



EVALUATION OF THE EFFECT OF VINCANIN HYDROCHLORIDE AND ITS DERIVATIVES ON BLOOD PRESSURE AND RESPIRATION UNDER EXPERIMENTAL CONDITIONS

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ABOUT ARTICLE

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Abstract: At the Yunusov Institute of Plant Chemistry of the Academy of Sciences of the Republic of Uzbekistan, a number of scientists conducted extensive pharmacotoxicological studies to study the biological activity of vincane hydrochloride and its derivatives. Based on these studies, a number of studies were conducted not only on the special pharmacological activity of the substances studied, but also on their effects on organs and systems, including respiration and blood pressure. Based on the conducted studies, it was found that in acute experiments on cats, vincanin hydrochloride and derivatives in doses of 0.3 – 5.0 showed a tendency to increase blood pressure and somewhat increased breathing. However, at higher doses, tonic clonic seizures occurred, leading to the death of experimental animals. This requires the use of these substances in very small doses, as far as possible, in order to achieve a therapeutic effect. In studies of changes in the body weight of experimental animals in dynamics, vincanin hydrochloride and pyrosaline chloride did not have a negative effect on the ratio between the control group, although they slightly changed the weight of animals, while pyrosaline iodomethylate did not have a negative effect on the change in body weight of experimental animals in dynamics compared with vincanin hydrochloride and pyrosaline chloride.

**ТАЖРИБА ШАРОИТИДА ВИНКАНИН ГИДРОХЛОРИДИ ВА УНИНГ
ҲОСИЛАЛАРИНИНГ ҚОН БОСИМИ ВА НАФАС ОЛИШГА ТАЪСИРИНИ
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МАҚОЛА ҲАҚИДА

Калит сўзлари: Артериал қон босими, нафас олиш, алкалоид, беморнинг кузатув Мониторинги, тоник клоник хуружлар, тутқаноқ, хайвонлар тана вазни

Аннотация: ЎзР ФА академик С.Ю.Юнусов номидаги Ўсимлик моддалари кимёси институтида бир қатор олимлар томонидан винканин гидрохлориди ва унинг ҳосилаларининг биологик фаоллигини ўрганиш бўйича кенг фармако-токсикологик тадқиқотлар олиб борилди. Ушбу тадқиқотлар асосида ўрганилаётган моддаларнинг нафақат специфик фармакологик фаоллиги, балки уларнинг органлар ва тизимларга, шу жумладан нафас олиш ва қон босимига таъсири борасида бирламчи тадқиқотлар ўтказилди. Тадқиқотлар асосида мушукларда ўтказилган ўткир тажрибаларда 0,3 – 5,0 дозалардаги винканин гидрохлориди ва унинг ҳосилалари таъсирида қон босимининг кўтарилиш тенденцияси кузатилди ва нафас олиш бироз тезлашди. Бироқ, юқори

дозаларда тоник клоник тутилишлар пайдо бўлиб, тадқиқот ҳайвонларнинг ўлимига олиб келди. Шу муносабат билан, даволаш мақсадида қўлланилганда терапевтик таъсирга эришиш учун ушбу моддаларни имкони борича жуда кичик дозаларда қўллаш талаб қилинади. Тажриба ҳайвонларининг тана вазнининг динамикадаги ўзгаришини ўрганишда винканин гидрохлориди ва пирозалин хлорид назорат гуруҳи нисбатан салбий таъсир кўрсатмади, гарчи ҳайвонларнинг вазни бироз ўзгарган бўлсада, пирозалин ёдометилат ҳам винканин гидрохлориди ва пирозалин хлорид каби тажриба ҳайвонларининг тана вазнининг динамикада ўзгаришига салбий таъсир кўрсатмади.

