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PHYSICAL ACTIVITY OF RATS UNDER ORAL EXPOSURE TO 2,6-DIMETHYL-N-PYRIDINE OXIDE (IVIN) IN THE ROTAROD TEST

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Background. Environmental and human lifestyle pollution with industrial chemicals, intensification of production, a long-lasting physical, emotional, and psychogenic stress lead to the occurrence of a variety of somatic diseases, fatigue, and memory disorders. This may be due to a reduced non-specific resistance and functional reserves of an organism, as well as the development of stressful conditions. Therefore, a current priority in preventive toxicology is the search for synthetic substances with adaptogenic properties that can enhance the immune system's resistance to adverse effects. In this regard, the task of this study was to investigate the physical activity of rats under the influence of 2,6-dimethylpyridine N-oxide (Ivin) and under conditions of additional chemical load with chlorpyrifos. The aim of the research was to study the Ivin's effect on the motor activity and coordination of Wistar Hannover rats and on the resistance of an organism to an additional chemical agent load.

Materials and Methods. 2,6-dimethylpyridine N-oxide, 99.9% (Ivin) was chosen for the study. Adaptogen Eleutherococcus was used as a comparison agent. The study was conducted on 50 male Wistar Hannover rats divided into 5 groups (10 rats per group): 1 – intact animals (not treated male rats), 2 – control animals (trained male rats were treated with distilled water as a vehicle), in groups 3 and 4 rats were treated with Ivin at doses of 13.0 and 0.013 mg/kg (1/100 and 1/100000 LD_{50}), respectively, 5 – male rats were treated with Eleutherococcus (as a positive control) at a dose of 50 mg/kg. The exposure period with oral administration lasted for 28 days. The physical activity of rats was studied using the rotarod test. Following the completion of Ivin treatment, the animals in the same experimental groups were administered chlorpyrifos (CHP)

at a single dose of 37.5 mg/kg to evaluate their physical activity under conditions of an additional toxic load.

Results and Conclusions. It was found that the time spent by rats on a rotating cylinder increased by more than 11 and 10 times after a single exposure to Ivin at a dose of 13.0 mg/kg and 0.013 mg/kg, respectively. Following 14 and 28 days of exposure to Ivin at a dose of 0.013 mg/kg, the covered distance was increased by 172.7 % and 291.5 %, and the time spent on the rod was increased by 2.5 and 3.5 times, respectively, in comparison with intact animals. Significantly relevant changes in the parameters caused by eleutherococcus were observed after the 28-day exposure. After administration of CHP at a dose of 37.5 mg/kg to intact and control (trained) rats, the time spent on the rod decreased by almost 2 times. In groups of animals that received CHP in combination with Ivin, the riding time of the rats was 27–30 % higher compared to the effect of the combination of eleutherococcus reference drug and CHP.

Thus, Ivin at a 13 mg/kg single exposure, and at a 0.013 mg/kg single and long-term exposure significantly increases the time spent by rats on a rotating rod (rotarod test), which indicates an increase in motor activity, balance, and muscle strength of animals. The efficacy of Ivin was comparable to, or greater than that of the reference drug, eleutherococcus. chlorpyrifos significantly reduces the physical activity of intact and control (physically trained) rats in the rotarod test. Ivin, at the tested doses, diminished the negative effect of chlorpyrifos on the physical performance of rats, indicating an increase of the organism resistance to additional chemical load.

Keywords: 2,6-dimethylpyridine N-oxide, physical activity, rats, rotarod test, chlorpyrifos

INTRODUCTION

Latest studies have shown that environmental and human environment pollution with chemicals, intensification of manufacturing processes, as well as long-lasting physical, emotional and psychogenic stress can lead to a variety of somatic diseases, fatigue, and memory disorders. These may be due to decreased nonspecific resistance and functional reserves of humans, and the development of stressful conditions (Vyunytska, 2018; Vyunytska *et al*., 2022; Zarudna & Mural, 2013; Kalka, 2015). Prevention of the adverse effects of stress by herbal preparations with adaptogenic properties has been suggested (Wiegant *et al*., 2009; Ajala, 2017; Salve *et al*., 2019). Herbal adaptogens are characterised by pleiotropic effects, such as antioxidant, antitoxic, cytoprotective, neuroprotective, anxiolytic, antidepressant, etc., which make it possible to correlate disturbances in the homeostasis and, specifically, in the state of the central nervous system, and to increase physical efficiency and cognitive functions of the human brain (Panossian & Wikman, 2010; Panossian & Wagner, 2011; Amir *et al*., 2023).

In this regard, the search for synthetic substances with adaptogenic properties, which would increase the resistance of an organism and prevent the occurrence of harmful effects in isolation or in combination with both chemical and physical factors, is an important aspect of preventive toxicology.

