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Exploring Rhodiola rosea: A Comprehensive Review of Its Adaptogenic Effects and Medical Relevance

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Abstract

Introduction

Rhodiola rosea L. is an adaptogen with an international reach, widely used in modern medicine. Scientific studies indicate that extracts obtained from Rhodiola rosea L. have a beneficial effect on various pathological conditions, including circulatory system diseases, neurological disorders and metabolic ailments. The wide range of applications of these compounds, combined with potentially low toxicity, makes Rhodiola rosea L. a promising candidate for integration in therapies supporting the treatment of diseases affecting various body systems. The aim of this review is to analyze contemporary research on the potential properties of Rhodiola rosea L., as well as to establish the foundation for further research and development of preparations based on this plant.

Materials and Methods

The review was conducted by searching PubMed and other scientific databases focusing on currently available publications. The literature available in the PubMed database was reviewed using the following keywords: “rhodiola rosea”, “adaptogen”, "cardiovascular diseases”, “neurological diseases”, “diabetes”. The analysis of 45 articles published between 1998-2023 was used to write the paper.

Keywords: “rhodiola rosea” “adaptogen” “diabetes” “cardiovascular diseases” “neurological disease”

Introduction

Rhodiola rosea, also known by names such as "golden root", "rose root"[1], is a perennial flowering plant from the Crassulaceae family.[2] In its natural environment, its occurrence can be observed in regions such as the Arctic lands of Europe (including Great Britain), Asia and North America.[3] Rhodiola Rosea is 5 to 40 centimeters tall, fleshy, and has several stems growing from a short, scaly rootstock. The flowers have 4 sepals and 4 petals, yellow to greenish yellow in color, sometimes with red tips, about 1 to 3.5 millimeters (0.039 to 0.138 in) long, and bloom in summer. Several shoots growing from the same thick root can reach a height of 5 to 35 centimeters (2.0 to 13.8 in). R. rosea is dioecious, which means it has separate female and male individuals.[1] There are about 140 chemical compounds in the underground parts of R. rosea.[4] Rhodiola rosea roots contain phenols, rosavin, rosin, roserine, organic acids, terpenoids, phenolic acids and their derivatives, flavonoids, anthraquinones, alkaloids, tyrosol and salidroside.[5] For these reasons, Rhodiola rosea has been used in traditional medicine in many European and Asian countries for centuries.[6] R. rosea has been used for centuries to increase physical endurance, work efficiency, longevity, resistance to altitude sickness, and to treat fatigue, depression, anemia, impotence, gastrointestinal complaints, infections, and nervous system disorders [7]. Thanks to its long-term use, Rhodiola rosea has become the subject of modern scientific research in order to use its potential positive impact on human health and functioning, which allowed the plant to be called an "adaptogen". The term "adaptogen" means a substance of plant origin that non-specifically increases the body's immunity, does not disturb normal biological parameters, and has a normalizing effect on physiology, which helps maintain homeostasis.[8] Plant adaptogens have the ability to direct physiological processes to initiate a generalized adaptation process (non-specific immunity) and cope with a stressful situation in a more resourceful way.[9] Currently, scientific research and clinical trials have largely confirmed that R. rosea is an effective adaptogen, providing various protective effects, such as antidiabetic, psychostimulant, antistress, antiaging, cardioprotective and neuroprotective effects.[10] Researchers have shown that in clinical practice and experimental studies, Rhodiola rosea L. preparations, extracts and active compounds perform many biological functions, including immune regulation, antioxidant activity and inhibition of the proliferation of cancer cells, making Rhodiola rosea L. a potential component of therapeutic therapies. diseases from groups such as cardiovascular diseases, neurological and neurodegenerative

diseases, metabolic diseases. [11] This study reviews the positive effects of Rhodiola rosea L. (preparation, extract and active substance) on the development of diseases of the cardiovascular system, neurological system, and metabolic diseases (diabetes).

