ± 10,0
6	4-BrBA	141,7 ± 8,3**..	131,0 ± 12,6**	75,0 ± 8,3	92,0 ± 9,7
7	SHBA	96,0 ± 8,0**	48,0 ± 8,0	48,0 ± 4,0**	36,0 ± 4,0*
8	SHBrBA	177,8 ± 8,3**..	250,0 ± 3,3**..	175,0 ± 8,3	111,7 ± 5,0**..

has reached the maximum on 5<sup>th</sup> h after administration. BA and SHBA also have demonstrated anxiolytic activity during 3 h and 5 h of the experiment. At the same time the data obtained with 4-BrBA and SHBrBA had no significant differences in comparison with control.

The values of «hole activity» (Tabl. 5) in OF-test have demonstrated correlation with exploratory activity in LDB-test (numbers of «peeps» from the «light box» to the «dark box»).

The data obtained during the experiment have supported sedation of complexes in 3 h, 5 h and 24 h after the experiment. The data obtained after SHBA administration represented its role in the sedation of complexes, in turn,

SHBrBA administration demonstrated pronounced anxiolytic effect. Probably the anxiolytic activity has occurred due to bromine atoms presence in the structure of the complexes that also supported by the study of our colleagues [21].

### Conclusions

The study of anxiolytic activity of the complex compounds of SnCl<sub>4</sub> with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde demonstrated that after the oral administration of these compounds the expressive neurotropic effect had observed during the 24 h of the experiment. The study of salicyloyl hydrazones of 4-bromobenzaldehyde indicated its significant contribution

into the anxiolytic effect of the C-II.

1. The cellular and molecular basis of major depressive disorder: towards a unified model for understanding clinical depression. E. Pitsillou, S. M. Bresnehan, E. A. Kagarakis et al. *Molecular biology reports*. 2020. V. 47 (1). P. 753–770. <https://doi.org/10.1007/s11033-019-05129-3>.

