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THE EFFECT OF THE MIXTURES WITH BIOLOGICALLY ACTIVE SUBSTANCES FROM *FRAXINUS EXCELSIOR* AND *PHLOMIS PUNGENS* ON THE RESISTANCE TO HYPOXIA IN WHITE RATS COMPARED TO THE ACTION OF A-TOCOPHEROL AND MEXIDOL

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Key words: hypoxia; α-tocopherol; mexidol; Fraxinus excelsior; Phlomis pungens

The aim of the work was to study the antihypoxic action of the biologically active mixtures obtained from Fraxinus excelsior (European ash) growing in Azerbaijan Guba region and Phlomis pungens (Jerusalem sage) from the Nakhichevan Autonomous Republic. The study was conducted in male and female white rats on the model of acute hypobaric hypoxia. As reference medicines α-tocopherol and mexidol in the doses of 200 mg/kg were used. The biologically active mixtures from Fraxinus excelsior (300 mg/kg), Phlomis pungens (400 mg/kg) and the reference medicines were injected into the abdominal cavity of the animals 40 min before the experiment. It has been found that by the effect of the body's resistance to hypoxia the substances under study can be arranged as follows: Fraxinus excelsior>Phlomis pungens>mexidol>α-tocopherol.

As a risk factor for many diseases hypoxia is one of the most pressing problems of modern medicine. Any pathological process in the body is more aggressive in the presence of hypoxia, or hypoxias themselves play a role in the pathogenesis of diseases [1, 12, 13, 14]. Ischemic diseases of the heart and brain, impaired supply of oxygen to the body organs, and even some infectious diseases occur as a result of hypoxia [1, 4, 6, 9]. Therefore, protection of the body from hypoxia and its undesirable effects is an urgent problem of practical medicine and is of great social importance [2, 7, 10, 11].

Methods for protection of the organism from hypoxia have not been fully studied by pharmacologists and pathophysiologists. These methods are divided into two types. The first one is the natural increase of the body's resistance to hypoxia, and the second type is the use of new drugs of the natural origin possessing the antihypoxic and antioxidant activity in the medical practice [8, 21]. Taking all of this into account the aim of our research was to study the antihypoxic action of the biologically active mixtures obtained from *Fraxinus excelsior* (European ash) growing in Azerbaijan Guba region and *Phlomis pungens* (Jerusalem sage) from the Nakhichevan Autonomous Republic [15-20] and compare their action with α-tocopherol and mexidol.

Materials and Methods

When conducting our study the methods of acute hypobaric hypoxia were used.

The model of acute hypobaric hypoxia was created using white rats in an airless pressure chamber. The pressure was measured by an altimeter, the rate of hoisting – by a variometer. The animals were hoisted at an altitude of 11.000 m and at the rate of 25 m/s (198.7-185 mmHg). This position was held for 10 min. Then the animals were returned to their previous position for 5 min. To eliminate hypercapnia the CO_2 absorber (30-35% alkali) was placed to the chamber. To create the same conditions of hypoxia simultaneously 3 animals of each group (experimental and control) were placed to the chamber. There was the own control group for each experimental group [5, 12]. The life span of animals and the number of surviving rats were calculated.

To compare the antihypoxic resistance of biologically active mixtures obtained from *Fraxinus excelsior* and *Phlomis pungens* with α-tocopherol and mexidol these substances were injected into the abdominal cavity of the animals 40 min before the experiments. The control group of animals was injected the same amount of physiological salt solution.

The data obtained during the experiments were statistically processed in accordance with the current requirements. The group results were arranged in a set of variations. For each group the arithmetic mean (M), its standard error (m), as well as the maximum (max) and minimum (min) limits were determined.

All calculations were performed in Excel spreadsheet [3], and the results were summarized in Table.

Results and Discussion

The resistance of biologically active mixtures obtained from *Fraxinus excelsior* and *Phlomis pungens* to hypoxia was studied compared to α-tocopherol and mexidol in male and female white rats on the background of hypobaric hypoxia. The similar experiments were also conducted on intact white rats. The rats were injected abdominally with the biologically active mixture from *Fraxinus excelsior* in the dose of 300 mg/kg, the bio-

logically active mixture from *Phlomis pungens* in the dose of 400 mg/kg and α-tocopherol and mexidol in the effective doses of 200 mg/kg.