Rhodiola rosea in neurological diseases

According to modern research, Rhodiola rosea has a potential effect on neurological disorders, including neuroprotective effects, improvement of cognitive functions, mood regulation, anti-inflammatory effects and modulation of neurotransmitters [12]. The adaptogenic and stimulating effect on the central nervous system is attributed to the activation of biogenic amines such as serotonin, dopamine and norepinephrine in the cerebral cortex, brainstem and hypothalamus and the stimulation of opioid peptides[13]. According to Perfumia and Mattioli's research conducted on mice treated with R. rosea extract for 10 days, the levels of noradrenaline and dopamine decreased in the cortex and brain stem, increased in the hypothalamus, and serotonin levels changed in opposite directions.[14] It is suspected that R. rosea has properties that inhibit the activity of monoamine oxidase and catechol-O-methyltransferase, responsible for the degradation of monoamines, thus influencing their levels.[15] Moreover, R. rosea has antioxidant and anti-inflammatory properties, which reduces inflammation and stress that can lead to the development and progression of diseases such as Alzheimer's disease or Parkinson's disease [16]. In Parkinson's disease, disease symptoms occur due to degenerative changes in nerve cells in the substantia nigra (Latin: substantia nigra), which causes reduced levels of dopamine in the striatum [17]. R. rosea works by ameliorating the disease at the cellular level, mitigating damage caused by free radical oxygen species [18]. Salidroside obtained from R.rosea reduces the decrease in cell viability, blocking the increase in the level of reactive oxygen species (ROS), malondialdehyde and 8-hydroxy-deoxyguanosine, and increasing the level of superoxide dismutase, the level of catalase, glutathione peroxidase and glutathione [18]. Additionally, salidroside can induce mesenchymal stem cells to differentiate into dopaminergic neurons [19]. Alzheimer's disease is characterized by the loss of neurons and synapses in the cerebral cortex and certain subcortical regions. This results in atrophy in the affected areas with degeneration in the temporal and parietal lobes, as well as in parts of the frontal lobes and cingulate gyrus.[20] Senile plaques and neurofibrillary tangles are clearly visible under a microscope in brains affected by Alzheimer's disease. Plaques form dense, mostly insoluble deposits of beta-amyloid peptides and cellular material outside cells, around neurons.[21] Salidroside extracted from R. rosea showed a protective effect against beta-amyloid-induced

neurotoxicity in Alzheimer's disease, improving behavior, the levels of soluble and insoluble beta-amyloid decreased, and the levels of synapse-related proteins increased. Salidroside protects cells against beta-amyloid-induced apoptosis by activating ERK1/2 and AKT signaling pathways [22]. As can be seen from the above, R.rosea has a neuroprotective effect by reducing oxidative stress and inflammation, potentially slowing down the progression of neurological disorders [23]. Additionally, it improves cognitive functions, including memory, attention and learning abilities [24]. Moreover, R. rosea modulates the levels of neurotransmitters such as serotonin, dopamine, and norepinephrine, which play a key role in mood regulation, cognitive functions, and motor neurological disorders [13].

Antidiabetic Effects of Rhodiola rosea

Diabetes is a group of metabolic diseases characterized by hyperglycemia, i.e. increased blood glucose levels, resulting from a defect in the production or action of insulin secreted by the beta cells of the pancreatic islets.[27] Chronic hyperglycemia is associated with damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. Due to the cause and course of the disease, we can distinguish: type 1 diabetes, type 2 diabetes, gestational diabetes and other, less common types.[25] Studies on mice and rats have shown that R. Rosea, and especially its active substance, salidroside, has antidiabetic effects [26]. Through its action, salidroside improves glucose tolerance, insulin sensitivity and β-cell and liver functions, and also inhibits adipogenesis, inflammation and conditions related to oxidative stress [28]. In a mouse model of type 2 diabetes, R. rosea extract significantly improved fasting blood glucose levels, altered the response to exogenous insulin, and reduced the transcript levels of circulating lipopolysaccharide and hepatic C-reactive protein [28]. In induced diabetic rats, R. rosea extract improved hyperglycemia by increasing the secretion of β-endorphins from the adrenal glands to activate opioid μ-receptors [29]. According to research, R. rosea has several beneficial effects in the treatment of diabetes, i.e. it helps regulate blood sugar levels by increasing glucose uptake, increasing insulin sensitivity and promoting insulin release in response to glucose [27]. Moreover, R. rosea has antioxidant and anti-inflammatory effects, soothing oxidative stress and inflammation that often accompanies diabetes[28]. Both clinical and experimental studies have shown that Rhodiola rosea L. also has a good therapeutic effect on diabetic complications, such as diabetic nephropathy, cardiovascular diseases, and neuropathy. In the case of diabetic nephropathy, clinical trials have shown that injection of R.rosea extracts improved test results such as BUN, Scr and urine protein levels[30]. Extracts obtained from R.rosea also have a lipid-lowering effect,

reducing the levels of total cholesterol, LDL cholesterol and triglycerides, while increasing the level of HDL cholesterol [31]. As a result, they may also protect against diabetes complications such as neuropathy and nephropathy by alleviating nerve damage and reducing kidney damage [32].

