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ANTIHYPOXIC PROPERTIES OF PHYTODRUGS

Actuality. *The article, based on its own research and literature sources, provides data on the antihypoxic properties of herbal drugs.The antihypoxic effect of herbal drugs is the basis of their effect on the cardiovascular and nervous systems, as well as on other organs. The basis of their mechanism of action as antihypoxants is the ability to restore the activity of energy production and energy consumption, antioxidant-prooxidant properties in relation to metabolic components.Previous works established the antioxidant, adaptogenic, membrane-protective properties of herbal drugs. At the same time, the occurrence of hypoxic conditions in the hospital, during competitions, heavy physical work, military conditions, requires the study of the antihypoxic effect of herbal drugs.*

The aim of the study *– to determine the antihypoxic properties of herbal drugs.*

Materials and research methods. *An analysis of domestic and foreign literature, information from printed and Internet publications regarding the determination of antihypoxic properties of herbal drugs was carried out.*

Research results and their discussion. *Defined types of hypoxic conditions in medicine and experiment. The classification of antihypoxants (cytoprotectors) is outlined. Mechanisms of antihypoxic action of herbal drugs have been revealed. Taking into account the fact that drugs of plant origin have less toxicity than synthetic ones, are more effective in terms of the «benefit/risk» ratio and are mostly cheaper to manufacture, their further research is important.*

Conclusions. *The results of the literature analysis made it possible to state that herbal drugs and some food additives have antihypoxic properties and, thanks to this, implement cardiotropic, neurotropic, and other organoprotective actions. These properties are based on their influence on energizing systems and indicators of pro-oxidant-antioxidant exchange, which are based on a positive influence on biochemical indicators of metabolism.*

Key words: *herbal drugs, antihypoxic properties, metabolism, organoprotection.*

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АНТИГІПОКСИЧНІ ВЛАСТИВОСТІ ФІТОПРЕПАРАТІВ

Актуальність. *У статті на основі власних досліджень та джерел літератури наведені дані щодо антигіпоксичних властивостей фітопрепаратів. Антигіпоксична дія фітопрепаратів лежить в основі їх впливу на серцево-судинну, нервову системи, а також на інші органи. В основі їх механізму дії в якості антигіпоксантів лежить властивість відновлювати активність енергоутворення і споживання енергії, антиоксидантні-прооксидантні властивості щодо компонентів метаболізму. Попередні роботи встановили антиоксидантні, адаптогенні, мембранопротекторні властивості фітопрепаратів. Разом з тим, виникнення гіпоксичних станів у лікарні, при змаганнях, важкій фізичній роботі, військових станах, потребує вивчення антигіпоксичної дії фітопрепаратів.*

Мета роботи *– визначити антигіпоксичні властивості фітопрепаратів.*

Матеріали та методи досліджень. *Був проведений аналіз вітчизняної та зарубіжної літератури, відомості з друкованих та інтернет-видань щодо визначення антигіпоксичних властивостей фітопрепаратів.*

Результати дослідження та їх обговорення. *Визначені види гіпоксичних станів у медицині і експерименті. Викладена класифікація антигіпоксантів (цитопротекторів). Розкриті механізми антигіпоксичної дії фітопрепаратів. Зважаючи на те, що препарати рослинного походження мають меншу токсичність ніж синтетичні, ефективніші за співвідношенням «користь/ризик» і здебільшого дешевші у виробництві, важливим є їх подальше дослідження.*

Висновки. *Результати аналізу літератури дозволили стверджувати, що фітопрепарати і деякі харчові добавки мають антигіпоксичні властивості, і завдяки цьому реалізують кардіотропну нейротропну та інші органопротекторні види дії. В основі цих властивостей лежить їх вплив на енергізуючі системи та показники прооксидантно-антиоксидантного обміну в основі яких лежить позитивний вплив на біохімічні показники метаболізму.*

Ключові слова: *фітопрепарати, антигіпоксичні властивості, метаболізм, органопротекція.*

Introduction. Actuality. Determination of the antihypoxic effect of herbal drugs allows to clarify the mechanism of their organoprotective properties in various pathological conditions, when signs of hypoxia are detected. The antihypoxic effect of herbal drugs is the basis of their effect on the cardiovascular and nervous systems, as well as on other organs. The basis of their mechanism of action as antihypoxants is the ability to restore the activity of energy production and energy consumption, antioxidant-prooxidant properties in relation to metabolic components.

The aim of the study – to determine the antihypoxic properties of herbal drugs.

Research materials and methods. The analysis of domestic and foreign literature was conducted on the determination of the properties of plant antihypoxants.