The biologically active mixtures obtained from both plants showed the antihypoxic action in female and male white rats. Thus, the biologically active mixture from *Fraxinus excelsior* in the dose of 300 mg/kg injected abdominally increased the resistance to hypoxia in both male and female rats. The results of the control group of male rats were 9.19±0.31 min, with introduction of the biologically active mixture from *Fraxinus excelsior* (300 mg/kg) the results increased to 12.20±0.04 min. Therefore, when using the biologically active mixture from *Fraxinus excelsior* in male rats the resistance to hypoxia statistically increased by 32.8%. The antihypoxic effect of the biologically active mixture from *Fraxinus excelsior* was also observed in female rats. The results of the control group were 8.59±0.16 min, while on the background of the biologically active mixture from *Fraxinus excelsior* (300 mg/kg) they were 11.23±0.05.

The results obtained have shown that the biologically active mixture of *Fraxinus excelsior* in the dose of 300 mg/kg increases the resistance of male rats by 32.8%, and female rats by 30.7% to hypoxia.

The similar powerful antihypoxic effect was observed with abdominal introduction of the biologically active mixture of *Phlomis pungens* in the dose of 400 mg/kg. he results of the control group were 0.31±9.19 min in male rats, while when using the biologically active mixture from *Phlomis pungens* (400 mg/kg) they were 10.64± ±0.33 min. This means that the biologically active mixture from *Phlomis pungens* in the dose of 400 mg/kg statistically increased the resistance to hypoxia by 15.8% ($p<0.01$) in male white rats. When introducing the biologically active mixture from *Phlomis pungens* in the dose of 400 mg/kg to female rats the results were 9.30±0.03 min, and the values of the control group were 8.59±0.16 min. Thus, the resistance to hypoxia of female white rats receiving the mixture from *Phlomis pungens* (400 mg/kg) statistically increased by 8.3%.

To check the efficiency of the results obtained the mixtures studied were compared to the action of the natural antioxidant α-tocopherol and the synthetic antioxidant mexidol. The research demonstrated that the abdominal injection of α-tocopherol in the dose of 200 mg/kg increased the resistance to hypoxia in the group of white male rats compared to the control. The results of the control group were 9.19±0.31 min, while the introduction of α-tocopherol (200 mg/kg) increased the results to 10.40±0.33 min. Thus, α-tocopherol statistically increased the resistance to hypoxia of male white rats by 13.2%. The antihypoxic effect was also observed in experiments with female rats. The results in the control group of female rats were 8.59±0.16 min, while when introducing α-tocopherol they increased to 9.30±0.03 min. Thus, α-tocopherol statistically increased the resistance in female white rats by 8.7% compared to the control group.

As a result of our studies conducted with mexidol it became clear that with its abdominal injection (200 mg/kg) the resistance to hypoxia of male white rats increased compared to the control group. The results of the control group were 9.19±0.31 min in male rats, while when using mexidol in the dose of 200 mg/kg the results increased to 11.60±0.42 min. Thus, when using mexidol the resistance to hypoxia of male white rats statistically increased by 26.2%. The antihypoxic effect was also observed in female rats. The results in the control group were 8.59±0.16 min, and the results with mexidol were (200 mg/kg) increased to 10.34±0.05 min. Therefore, when using mexidol the resistance to hypoxia of female white rats compared to the control group statistically increased by 20.3%.

Table

The effects of biologically active mixtures obtained from *Fraxinus excelsior* in the dose of 300 mg/kg and *Phlomis pungens* in the dose of 400 mg/kg on resistance to hypoxia compared to the action of 200 mg/kg of α-tocopherol and 200 mg/kg of mexidol (M±m, n = 10)

Study groups	Gender	
	Male	Female
Intact (0.9% NaCl) (n = 10)	9.19±0.31 (8.31-11.26)	8.59±0.16 (8.18-9.51)
Mexidol – 200 mg/kg (n = 10)	11.60±0.42 (10.03-14.14)**	10.34±0.05 (10.12-10.58)**
Vitamin E – 200 mg/kg (n = 10)	10.40±0.33 (9.18-12.16)*	9.34±0.06 (9.12-9.56)**
Phlomis pungens– 400 mg/kg (n = 10)	10.64±0.33 (9.2-12.29)**	9.30±0.03 (9.14-9.48)*
Fraxinus excelsior– 300 mg/kg (n = 10)	12.20±0.04 (12-12.44)**	11.23±0.05 (11.02-11.43)**

Note: statistical correlation of the values of the intact group and the difference: * – $p<0.05$; ** – $p<0.01$

The results of the study are given in Table.

