групп по живой массе, установленный в начале эксперимента, также был отмечен в конце исследования. Полученные данные по межгрупповым различиям по живой массе в конце опыта обусловлены во многом наряду с разным её уровнем в начале опыта неодинаковой величиной её абсолютного прироста в период наблюдений. При этом лидирующее положение по уровню валового прироста живой массы занимали коровы-первотелки голштинской породы немецкой селекции II группы. Полученные экспериментальные материалы и их анализ свидетельствуют о межгрупповых различиях в значении анализируемого показателя с преимуществом коров-первотелок зарубежной селекции. Так, чистопородные животные II и III групп превосходили по относительному темпу роста чистопородных сверстников черно-пестрой породы I группы по показателю относительного темпа роста за период эксперимента на 0,51% и 0,45% соответственно, помесей IV группы-на 0,37% и 0,31%, помесей V группы – на 0,46% и 0,40 %.

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STUDY OF THE EFFECT OF ABAMEKUR ON THE LIFESPAN OF RATS

Annotation

The article shows the achievements of the last decades, which led to the emergence of new directions in the manufacture of medicines, to the revision and reassessment of a number of theoretical positions and traditional techniques. The most significant influence on the development of dosage forms was the establishment of the dependence of the therapeutic effect of medicinal substances not only on the chemical structure and physiological activity, but also on other factors, such as the technology of drug manufacture, the degree of dispersion of medicinal substances, their physical condition, the type of dosage form, etc. The rational way to find new drugs, namely antiparasitic ones, is still to vary the structure of the molecules of known chemical compounds, for example, avermectins, and to optimize them-to strengthen the desired and weaken the side effect by creating a dosage form.

Until recently, the dosage form was considered from the point of view of its compliance with purely technological requirements, i.e., as a more or less convenient form of the active substance that has the appropriate properties: particle size, consistency, hardness, fusibility, flowability, surface appearance, smell, taste, mass. At the same time, the dosage form has a significant effect on the effect of the drug substance included in it. It is the whole set of properties, and not only the active substance, affects a certain process in the body.

Thus, the inclusion of abamecur in the diet of rats at a therapeutic dose of 0.2 mg / kg for DV and a 5-fold increased dose of 1 mg/kg for DV throughout life, starting from 2 months of age, did not have a negative effect on the life expectancy of the animals. It should also be noted that the causes of death of rats when abamecur was included in their diet at a therapeutic and 5-fold higher dose did not differ from those in the control, it is especially important that no tumors were isolated in the rats during the experiment.

Keywords*: pharmaceuticals, antiparasitic, amabecur, rats, life expectancy.*

Introduction. Until recently, a dosage form was considered in terms of its compliance with purely technological requirements, i.e. as a more or less convenient form of the active substance with appropriate properties: particle size, consistency, hardness, malleability, friability, surface appearance, odor, taste, mass. At the same time dosage form has a significant impact on the action of the included drug substance. It has all the properties, not just the active substance, affect a particular process in the body [1-7].

To treat and prevent ecto- and endoparasitic diseases of cattle, a new highly effective broad-spectrum antiparasitic drug based on avermectin - abamekur - was developed and offered to veterinary practice [8-14]. It is known that the drugs are characterized by a pronounced specificity of their action. However, a therapeutic agent does not act on the organism in isolation, but can have joint action, i.e. it can affect organs and tissues or other processes in the animal. In particular, it is of interest to study abamekur on the longevity of animals [14-22].

Materials and methods of research. The work was carried out according to the «Methodical recommendations for the study of the carcinogenic properties of pharmacological and medicinal agents. Bulletin of Pharmacological Committee. 1998, No. 1, pages 21-24» on male rats of VISTAR line. The animals were divided into 3 groups: control and 2 experimental groups of 20 rats in each group. The rats of the control group received a common diet throughout their lives. The rats of the first experimental group were orally given abamekur in a therapeutic dose (0.2 mg/kg body weight by DV). Rats of the second group were given abamekur at 5 times the therapeutic dose (1 mg/kg body weight by DV). Abamekur was included in the diet of rats from 2 months of age until the end of life. The animals were observed throughout their lives. Each dead rat was dissected open and macroscopic morphological studies were performed.

