UDC 615.03.68:616.891

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To cite this article: Gorchakova N., Belenichev I., Harnyk T., Zaichenko G., Klymenko O., Gorova E., Shumeiko O., Maslova I. (2024). Stresprotektorni vlastyvosti fitopreparativ [Stress protective properties of phytodrugs]. *Fitoterapiia. Chasopys – Phytotherapy. Journal,* 3, 5–14, doi: https://doi.org/10.32782/2522-9680-2024-3-5

STRESS PROTECTION PROPERTIES OF PHYTODRUGS

Actuality. *Since ancient times, in folk and non-traditional medicine, attention has been paid to medicinal products prescribed for emergency conditions. The state of stress was highlighted separately. This condition requires protection and warning. Protective agents*

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affecting the nervous, cardiovascular, and hormonal system are now being released. Among synthetic medicines, a number of side effects are distinguished, which also require prevention and correction. phytodrugs are considered to be less toxic, which, moreover, have a lower cost, and therefore, in stressful situations, they represent the main group of medicines.

***The aim of the study** – to identify phytodrugs that have a stress protective effect.*

***Research methods** – bibliosemantic, analytical, logical, and generalization methods. We explored the bibliographic database of life science and biomedical information MEDLINE, EMBASE, Medline (PubMed), the Web of Science, and the Cochrane Central to search for English publications satisfying the keywords of this study. All authors independently selected articles, evaluated the quality of the data, presentation, and interpretation correspondence to the main idea of the study, and constructed the final list of the references.*

***Research results.** It has been proven that the main group of drugs prescribed for stress are phytodrugs. Stress is a state of violation of non-specific adaptation mechanisms, which occurs when organs are affected by excessive force or pathogenic factors and clinically represents a complex of structural, functional and biochemical changes, which are called general adaptive changes. At the same time, hypertrophy of the cortex of the adrenal glands is possible, accidental involution of the thymus (atrophy of the flagellar glands and lymphocyte nodes), creation of ulcers and erosion in the stomach and intestines.*

Stress is a non-specific reaction of the body that occurs under the influence of various strong stress factors and is accompanied by the restructuring of the body's defense systems.

***Conclusions.** In the conditions of stressful conditions of acute chronic stress for prevention and treatment, preference should be given to phytodrugs, which, unlike synthetic ones, have greater safety and a greater "benefit/risk" ratio.*

***Key words:** stressful conditions, phytodrugs, prevention, treatment, neurotropic, cardiotropic activity.*

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Бібліографічний опис статті: Горчакова Н., Бєленічев І., Гарник Т., Зайченко Г., Клименко О., Горова Е., Шумейко О., Маслова І. (2024). Стреспротекторні властивості фітопрепаратів. *Фітотерапія. Часопис,* 3, 5–14, doi: https://doi.org/10.32782/2522-9680-2024-3-5

СТРЕСПРОТЕКТОРНІ ВЛАСТИВОСТІ ФІТОПРЕПАРАТІВ

Актуальність. *Із давніх часів у народній і нетрадиційній медицині звертали увагу на лікарські засоби, які призначають при невідкладних станах. Окремо виділяли стан стресу. Цей стан вимагає захисту і попередження. Зараз виділяють захисні засоби, які впливають на нервову, серцево-судинну гормональну системи. Серед синтетичних лікарських засобів виділяють низку побічних ефектів, які також потребують профілактики і корекції. Менш токсичними вважають фітопрепарати, що до того ж мають меншу вартість і тому при стресових ситуаціях вони є головною групою лікарських засобів.*

Мета дослідження *– визначити фітопрепарати, які мають стреспротекторну дію.*

Матеріал і методи *– бібліосемантичний, аналітичний, логічні та методи узагальнення. Ми досліджували бібліографічну базу даних наук про життя та біомедичної інформації MEDLINE, EMBASE, Medline (PubMed), Web of Science і Cochrane Central, щоб знайти публікації англійською мовою, які відповідають ключовим словам цього дослідження. Усі автори самостійно відбирали статті, оцінювали якість даних, відповідність викладу та інтерпретації основній ідеї дослідження та формували остаточний список літератури.*

Результати дослідження. *Доведено, що основною групою лікарських засобів, які призначають при стресі, є фітопрепарати. Стрес – це стан порушень неспецифічних адаптаційних механізмів, який виникає у разі дії на органи надмірних за силою або патогенних чинників та клінічно є комплексом структурних функціональних і біохімічних змін, які називають загальними адаптаційними змінами. При цьому можливі гіпертрофія кори надниркових залоз, акцидентальна інволюція тимуса (атрофія вінникових залоз та лімфоцитарних вузлів), створення виразок і ерозії у шлунку і кишках.*

Стрес – неспецифічна реакція організму, що виникає під впливом різних сильних чинників стрес-факторів та супроводжується перебудовою захисних систем організму.