According to M. Amir *et al*., (2023), adaptogens are required to meet the following criteria: to be low-toxic and cause minimal disturbances in the physiological functions of an organism, to have a multivalent mechanism of action and pharmacological effect on adaptation and survival, to have a nonspecific effect, i.e. to increase resistance to

adverse effects of a wide range of physical, chemical and biological factors, to have a normalising effect despite the orientation of pathological changes. The plant growth regulator (PGR) – Ivin (2,6-dimethylpyridine N-oxide) can meet these criteria, as it is a low-toxic substance, and when combined with pesticides of different chemical groups, it reduces their toxicity and intoxication. It decreases lipid peroxidation, provides antioxidant, antihypoxic, hepatoprotective, genoprotective, membrane-stabilising effects, intensifies protein and nucleic acid synthesis, which can play an important role in both xenobiotic toxicity and stabilisation of homeostasis (Vasetska *et al.,* 2023).

In the plant organism, Ivin increases the intensity of transcription and translation processes, promotes the activation of gene expression, activates RNA and protein synthesis, affects membrane processes, active ion transport, and the system of regulation of H^+-ATPase activity. The effect of this agent on plants is determined by the unique features of its structure and thermal movement of the molecule (Ponomarenko, 1999; Ponomarenko & Iutynska, 2011; Iutynska *et al.*, 2010; Ribchenko & Palladina, 2012). Ivin has an ability to protect plants from physical and chemical factors (temperature, salt stress, heavy metals) (Ponomarenko & Iutynska, 2011; Grishko & Demura, 2009; Havrys *et al*., 2013; Ryabchenko *et al*., 2006).

Considering the biological properties of Ivin, its increased resistance to stress under the influence of factors of different nature, in particular resistance to physical activity under the influence of chemicals, can be expected. In this regard, the task of this study was to investigate the physical activity of rats under the influence of 2,6-dimethylpyridine N-oxide (Ivin) and under conditions of additional chemical load with chlorpyrifos.

The aim of the research was to study the effect of Ivin on the motor activity and coordination of Wistar Hannover rats and on the resistance of an organism to an additional chemical agent load.

MATERIALS AND METHODS

The PGR Ivin – 2,6-dimethylpyridine N-oxide (99.9%, liquid, clear from colourless to yellowish, miscible with water), produced by NE ISTC 'Agrobiotech', Kyiv, Ukraine, was used in the present study. The adaptogen Eleutherococcus extract (manufactured by PJSC FF 'Viola', Zaporizhzhia, Ukraine (UA/11560/01/01)) was selected as a reference substance (Todorova, 2021). The organophosphate insecticide chlorpyrifos, 97.5% (O-3,5,6-trichloropyridyl-2)-O,O-diethyl thiophosphate), was used for additional chemical exposure to animals administered with Ivin. Chlorpyrifos was chosen as a model of toxic load due to its known neurotoxic effect and ability to reduce physical activity in rodents (Hallal *et al.*, 2019; Moser *et al.*, 2005).

The experiments were conducted on mature Wistar Hannover male rats (50 animals weighing 230–240 g). The rats were taken from the Specific Pathogen Free (SPF) nursery of the State Enterprise "L. I. Medved Research Center of Preventive Toxicology, Food and Chemical Safety", the Ministry of Health of Ukraine, and placed in a conventional vivarium. The animals underwent a 7-day acclimatization period under veterinary supervision. According to the experimental design, animals were divided into five groups (10 rats per group): group 1 – intact animals (untreated male rats); group 2 – control animals (treated with distilled water as a vehicle); group 3 – male rats treated with Ivin at a dose of 13.0 mg/kg body weight (1/100 LD_{50}, subtoxicity dose); group 4 – male rats treated with Ivin at a dose of 0.013 mg/kg body weight (1/100000 LD_{50}, no effect dose); group 5 – male rats treated with Eleutherococcus (as a positive control) at a dose

of 50 mg of extract/kg body weight (therapeutical dose). Solutions of the test substances were prepared extempore with distilled water as a solvent (vehicle).

The test substances were orally administered to rats during 28 days in the morning at the same time. The volume of the solution administered to the stomach did not exceed 1.0 mL per 100 g of animal weight. Male rats were kept in standard vivarium conditions for studying the functional state of the central nervous system.

Daily clinical examination of animals was carried out to identify possible symptoms of intoxication and neurological disorders (Moser, 2000).

Behavioural reactions were tested according to the Guidelines (Stefanov, 2001) in compliance with the stable environment (temperature, lighting regime and air humidity), free access to feed and water, etc. (Hånell & Marklund, 2014).

The physical activity of animals was studied in the test of balancing on a rotating rod or rotarod test, which was proposed by N. W. Dunham and T. S. Miya (1957) for assessing the effect of drugs on animal behavior, in particular on neuromuscular coordination (Williams & Porsolt, 2007; Cenci & Lundblad, 2005). The rotarod is composed of a rod with a diameter of 7 cm that rotates at a constant speed of 20 rotations per minute. The rod installed at 15 cm above the floor has blades (drums) allowing simultaneous testing several animals. For the experiments, animals with medium endurance were selected. The experimental scheme is illustrated in **Fig. 1**. The testing was conducted on days 0 (before treatment), 1, 14, and 28 of exposure at the same time in the morning. The riding distance and the total riding time (in seconds) on a rotating rod were determined. During intervals between tests, the animals of groups 2–5 were trained twice a week with a 50 % load (i.e., 50% of the time from the previous test). During testing, the possible signs of dangerous overfatigue (weakness, nosebleeds, etc.) were monitored.