ОЦЕНКА ВЛИЯНИЯ ВИНКАНИНА ГИДРОХЛОРИДА И ЕГО ПРОИЗВОДНЫХ НА АРТЕРИАЛЬНОЕ ДАВЛЕНИЕ И ДЫХАНИЕ В ЭКСПЕРИМЕНТАЛЬНЫХ УСЛОВИЯХ

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О СТАТЬЕ

Ключевые слова: Артериальное давление, дыхание, алкалоид, Монитор пациента, тонические клонические припадки, судороги, масса тела животных

Аннотация: В Институте химии растительных веществ им. С.Ю. Юнусова АН РУз ряд ученых провели обширные фармако-токсикологические исследования по изучению биологической активности винкана гидрохлорида и его производных. На основе этих исследований был проведен ряд исследований не только особой фармакологической активности изучаемых веществ, но и их влияния на органы и системы, включая дыхание и артериальное давление. На основании проведенных исследований установлено, что в острых опытах на кошках винканин гидрохлорид и производные в дозах 0,3 – 5,0 проявляли тенденцию к повышению артериального давления и несколько учащали дыхания. Однако при более высоких дозах возникали тонические клонические припадки, приводящие к смерти подопытных животных. Это требует использования этих веществ в очень малых дозах, насколько это возможно, с целью достижения терапевтического эффекта. В исследованиях изменения массы тела подопытных животных в динамике винканин гидрохлорид и пирозалин хлорид не оказывали отрицательного влияния на соотношение между контрольной группой, хотя и незначительно изменяли вес животных, в то время как пирозалин йодметилат не оказывал отрицательного влияния на изменение массы тела подопытных животных в динамике по сравнению с винканином гидрохлоридом и пирозалином хлоридом.

INTRODUCTION

It is known that the growth and development of the body is effectively and ineffectively influenced not only by the external environment, but also by nutrition, and medicines are no

exception. A direct relationship has been established between the ecology of the habitat, the presence of various harmful components in it and medicines used for medicinal purposes, in the development of severe pathological processes or during the course of emerging diseases [1]. In recent years, thanks to the scientific achievements of scientists working in the field of medicine and pharmacology, thanks to the development of their ideas about the side effects of drugs, the concept of "toxic effect of drugs" has appeared. These effects are reactions caused by overdose, rapid saturation of the body, rapid administration of medium and even minimal doses, disruption of the normal functioning of excretory organs or detoxification processes of drugs in the body (for example, with primary hepatic or renal insufficiency) [2]. The toxic effect of the drugs is manifested by symptoms of mild, moderate and severe severity. Side effects of medicines include not only the occurrence of allergic reactions during their administration, but also the inconvenience of their use due to concomitant diseases, narrowing of the spectrum of their use, as well as contraindications to use [3]. The results obtained on the basis of scientific research by a number of scientists have shown that alkaloids have various pharmacotherapeutic effects and can affect the processes occurring in various organ systems of the human body. Having an alkaloid structure, drugs affect the cardiovascular and central nervous systems, peripheral neurotransmitter processes and afferent nerve endings. Perhaps such a wealth of therapeutic effects is due to the complex and diverse chemical structure of these biologically active substances. In addition, in accordance with the fundamentals of the production of alkaloid preparations, they have their own characteristics, depending on the purpose for which the drug is produced. Clinical studies and clinical studies analyzed by scientists and researchers allow us to conclude that little is known about the group of substances with an alkaloid structure. It is known that alkaloids can be converted into active substances in the body, which means that they have a wide range of therapeutic effects, as well as various drugs of pharmacological groups. Thus, the use of these biologically active substances is relevant and promising in modern medicine [4-9]. In this regard, in the course of scientific research on the effect of indole alkaloids with antitumor activity on organs and systems, their effect on respiration and blood pressure was studied [10].

THE MAIN RESULTS AND FINDINGS

Study of the effect of indole alkaloids on respiration and blood pressure, as well as on the dynamics of body weight of experimental animals.