Висновок. *В умовах стресових станів гострого хронічного стресу для профілактики і лікування перевагу слід надавати фітопрепаратам, які на відміну від синтетичних мають більшу безпечність і більше співвідношення «користь/ризик».*

Ключові слова: *стресові стани, фітопрепарати, профілактика, лікування, нейротропна, кардіотропна активність.*

Introduction. Topicality. Stress is a state of violation of non-specific adaptation mechanisms that occurs when the body is exposed to excessive force or pathogenic factors and clinically represents a complex of structural, functional and biochemical changes, which are called general adaptive changes. The impact of stress is manifested in diseases of various systems and organs. Stress is a common phenomenon in the current situation. They arise as a result of physical and mental stress, during operative interventions. During military operations, a combat and operational stress situation occupies a special place (Chaban, Khaustova & Omelianovych, 2023).

Stressful conditions in the military lead to adjustment disorder. This includes:

1) An alarm response when the fight or flight response is triggered. There is an activation of the sympathetic nervous system, which mobilizes functional reserves for combating stress. Acceleration of heartbeat, breathing, mydriasis, tunnel vision, tremors and other symptoms may be observed;

2) Resistance (adaptation). When stress is not dealt with immediately, the endocrine system helps support the response through the hypothalamic-pituitary-adrenal system. Cortisol is released, glucose metabolism is stimulated, the immune system is suppressed, and balance is established. During this stage, there may be a decrease in work capacity and desire to perform any physical activity, increased appetite and other non-specific reactions;

3) Exhaustion. This stage occurs when the body can no longer withstand stress and the body's resources are depleted. More often, the reason for this is long-term stress that is constantly repeated. In this stage, the disease develops as a result of exhaustion of adaptive reserves. Manifestations of this maladaptation relate to the emotional, cognitive, somatic sphere (Casey & Bailey, 2011).

For the prevention and elimination of stress states and improvement of adaptation based on the sources of folk and complementary medicine, phytodrugs were proposed, which can be used as anti-stress measures or stress protectors due to their protective effect on the nervous, cardiovascular, endocrine and immune systems (Kyrychok, 2008).

The aim of the study – to identify phytodrugs that have a stress protective effect.

Research methods – bibliosemantic, analytical, logical, and generalization methods. We explored the bibliographic database of life science and biomedical information MEDLINE, EMBASE, Medline (PubMed), the Web of Science, and the Cochrane Central to search for English publications satisfying the keywords of this study. All authors independently selected articles, evaluated the quality of the data, presentation, and interpretation correspondence to the main idea of the study, and constructed the final list of the references.

Research results. Protectors acting on the nervous system can have a calming, anti-depressant, possibly tonic effect. When affecting the cardiovascular system, they can lower and raise blood pressure, more often have a vasodilating effect, inhibit the manifestations of ischemia. Stress protectors can have a bradycardic and tachysystemic effect on heart pressure, depending on the type of arrhythmia.

Often, stress protectors normalize metabolic reactions in the nervous and cardiovascular systems. phytodrugs are antioxidants, so they reduce the manifestations of oxidative stress and reduce the level of free radicals. They can reduce elevated lipid content, normalizing the ratio of fatty acids. Many experiments aimed at investigating the mechanisms of this antioxidant action have been conducted (Liang et al., 2021).

Now one of the researchers' tasks is to identify the relationship between the development of anxiety states within the framework of diseases of civilization and manifestations of chronic, less often acute, stress. And although all the possibilities of anxiolytics are not defined, more effective drugs of this group are introduced, which are still not completely safe (Burshynskyi, 2023). This is also the basis for the use of phytodrugs for anxiety disorders.

Free oxygen radicals are formed when smoking cigarettes, which increases pollution of substances by radiation. These influences destroy cell membranes, enzymes, DNA, lead to the emergence of diseases such as cancer, atherosclerosis, malaria, coronavirus, rheumatoid arthritis, neurodegenerative diseases. This process occurs when the balance between free radicals and antioxidants is disturbed. Due to the fact that antioxidants are scavengers of free radicals and are responsible for the cell code, an increase in the content of fruits and vegetables containing antioxidants in the diet suppresses oxidative stress. Natural products demonstrate a wide range of biological effects, such as anti-inflammatory, anti-aging, anti-tuberculosis, anti-tumor (Akbari et al., 2022; Liang et al., 2021).