The initial weight of the rats was 80-90 g, the initial age of the rats was 2 months.

Results of the study and their discussion. Throughout the whole life the rats of the experimental groups did not differ from the control groups in appearance and general condition. The body weight of the rats was given in Table 1.

Table 1 – Body weight of rats when adding abamekur to their diet

Age of rats, months	Groups		
	Control (g)	1st experimental group (g)	2nd experimental group (g)
1	2	3	4
2,0	86,6±4,5	84,8±4,0	86,3±6,3
2,25	122,4±6,3	121,8±6,0	120,2±2,7
2,5	145,8±4,5	148,9±8,1	155,0±3,4
2,75	166,8±5,4	165,7±5,4	166,3±4,9
3,0	187,5±6,4	188,8±6,8	189,7±4,9
3,5	224,0±6,5	220,6±5,9	213,8±10,3
4,0	264,0±7,6	271,5±4,6	268,2±9,4
4,5	297,7±7,1	303,8±6,5	304,4±8,1
5,0	305,0±6,7	309,6±7,4	316,6±8,9
6,0	332,5±9,7	338,0±12,8	332,2±6,5
7,0	379,0±9,9	370,8±6,9	368,4±11,9
8,0	384,0±11,2	381,6±15,6	379,0±13,5
9,0	438,0±11,7	436,6±18,0	430,0±13,8
10	442,0±9,2	440,5±15,0	439,7±12,2
11	449,0±10,2	441,3±13,4	430,0±12,5
12	457,5±10.2	434,2±11,5	429,6±11,8

1	2	3	4
13	462,2±12,2	448,7±13,5	445,4±14,6
14	473,0±7,0	465,5±17,2	462,8±15,0
15	481,4±19,8	471,6±19,4	470,0±12,1
16	488,2±8,8	472,0±26,12	470,5±24,9
17	496,6±14,7	485,0±24,9	478,0±30,7
18	495,0±13,7	492,2±45,5	486,0±28,1
19	498,0±14,6	493,3±30,6	486,6±35,1
20	501,5±28,6	497,3±35,2	490,6±52,3

As can be seen from Table 1, the body weight of the animals during the experiment in the rats of the experimental groups did not statistically reliably differ from the control. At the 20th month of life, there was no statistically significant increase in the body weight of the rats of both experimental groups compared with the control. Table 2 shows the lifespan of each rat taken for the study.

Experimental studies showed that the rats began to die at the age of 12.6 months (first experimental group), 13.7 months (control) and 14.8 (second experimental group). The longest lifespan was 25.8 months in the control group, and 750 days (25 months) in the rats with the inclusion of abamekur in their diet.

Table 2 – Lifespan of rats treated with abamekur

Number of animals	Groups		
	Control (days)	Experimental group 1 (days)	Experimental group 2 (days)
1	412	378	444
2	445	390	447
3	457	441	477
4	489	469	501
5	531	498	549
6	570	567	552
7	615	600	552
8	618	618	598
9	649	750	690
10	769	750	750

The indices of average life expectancy are presented in Table 3.

Table 3 – Average life expectancy of rats when abamekur was included in their diet at doses of 0.2 and 1 mg/kg

Life expectancy	Group		
	Control	1 Experimental group	2 Experimental group
months	18,44±1,09	17,94±1,39	18,53±1,06

The average data from 10 animals at $p>0.05$ are presented. As can be seen, the inclusion of abamekur in the diet of rats from 2 months of age to the end of life did not lead to a statistically significant change in the life expectancy of the animals.

Table 4 presents data on longevity and causes of death for each rat taken in the experiment.