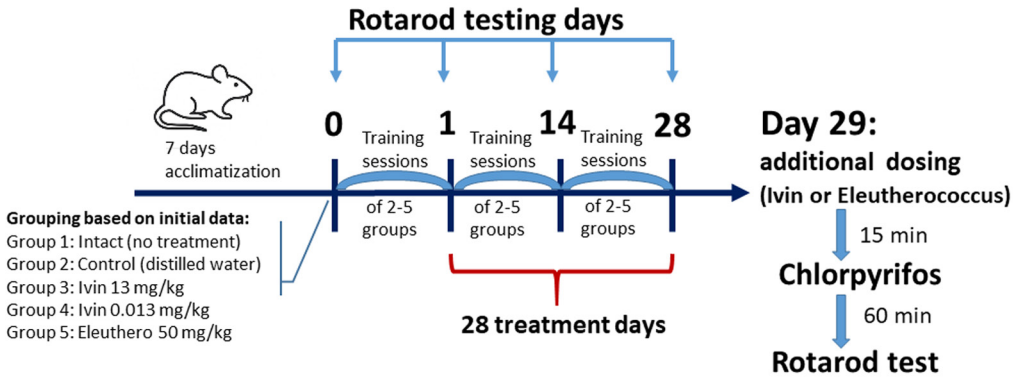

Fig. 1. Scheme of the experiment

In the case of observed improvement in physical performance of animals under the influence of Ivin, it was important to investigate whether high physical activity in rats would be maintained under additional chemical load. The day following the final testing, rats were orally administered Ivin at doses of 13 and 0.013 mg/kg, or Eleutherococcus at a dose of 50 mg/kg, and 15 min later with chlorpyrifos (CHP) at a dose of 37.5 mg/kg (1/2 LD_{50}). Through 60 min after administration of CHP, the animals have been tested in the rotarod test.

The animal model study was conducted in accordance with the principles of bioethics and the requirements of the Medical and Biological Research Ethics Commission of the L. I. Medved Research Center of Preventive Toxicology, Food and Chemical, Ministry of Health, Ukraine (State Enterprise) (Minutes No. 9/1 dated 09.05.2020).

Statistical processing of the obtained data was carried out using one-way or two-way ANOVA with the factors being the effects of treatment (five experimental groups) and treatment duration (0, 1, 14, or 28 days) followed by Fisher's LSD or Student's – *t*-test when appropriate. The data were tested for normality of distribution according to Shapiro–Wilk test. The results were presented in the form of mean values and square deviation of the mean (M ± m). Differences were considered significant at $p \leq 0.05$ for all tests.

RESULTS AND DISCUSSION

Exposure to Ivin did not result in clinical symptoms of intoxication, behaviour changes, or mortality in experimental animals.

The physical performance is an integral indicator of the functiona strength of an organism. The rotarod test allows assessing physical endurance after the injection of adaptogenic substances (Ray *et al.*, 2016). As is known, during the test on a rotating rod, the results depend on two parameters – motor coordination and muscle strength. To eliminate the effect of motor coordination, a fixed standard rotation speed of the rod is applied, which is usually used for all healthy animals (Hamm, *et al.*, 1994).

The effect of Ivin and the reference substance Eleutherococcus on the physical activity of male rats is shown in **Fig. 2**. The two-way ANOVA analysis of the obtained data demonstrated significance for the main effects of the treatment factor ($p = 0.005$, $F(4, 180) = 3.854$) and the treatment duration factor ($p = 0.0001$, $F(3, 180) = 1.582$). However, no significance was observed for the interaction factors ($p = 0.49$, $F(12, 180) = 0.9520$). Analysis of the dynamics of physical performance under the conditions of the present experiment showed that a single administration of Ivin at a dose of 13 mg/kg significantly increased ($p = 0,04$, by Student's *t*-test) the total riding time of rats on a rotating rod and, accordingly, the riding distance, in comparison to intact animals. A comparable trend was observed with the exposure to Ivin at a dose of 0.013 mg/kg and the reference drug Eleutherococcus.

As illustrated in **Fig. 2*A***, after a single administration of Ivin at both 13.0 mg/kg and 0.013 mg/kg statistically significant changes in riding time were observed compared to the initial data (day 0). Specifically, the former group exhibited an increase of more than 11 times the initial value ($p = 0.02$, by Fisher's LSD test), the latter group demonstrated an increase of over 10 times the initial level ($p = 0.02$, by Fisher's LSD test). In the Eleuthero group, an increase in riding time was also noted compared to the initial values ($p = 0.04$, by Fisher's LSD test).

