



STUDY OF THE EFFECT OF ALKALOIDS ISOLATED FROM THE VINCA ERECTA PLANT ON CARDIAC ACTIVITY UNDER EXPERIMENTAL CONDITIONS

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ABSTRACT

In the presented research paper on the study of the effect of vincanine hydrochloride and its derivatives on cardiac activity, changes caused by the action of therapeutic and subtoxic doses of these substances are presented. Studies have shown that the studied substances slightly reduced the heart rate in therapeutic doses, while in high doses there was pronounced bradycardia and even death as a result of asystole. It was also found that the studied substances slightly reduce the generation of pulses at the sinus node in all studied doses, in high doses can even cause cardiac arrest.

Introduction. As is known, a tumor is a pathological process manifested by an undifferentiated proliferation of healthy body tissues at the local level. Because tumor cells have different properties, they are different from healthy cells and cannot mature and develop into healthy cells. Antitumor drugs exhibit a specific pronounced cytostatic effect, inhibiting cell growth and proliferation. However, it should be borne in mind that chemotherapeutic agents used in the treatment of oncological diseases have a cytostatic effect not only on tumor cells, but also on healthy cells of the body. At the same time, medicinal cytostatic drugs have

a toxic effect on the body, since they also inhibit the growth of healthy cells, which are characterized by rapid growth and reproduction, for example, cells of hematopoietic organs, germ cells, cells of the mucous membranes of the gastrointestinal tract, etc. [1-3]. Currently, in modern cancer therapy, many drugs are used that differ in their mechanisms of action and origin, and in the field of oncotherapy, there are opportunities to find substances isolated from natural compounds with a new mechanism of action and low toxicity, which are considered a promising object of research. In this regard, currently, based on the



analysis of the structure of natural compounds, the most promising substances have been identified, such as quinones, alkaloids, terpenoids, having a polycyclic structure of molecules exhibiting antitumor properties. Many of these newly identified compounds are used in clinical practice, but at the same time, further studies of the properties of natural compounds are continuing to determine effective anticancer agents [4-9]. At the Institute of Plant Chemistry named after S.Yu. Yunusov of the Academy of Sciences of the Republic of Uzbekistan, Professor P.H. Yuldashev and other scientists synthesized a new chemical compound from the alkaloid norfluorocurarin isolated from *Vinca erecta* showing antitumor properties. In the course of scientific research on the effect of chemicals on organs and systems, the general toxicological and pharmacological properties of these secreted substances are studied [10-12].

The purpose of the study. Study of the effect of vincanin hydrochloride derivatives on cardiac activity.

Materials and methods. Research work to study the effect of vincanin hydrochloride and its derivatives on cardiac activity was carried out on mongrel laboratory white rats weighing 180-220 g. Before the study, experimental animals were kept in a vivarium under standard conditions for 14 days, and experiments were carried out in accordance with the requirements of international recommendations of the European Convention for the Protection of Vertebrates [13]. As for the study of the effect of the substances studied on cardiac activity, the studies were conducted in accordance with the recommendations set out in the manual, and changes in cardiac

activity caused by the substances were recorded on an ECG [14, 15]. ECG readings were studied in white rats on a 3-channel AT-1 Schiller electrocardiograph (Switzerland) by injecting 40 mg/kg of sodium ethaminal into the abdominal cavity. At the same time, all the studied substances were administered in different doses intravenously, after which they were observed for 5-6 hours until the animals woke up or died. The results of the study were evaluated by comparison with animals in the intact group that were not injected with the test substance, and statistical processing of the results was carried out by the tabular method proposed by R.B. Strelkov [16].

Results and their discussion. It is known that the toxicity or undesirable reaction of drugs depends on many factors, one of which is the functional state of the body and its individual organs and systems, which in turn change over time, since the spatiotemporal organization of living matter determines the frequency of fluctuations in the intensity of processes occurring in the body.

1. The effect of therapeutic to low-toxic doses of vincanin hydrochloride on the activity of the heart by the effect of substances on the rat ECG. In studies conducted in the studied doses of vincanin hydrochloride, an effect on cardiac activity was manifested in the following at a dose of 0.5 mg / kg, a decrease in F.H.C. was noted from 330 to 320 beats. in min., and the height of the prong P decreased by 9%. At a dose of 1 mg / kg, there was a decrease in F.H.C. from 320 to 295 beats per minute. The height of the prong P decreased by 4%. At a dose of 3 mg / kg, there was an increase in F.H.C. from 330 to 310 units. in min. The height of the prong P decreased



by 6.7%. At a dose of 5 mg / kg, there was a decrease in F.H.C. from 320 to 270 beats. in min. Without affecting the index of the

prong P . At a dose of 10 mg/kg, clonic seizures and death were noted (Table 1)

Table 1. Evaluation of the effect of vincanine hydrochloride on the activity of the heart.

