

The effect of a complex herbal remedy on the sexual activity of male rats L.N. Shantanova<sup>1</sup>, EAT. Krivosheeva<sup>2</sup>, L.V. Osadchuk<sup>3</sup>, P.B. Lubsandorzheeva<sup>1</sup>, A.G. Mondodoev<sup>1</sup>, S.T.

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Effect of the complex plant remedy on the sexual activity of male rats

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#### SUMMARY

On the basis of a Tibetan prescription recipe, a complex natural remedy "adaptofit-28" has been developed. It was found that the specified agent, when administered repeatedly to white rats, stimulates the sexual activity of male rats, which is due to an increase in testosterone levels. The most pronounced aphrodisiac effect of the agent was found in relation to old male rats. Using the "pharmacological castration" method, it was shown that "adaptofit-28" activates the process of testosterone restoration to 5 $\alpha$ -dihydrosterone, increases the sensitivity of androgen receptors, and also has an antiestrogenic effect.

Key words: Tibetan medicine, adaptogens, sexual activity of male rats.

#### RESUME

A complex natural remedy "adaptophyt-28" has been developed on the base of the Tibetan medicine formula. It has been established that the repeated administration of the given remedy to white rats stimulates the sexual activity of male rats due to the increase in the level of testosterone. The remedy has manifested a strongly pronounced aphrodisiac effect in old male rats. The use of the "pharmacological castration" method has revealed that "adaptophyt-28" activates the transformation process of testosterone into 5 $\alpha$ -dihydrosterone, increases the sensitivity of androgene receptors as well as it has antiestrogenic effect.

Keywords: Tibetan medicine, adaptogenes, sexual activity of male rats.

#### INTRODUCTION

Currently, more than one third of the population of developed countries, due to high psycho-emotional stress, deteriorating environmental situation, various kinds of abuse (tobacco, alcohol, medications), develop chronic fatigue syndrome, accompanied by a high level of depressive disorders and psychosomatic diseases. The social significance of this problem lies in the fact that chronic fatigue syndrome not only negatively affects physical and intellectual abilities, significantly reducing the quality of life of the working-age population, but, as a rule, leads to a significant decrease in the reproductive potential of the male population [5, 2]. So, in Russia, according to various sources,

The main method of treating sexual dysfunctions, mainly related to increasing sexual potency, is the use of drugs belonging to different pharmacological groups: adrenergic blockers, dopamine receptor antagonists, neuroleptics, androgens, phosphodiesterase-5 inhibitors, peripheral vasoactive drugs, etc. [7]. However, many of them have side effects and serious negative consequences in the form of the development of cardiovascular pathologies, mental disorders, dysfunctions of the urinary system, etc. [1]. In this regard, the use of adaptogenic agents of natural origin is more justified - preparations of ginseng, golden root, leuzea, antlers, etc., capable of correcting sexual dysfunctions.

A promising direction in the search and development of new adaptogenic drugs with aphrodisiac properties is the study of the heritage of traditional Tibetan medicine, which has a significant amount of tonic drugs, called "rudlains". "Zhudlans" are prescribed for the treatment of chronic and "debilitating" diseases, to increase the adaptive capabilities of practically healthy individuals in the conditions of high-mountainous Tibet, and are also used in gerontological practice and to increase reproductive potential. In the canon of Tibetan medicine "Chzhud-shi" [12], 3 sections are devoted to such means: "Treatment of infertility", "Strengthening potency", "Treatment of diseases of old age", which describe more than 30 names of "zhudlans". In the recipe reference book of the XIX century. "Kunsal-Nanzod" [8] provides a recipe for a multicomponent collection called "Rejuvenating-35", which includes 35 components of natural origin. The remedy has general tonic and aphrodisiac properties and is used in gerontological practice, because, as stated in the above treatise, "the collection strengthens the elderly and is the best nectar for the body. There is no lower body disease that cannot be overcome with this medicine."