Following exposure to Ivin over a period of 14 and 28 days (**Fig. 2*B*,*C***), a statistically significant increase in physical activity was observed only at a dose of 0.013 mg/kg. Specifically, the duration of riding increased by more than 2.5 and 3.5 times that of intact animals, respectively.

Correspondingly, the distance traversed increased by 172.7 % ($p = 0.05$ by Student's *t*-test, $p = 0.037$ by Fisher's LSD test) and by 291.5 % ($p = 0.01$ by Student's *t*-test; $p = 0.001$ by Fisher's LSD test), respectively. Furthermore, there was a 144 % increase ($p = 0.009$ by Fisher's LSD test) in running time when compared to the control group.

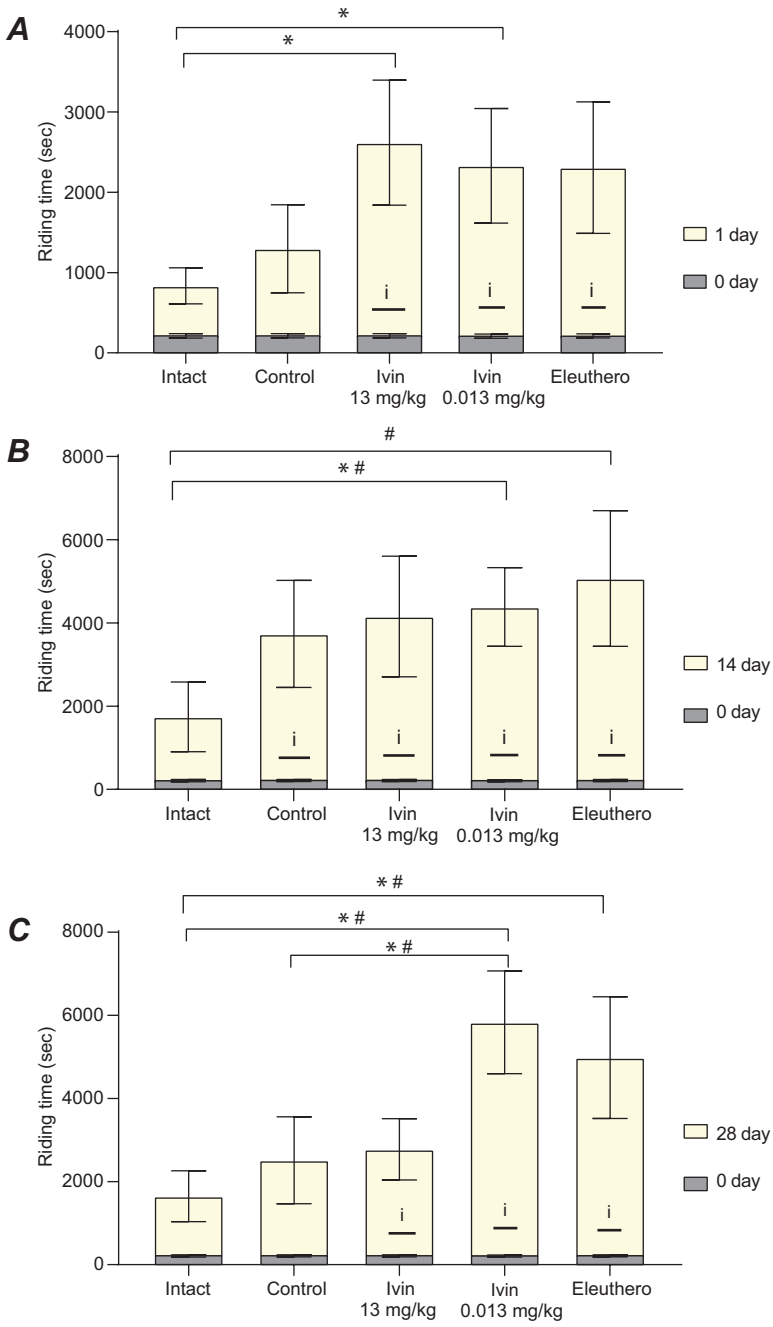

Fig. 2. The effect of Ivin on physical activity of rats in the rotarod test (M±m, n = 10 per group): ***A*** – before (0 day) and after single administration of Ivin and Eleutherococcus; ***B*** – after 14 days of administration; ***C*** – after 28 days of administration

Notes: i – the difference is significant compared to the initial data; * – P ≤0.05 the difference is significant by Student's *t*-test, # – P ≤0.05 the difference is significant using two-way ANOVA followed by Fisher's LSD test

Significant changes in the parameters were observed only after 28 days of exposure to Eleutherococcus. The riding distance was 232 % longer, and the total riding time on the rod increased by 3.3 times compared to intact animals (p = 0.05 by Student's *t*-test; p = 0.009 by Fisher's LSD test). As reported (Patel, 2024), endurance to physical load increased in animals administered an aqueous extract of Eleutherococcus. The ingestion of the Eleutherococcus extract by athletes promoted fatigue reduction during training.