2. Current concept of anxiety: implications from Darwin to the DSM-V for the diagnosis of generalized anxiety disorder. F. C. Coutinho, G. P. Dias, M. C. do Nascimento Bevilaqua et al. *Expert. Rev. Neurother.* 2010. V. 10, № 8. P. 1307–1320.
3. Hyman S. E. How mice cope with stressful social situations. *Cell.* 2007. V. 131 (2). P. 232–234. <https://doi.org/10.1016/j.cell.2007.10.008>.
4. A frontal-vagal network theory for Major Depressive Disorder: Implications for optimizing neuro-modulation techniques. T. A. Iseger, N. van Bueren, J. L. Kenemans et al. *Brain stimulation.* 2020. V. 13 (1). P. 1–9. <https://doi.org/10.1016/j.brs.2019.10.006>.
5. Mula M., Pini S., Cassano G. B. The role of anticonvulsant drugs in anxiety disorders: a critical review of the evidence. *J. Clin Psychopharmacol.* 2007. V. 27. P. 263–272.
6. Effectiveness of antiepileptic drugs for the treatment of bipolar disorder: findings from a systematic review. C. L. Melvin, T. S. Carey, F. Goodman et al. *J. Psychiatr Pract.* 2008. V. 14 (Suppl. 1). P. 9–14.
7. Guillot J., Maumus-Robert S., Bezin J. Polypharmacy: A general review of definitions, descriptions and determinants. *Therapie.* 2020. V. 75 (5). P. 407–416. <https://doi.org/10.1016/j.therap.2019.10.001>.
8. Протисудомна й антидепресивна активність нових комплексів SnCl<sub>4</sub> з саліцилоїлгідразонами бензальдегіду та 4-бромбензальдегіду при пероральному введенні. О. І. Александрова, І. А. Кравченко, О. Г. Прокопчук та ін. *Одеський медичний журнал.* 2015. № 5 (151). С. 24–27.
9. Prokopchuk E., Aleksandrova A., Kravchenko I. Analgesic activity of new complex compounds SnCl<sub>4</sub> with salicyloylhydrazones of benzaldehyde and brombenzaldehyde. *Journal of Education, Health and Sport.* 2019. № 9 (2). P. 156–164.
10. Прокопчук О. Г., Александрова О. І., Кравченко І. А. Anti-inflammatory activity of complex compounds tin (IV) chloride (SnCl<sub>4</sub>) with salicyloyl hydrazones benzaldehyde and 4-bromobenzaldehyde on carrageenan and formalin-induced inflammation. *Актуальні проблеми транспортної медицини.* 2019. № 1 (55). С. 63–68.
11. Противовоспалительная активность новых комплексов SnCl<sub>4</sub> с салицилоилгидразами бензальдегида и 4-бромбензальдегида. А. И. Александрова, Е. Г. Прокопчук, Н. В. Шматкова, И. И. Сейфулліна, И. А. Кравченко. *Актуальні проблеми транспортної медицини.* 2017. № 2 (48). С. 136–141.
12. European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Strasbourg, Council of Europe. 1986. № 123. 51 p.
13. Ghosh M. N. Fundamentals of Experimental Pharmacology. 5<sup>th</sup> ed. Kolkata : S.K. Ghosh and Others, 2011. 287 p.
14. Takao K., Miyakawa T. Light/dark transition test for mice. *Journal of Visualized Experiments.* 2006. V. 13 (1). P. 104. <https://doi.org/10.3791/104>.
15. Лапин И. П. Модели тревоги на мышах: оценка в эксперименте и критика, методики. Москва : Медицина, 2000. 361 с.
16. Ennaceur A. Tests of unconditioned anxiety – Pitfalls and disappointments. *Physiology & Behavior.* 2013. V. 135. P. 55–71. <https://doi.org/10.1016/j.physbeh.2014.05.032>.
17. Borsini F., Podhorna J., Marazziti D. Do animal models of anxiety predict anxiolytic-like effects of antidepressants? *Psychopharmacology.* V. 163. P. 121–141. <https://doi.org/10.1007/s00213-002-1155-6>.
18. General practitioners' experiences and perceptions of benzodiazepine prescribing: systematic review and meta-synthesis. C. Sirdifield, S. Antheriens, H. Creupelandt et al. *BMC family practice.* 2013. V. 14. P. 191. <https://doi.org/10.1186/1471-2296-14-191>.
19. Буреш Я. Методики и основные эксперименты по изучению мозга и поведения. Москва : Высшая школа, 1991. 399 с.
20. Ivinkis A. A study of validity of open-field measures. *Austral. J. Psychol.* 1970. V. 22. P. 175–183.
21. A Novel Bromine-Containing Paroxetine Analogue Provides Mechanistic Clues for Binding Ambiguity at the Central Primary Binding Site of the Serotonin Transporter. R. D. Slack, A. M. Abramyan, H. Tang et al. *ACS chemical neuroscience.* V. 10 (9). P. 3946–3952. <https://doi.org/10.1021/acscchemneuro.9b00375>.

**E. G. Prokopchuk, A. I. Aleksandrova, I. A. Kravchenko**  
**Neurotropic properties of new complex compounds of SnCl<sub>4</sub> with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde**

Existing data demonstrate that various medicines used for depressive disorders therapy had a number of additional effects such as sedation and mood improvement. In fact, signals from the environmental stress factors such as life-threatening hazards, social stressors and reaction to injury in the organism, firstly transmitted by the sensory nervous system and then this information are processed by the so-called emotional patterns in the brain. Treatment of various diseases that usually accompanied with neuropsychic disorders leads to «polypragmasia» – prescription of many medicines (5 and more) at the same time. Therefore, there is a big of interest to develop complex medicine with broad spectrum of the pharmacological action for the

treatment of depressive disorders. Our previous research was focused on the anti-depressive properties of the complex compounds of  $\text{SnCl}_4$  with salicyloyl hydrazones of benzaldehyde (C-I) and 4-bromobenzaldehyde (C-II) and their functional aspects.

The aim of the study is to determine anxiolytic and sedative activity of new complex compounds of  $\text{SnCl}_4$  with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde in: «Open-field test» and «Light-dark box».