After modifying the original recipe, we developed a new composition consisting of 28 components, conventionally called "adaptophyt-28". The collection includes raw materials from plants such as *Tribulus terrestris* L., *Paeonia anomala* L., *Poligonatum odoratum* (Mill.) Druce, *Peucedanum morisonii* Bess. Ex Spreng, *Polygonum aviculare* L., *Orthosiphon stamineus* Benth., *Acorus calamus* L., *Juniperus communis* L., *Althaea officinalis* L., *Lespedeza juncea* (L. Fil.) Pers., *Equisetum arvense* L., *Calendula officinalis* L., *Inula helenium* L., *Sophora flavescens* Soland., *Bergenia crassifolia* L. et al. The collection was prepared in the form of a decoction 1:10. Phytochemical studies carried out using titrimetric and differential spectrophotometric methods [6, 11] showed that in the aqueous extract (1:10) the content of polyphenols is 2.3%; flavonoids - 1.1%, ascorbic acid - 0.3%. The aim of this work was to determine the effect of the complex herbal remedy "adaptofit-28" on the sexual activity of white rats.

## MATERIALS AND METHODS

The experiments were carried out on mature and old male Wistar rats weighing 210–230 g and 250–380 g, respectively. In the first series of experiments, the effect of the complex agent on the sexual activity of intact male rats was investigated. Before the experiments, the animals were isolated from females for 30 days. The rats of the experimental group were injected intragastrically with a decoction of "adaptofit-28" (prepared in a ratio of 1:10) in a volume of 10.0 ml / kg once a day for 7 days before testing. The rats of the control group were injected with an equal volume of distilled water according to a similar scheme. To determine the effect of the test agent on the indicators of sexual behavior of male rats, the number of sniffs, licks, cages and ejaculations during mating of males with females in a state of estrus was assessed [9]. The indicators of the sexual behavior of male rats were recorded for 15 minutes. The state of estrus was induced by subcutaneous administration of 0.05 ml of 2% synestrol for 5 days. The phase of the cycle was determined on the basis of cytological examination of vaginal smears [4]. Along with the indicators of sexual behavior, the serum testosterone content was determined by enzyme immunoassay using a standard set "Sterotide ELISA-testosterone-01". In the second series of experiments, the sexual behavior of male rats was investigated against the background of "pharmacological castration". To reproduce the model of "pharmacological castration" antiandrogenic drugs with different mechanisms of action were used: androkur (blocker of androgen receptors), proscar (specific inhibitor of 5- $\alpha$  reductase that activates testosterone); Sinestrol (an estrogenic androgen antagonist hormone). These drugs were administered enterally once a day for 30 days prior to the experiment: Androkur - at a dose of 150 mg / kg, Proscar - at a dose of 1 mg / kg, Sinestrol - at a dose of 40 mg / kg. The animals of the experimental group, simultaneously with antiandrogenic drugs, were injected intragastrically with adaptofit-28 decoction in a volume of 10 ml / kg. Five days before testing, the females were induced to oestrus and the indicators of the sexual behavior of male rats were assessed using the above method. Statistical processing of the data obtained was carried out using the Mann-Whitney test. Differences were considered significant at  $p \leq 0.05$ . The data obtained are shown in table. 12. The animals of the experimental group, simultaneously with antiandrogenic drugs, were injected intragastrically with adaptofit-28 decoction in a volume of 10 ml / kg. Five days before testing, the females were induced to oestrus and the indicators of the sexual behavior of male rats were assessed using the above method. Statistical processing of the data obtained was carried out using the Mann-Whitney test. Differences were considered significant at  $p \leq 0.05$ . The data obtained are shown in table. 12. The animals of the experimental group, simultaneously with antiandrogenic drugs, were injected intragastrically with adaptofit-28 decoction in a volume of 10 ml / kg. Five days before testing, the females were induced to oestrus and the indicators of the sexual behavior of male rats were assessed using the above method. Statistical processing of the data obtained was carried out using the Mann-Whitney test. Differences were considered significant at  $p \leq 0.05$ . The data obtained are shown in table. 12. 05. The data obtained are shown in table. 12. The data obtained are shown in table. 12.