Stress conditions are observed in some types of acute and chronic pain of the musculoskeletal system. Arnica extracts and gel or cream from it relieve pain, therefore, together with anti-inflammatory, antimicrobial, antioxidant effects, they can also have an anti-stress effect (Smith et al., 2021).

Under stress, there is a reaction of exhaustion. Plant polyphenols have antioxidant, analyzing and cysteine-normalizing effects (Hano & Tungmunnithum, 2020). Attention is drawn to new phytodrugs and to combined medicinal products, which include phytodrugs, the effects of which can affect glucocorticoid receptors associated with proteins during stress reactions, because the degree of lipid phosphorylation is reduced. When the peptide is active, it prevents spasm, which can prevent the development of a stress response (Li et al., 2020; Timchenko et al., 2022).

Among cardiovascular drugs, drugs with cardioprotective and antihypertensive effects are often prescribed as anti-stress agents. Of the drugs with a psychotropic effect, tranquilizers and antidepressants are mandatory.

One of the plants that has a pronounced anti-stress effect is Ginkgo Biloba. The drug has a metabolic, antioxidant, antidepressant, sedative effect, improves the biochemical properties of blood, the microcirculation of cerebral circulation (Nash & Shah, 2015). Similar pharmacodynamics have been determined in the leaves and fruits of modern Chinese plants (Liang et al., 2021).

Flavonoids are a large group of polyphenols found in fruits, vegetables, and berries. Most flavonoids include flavonols, anthocyanins, isodonols, flavones and other groups. Flavonoids are considered indispensable in herbal pharmacological agents. They prevent the occurrence of diseases and contribute to their treatment thanks to their antioxidant, antiatherogenic, and antiplatelet effects. In addition, flavonoids are part of red wine. The importance of using flavonoids in the treatment of COVID has now been established. They reduce the risk of disease and disability. Flavonoids contribute to the creation of new molecules (Khan et al., 2021).

Research on establishing the neurotropic effect of phytodrugs has intensified in recent years. Thus, it was experimentally established that the alcoholic extract of Stephania japonica had sedative, soporific, antidepressant activity according to tests of the motor activity of rats (Dhar et al., 2020). Indian prickly pear extract has a sedative and tranquilizing effect due to the content of glycosides and rhamnoside. In the world, they are also prescribed for kidney diseases, diabetes, rheumatism, bronchial asthma, for healing burns (Akkol et al., 2020). A calming and tranquilizing effect is also found in the liquid extract of the kratom or mirage plant. (Novindriani et al., 2021). It is believed that lettuce of the aster family has a sedative effect due to the content of sesquiterpene lactones (Ilgün et al., 2020).

While synthetic sedatives have a significant number of side effects, the sedative herbal remedies of prickly pear

and kelp may have only minor side effects. Their action is due to polyphenols, like many other phytodrugs (Shanaida et al., 2021). The fruits and leaves of the theobroma cacao plant have a sedative, analgesic effect and can have a vasodilating effect (Hassan et al., 2021). Plants containing bioflavonoids, catechins, quercetin have a significant cardiotrophic effect, which makes them necessary for inclusion in the pharmacotherapy of COVID (Mounika et al., 2021).

In clinical studies with the participation of volunteers who complained of restlessness, insomnia, lack of appetite, the effect of the Ayurvedic drug Orcinum multiflorum extract was tested. Subjects took the extract twice a day for a month. A month later, a reduction in the impact of stress, improvement in sleep, and food intake were established. A decrease in the level of cortisol in hair and saliva was noted, which confirmed the anti-stress effect (Lopresti et al., 2022).

With the occurrence of neurodegenerative diseases, as well as with atherosclerosis, malaria, bronchial asthma, as well as with stressful conditions, including under the influence of radiation, the content of free radicals that destroy enzymes, DNA, and cause oxidative stress increases. This requires taking plant foods that contain antioxidants and medicinal plants with significant antioxidant content, such as flavonoids, catechins (Akbari et al., 2022).). Our studies have established that bioflavonoids, being inhibitors of the transthyretin protein and scavellers of cytotoxic forms of NO, are capable of exhibiting significant neuroprotective effects in the multiple sclerosis model (Belenichev, 2024). We have also established the neuroprotective activity of bioflavonoids in the premenopausal model. For the first time, one of the mechanisms of the neuroprotective action of bioflavonoids was identified, which consists in inhibition of neuroapoptosis (Zaichenko, 2023).