The data obtained from the rotarod test showed that rats treated with Ivin showed an increase in the average group indicators of their physical activity compared with the intact male group and the initial data. Since the increase in the riding time on the rotarod indicates a slowing down of the rate of fatigue in the animals (Zhang *et al.*, 2019), it can be assumed that Ivin causes a redistribution of the animals in the endurance structure: namely from the "medium endurance" group to the "high endurance" group, which characterises it as an adaptogen.

Physical activity of animals under additional chemical exposure. After oral administration of chlorpyrifos at a dose of 37.5 mg/kg to intact and control (trained) animals, the time of their holding on the rod decreased almost by 2 times, which indicates a reduction in physical activity of the organism under extra chemical exposure (chlorpyrifos). This may be due to its toxic effect (**Fig. 3**), which is in compliance with the literature data on the ability of chlorpyrifos to reduce motor activity and behaviour in rodents (Hallal *et al.*, 2019, Moser *et al.*, 2005).

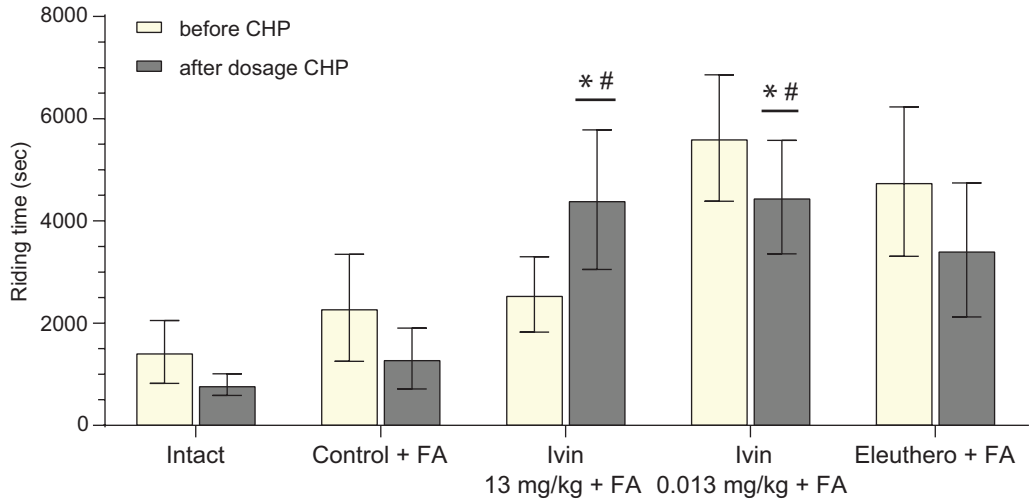

Fig. 3. Effect of Ivin on physical activity of male rats in the rotarod test after administration of chlorpyrifos (CHP)

Notes: PL – physical load; * – P ≤0.05 significant difference compared to intact animals; # – P ≤0.05 significant difference compared to control animals (using ordinary one-way ANOVA followed by Fisher's LSD test)

In both Ivin-treated groups, after administration of chlorpyrifos, the riding time on the rod equally increased. These changes were significant in relation to intact and control trained animals also with chlorpyrifos, testifying to an increasing physical performance of rats.

However, it should be noted that, at a dose of 13 mg/kg, despite the effect of chlorpyrifos, the time on the rotating rod for rats was 72 % longer than before chlorpyrifos administration. This suggests that Ivin contributed to an increase in the body's adaptive reactions to the chemical factor.

In the group of Ivin in a lower dose and in the group of the reference substance Eleutherococcus, after the administration of chlorpyrifos, the riding time of the animals on the rod was shorter (by 21 % and 28 %, respectively) compared to chlorpyrifos pre-injection. It should be noted that after the administration of chlorpyrifos to Ivin-treated groups, the riding time of rats was 27–30 % longer than that observed in the Eleutherococcus-treated group.

Therefore, the obtained results confirm that Ivin enhances physical activity of rats under an additional chemical load, such as chlorpyrifos, and to a greater extent than Eleutherococcus.

CONCLUSIONS

1. Ivin at a 13 mg/kg single exposure, and at a 0.013 mg/kg single and long-term exposure significantly increases the time spent by rats on a rotating rod (rotarod test), which indicates an increase in motor activity, balance, and muscle strength of animals. The efficacy of Ivin was comparable to or greater than that of the reference drug, Eleutherococcus.
2. Chlorpyrifos significantly reduces the physical activity of intact and control (physically trained) rats in the rotarod test. Ivin, at the tested doses, diminished the negative effect of chlorpyrifos on the physical performance of rats, indicating an increase of the organism's resistance to an additional chemical load.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: there were no commercial or financial relationships that could be interpreted as a potential conflict of interest.

Human Rights: this article does not contain any studies with humans.

Animal studies: all international, national, and institutional guidelines for the care and use of laboratory animals were followed.