Table 1

Influence of "adaptofit-28" on sexual behavior and testosterone content in blood serum male white rats

Показатели	Группы			
	половозрелые самцы		старые самцы	
	Интактная n = 15	Опытная (адаптофит) n = 10	Интактная n = 10	Опытная (адаптофит) n = 10
Количество обнюхиваний	17,6 ± 1,63	7,4 ± 0,82*	4,8 ± 0,48	10,2 ± 0,77*
Количество облизываний	7,2 ± 1,14	5,4 ± 0,96	1,9 ± 0,51	6,3 ± 0,83*
Количество садок	6,0 ± 1,8	17,3 ± 2,58*	0,8 ± 0,22	1,5 ± 0,14*
Количество эякуляций	1,9 ± 0,68	17,1 ± 1,06*	0,0	0,9 ± 0,91*
Суммарный показатель	32,7 ± 3,06	46,6 ± 2,66*	7,5 ± 0,69	18,9 ± 1,19*
Тестостерон, нмоль/л	11,0 ± 0,71	33,2 ± 0,93*	0,79 ± 0,04	15,8 ± 2,14*

Примечание: \* – различия достоверны по сравнению с данными интактных животных при  $P \leq 0,05$ ; n – количество крыс в группе.

table 2

Influence of "adaptofyt-28" on the sexual activity of sexually mature male rats and testosterone on the background of "pharmacological castration"

Группы	Показатели					Содержание тестостерона, нмоль/л
	Половая активность					
	Кол-во обнюхиваний	Кол-во облизываний	Кол-во садок	Кол-во эякуляций	Суммарный показатель	
Интактная	17,6 ± 1,63	7,2 ± 0,94	6,0 ± 1,80	1,9 ± 0,38	32,7 ± 3,06	11,0 ± 0,71
кастрация проскарром						
Контрольная (проскар)	6,1 ± 0,84*	3,0 ± 0,85*	1,4 ± 0,36*	0,0*	10,5 ± 1,94*	3,5 ± 0,18*
Опытная (проскар + адаптофит)	10,7 ± 1,03	9,2 ± 0,75	3,7 ± 0,87*	2,0 ± 0,57**	25,6 ± 2,79**	5,2 ± 0,48**
кастрация синестролом						
Контрольная (синестрол)	12,2 ± 1,57*	2,7 ± 0,68*	7,5 ± 1,18	0,7 ± 0,06*	23,1 ± 2,71*	3,7 ± 0,13*
Опытная (синестрол + адаптофит)	15,3 ± 1,08	6,4 ± 0,85**	12,0 ± 1,55**	2,4 ± 0,35**	36,1 ± 3,92**	12,0 ± 0,54**
кастрация андрокуром						
Контрольная (андрокур)	9,9 ± 0,98*	4,8 ± 0,92*	2,6 ± 0,40*	0,9 ± 0,09*	18,2 ± 1,81*	2,4 ± 0,44*
Опытная (андрокур + адаптофит)	11,4 ± 1,63	8,8 ± 0,59**	1,4 ± 0,62	0,1 ± 0,0**	21,7 ± 2,79	4,9 ± 0,54**

Примечание: \* – различия достоверны по сравнению с данными интактных животных; \*\* – различия достоверны по сравнению с данными крыс контрольной группы при  $P \leq 0,05$ .

## RESULTS

It was found that the course administration of the complex herbal remedy "adaptofit28" has a pronounced stimulating effect on the sexual behavior of both sexually mature and old male rats (Table 1).