The majority of experimental works indicate that disorders of mental activity are associated with the accumulation of free oxygen radicals, which requires the appointment of antioxidants, including those of plant origin. At the same time, the anti-stress and calming effect of such plants as valerian and leuzea is associated with the content of polyphenols (Chandran & Abrahamse, 2020).

Depression is one of the most frequent consequences of stress. Taking phytodrugs allows you to reduce the impact of stress and improve mental activity. The occurrence of depression is associated with hypothalamic-pituitary-adrenal system, therefore, they are looking for anti-stress phytodrugs that have not only a calming, antidepressant effect, but can also have an effect on hypothalamic-pituitary-adrenal system (Dai et al., 2022).

In recent years, the effect of phytodrugs with not only a calming, but also an antidepressant effect, includes oils and extracts from lavender, yarrow, which significantly improve the mental state of patients (Zhang et al., 2021). It is known that during pregnancy, women develop stressful conditions, which manifest themselves more often as manic-depressive disorders. Among phytodrugs, ginger, raspberry leaves, and Kalanchoe reduce the manifestations of these conditions. It is important that these drugs are non-toxic and well tolerated (Gantner et al., 2021).

In experiments on rats and rabbits, when simulating four types of depression, the antidepressant effect of traditional Chinese folk medicine was established, which once again confirmed the inclusion of phytodrugs in the pharmacotherapy of depressive states (Dai et al., 2022). In experiments on normotensive and hypertensive rats, a hypotensive effect was shown during stress modulations of parsley extract due to the content of phenolic acids. flavonoids, including quercetin. A similar effect of the extract was recognized in experiments on mice (Gonçalves et al., 2020). Dry extract of Crotalaria burpia, which is dissolved in 70% alcohol, when administered intravenously to normotensive and hypertensive rats showed antihypertensive, vasodilator, diuretic, cardiotonic effects, which are associated with the blockade of calcium channels (Raza & Imran, 2020). Some plant extracts have a hypotensive effect due to diuretic activity, blockade of antihypertensive receptors or inhibition of ATP. This was proved by the introduction of extract of celery, blueberry (Ajebli & Eddouks, 2020).

Thanks to polyphenols, plants have a versatile effect on the cardiovascular system, which is based on an antioxidant effect. Thus, polyphenols also provide an antioxidant, vasodilating, anti-inflammatory effect (Alotaibi et al., 2021). Olean and oleic acids contained in olives have an antihypertensive effect (Sureda et al., 2020).

People with hypertension are recommended to eat food containing an extract of the medicinal plant. In addition, the extract of the medicinal plant can have a vasodilating effect, the mechanism of which is associated with the accumulation of NO, cGMP, and Ca+ blockade through the membrane. Therefore, this product should be part of the food, especially for the elderly (Jung et al., 2023). An extract from the leaves of the plantain can lower blood pressure in hypertensive rats on the background of adrenaline. The antihypertensive effect is associated with the blockade of L-type calcium channels and the slowing down of signaling in the endothelium (Fidelis-de-Oliveira et al., 2020). In the conditions of adrenal hypertension, it was established that the aqueous extract of Amon muricata and Perseus americano, as well as their combination, has a hypotensive and anti-hypotensive effect, and also has low toxicity, therefore it is safe to use (Sokpe et al., 2020).

Lemon balm preparations began to be prescribed more often for cardiovascular diseases. Previously, only its sed-

ative effect was used. The active substances contain terpenoids (monoterpenes, sesquiterpenes, and others), as well as polyphenolic compounds (rosmarinic acid, quercetin, luteolin, and others). Melissa, on the one hand, improves memory, consciousness, and also has an antiarrhythmic, negative chronotropic and anti-anxiety effect, hypotensive, vasodilating effect. The mechanism of action can be associated with its antioxidant effect due to polyphenols. In recent years, it has been established that lemon balm has an anti-inflammatory effect, activates M2-cholinoreceptors, blocks S3-receptors of the heart, and also blocks free-dependent Ca+ channels. Now she is being studied in a cardiology clinic (Draginic et al., 2021).