Behaviour of experimental animals (mouse) was analysed by means of the test «light-dark box». It was conducted during 5 min in 1 h, 3 h, 5 and 24 h after the oral administration of substances, registering the following values: residence time in the light box and number of peeps from black to light box. Study of anxiety was conducted by means of «open-field test» during the equal time (1 h, 3 h, 5 h and 24 h). Examination was conducted during 5 min, registering numbers of stands on the hind paws (vertical mobility), numbers of peeps into holes (exploratory activity) and numbers of crossings the boxes (locomotor activity). To determine whether the complexes and functional groups that contained in C-I and C-II demonstrate anxiolytic effect, the anxiolytic action of benzaldehyde, 4-bromobenzaldehyde, salicyloyl hydrazone of benzaldehyde, salicyloyl hydrazones of 4-bromobenzaldehyde have been tested.

The results of anxiolytic activity study of the complex compounds of  $\text{SnCl}_4$  with salicyloyl hydrazones of benzaldehyde and 4-bromobenzaldehyde demonstrated that after oral administration of these compounds the expressive neurotropic effect had observed during the 24 h of the experiment. The study of salicyloyl hydrazones of 4-bromobenzaldehyde indicated its significant contribution into the anxiolytic effect of the C-II. Probably the anxiolytic activity has occurred due to bromine atoms presence in the structure of the complexes.

*Key words: sedative effect, anti-anxiety drugs, salicyloyl hydrazone complexes*

### **О. Г. Прокопчук, О. І. Александрова, І. А. Кравченко** **Нейротропні властивості нових комплексних сполук $\text{SnCl}_4$** **з саліцилоїлгідрозонами бензальдегіду та 4-бромбензальдегіду**

Існують дані, що багато препаратів, які призначаються для лікування депресивних розладів, мають низку додаткових ефектів, таких як седация та покращання настрою. Відомо, що сигнали від стресових факторів навколишнього середовища, таких як небезпека для життя, соціальні стресори та реакції на травму в організмі, спочатку передаються сенсорною нервовою системою, а потім послідовно інформація обробляється так званими емоційними контурами в мозку. Лікування низки захворювань, що часто супроводжуються нейropsychічними розладами, призводить до явища «поліпрагмазії» – призначення 5 і більше лікарських препаратів. Саме тому важливі пошук і розробка комплексного засобу з широким спектром дії, а засоби, що здатні усувати відчуття тривоги та/або седацию мають особливий інтерес. Раніше нами були встановлені антидепресивні властивості комплексних сполук  $\text{SnCl}_4$  з саліцилоїлгідрозонами бензальдегіду (K-I) та 4-бромбензальдегіду (K-II) та їхніх функціональних складових.

*Мета дослідження* – визначення анкіолітичної та седативної активності нових комплексних сполук  $\text{SnCl}_4$  з саліцилоїлгідрозонами бензальдегіду та 4-бромбензальдегіду в тестах «Відкрите поле» і «Світла–темна камера».

Аналіз поведінки експериментальних тварин (мишей) у тесті «Світла–темна камера» проводили протягом 5 хв через 1, 3, 5 і 24 год після перорального введення сполук, що вивчались, реєструючи наступні показники: час перебування в світлому відсіку та кількість виглядань у світлий відсік з темного. Дослідження тривожності проводили в тесті «Відкрите поле» через визначені проміжки часу (1, 3, 5 і 24 год). Спостереження проводили впродовж 5 хв, реєструючи число вставань на задні лапи (вертикальні переміщення), число заглядань у отвори (дослідницька активність) і кількість перетинів квадратів (локомоторна активність). Для виявлення внеску в анкіолітичну активність комплексних сполук K-I і K-II функціональних груп, що входять до їхньої структури, було досліджено анкіолітичну дію таких сполук: бензальдегід, 4-бромбензальдегід, саліцилоїлгідрозони бензальдегіду і 4-бромбензальдегіду.