The study of the effect of vincanine hydrochloride and its derivatives on respiration and blood pressure was carried out using a multi-channel patient monitor (Model: IM 100, ZOOMED, ЗАО "Ист Медикал" Москва, Россия). All studies were conducted on anesthetized (sodium ethaminal 50 mg/ kg in/ab) cats with a body weight of 2.5-3.0 kg, which were kept in standard vivarium conditions for two weeks. At the same time, a special cuff suitable for the animal's leg

was installed on the upper 2/3 of the front part of the experimental animal's leg to measure blood pressure, and as a result of filling the cuff with air, blood pressure readings were displayed on the monitor for 20 seconds. During the studies, data on the amount and timbre of the respiratory rhythm were presented on a monitor based on data from a special sensor that determines the level of oxygen saturation in peripheral blood vessels, and standard ECG leads installed in the language of the experimental animal. The studied substances were injected in the form of an aqueous solution through a special catheter inserted into a vein in the shin area of the experimental animal. On the other hand, animals in the control group were injected with a saline solution in accordance with the volume of the test substance. In addition to these experiments, studies of the effect of the substances studied on the body weight of experimental animals were also conducted on mongrel laboratory white mice with a body weight of 22-24 g. Prior to the start of the experiments, for 14 days and throughout the entire period of the experiments, the experimental animals were kept and cared for in standard vivarium conditions. In order to study the effect of the studied substances on the body weight of experimental animals, high effective doses of these substances were administered orally for 22 days and during this time an equal volume of distilled water was administered to the animals of the control group. The results obtained on the basis of the conducted studies were discussed in comparison with the control group and statistical processing of the obtained results was carried out by the tabular method proposed by R.B. Strelkov [11].

1. Study of the effect of vincanine hydrochloride on respiration and blood pressure. It is known that the acute toxicity of vincanine hydrochloride and its derivatives is very high, studied with intravenous administration, which requires strict caution when using it [12, 13, 14]. At a dose of 0.5 mg / kg, it caused a slowly developing increase in blood pressure by 22 mm.m.b., followed by a return to the baseline after 2 hours. There is no effect on breathing. At doses of 1.0 and 3.0 mg/kg, it caused a slowly developing decrease in blood pressure by 28 mm.m.b. and 32 mm.m.b. with a subsequent return to the original after 2 hours. The number, timbre and frequency of respiration are also increased, followed by a return to the original after 2 hours. When administered at a dose of 10 mg / kg, clonic seizures and death of the animal developed after administration.

2. The effect of pyrazoline chloride 1 mg/kg on blood pressure and respiration in an acute experience on a cat. According to acute experience on a cat, pyrazoline chloride at a dose of 1 mg / kg i/v caused an increase in blood pressure to 34 mm.m.b. for a duration of 2 hours with a subsequent decrease to the baseline level. The breathing increased somewhat. In doses of 10-15 mg/ kg, clonic seizures leading to the death of cats are noted in acute experiments.

3. Investigation of the effect of pyrosaline iodine methylete on respiration and blood pressure. Pyrosaline iodine methylete at a dose of 0.3 mg / kg i/v caused a slight increase in the

increase in blood pressure. However, at higher doses, tonic clonic seizures with a fatal outcome were observed, observed when exposed to vincanine hydrochloride and pyrosaline iodine methylete.

4. Study of the effect of vincanine hydrochloride and its derivatives on the dynamics of body weight of experimental animals. In the conducted studies, it was noticed that the body weight of the control group animals decreased by 5.15 g and 4.2 g, respectively, on days 9 and 15 of the experiment, and increased by 1.4 g on day 22 compared to the baseline. When exposed to vincanine hydrochloride at a dose of 0.1 mg/kg and 10 mg/kg, a decrease in animal body weight was observed in dynamics from 0.1 g to 0.6 g compared with baseline values, and at a dose of 10.0 mg/kg, an increase in dynamics to 0.5; 0.8 and 1.0 g, respectively (see Table - 1).