Research results and their discussion. Actoprotective, anabolic, and membranotropic properties have been established for most herbal drugs. However, there are phytodrugs that are used in conditions where they, like other metabolitotropic drugs, can prevent the manifestations of hypoxia in the conditions of the clinic, training, in extreme situations, including the military (Bahmut et al., 2020).

It has been determined that hypoxia is at the basis of the development of many diseases, postoperative conditions, physical exertion, military conditions and other circumstances accompanied by stress. This requires the study of the pathogenesis of the occurrence and changes of vital systems and organs for a more targeted construction of preventive protection and treatment in these conditions (Ordynskyi et al., 2019). Hypoxia is a typical pathological process that occurs when tissues are insufficiently saturated with oxygen or its utilization by various tissues is impaired.

At the same time, many pathogenetic factors are identified, which are observed as a violation of the body's structures. One of them is the disruption of mitochondrial membranes, which occurs when the effectiveness of biological oxidation is suppressed due to the uncoupling of respiration and oxidative phosphorylation (Yelins'ka & Kostenko, 2018).

At the end of the last century, thanks to the works of Ukrainian scientists-physiologists, the imagination regarding the physiology of sports, the pathological physiology of hypoxic conditions changed due to high-altitude, space, aviation physiology, and occupational hygiene. Concepts regarding the mechanisms of action of hypoxia on the human body have expanded significantly, which became the foundation for the subsequent determination of the mechanisms of action of antihypoxants (Kolchinskaya, 1993).

It is believed that hypoxia is a pathological condition that occurs as a result of insufficient biological oxidation and suspension of energy supply of vital processes (Slipchenko, 2015). Hypoxia can be classified depending on the causes of its occurrence into exogenous (hypobarogenesis, hyperbarogenesis), respiratory (respiratory), circulatory (cardiovascular), overload (load hypoxia), substrate. According to the prevalence, local and general hypoxia are distinguished, according to the speed of development and duration – fulminant, acute, subacute, chronic, hypoxia, according to the degree of severity – mild, moderate, severe, critical (fatal) hypoxia.

Experimental studies of antihypoxic agents are carried out in accordance with the recommendations of the SEC of the Ministry of Health of Ukraine in experiments on rats in the simulation of hemic, hypoxic hypoxia (Luk'yanchuk et al., 2002).

Modern antihypoxants of synthetic origin are divided into (Egorova & Garmash, 2017; Baraboy, 2006; Lesiovskaya, 2012):

1. Intramitochondrial cytoprotectors affecting:
1.1. Inhibition of fatty acid oxidation (trimetazidine);
1.2. Fatty acid transport inhibition (meldonium);
1.3. Stimulation of the cytochrome chain (coenzyme Q);
2. Cytoprotectors affecting the transport of energy substrates into the cell (phosphocreatinine, glucose-insulin mixture, succinic acid, cytoflavin);
3. Glucose and galactose transport stimulators (thiotriazoline);
4. Antioxidants and cytoprotectors with antioxidant effect.

Considering the fact that herbal drugs have less toxicity than synthetic ones, are more effective in terms of the "benefit/risk" ratio and are mostly cheaper to produce, their research is important.

Recent years have also been characterized by new research into the composition and effect of phytodrugs as antioxidants, antihypoxants, and cytoprotectors.

The antihypoxic effect of plant polyphenols, which prevented the development of caries in the offspring, despite the cariogenic diet, was established. In addition, in the liver of rats, plant polyphenols normalized the activity of antioxidant enzymes (catalase, glutathione peroxidase) and had a certain protective effect on periodontal tissues (Ivanov et al., 2021).

Despite the fact that the liquid extract of hawthorn is known as a cardioprotector, antioxidant, and membranotropic agent, further research reveals its new properties. It was established that the liquid extract and tincture of hawthorn have not only a membrane-protective, but also an antihypoxic effect. A more pronounced antihypoxic effect is determined by the drug Kratal, which includes a liquid extract of hawthorn, which is prescribed for the treatment of acute, hemic, hypoxic, circulatory hypoxia (Yakovleva, 2007). Studying the mechanism of the antihypoxic action of Kratal in circulatory hypoxia, it was established that in the brain tissue of rats, Kratal prevents a decrease in the content of ATP, components of the thiol-disulfite system, and the content of RNA activity of SDH and TCHO. The antihypoxic properties of hawthorn drugs are manifested in the fact that it can eliminate the symptoms of insomnia, heart pain, and arrhythmia.

Antihypoxic properties have also been established in the medicinal valerian preparation due to its components (valerian essential oil), which makes it possible to prescribe them for insomnia and nervous excitement (Baker et al., 2014).

