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Study Of The Chrono-Correcting Action Of A New Drug With Dry Extract Of Eleuthorococcus And Pabuda

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Abstract: The data obtained in the course of this study on the study of the chrono-correcting effect of a new drug - capsules with Eleutherococcus and Pabuda extract in comparison with Melaxen®, coated tablets (INN metalonin) indicate that EP EPDM has a desynchronizing effect, which was expressed in a decrease in research activity, swimming time of animals, negative influence (depletion) of stress-competent organs (liver, spleen, thymus, adrenal glands) and a decrease in the content of antioxidants in the blood serum of rats.

Keywords: desynchranosis, dry extract, Eleutherococcus, Paraguayan holly,

INTRODUCTION

Desynchronosis - (de- + Greek synchronismos coincidence in time, simultaneity + -oz) is a painful condition caused by desynchronization of biological rhythms and manifested by disturbed sleep, appetite, decreased performance [1]. The most striking manifestation of this condition is a decrease in working capacity as a result of the rapid onset of fatigue, accompanied by a poor reaction to external stimuli and impaired psychomotor activity, manifested in a reduced concentration of attention, irritability and depletion of the nervous system with moderate depression, and, as a result, a violation of physical activity. The development of the pathological process involves the endocrine, antioxidant,

autonomic nervous, cardiovascular, immune systems and digestive organs.

According to modern concepts, the main hormonal regulator of biorhythms is the hormone melatonin (N-acetyl-5-methoxytryptamine), which is synthesized in the secretory cells of the pineal gland and enters the blood from there [2, 3]. The production of melatonin by the pineal gland depends on the time of day and is directly related to light exposure. Information about day or night (light level) is transmitted by a light pulse through the retina of the photosensitive ganglion cells of the eyeball. In response to this information, melatonin is either produced in the body or not. Once in the bloodstream, melatonin acts as an endocrine hormone and controls biological functions in the regulation of circadian rhythms, such as the sleep-wake cycle. Melatonin is a rare example of a hormone to which it is available as membrane [4, 5].

In connection with the above, the purpose of this study is to study the chrono-correcting effect of a new drug - capsules with Eleutherococcus and Pabuda extract in comparison with Melaxen®, film-coated tablets (INN metalonin).

MATERIALS AND METHODS

Paraguayan holly leaves and petioles (sample of industrial raw materials "Martin & Cia LTDA.SA", trade mark "DON LUCAS", series AC14097, valid until 10.2018, certified by INAL - Instituto Nacional De Alimentos (National Institute of Nutrition), weight of raw materials in 1 pack - 500 g;

Eleutherococcus dry extract, dry substance-extract (LLC "Kharms", Russia), No. LSR-004059/09 (in accordance with FS 2.5.0053.15);

Succinic acid, substance-powder (JSC "Marbiopharm", Russia), R N000493 / 01;

Melaxen®, film-coated tablets (Unipharm Inc., USA), No. P N015325 / 01.

In the course of the research, the developed drug (MP), capsules "Means for correction with Eleuthorococcus and Pabud" (EPDM) were studiedin comparison with Melaxen®... [6]

The calculation of doses of the investigated substances equivalent for animals is presented in Table 1.

Table 1. The studied doses of substances in the study of the effectiveness of the drug "SKEP" when modeling light desynchronosis

№.	Test substance	TDdays	ETDmice	ETD rats
1	Melaxen®	0.04 mg / kg	0.52 mg / kg	0.24 mg / kg
2	LP SKEP	16.57 mg / kg	215.41 mg / kg	99.42 mg / kg
3	dryextractofEleutherococcus	2.86 mg / kg	37.18 mg / kg	17.16 mg / kg
4	hollyextractdry	7.14 mg / kg	92.82 mg / kg	42.84 mg / kg
5	succinicacid	2.86 mg / kg	37.18 mg / kg	17.16 mg / kg
6	dry extract of Eleutherococcus + dry holly extract	10 mg / kg	130 mg / kg	60 mg / kg
7	dry extract of Eleutherococcus + succinic acid	4.26 mg / kg	55.38 mg / kg	25.56 mg / kg
8	dry holly extract + succinic acid	8.57 mg / kg	111.41 mg / kg	51.42 mg / kg

For the study, experimental groups of animals (10 groups of 16 (male rats) and 20 (male mice)) were injected with the test solutions at a dose of 1ETD: 1 - intact, received intragastrically 1% starch solution;

2 - control, received intragastrically 1% starch solution; 3 - received intragastrically as a suspensionMelaxen®; 4 - a granulate of a mixture of Paraguayan holly and Eleutherococcus prickly extracts and a substance-powder of succinic acid was obtained; 5 - received intragastric dry extract of Eleutherococcus; 6 - received an intragastric dry holly extract; 7 - received succinic acid intragastrically; 8 - received intragastrically a mixture of extracts of Eleutherococcus dry and holly dry; 9 - received intragastric extract of Eleutherococcus dry and succinic acid; 10 - received intragastrically dry holly extract and succinic acid. All groups, with the exception of the intact, were exposed to desynchronosis

Modeling of light desynchronosis was carried out according to the scheme of continuous illumination with fluorescent lamps (BEURER TL40, Germany) for 21 days. The illumination of the cells was 1.51 Lux / cm2.