Table – 1. Effects of vincanine hydrochloride on the dynamics of body weight of experimental animals

№	Groups and substances	Doses in mg/kg	Change in body weight			
			Initial indicators	After 9 days	After 15 days	After 22 days
1.	Control	Dis.water	23,4±0,48	18,25±0,24	19,2±0,48	24,8±0,36
2.	Vincanine hydrochloride	0,1	23,7±0,24*	23,6±0,48*	23,1±0,36*	23,3±0,24*
		1,0	23,3±0,36*	23,8±0,24*	24,1±0,48*	24,3±0,48*
		10,0	23,5±0,48*	23,1±0,36*	23,3±0,24*	23,5±0,24*

Note. *P≤0.05 comparison with the control group

In the conducted studies, the studied doses of vincanin hydrochloride did not have a negative effect on the body weight of experimental animals in dynamics and, compared with experimental animals, can even be increased several times.

In parallel with the above studies, it was observed that when exposed to a dose of 0.1 mg/kg pyrosaline chloride, the body weight of experimental animals increased by 0.7 g, respectively, after 9 and 22 days, decreasing by 1.6 g after 15 days of the study, while at a dose of 1.0 mg/kg it increased by 0.5; 0.45 and 1.1 g, and at a dose of 10.0 mg / kg, a decrease from 5.05 g to 7.5 g. The results obtained on the basis of the conducted studies are shown in Figure 1.

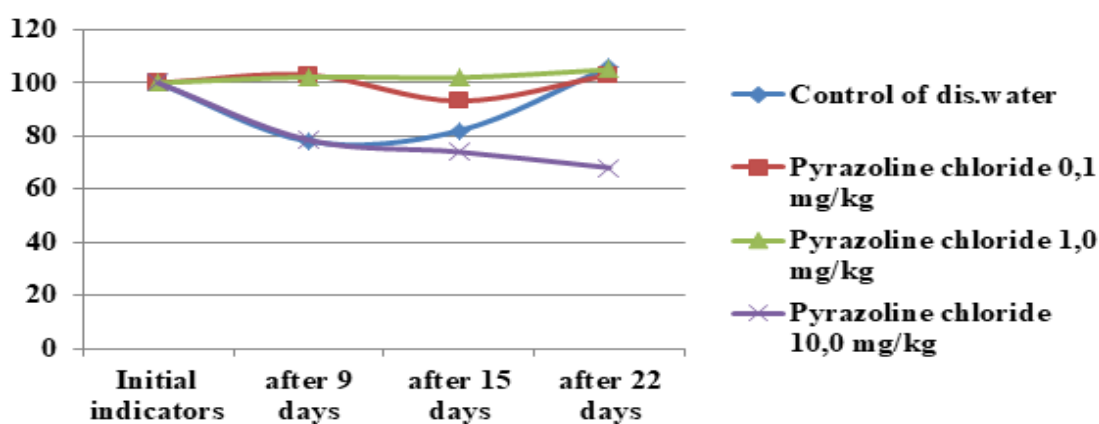


Figure – 1. Effects of pyrazoline chloride on the dynamics of body weight of experimental animals

As shown in the figure, the doses of pyrazoline chloride 0.1 and 1.0 mg/kg did not have a negative effect on the body weight of mice compared to the control group and even increased to baseline values at the end of the experiment, but at a dose of 10.0 mg/kg, a significant decrease in the body weight of the experimental animal was observed throughout the study.

In the above results of the effects of vincanine hydrochloride and pyrazoline chlorides on the body weight of laboratory white mice, one can see the tendency of animals to increase or decrease body weight. However, when exposed to all the studied doses of pyrazoline iodine methylate, no significant changes in the mass of experimental animals were observed (see Figure - 2).