Результати дослідження анкіолітичної активності комплексних сполук  $\text{SnCl}_4$  з саліцилоїлгідрозонами бензальдегіду та 4-бромбензальдегіду показали, що пероральне введення даних комплексів викликає виражений протитривожний ефект упродовж 24 год експерименту. Дослідження саліцилоїлгідрозону 4-бромбензальдегіду свідчить про його внесок у протитривожну активність комплексу II. Імовірно, саме наявність атому бромю в структурі сполук обумовлює анкіолітичний ефект.

*Ключові слова: седативний ефект, протитривожні засоби, комплексні сполуки саліцилоїлгідрозонів*

### **Е. Г. Прокопчук, А. И. Александрова, И. А. Кравченко** **Нейротропные свойства новых комплексных соединений $\text{SnCl}_4$** **с салицилоилгидразонами бензальдегида и 4-бромбензальдегида**

Существуют данные, что многие препараты, предназначенные для лечения депрессивных расстройств, имеют ряд дополнительных эффектов, таких как седация и улучшение настроения.

---

---

Известно, что сигналы от стрессовых факторов окружающей среды, таких как опасность для жизни, социальные стрессоры и реакции на травму в организме, сначала передаются сенсорной нервной системой, а затем последовательно информация обрабатывается так называемыми эмоциональными контурами в мозге. Лечение ряда заболеваний, часто сопровождающихся нейропсихическими нарушениями, приводит к «полипрагмазии» – назначению 5 и более лекарственных препаратов. Именно поэтому представляет интерес поиск и разработка комплексного средства широкого спектра действия, а средства, способные устранять чувство тревоги и / или седацию представляют отдельный интерес. Ранее нами были установлены антидепрессантные свойства комплексных соединений SnCl<sub>4</sub> с салицилоилгидразолами бензальдегида (K-I) и 4-бромбензальдегида (K-II) и их функциональных составляющих.

*Цель исследования* – определение анксиолитической и седативной активности новых комплексных соединений SnCl<sub>4</sub> с салицилоилгидразолами бензальдегида и 4-бромбензальдегида в тестах «Открытое поле» и «Светлая–темная камера». Анализ поведения экспериментальных животных (мышей) в тесте «Светлая–темная камера» проводили в течение 5 мин через 1, 3, 5 и 24 ч после перорального введения соединений, которые изучались, регистрируя следующие показатели: время пребывания в светлом отсеке и количество заглядываний в светлый отсек из темного. Исследование тревожности проводили в тесте «Открытое поле» через определенные промежутки времени после введения комплексных соединений (1, 3, 5 и 24 ч). Наблюдение проводили в течение 5 мин, регистрируя число подъемов на задние лапы (вертикальные стойки), число заглядываний в отверстия (исследовательская активность) и количество пересеченных квадратов (локомоторная активность). Для выявления вклада в анксиолитическую активность комплексных соединений I и II функциональных групп, входящих в их структуру, было исследовано анксиолитическое действие таких соединений: бензальдегид, 4-бромбензальдегид, салицилоилгидразоны бензальдегида и 4-бромбензальдегида.

Результаты исследования анксиолитической активности комплексных соединений SnCl<sub>4</sub> с салицилоилгидразолами бензальдегида и 4-бромбензальдегида показали, что пероральное введение данных комплексов вызывает выраженный противотревожный эффект в течение 24 ч эксперимента. Исследование салицилоилгидразона 4-бромбензальдегида свидетельствует о его вкладе в противотревожную активность комплекса II. Вероятно, именно наличие атома брома в структуре соединений обуславливает анксиолитический эффект.

*Ключевые слова:* седативный эффект, противотревожные средства, комплексные соединения салицилоилгидразонов

---

Надійшла: 1 жовтня 2020 р.

Прийнята до друку: 2 грудня 2020 р.

**Контактна особа:** Прокопчук Олена Геннадіївна, старший викладач, Одеський національний політехнічний університет, буд. 31, вул. Володимира Винниченка, м. Одеса, 65006.  
Тел.: + 38 0 98 555 12 61. Електронна пошта: pochawt@me.com