As follows from the data presented in table. 1, mature rats treated with the test agent are characterized by high sexual activity, as indicated by an almost 3-fold increase in the number of cages, accompanied in each case by ejaculation. At the same time, a decrease in such an indicator of sexual behavior as the number of licks was noted. The total index of sexual activity in rats treated with "adaptofit" was 42% higher than in intact rats. It was found that an increase in sexual activity in rats of the experimental group is associated with a significant increase in the level of testosterone: its concentration in the blood increased by 3 times in comparison with the physiological norm. More pronounced aphrodisiac properties of "adaptofyt" were established when it was administered to old male rats. In old intact males, sexual activity is at a low level: in the presence of a certain sexual interest in females in estrus, as indicated by such indicators as sniffing and licking, cages were recorded in only half of the animals in the group, there were no ejaculations. The content of testosterone in the blood of old males decreases 10 times compared with that in sexually mature rats. Course introduction of "adaptofit" was accompanied by an increase in the number of sniffs and licks, respectively, 2 and 3 times

comparison with similar data in intact old rats; an increase in the number of cages by 2 times and the appearance of ejaculation in 3 animals of this group. The total index of sexual activity, as well as the content of testosterone in rats treated with the test agent, increased by 2.5 and 19 times, respectively, in comparison with the data of intact old rats.

As follows from the data given in table. 2, "pharmacological castration" with antiandrogenic drugs is accompanied by a significant decrease in the sexual activity of male rats, as indicated by a 3-fold decrease in the total index of sexual activity when using Proscar, 2 times when using sinestrol, and 1.8 times when using androkur. data from intact rats. The oppression of the copulative component of sexual activity was especially pronounced with the introduction of Proscar and Androkur. Along with this, the rats of the control groups showed a more than threefold decrease in the level of testosterone in the blood serum. It was found that the course administration of "adaptofit-28" contributed to the restoration of the sexual activity of animals with "pharmacological castration" in all experimental groups. So, the total index of sexual activity in rats of the experimental groups against the background of the introduction of proscar increased by 2.4 times, sinestrol - by 56%, androkur - 20% compared to the analogous indicators of animals in the control groups. At the same time, the sexual activity in rats that received the test agent against the background of "castration" with synestrol reached the level of that in intact rats. It was shown that in the animals of the experimental groups that received the test agent, an increase in the level of testosterone was noted: against the background of proscar, its content increased by 48%, sinestrol - 3.4 times, androkur - 2.0 times compared with similar indicators of rats in the control groups ... who received the test agent against the background of "castration" with synestrol reached the level of that in intact rats. It was shown that in the animals of the experimental groups that received the test agent, an increase in the level of testosterone was noted: against the background of proscar, its content increased by 48%, sinestrol - 3.4 times, androkur - 2.0 times compared with similar indicators of rats in the control groups ... who received the test agent against the background of "castration" with synestrol reached the level of that in intact rats. It was shown that in the animals of the experimental groups that received the test agent, an increase in the level of testosterone was noted: against the background of proscar, its content increased by 48%, sinestrol - 3.4 times, androkur - 2.0 times compared with similar indicators of rats in the control groups ...

#### DISCUSSION AND CONCLUSIONS

Thus, the data obtained indicate that the multicomponent agent "adaptofit-28" has a significant aphrodisiac activity, increasing the sexual activity of male white rats, including its copulative component. The activation of sexual activity correlated with the level of testosterone in the blood and was more indicative in relation to old males, which indicates the ability of the test agent to arrest the signs of age-related hypogonadism. Considering the obtained data on the increase in sexual activity and testosterone content in rats of the experimental group against the background of "pharmacological castration", it can be assumed that "adaptofit-28" has both central and peripheral gonadotropic effects, preventing the antiandrogenic effect of drugs with different mechanisms of action. In particular, The test agent activates the process of testosterone restoration to 5 $\alpha$ -dihydrosterone in prostatic cells, increases the sensitivity of the androgen receptors of target cells to testosterone, and also has an antiestrogenic effect. The data obtained on the high aphrodisiac activity of "adaptofit28" justify the expediency of further research, including its full preclinical testing and implementation in practical health care.

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