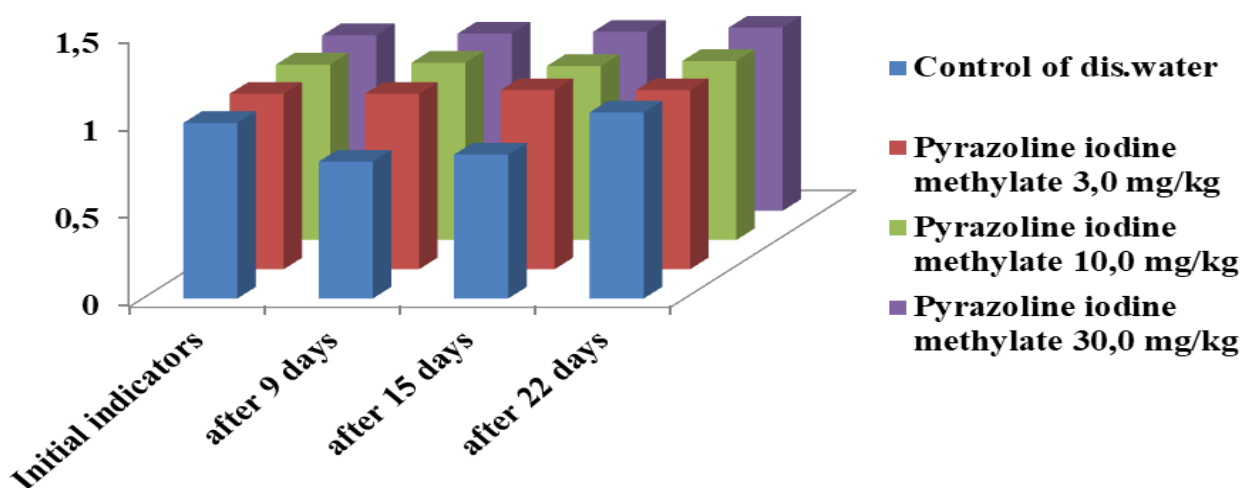


Figure – 2. Effects of Pyrazoline iodine methylate on the dynamics of body weight of experimental animals

As can be seen in Figure 2, pyrazoline iodomethylate did not have a negative effect on the change in body weight of experimental animals in dynamics proportional to all the studied doses, unlike vincanine hydrochloride and pyrazoline chloride. Taking into account that the studied substances and the control group were contained and cared for under standard vivarium conditions, as well as that all studies were conducted under standard vivarium conditions, it can be noted that vincanin and its derivatives do not have a negative effect on the absorption of nutrients from the gastrointestinal tract or the appetite of animals. This, in turn, requires conducting scientific research in this direction more fully and on a wider scale.

CONCLUSION

In acute experiments on cats, vincanin and derivatives in doses of 0,3 – 5,0 showed a tendency to increase blood pressure and somewhat increased breathing. However, at higher doses, tonic clonic seizures occurred, leading to the death of experimental animals.

This requires the use of these substances in very small doses, as far as possible, in order to achieve a therapeutic effect. The acute toxicity of vincanin hydrochloride and its derivatives is somewhat lower with oral administration, which means that the presence of a less toxic toxicity class creates the basis for extensive research on the search and implementation of oral remedies.

In studies of changes in the body weight of experimental animals in dynamics, vincanin hydrochloride and pyrosaline chloride did not have a negative effect on the ratio between the control group, although they slightly changed the weight of animals, while pyrosaline iodomethylate did not have a negative effect on the change in body weight of experimental animals in dynamics compared with vincanin hydrochloride and pyrosaline chloride.