Physical endurance was assessed according to the method of forced swimming with a load [7, 8, 9].

Discussion

Experiments have shown that in all control groups of animals, a powerful desynchronizing effect was observed, which was expressed in a decrease in exploratory activity, swimming time of animals, a negative effect (depletion) of stress-competent organs (liver, spleen, thymus, adrenal glands) and a decrease in the content of antioxidants in blood serum Rats [10, 11].

In the group of animals that received the reference drug Melaxen®, research activity increased and had a positive effect on stress-competent organs, but the duration of swimming and AOA did not increase [12].

In contrast to the control groups, in animals receiving LP "CCEP ", increased exploratory activity, swimming duration, had a positive effect on stress-competent organs, and the highest AOA was observed in the blood serum of rats with simulated two-week desynchronosis. The actoprotective effect was expressed in an increase in the swimming time, thereby increasing the nonspecific resistance of animals under intense physical activity.

Table 2. Influence LP SKEP on the dynamics of changes in the swimming time of male rats (M ± m, s) with simulated light desynchronosis

Groups	Swimming		
	1 day	Day 7	21 day
Intact	226.8 ± 18	274.7 ± 11.6 *, **	381.5 ± 16.3 *, **
Control	235.6 ± 13	245.7 ± 17.8	198.2 ± 12.1 *, **
Melaxen®	230.7 ± 15.4	272.1 ± 12 *, **	258 ± 8.1 *, **
GLF SKEP	230.3 ± 18.1	356 ± 8.8 *, **	439.1 ± 17 *, **
dryextractofEleutherococcus	226.8 ± 17.7	296.8 ± 19.1 *, **	344.6 ± 13.7 *, **
hollyextractdry	236.7 ± 19.9	349.3 ± 19	397.9 ± 18.2 *, **
succinicacid	228.3 ± 19.7	274 ± 11.2 *, **	349.1 ± 12 *, **
dry extract of Eleutherococcus + dry holly extract	212.2 ± 21.3	322.4 ± 18 *, **	372 ± 12.2 *, **
dry extract of Eleutherococcus + succinic acid	233.9 ± 19.1	276 ± 14.9 *, **	331.2 ± 20.6 *, **
dry holly extract + succinic acid	225 ± 17.6	340.3 ± 20.3	366 ± 17.6 *, **

* - significant difference from the intact group at P≥0.95;

** - significant difference from the control group at P≥0.95

Table 3. InfluenceLP SKEP on the dynamics of changes in the swimming time of male mice (M ± m, s) with simulated light desynchronosis

Groups	Swimming		
	1 day	Day 7	21 day
Intact	423.1 ± 13.4	467.4 ± 19.8	564.1 ± 19.7 *, **
Control	424.2 ± 13	363.1 ± 13.5 *, **	312.1 ± 19.2 *, **
Melaxen®	420.7 ± 16	432 ± 16.2	374.5 ± 17.6 *, **
GLF SKEP	420.2 ± 15.4	565.1 ± 16.1 *, **	627 ± 17.5 *, **
dryextractofEleutherococcus	422 ± 17.6	477 ± 19.2 *, **	520.8 ± 15.5 *, **
hollyextractdry	416.7 ± 13	522.7 ± 21.3 *, **	597.3 ± 15.3 *, **
succinicacid	429 ± 15.2	502 ± 16.1 *, **	508.2 ± 16.2 *, **
dry extract of Eleutherococcus + dry holly extract	412.5 ± 16.4	531.1 ± 19.2 *, **	602.5 ± 15.3 *, **
dry extract of Eleutherococcus + succinic acid	422.5 ± 17.2	499.5 ± 15.5 *, **	510.6 ± 18.2 *, **
dry holly extract + succinic acid	416.2 ± 18.8	512.3 ± 15 *, **	582.4 ± 16.2 *, **

* - significant difference from the intact group at P≥0.95;

** - significant difference from the control group at P≥0.95

As follows from the data presented in tables 2 and 3, 21-day administration LP SKEPensured almost complete preservation of physiological functions in animals compared to intact animals: the increase in swimming time was 32 and 23% (rats and mice, respectively), significantly different from the increase in swimming time in intact animals. At the same time, the duration of swimming of the animals of the EPDM group increased by 110 and 68% (rats and mice, respectively) compared to the control (p≤0.05). The reference drug - Melaxen®, increased the swimming duration of animals by 30 and 16% (rats and mice, respectively) compared to the control (p≤0.05), however, when comparing the swimming indicators of this group of animals with those of intact animals, a decrease is observed 56 and 44% (rats and mice, respectively) of the duration of swimming (p≤0.05). Thus, to the extent that compensatory reactions occur,

The data obtained during the study of antioxidants (AOA) indicate the highest AOA in the blood serum of rats in the group receiving EP EPDM (357.4 ± 12.7 μmol / L). In the blood serum samples of rats of other groups, there was also a tendency to an increase in the level of AOA in comparison with the intact group (table 4)