Antihypoxic properties have been established in drugs of lemon balm, which help with physical exertion and convulsions (Chen et al., 2023). The effectiveness of lemon balm in galenic dosage forms has shown its effectiveness in the treatment of nervous diseases in the inhabitants of Africa. A significant effect was observed when using an alcohol tincture of lemon balm, but for a long time there was no experimental confirmation of this effect. Therefore, the antihypoxic effect of the alcoholic extract of lemon balm was proven in experiments on mice in the simulation of hemic hypoxia (Akinpelu Lateef Abiola et al., 2020).

Antihypoxic and cardioprotective properties have been established in the Chinese plant Tongmai Yangxin, which was administered intraperitoneally to rats in which myocardial infarction was simulated. Electrophysiological biochemical indicators were determined on the 3rd and 28th day after the simulation of a heart attack. The drug was administered in 3 doses – 1 mg/kg, 2 mg/kg, 4 mg/kg. On the 28th day of the experiment, the infarct zone was reduced, contractility was restored. The studied compound had antioxidant and anti-inflammatory properties (Chen et al., 2023).

Dry extract of the Baikal scutella (Scutellaria Adenostegia), belonging to the herbaceous family, contains 46% polysaccharides and 5.8% flavonoids. When administered to rats in a dose of 100 mg/kg, it showed significant antihypoxic activity (Ergasheva et al., 2021).

Cardioprotective action of the Qili Qiangxin herb component, which is used in China for heart failure, was determined by modeling myocardial disorders of HER2 cells under apoptosis conditions (Fan et al., 2022).

In clinical conditions, the antihypoxic effect of rhodiola extract (2 capsules) was studied on volunteers under hypoxia simulation conditions. Hypoxia lasted 30 minutes, subjects received 2 capsules of 627 mg each. While hypoxia saturation decreased, rhodiola extract prevented all changes, showing antihypoxic effects (Lee et al., 2023).

The Chinese ascomycete mushroom plant cordyceps targets endothelial vascular factor, which gives the plant antihypoxic properties (Long et al., 2021).

The antihypoxic effect of cat's fur was determined in experiments on rats in hypertensive, hemic, histotoxic hypoxia, which is associated with the normalization of the level of ATP, lactate, malate, components of the glutathione system by the antioxidant effect (Razuvaeva et al., 2021).

In experiments on rats, the presence of an antihypoxic effect of dry and crushed sage extract was tested in experiments on rats, which were simulated hypoxia. In hypoxic rats, an antihypoxic effect associated with an antioxidant effect was established (Wang et al., 2020). The antihypoxic effect of sage is associated with its selective components, which include rosmarinic acid, mitopermicinic acid, salvinic acid and other active ingredients. The activity of sage is associated with the ability to normalize the activity of superoxide dismutase, indicators of antioxidant protection and the glutathione system (Wang et al., 2020).

Antihypoxic properties have been identified in green tea, the effect of which increases resistance to long-term training (Rahimi & Falahi, 2017).

Antihypoxic properties have been identified in curcumin, which makes it possible to recommend it to overcome stress before and after competition (Nakhostin-Roohi et al., 2016).

Antihypoxic action of apricot and gooseberry juices was established in case of hemic hypoxia simulated in experiments on rats. In conditions of hemic hypoxia, when these juices were administered intraperitoneally at a dose of 500 mg/kg for 10 days, they prevented changes

in the activity of antioxidant enzymes (SOD, glutathione peroxidase, and the level of reduced glutathione) and cytochrome C oxidase activity in the liver and myocardium of rats (Gorchakova & Chekman, 2018).

Antihypoxic properties were reported by pharmacologists when studying grape and pomegranate juice, which was associated with an effect on the indicators of the adenyl system, creatine phosphate, and an antioxidant effect.

With hypoxia, all types of metabolism suffer, and primarily energy metabolism (Portnichenko et al., 2012). That is why herbal drugs, due to their effectiveness and low toxicity, are useful in clinical conditions, during sports competitions and in stressful situations (Koval et al., 2018).

Conclusions

The analysis of scientific literature allowed us to state that phytodrugs and some food additives, which have antihypoxic properties, have cardioprotective, neuroprotective and other organoprotective effects. These properties are based on their influence on energizing systems and indicators of pro-oxidant-antioxidant exchange, which are based on a positive influence on biochemical indicators of metabolism. The cited literary data confirm the statement: "Nature heals, but doctors must know well pharmacology, pharmacy and clinical biochemistry in order to correctly prescribe herbal medicines and avoid overdose processes".

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