Summarizing our studies it has been concluded that along with the absence of the toxic action both biologically active mixtures are competitive with the natural antioxidant a-tocopherol and the synthetic antioxidant mexidol in increasing the body's resistance to hypoxia. According to the research results the biologically active mixture from *Fraxinus excelsior* in the dose of 300 mg/kg has the strongest antihypoxic action; the next is the mixture from *Phlomis pungens* in the dose of 400 mg/kg. By the effect to the hypoxia resistance these substances can be arranged as follows: *Fraxinus excelsior* >*Phlomis pungens* > mexidol > α-tocopherol.

CONCLUSIONS

The biologically active mixture from *Fraxinus excelsior* in the dose of 300 mg/kg, and the biologically active mixture from *Phlomis pungens* in the dose of 400 mg/kg have increased the resistance of white rats with hypoxia compared to α-tocopherol and mexidol in the doses of 200 mg/kg.

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ДІЯ СУМИ БІОЛОГІЧНО АКТИВНИХ СУМІШЕЙ, ОДЕРЖАНИХ З ЯСЕНЯ ЗВИЧАЙНОГО (*FRAXINUS EXCELSIOR*) ТА ЗОПНИКА КОЛЮЧОГО (*PHLOMIS PUNGENS*), НА ОПІРНІСТЬ ДО ГІПОКСІЇ БІЛИХ ЩУРІВ У ПОРІВНЯННІ З ДІЄЮ МЕКСИДОЛУ ТА α-ТОКОФЕРОЛУ

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***Ключові слова**: гіпоксія; α-токоферол; мексидол; Fraxinus excelsior; Phlomis pungens*

Метою даної роботи стало вивчення антигипоксантної дії біологічно активних сумішей, одержаних з Ясеня звичайного (Fraxinus excelsior), що росте в Губинському районі Азербайджану, та Зопника колючого (Phlomis pungens), що росте в Нахічеванській Автономній Республіці. Дослідження проведене на моделі гострої гіпобаричної гіпоксії на щурах-самцях та щурах-самицях. В якості препаратів порівняння використовували α-токоферол та мексидол у дозах 200 мг/кг. Біологічно активні суміші з Ясеня звичайного (300 мг/кг) та Зопника колючого (400 мг/кг) і референт-препарати вводили внутрішньоочеревинно за 40 хвилин до початку експерименту. Встановлено, що за дією на опірність організму до гіпоксії досліджувані речовини можна розташувати наступним чином: Ясень звичайний > Зопник колючий > мексидол > α-токоферол.

ДЕЙСТВИЕ СУММЫ БИОЛОГИЧЕСКИ АКТИВНЫХ СМЕСЕЙ, ПОЛУЧЕННЫХ ИЗ ЯСЕНЯ ОБЫКНОВЕННОГО (*FRAXINUS EXCELSIOR*) И ЗОПНИКА КОЛЮЧЕГО (*PHLOMIS PUNGENS)*, НА СОПРОТИВЛЯЕМОСТЬ К ГИПОКСИИ БЕЛЫХ КРЫС В СРАВНЕНИИ С ДЕЙСТВИЕМ МЕКСИДОЛА И α-ТОКОФЕРОЛА

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***Ключевые слова**: гипоксия; α-токоферол; мексидол; Fraxinus excelsior; Phlomis pungens*

Целью данной работы стало изучение антигипоксантного действия биологически активных смесей, полученных из произрастающего в Губинском районе Азербайджана Ясеня обыкновенного (Fraxinus excelsior) и Зопника колючего (Phlomis pungens), произрастающего в Нахичеванской Автономной Республике. Исследование проведено на модели острой гипобарической гипоксии на крысах-самках и крысах-самцах. В качестве препаратов сравнения использованы α-токоферол и мексидол в дозах 200 мг/кг. Биологически активные смеси, полученные из Ясеня обыкновенного (300 мг/кг) и Зопника колючего (400 мг/кг), и референт-препараты вводили внутрибрюшинно за 40 минут до начала эксперимента. Установлено, что по воздействию на сопротивляемость организма к гипоксии исследуемые вещества можно расположить следующим образом: Ясень обыкновенный>Зопник колючий>мексидол> α-токоферол.