AUTHOR CONTRIBUTIONS

Conceptualization, [V.O.; P.M.]; methodology, [V.O.; R.I.]; validation, [V.O.; R.I.]; formal analysis, [V.O.; R.I.]; investigation, [V.O.; R.I.]; writing – original draft preparation, [V.O.]; writing – review and editing, [V.O.; P.M.]; visualization, [V.O.; R.I.]; project administration, [V.O.; P.M.].

All authors have read and agreed to the published version of the manuscript.

REFERENCES

Ajala, T. (2017). The effects of adaptogens on the physical and psychological symptoms of chronic stress. *Discovery: Georgia State Honors College Undergraduate Research Journal*, 4(2). doi:10.31922/disc4.2
Crossref ● Google Scholar

Amir, M., Vohra, M., Raj, R. G., Osoro, I., & Sharma, A. (2023). Adaptogenic herbs: a natural way to improve athletic performance. *Health Sciences Review*, 7, 100092. doi:10.1016/j.hsr.2023.100092
Crossref ● Google Scholar

Cenci, A., & Lundblad, M. (2005). Utility of 6-hydroxydopamine lesioned rats in the preclinical screening of novel treatments for Parkinson disease. In: M. LeDoux (Ed.), *Animal models of movement disorders* (pp. 193–208). Academic Press. do:10.1016/b978-012088382-0/50016-5
Crossref ● Google Scholar

Grishko, V. M., & Demura, T. A. (2009). Vplyv rehulyatoriv rostu na stiykist' prorostkiv kukurudzy, rozvytok protsesiv perekysnoho okyslennya lipidiv i vmist askorbinovoyi kysloty za sumisnoyi diyi kadmiyu i nikelyu [Influence of growth regulators on maize seedlings resistance, lipid peroxidation processes development and ascorbic acid content at cadmium and nickel joint action]. *Physiology and Biochemistry of Cultivated Plants,* 41(4), 335–43. (In Ukrainian)
Google Scholar

Hallal, N., El Khayat El Sabbouri, H., Salami, A., Ramadan, W., Khachfe, H., Moustafa, M. E., Khalil, M., & Joumaa, W. H. (2019). Impacts of prolonged chlorpyrifos exposure on locomotion and slow- and fast-twitch skeletal muscles contractility in rats. *Toxicology Reports*, 6, 598–606. doi:10.1016/j.toxrep.2019.06.006
Crossref ● PubMed ● PMC ● Google Scholar

Hamm, R. J., Pike, B. R., O'Dell, D. M., Lyeth, B. G., & Jenkins, L. W. (1994). The rotarod test: an evaluation of its effectiveness in assessing motor deficits following traumatic brain injury. *Journal of Neurotrauma*, 11(2), 187–196. doi:10.1089/neu.1994.11.187
Crossref ● PubMed ● Google Scholar

Hånell, A., & Marklund, N. (2014). Structured evaluation of rodent behavioral tests used in drug discovery research. *Frontiers in Behavioral Neuroscience*, 8, 252. doi:10.3389/fnbeh.2014.00252
Crossref ● PubMed ● PMC ● Google Scholar

Havrys, I. L., Tsygankova, V. A., & Ponomarenko, S. P. (2013). *Vykorystannia rehulyatoriv rostu na roslynakh pomidora u zymovykh teplytsyakh* [*The use of growth regulators on tomato plants in winter greenhouses*], Vinnytsia: Nilan. (In Ukrainian)
Google Scholar

Iutinskaya, G. A., Ponomarenko, S. P., & Andreyuk, E. I. (2010). *Bioregulyatsiya mikrobno-rastitelnikh sistem* [*Bioregulation of microbial-plant systems*]. Kyiv: Nichlava. (In Russian)
Google Scholar

Kalka, N. M. (2015). *Profilaktyka i podolannia syndromu khronichnoi vtomy u pratsivnykiv OVS* [*Prevention and overcoming of chronic fatigue syndrome in employees of the Internal Affairs*]. Lviv: LvDUVS. (In Ukrainian)
Google Scholar

Moser, V. C. (2000). The functional observational battery in adult and developing rats. *Neurotoxicology*, 21(6), 989–996.
PubMed ● Google Scholar

Moser, V. C., Phillips, P. M., McDaniel, K. L., Marshall, R. S., Hunter, D. L., & Padilla, S. (2005). Neurobehavioral effects of chronic dietary and repeated high-level spike exposure to chlorpyrifos in rats. *Toxicological Sciences*, 86(2), 375–386. doi.org/10.1093/toxsci/kfi199
Crossref ● PubMed ● Google Scholar

Panossian, A., & Wagner, H. (2011). Adaptogens: a review of their history, biological activity, and clinical benefits. *HerbalGram*, 90, 52–63.
Google Scholar

Panossian, A., & Wikman, G. (2010). Effects of adaptogens on the central nervous system and the molecular mechanisms associated with their stress-protective activity. *Pharmaceuticals,* 3(1), 188–224. doi:10.3390/ph3010188
Crossref ● PubMed ● PMC ● Google Scholar