№	Name of the group and substance	Doses in mg/kg	F.H.C. before the introduction of the substance	F.H.C. after the introduction of the substance	Difference F.H.C.
1.	Control	saline solution.	330±3,62	328±4,82	-2
2.	Vincanine hydrochloride	0,5	330±6	320±2,41	-10
		1,0	320±4,8	295±4,32	-25
		3,0	330±5,76	310±7,2	-20
		5,0	320±2,41	270±1,2	-50
		10,0	325±4,96	asystole	death

Note. $P \leq 0.05$ comparison with the control group

Thus, in all studied doses of vincanin hydrochloride, the heart rate decreased, i.e. bradycardia, especially at a dose of 5.0 mg/kg, pronounced bradycardia was observed, and at a dose of 10.0 mg/kg, death was observed in a short time. Also, a significant decrease in the voltage of the P wave was observed on the ECG. It was shown that this substance slightly reduces the generation of pulses at the sinus node.

2. The effect of therapeutic to low-toxic doses of pyrazoline chloride on the activity of the heart by the effect of substances on the rat ECG. The effect of the studied doses of pyrazoline chloride on the activity of the heart on the effect of substances on the rat ECG when administered intravenously was further studied. The study showed that

pyrazoline chloride at a dose of 1.0 mg, kg i / v did not cause changes on the part of the rat ECG. At a dose of 1 mg / kg i / v, there was a decrease in heart rate (F.H.C.) From 375 to 350 beats. in min. At a dose of 3 mg / kg h.s. from 360 to 330 units. in min. The effect on the height of the prong P was not noted. At a dose of 5 mg / kg F.H.C. from 340 to 320 units . in min. or 12-14% The height of the prong P decreased by 22%. At a dose of 10 mg / kg, after administration, there was a decrease in F.H.C. from 333 to 275 beats per minute or by 14%. The height of the prong P decreased from 7 to 3.5 mm, i.e. by 2 times. At a dose of 15 mg/kg, clonic seizures and death were noted.

Table 2. Evaluation of the effect of pyrazoline chloride on the activity of the heart.

№	Name of the group and substance	Doses in mg/kg	F.H.C. before the introduction of the substance	F.H.C. after the introduction of the substance	Difference F.H.C.
1.	Control	saline solution.	330±3,62	328±4,82	-2
2.	Pyrazoline chloride	1,0	375±5,23	350±4,32	-25
		3,0	360±6,72	330±3,36	-30
		5,0	340±3,62	320±4,56	-20



		10,0	333±2,4	275±6	-58
		15,0	345±5,76	asystole	death

Note. $P \leq 0.05$ comparison with the control group

Thus, pyrazoline chloride, starting with a dose of 5 mg / kg with intravenous administration, began to reduce HP by 12-14% and inhibit myocardial contractility by up to 20%. At a dose of 10 mg / kg IV, pronounced bradycardia was noted, and at a dose of 15 mg / kg after 3-5 minutes, asystole and death were noted. Also, a significant decrease in the voltage of the P wave, such as vincanin hydrochloride, was observed on the ECG, which showed that this substance slightly reduces the generation of pulses at the sinus node.

3. The effect of therapeutic to low-toxic doses of pyrazoline iodine methylete on the activity of the heart by the effect of substances on the rat ECG. The study showed that pyrazoline iodide at a dose of 0.1 mg / kg IV did not cause changes on the

part of the rat ECG. At a dose of 0.5 mg / kg, there was a decrease in F.H.C. from 380 to 360 beats. in min. Without affecting the index of the prong P . At a dose of 1 mg / kg, there was an increase in F.H.C. from 370 to 400 units. in min. or 7.5%. Without affecting the index of the prong P . At a dose of 2.5 mg / kg, there was an increase in F.H.C. from 330 to 365 beats per minute. or by 10%. Without affecting the index of the prong P . At a dose of 5 mg / kg, there was a decrease in F.H.C. from 350 to 300 units. in min. or by 11%. The height of the prong P increased by 11%. At a dose of 10 mg / kg, there was a decrease from the initial F.H.C. from 330 to 190 units. in min. on the 5th minute. The height of the prong P decreased by 25%. In the future, after 14 minutes, cardiac arrest was noted

Table 3. Evaluation of the effect of pyrazoline iodomethylete on heart activity.

№	Name of the group and substance	Doses in mg/kg	F.H.C. before the introduction of the substance	F.H.C. after the introduction of the substance	Difference F.H.C.
1.	Control	saline solution.	330±3,62	328±4,82	-2
2.	Pyrazoline iodine methylete	0,5	380±6,26	360±5,3	-20
		1,0	370±6,5	400±6,75	+30
		2,5	330±6,26	365±5,78	+35
		5,0	350±6,99	300±6,5	-50
		10,0	330±4,82	190±5,3	-140

Note. $P \leq 0.05$ comparison with the control group

Studies have shown that pyrosaline iodine methylete caused bradycardia when exposed to a dose of 0.5 mg/kg, and tachycardia at doses of 1.0 and 2.5 mg/kg, pronounced bradycardia at doses of 5.0 and 10 mg/kg, and cardiac arrest was noted after 14 minutes. In the studied doses, no changes in the teeth were observed on the ECG, which allows us to

conclude that these substances do not affect the heart rate.

Conclusion. Thus, when administered intravenously to white rats, these substances in doses of 1-3 mg / kg do not significantly affect the activity of the heart. In doses of 5-10 mg / kg, the heart rate is reduced and the amplitude of contractions



is reduced, and in part of the experiments lead to cardiac arrest.

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