REFERENCES

1. Усачев И.И., Бурденюк Е.А., Агапова К.А., Карпечкина С.В., Толстая Н.В. Влияние различных фармакологических препаратов на динамику массы тела и сохранность щенков собак породы алабай. Вестник брянской государственной сельскохозяйственной академии. 2021. С.37-41. DOI: 10.52691/2500-2651-2021-85-3-37-41
2. Викторов А.П., Мальцев В.И., Матвеева Е.В., Логвина И.А. **Механизмы развития побочного действия лекарственных средств: проблемы терминологии и классификации. издание для врача-практика.** Раціональна фармакотерапія науково практичне видання для лікарів издание для врача-практика 2(3) ' 2007.
3. Малыхин Ф.Т., Батулин В.А. Возможные побочные эффекты лекарственных препаратов у пожилых пациентов с хронической обструктивной болезнью легких и сопутствующей патологией. Терапевтический архив 3, 2016. ст. 100-107. doi: 10.17116/terarkh2016883100-107
4. Семёнова Е.В., Никулина О.И. Исследование свойств алкалоидов лекарственных растений // Научное обозрение. Медицинские науки. – 2021. – № 1. – С. 20-24; URL: <https://science-medicine.ru/ru/article/view?id=1166> (дата обращения: 17.10.2022).
5. Лугманова М.Р. Алкалоидоносные виды флоры Предуралья: выявление, эколого-ценотические закономерности распространения, перспективы ресурсного использования: автореф. дис. ... канд. биол. наук. Уфа, 2007. 22 с.
6. Кедик С.А., Марахова А.И. Алкалоиды: синтез, методы выделения и анализа. М.: Институт фармацевтических технологий, 2010. 246 с.

7. Ветрова Е.В., Борисенко Н.И., Хизриева С.С., Бугаева А.Ф. Изучение антиоксидантной активности апорфинового алкалоида глауцина и полученного в субкритической воде фенантренового алкалоида дес-глауцина // Химия растительного сырья. 2017. № 1. С. 85–91.

8. Турсунова Н.В., Чурин Б.В., Клиникова М.Г. Противоопухолевая активность соединений природного происхождения // Современные проблемы науки и образования. 2018. № 5. URL: <http://science-education.ru/ru/article/view?id=28056> (дата обращения: 03.02.2021).

9. Рабжаева А.Н. Особенности накопления биологически активных веществ *Thymus baicalensis* в зависимости от экологических факторов: автореф. дис. ... канд. биол. наук. Улан-Удэ, 2011. 24 с.

10. Изучение физико-химических и технологических свойств субстанции пирозалина гидрохлорида // Universum: технические науки : электрон. научн. журн. Рахимова О.Р. [и др.]. 2021. 9(90). URL: <https://7universum.com/ru/tech/archive/item/12260>

11. Стрелков Р.Б. Статистические таблицы для ускоренной количественной оценки фармакологического эффекта. Фармакология и токсикология 1986. №4 с.100-104.

12. Mirzaev Yu.R., Khamroev T.T., Ruzimov E.M., Khamdamov B.N., Abduazimov B.B., Adizov Sh.M., Yuldashev P.Kh., & Elmurodov B.J. (2022). Comparative assessment of acute toxicity of vincanin hydrochloride derivatives in research conditions. International Journal of Medical Sciences And Clinical Research, 2(10), 9–15. <https://doi.org/10.37547/ijmscr/Volume02Issue10-03>

13. Mirzaev Yu.R., Khamraev T.T., Ruzimov E.M., Khamdamov B.N., Abduazimov B.B., Adizov Sh.M., Elmurodov B.J., Yuldashev P.H. (2022). Study of the effect of alkaloids isolated from the vinca erecta plant on cardiac activity under experimental conditions. Eurasian journal of medical and natural sciences, 2(11), 250–255. <https://doi.org/10.5281/zenodo.7220861>

14. Yu.R. Mirzaev, T.T. Khamraev, E.M. Ruzimov, Sh.M. Adizov, B.B. Abduazimov, B.N. Khamdamov, B.J. Elmurodov, P.H. Yuldashev. (2022). Toxicological characteristics of vincanin hydrochloride and its derivatives in an experimental condition. Eurasian journal of academic research, 2(11), 1027–1033. <https://doi.org/10.5281/zenodo.7244593>