Patel, K. (2024). Eleuthero. Examine database. Retrieved from https://examine.com/supplements/eleuthero/research

Ponomarenko, S. P. (1999). *Regulyatory rosta rasteniy na osnove N-oksidov proizvodnykh piridina* (*Fiziko-khimicheskiye svoystva i biologicheskaya aktivnost'*) [*Plant growth regulators based on N-oxides derived from pyridine* (*Physico-chemical properties and biological activity*)]. Kyiv: Tekhnika. (In Russian)
Google Scholar

Ponomarenko, S. P., & Iutynska, H. O. (Eds.). (2011). *New plant growth regulators: basic research and technologyes of application*. Kyiv: Nichlava.
Google Scholar

Ray, A., Gulati, K., & Anand, R. (2016). Stress, adaptogens and their evaluation: an overview. *Journal Pharma Reports*, 1(110), 2.
Google Scholar

Ribchenko, Z.hI., & Palladina, T. O. (2012). The action of adaptogenic preparations on vacuolar proton pumps activity in corn root cells under salt stress conditions. *Ukranian Biochemical Journal,* 84(3), 88–94. (In Ukrainian)
PubMed ● Google Scholar

Ryabchenko, N. A., Mochalov, V. V., & Lisitskaya, S. M. (2006). Vliyanie regulyatorov rosta rastenii na vozmozhnost snizheniya insektitsidnoi nagruzki v agrotsenozakh ozimoi pshenitsi [Effect of plant growth regulators on possibility of reduction of insecticide load in agrocenoses of winter wheat]. *Visnyk of Dnipropetrovsk University. Biology, ecology*, 1(14), 160–164. Retrieved from https://www.dnu.dp.ua/docs/visnik/fbem/program_5e53fc4167202.pdf (In Russian)
Google Scholar

Salve, J., Pate, S., Debnath, K., & Langade, D. (2019). Adaptogenic and anxiolytic effects of ashwagandha root extract in healthy adults: a double-blind, randomized, placebo-controlled clinical study. *Cureus*, 11(12), e6466. doi:10.7759/cureus.6466
Crossref ● Google Scholar

Stefanov, O. V. (Ed.). (2001). *Doklinichni doslidzhennia likarskykh zasobiv* [*Preclinical studies of medicinal products*]. Kyiv: Avicena. Retrieved from https://pubmed.com.ua/xmlui/handle/123456789/77 (In Ukrainian)
Google Scholar

Todorova, V., Ivanov, K., Delattre, C., Nalbantova, V., Karcheva-Bahchevanska, D., & Ivanova, S. (2021). Plant adaptogens-history and future perspectives. *Nutrients*, 13(8), 2861. doi:10.3390/nu13082861
Crossref ● PubMed ● PMC ● Google Scholar

Vasetska, O. P., & Zhminko, P. H. (2021). Biolohichna aktyvnist i toksykolohichni vlastyvosti rehuliatoriv rostu roslyn – metylnykh pokhidnykh pirydyn-*N*-oksydu [Biological activity and toxicological properties of plant growth regulators – methyl derivatives of *N*-oxidepyridine]. In: A. I. Vovk (Ed.), *Syntez i bioaktyvnist funktsionalizovanykh azotovmisnykh heterotsykliv* [*Synthesis and bioactivity of functionalized nitrogen-containing heterocycles*] (pp. 288–324). Kyiv: Interservice. Retrieved from https://drive.google.com/file/d/1pNYtByPb-H-XxZKdrY0LzOUXOEC628t4/view (In Ukrainian)
Google Scholar

Vasetska, O. P., Prodanchuk, M. G., & Verys, T. M. (2023). The state of the prooxidant and antioxidant systems of the rat under the single application of some methyl derivatives of pyridine N-oxide – Ivin and Poteitin. *Ukrainian Journal of Modern Toxicological Aspects*, 94(1), 55–71. doi:10.33273/2663-4570-2023-94-1-55-71
Crossref ● Google Scholar

Vyunytska, L. V. (2018). Funktsional'ni mekhanizmy systemy homeostazu yak komponent stres-vidpovidi [Functional mechanisms of the homeostasis system as a component of the stress response]. *Laboratory Diagnostics*, 2(81), 20–30. (In Ukrainian)
Google Scholar

Vyunytska, L. V., Yuzvenko, T. Yu., Dashuk, T. I., & Pankiv, V. I. (2022). Stress-induced changes in a body's vital functions. Review. *Clinical Endocrinology and Endocrine Surgery*, 2(78), 49–60. doi:10.30978/cees-2022-2-49 (In Ukrainian)
Crossref ● Google Scholar

Wiegant, F. A., Surinova, S., Ytsma, E., Langelaar-Makkinje, M., Wikman, G., & Post, J. A. (2009). Plant adaptogens increase lifespan and stress resistance in *C. elegans*. *Biogerontology*, 10(1), 27–42. doi:10.1007/s10522-008-9151-9
Crossref ● PubMed ● Google Scholar