Antihypertensive effect was determined in such plants as soy, carrots and algae. Studies have shown that this effect is due to the content of peptides, and some of them can also inhibit ACE (Shobako, 2021). The hypotensive effect was also determined in the extracts of hawthorn, celery, and saffron plants. It is also noted that extracts from these plants have an immunomodulatory effect (Verma et al., 2020).

It is necessary to start treating the disease from the first symptoms, because atherosclerosis, hypertension, hypertensive crisis, and myocardial infarction develop rapidly. At the first complaints from the cardiovascular system, it is necessary to prescribe low-toxic phytodrugs (Kamyab et al., 2020). One of the main components of plants, quercetin and its derivative ramiosides are often prescribed for cardiovascular diseases, which are accompanied by oxidative stress and are included in the treatment regimens for COVID (Ferenczyova et al., 2020).

It was established that the protein content of phytodrugs plays a role in the prevention of cardiovascular diseases. At the same time, proteins contained in phytodrugs are less toxic than proteins in animal organs (Del Re & Aspry, 2022). Complex phytodrugs are now being created, the components of which affect the nervous and cardiovascular systems, an example of which is corvelis. In connection with the positive effect of stressful conditions on the nervous and cardiovascular, hormonal, and immune systems, it is advisable to prescribe immunomodulators echinacea, pomegranate, garlic (Checkman, 2003).

The study and development of new phytodrugs with anti-stress effects, especially during wartime, is a priority task. New opportunities for the treatment of cardiovascular diseases under stress were obtained by the use of combined drugs. Combined drugs can contain separate herbal remedies, an example of which is carvelis, which has proven itself in conditions of chronic stress in patients with cardiovascular pathology (Romanova et al., 2023). Usually, in parallel, less toxic and more active synthetic agents are researched and searched for, while without the inclusion of phytodrugs (Kyrychek, 2008).

Karvelis includes European hawthorn, valerian, nettle, and lemon balm. Hawthorn, the active substance of which are flavonoids, triterpenic acids, phenolic acids, has antioxidant, antiarrhythmic (prolongs the III phase of the action potential, blocks potassium channels), anti-inflammatory, positive and nootropic effects. Valerian belongs to sedative drugs, has a hypnotic effect, and normalizes heart rhythm. Stinging nettle contains alkaloids, choline, tannins, essential oil, flavonoids, glycosides, etc., which provide anticonvulsant, cardiotropic, antiarrhythmic, and diuretic effects. The herb lemon balm contains essential oil, tannins, organic acids, mineral salts, which cause a sedative, antispasmodic, hypotensive, diuretic, bactericidal effect.

Complex phytodrugs also include herbastres, which are prescribed for the treatment of stress and post-traumatic stress disorders. Herbastres contains passion flower extract, chamomile flowers, hop blossoms, oat grains, Siberian Eleutherococcus roots, ginseng, vitamins B6 and B12. Passionflower extract significantly reduces preoperative anxiety. The composition of hops includes alpha-acids, isoalpha-acids, beta-acids, which have an antitumor effect, suppress cell proliferation and induce apoptosis. The active substances of chamomile have a wide range of pharmacological effects in relation to anxiety disorders, anti-inflammatory, immunomodulatory, anti-stress effects. Eleutherococcus, like ginseng, has anti-stress activity (Chaban & Bezsheiko, 2014).

Enterosorbents, especially silica, which has an antioxidant, anti-stress and anti-radiation effect, are often added to phytodrugs in order to increase their antioxidant effect. (Volodina et al., 2017; Golembiovska et al., 2019).

Many pathological conditions are accompanied by the development of oxidative stress, when there is an intensive production of free oxygen radicals in the body, which cannot be removed due to intensive oxidative processes and cause damage to cells and tissues. It is oxidative stress that occurs in a significant number of diseases, and the use of antioxidants in complex pharmacotherapy can reduce the manifestations of oxidative stress. Studies have shown that most Chinese herbal medicines are antioxidants, although they have different pharmacological effects and complications. Currently, in the therapeutic effect of phytodrugs, Chinese medicine emphasizes the presence of antioxidant action in them. Further research expands the range of use of phytodrugs, specifying their indications.

Conclusions

In conditions of stressful conditions (acute, chronic stress) for prevention and treatment, preference should be given to phytodrugs, which, unlike synthetic ones, have greater safety and a greater "benefit/risk" ratio.

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Стаття надійшла до редакції 03.04.2024.
Стаття прийнята до друку 31.05.2024.

The authors declare no conflict of interest.
Contribution of the authors:
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