Table 4 – Longevity and causes of death in rats when abectin B was included in their diet

Cause of dying	Life expectancy, months											
	12	13	14	15	16	17	18	19	20	23	25	Total
Control												
Abscessive bilateral pneumonia								1	1			2
Abscessive unilateral pneumonia				1								1
Bilateral pneumonia			1									1
Multiple colonic abscesses		1										1
Natural death					1	1		1		1	1	5
Total:		1	1	1	1	1		1	3		1	10
1 Experimental group												
Abscessive bilateral pneumonia	1	1		1			1					4
Abscessive unilateral pneumonia					1		1					2
1	2	3	4	5	6	7	8	9	10	11	12	13
Bilateral pneumonia											1	1
Natural death			1						1	1	2	5
Total:	1	1	1	1	1		2		1		2	10
2 Experimental group												
Abscessive bilateral pneumonia										1		1
Abscessive unilateral pneumonia							1					1
Bilateral pneumonia			1									1
Unilateral pneumonia				1				1				2
Intestinal and limb paresis, intoxication			1								1	2
Natural death		1			1		1			1	1	4
Total:			2	1	1		3	1		1	1	10

As can be seen from Table 4, the most frequent cause of death in the rats in the experiment was natural (14 rats out of 30). This cause of death was observed in all groups of rats in approximately equal numbers (5 - in the control group, 5 - in the first experimental group, 4 - in the second experimental group). It should be noted that bilateral or unilateral abscessing pneumonia was more common (13 cases of pneumonia).

In one case more rare pathological changes were noted: in the control - multiple colonic abscesses, in the second experimental group - intestinal and limb paresis, intoxication.

In the course of the whole experiment we found no tumors at autopsy of dead rats.

Conclusions. Thus, the inclusion of abamekur in the diet of rats at the therapeutic dose of 0.2mg/kg DV and 5 times the increased dose of 1 mg/kg DV throughout the life span, starting at 2 months of age, had no adverse effect on the life span of the animals. It should also be noted that the causes of death in rats when abamekur was included in their diet at a therapeutic and 5-fold higher dose were virtually the same as those in the control, especially important is the fact that no tumors were isolated in the rats during the experiment.

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ТҮЙІН

Мақалада дәрі-дәрмектерді өндіруде жаңа бағыттардың пайда болуына, бірқатар теориялық ережелер мен дәстүрлі әдістерді қайта қарауға және қайта бағалауға әкелген соңғы онжылдықтардың жетістіктері көрсетілген. Дәрілік формалардың дамуына дәрілік заттардың емдік әсерінің химиялық құрылымы мен физиологиялық белсенділігіне ғана емес, сонымен қатар дәрі-дәрмектерді дайындау технологиясы, Дәрілік заттардың дисперсия дәрежесі, олардың физикалық жағдайы, дәрілік форманың түрі және т. б. сияқты басқа факторларға тәуелділігін анықтау айтарлықтай әсер етті. Жаңа дәрі – дәрмектерді, атап айтқанда анти-паразитті іздеудің ұтымды жолы белгілі химиялық қосылыстардың молекулаларының құрылымын өзгерту болып қала береді, мысалы, авермектиндер және оларды оңтайландыру-дәрілік форманы құру арқылы қажетті және жанама әсерлердің күшеюі.

РЕЗЮМЕ

В статье показаны достижения последних десятилетий, приведшие к появлению новых направлений при изготовлении лекарств, к пересмотру и переоценке ряда теоретических положений и традиционных приемов. Наиболее значительное влияние на разработку лекарственных форм оказало установление зависимости терапевтического действия лекарственных веществ не только от химической структуры и физиологической активности, но и от других факторов, как технология изготовления лекарств, степень дисперсности лекарственных веществ, их физическое состояние, вид лекарственной формы и др. Рациональный путь поиска новых лекарственных средств, а именно антипаразитарных, пока еще остается варьирование структуры молекул известных химических соединений, например, авермектины и их оптимизация – усиление нужного и ослабление побочного действия за счет создания лекарственной формы.

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