Williams, M., & Porsolt, R. D. (2007). CNS safety pharmacology. In: S. J. Enna & D. B. Bylund (Eds.), *xPharm: the comprehensive pharmacology reference* (pp. 1–13). Elsevier. doi:10.1016/B978-008055232-3.63682-7
Crossref ● Google Scholar

Zarudna, O. I., & Mural, N. I. (2013). Syndrom khronichnoyi vtomy ta suchasne suspil'stvo [Chronic fatique syndrom and modern society]. *Nursing*, 4, 58–60. Retrieved from https://ojs.tdmu.edu.ua/index.php/nursing/article/view/5393/4957 (In Ukrainian)
Google Scholar

Zhang, X., Jing, S., Lin, H., Sun, W., Jiang, W., Yu, C., Sun, J., Wang, C., Chen, J., & Li, H. (2019). Anti-fatigue effect of anwulignanviathe NRF2 and PGC-1α signaling pathway in mice. *Food & Function*, 10(12), 7755–7766. doi:10.1039/c9fo01182j
Crossref ● PubMed ● Google Scholar

ФІЗИЧНА АКТИВНІСТЬ ЩУРІВ ЗА ПЕРОРАЛЬНОГО ВПЛИВУ 2,6-ДИМЕТИЛ-N-ОКСИД ПІРИДИНУ (ІВІНУ) В РОТАРОД-ТЕСТІ

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Обґрунтування. Доведено, що забруднення довкілля і середовища життєдіяльності людини хімічними речовинами, інтенсифікація виробничих процесів, а також тривале фізичне, емоційне та психогенне навантаження на організм сприяють формуванню низки різних соматичних захворювань, втоми, порушення пам'яті, що може бути наслідком зниження неспецифічної опірності й функціональних резервів організму, розвитку стресових станів. Тому актуальною проблемою профілактичної токсикології є пошук синтетичних речовин з адаптогенними властивостями, які сприяли би підвищенню опірності організму і запобігали б виникненню шкідливих ефектів. У зв'язку з цим завданням нашої роботи було дослідити фізичну активність щурів за впливу 2,6-диметил-N-оксид піридину (Івіну) та за умов додаткового хімічного чинника Хлорпірифосу.

Мета дослідження. З'ясувати вплив Івіну на рухову активність і координацію рухів щурів Wistar Hannover, а також здатність опірності організму на додатковий хімічний чинник у Ротарод-тесті.

Матеріали та методи. У роботі використано N-оксид-2,6-диметил піридину (99,9%). Препаратом порівняння слугував адаптоген Елеутерокок. Дослідження проведено на 50 самцях щурів Wistar Hannover. Кожна група налічувала 10 тварин: 1 – інтактні тварини, 2 – контроль (треновані тварини, дистильована вода), 3 і 4 – Івін у дозах 13,0 і 0,013 мг/кг відповідно, 5 – Елеутерокок у дозі 50 мг/кг.

Експозиція – 28 днів, перорально. Фізичну витривалість тварин вивчали в Ротарод-тесті. Наприкінці досліджень на тих самих групах щурів вивчено фізичну активність за додаткового навантаження хімічною речовиною Хлорпірифосом у дозі 37,5 мг/кг (однократно).

Результати. Встановлено, що за однократної дії Івіну в обох дозах час перебування щурів на циліндрі, що обертається, зростав більш ніж в 11 і 10 разів, відповідно. Через 14 і 28 днів впливу Івіну в дозі 0,013 мг/кг збільшувалися пройдена дистанція на 172,7 % та 291,5 %, сумарний час утримання щурів на циліндрі у 2,5 та 3,5 рази відповідно, порівняно з інтактними тваринами. Елеутерокок спричиняв вірогідно значущі зміни показників після 28-денної експозиції. Після введення Хлорпірифосу в дозі 37,5 мг/кг інтактним і контрольним (тренованим) щурам час утримання їх на циліндрі скоротився майже удвічі. У групах тварин, які отримували Хлорпірифос на тлі Івіну, час утримання на обертовому циліндрі був на 27–30 % вищим, ніж за впливу референтного препарату Елеутерококу і Хлорпірифосу.

Висновки. Отже, Івін за однократного впливу в дозі 13 мг/кг, за однократного і тривалого впливу в дозі 0,013 мг/кг значно збільшує час утримання щурів на обертовому стержні у Ротарод-тесті, що свідчить про підвищення моторної активності, балансу та м'язової сили тварин. Ефективність Івіну за дослідженим показником не поступалась або була вище референс-препарату Елеутерококу. Хлорпірифос суттєво знижує фізичну активність інтактних і контрольних (фізично тренованих) щурів у Ротарод-тесті. Івін у досліджених дозах послаблює негативний вплив Хлорпірифосу на фізичну працездатність щурів, що свідчить про підвищення опірності організму до додаткового хімічного навантаження.

Ключові слова: 2,6-диметил-N-оксид піридину, фізична активність, щури, Ротарод-тест, Хлорпірифос

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