Table 4. Influence LP SKEP on the AOA of the blood of male rats with simulated light desynchronosis

Group	Average value of trolox concentration, (μmol / l)
Intact	175.5 ± 7.6 **
Control	224.5 ± 4.8 *

Group	Average value of trolox concentration, (μmol / l)
Melaxen®	231.7 ± 4.3 *
GLF SKEP	357.4 ± 12.7 *, **
dryextractofEleutherococcus	272.6 ± 10.3 *, **
hollyextractdry	241.8 ± 15.3 **
succinicacid	252.9 ± 9.7 **
dry extract of Eleutherococcus + dry holly extract	299.2 ± 11.6 *, **
dry extract of Eleutherococcus + succinic acid	302.8 ± 10.8 *, **
dry holly extract + succinic acid	287.1 ± 12.5 *, **

* - significant difference from the intact group at P≥0.95;

** - significant difference from the control group at P≥0.95

Table 5. Influence LP SKEP on changes in body mass of male rats (M ± m) with simulated light desynchronosis

Group	Organmass			
	Liver, %	Spleen,%	Thymus,%	Adrenalglands,%
Intact	3.8 ± 0.1 **	0.33 ± 0.04 **	0.16 ± 0.01 **	0.016 ± 0.001 **
Control	3.1 ± 0.1 *	0.26 ± 0.02 *	0.09 ± 0.03 *	0.011 ± 0.001 *
Melaxen®	3.2 ± 0.1	0.3 ± 0.04 **	0.14 ± 0.03	0.012 ± 0.002
GLF SKEP	3.4 ± 0.1 *	0.34 ± 0.02 **	0.15 ± 0.01 **	0.015 ± 0.001 **
dryextractofEleutherococcus	3.4 ± 0.1 *	0.33 ± 0.02 **	0.13 ± 0.02	0.014 ± 0.001 **
hollyextractdry	3.3 ± 0.1	0.29 ± 0.03 *	0.12 ± 0.02	0.013 ± 0.002
succinicacid	3.2 ± 0.1 *	0.3 ± 0.03 *	0.12 ± 0.01 *	0.012 ± 0.002
dry extract of Eleutherococcus + dry holly extract	3.5 ± 0.1 **	0.31 ± 0.02 *	0.13 ± 0.02	0.014 ± 0.002
dry holly extract + succinic acid	3.4 ± 0.1 *	0.3 ± 0.02 *	0.14 ± 0.02	0.013 ± 0.002

* - significant difference from the intact group at P≥0.95;

** - significant difference from the control group at P≥0.95

Table 6. Influence GLF SKEP on changes in body mass of male mice (M ± m) with simulated light desynchronosis

Group	Organmass			
	Liver, %	Spleen,%	Thymus,%	Adrenalglands,%
Intact	5.8 ± 0.3 **	0.88 ± 0.31 **	0.18 ± 0.07 **	0.021 ± 0.004 **
Control	4.5 ± 0.8 *	0.4 ± 0.2 *	0.09 ± 0.04 *	0.009 ± 0.005 *
Melaxen®	4.8 ± 0.5 *	0.69 ± 0.39	0.13 ± 0.05	0.011 ± 0.005 *
GLF SKEP	4.8 ± 0.2 *	0.7 ± 0.18 **	0.19 ± 0.03 **	0.02 ± 0.003 **
dryextractofEleutherococcus	4.8 ± 0.3 *	0.68 ± 0.17 **	0.17 ± 0.04	0.018 ± 0.004

Group	Organmass			
	Liver, %	Spleen,%	Thymus,%	Adrenalglands,%
hollyextractdry	4.7 ± 0.3 *	0.51 ± 0.19	0.15 ± 0.04	0.012 ± 0.004 **
succinicacid	4.9 ± 0.2 *	0.45 ± 0.13	0.15 ± 0.03	0.015 ± 0.003
dry extract of Eleutherococcus + dry holly extract	4.9 ± 0.2 *	0.6 ± 0.17	0.18 ± 0.04	0.019 ± 0.003
dry extract of Eleutherococcus + succinic acid	5.2 ± 0.2 *	0.61 ± 0.17	0.17 ± 0.03	0.021 ± 0.004 **
dry holly extract + succinic acid	4.8 ± 0.3 *	0.39 ± 0.2	0.16 ± 0.04	0.015 ± 0.003

* - significant difference from the intact group at P≥0.95;

** - significant difference from the control group at P≥0.95

The results of weighing data from stress-competent authorities (Tables 5, 6) confirm the positive impact LPSKEP on adaptive mechanisms in simulated desynchronosis. In the model of light desynchronosis, EPDM with repeated administration showed a significant antidesyn chronizing effect, reducing the depletion of the spleen, thymus and adrenal glands in comparison with the control group by 18, 27 and 20% in rats and by 50, 48 and 45% in mice, respectively.

CONCLUSION

The experimental data presented indicate that EP EPDM has a chrono-correcting effect and also has a pronounced adaptogenic activity. Combinations of the studied drug are able to reduce the negative effect in desynchronosis. The planned daily dose of active substances is able to provide a chrono-correcting effect without undesirable effects for the body.

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