Rhodiola rosea in cardiovascular diseases

Cardiovascular disease (CVD) is a general term for heart and vascular diseases, mainly including ischemic heart disease, cerebrovascular disease, peripheral vascular disease, rheumatic heart disease, arrhythmias, valvular heart disease, cardiomyopathy, heart failure, stroke and hypertension. In Europe, CVD causes 49% of deaths, which is the leading cause of premature mortality and disability-adjusted life years in Europe. [33]

A study by Gao et al showed that salidroside could effectively improve the vasoconstrictor function of vascular endothelium and promote angiogenesis of ischemic myocardium in rats by affecting the expression of vascular endothelial growth factor (VEGF). It may also improve ischemic myocardial angiogenesis in rats and protect against myocardial ischemia-reperfusion injury.[34] It is concluded that salidroside inhibits HIF-1α and ET-1 gene expression and promotes eNOS expression as well as the expression of vascular endothelial contractile factors. Salidroside promotes the expression of vascular endothelial relaxant factors and improves vascular endothelial function.[34] Leung et al. in their study, they describe the effect of salidroside on aortic function in rats and demonstrate that salidroside is effective in preserving NO bioavailability and thus protects against impairment of endothelium-dependent relaxation. [35]

In the case of myocardial ischemia, the heart muscle will be ischemic and hypoxic. Oxygen free radicals will be produced in the ischemic part. Then the body's antioxidant activity will decrease and the antioxidant capacity will be insufficient, resulting in oxidative stress. In the study by Gupta et al. Rhodiola rosea extracts have been shown to inhibit malondialdehyde (MDA) and lactate dehydrogenase (LDH) in the blood, liver and muscle of rats, and also increase the reducing activity of glutathione (GSH) and superoxide dismutase (SOD) in the blood. [36] This process reduces the activity of free radicals, which in turn leads to protection against cardiomyocyte damage and their death.

There is an association between apoptotic loss of myocytes and the progression of heart disease, including heart failure. [37,38] In the study by Zhong et al. the protective effect of salidroside on mitochondrial damage has been described based on various mechanisms.[39] These include the rate of cardiomyocyte apoptosis and the expression of cytochrome C (Cyto-

C), the expression of which is related to the degree of opening of pores permeable by the mitochondrial membrane. And here, according to research, salidroside affects the release of Cyto-C from mitochondria into the cytoplasm by promoting the expression of Bcl-2 protein, inhibiting the expression of Bax protein, and then inhibiting a number of further activities of caspase-3 and caspase-9 proteins and realizing the inhibitory effect on cardiomyocyte apoptosis. [40] Rhodiola rosea affects the process of cardiac muscle fibrosis. There was a relationship between the use of salidroside and protection against myocardial fibrosis in mice with myocardial infarction. This is due to lower expression of TNF-α, TGF-β 1, IL-1β and Bax and higher expression of Bcl-2, VEGF, Akt and eNOS. [41]

Another study focused on discussing the effect of salidroside on the renin-angiotensin-aldosterone system (RAAS). This system plays a key role in regulating blood pressure and fluid volume in the body. Its action may be particularly important in the context of heart failure, as its hyperactivity may contribute to the deterioration of the patient's condition. It has been shown that salidroside can inhibit the activity of this system in rats. It also inhibits the expression of interleukin 17, which reduces the level of fibrosis and apoptosis of cardiomyocytes[42]. In addition, the ethanol extract from Rhodiola rosea increases the contractility of the heart muscle, which has a preventive effect on heart failure. [41]

Another effect of salidroside is its protective effect against thrombosis. The factors causing it are Virchow's triad, i.e. injury to the vessel wall, excessive blood clotting and blood flow disorders. In the study by Zhang et al. treatment with salidroside resulted in a shortening of the clot length, a decrease in the rate of platelet aggregation and a decrease in blood viscosity. [43]

Another effect of rhodiola rosea is its antiarrhythmic effect, which was presented in a study conducted by Liu et al.[44] It has been confirmed that Rhodiola rosea has a stabilizing effect on ion pumps and calcium channels on the cell membrane (it is associated with μ-opioid receptors in the heart muscle), and also rebuilds the atrial potential in rabbits with heart failure, inhibits atrial fibrillation, reduces atrial fibrosis, and eliminates ectopic rhythm. [44] The literature also describes the beneficial effect of Rhodiola rosea extract on the treatment of essential hypertension in rats. The mechanism involves inducing the release of β-endorphins, which results in a reduction in systolic blood pressure. [45]

Conclusion

Rhodiola rosea, as an adaptogen, has an effect on a number of disease states, such as cardiovascular diseases, neurological diseases and metabolic diseases. Extracts obtained from

Rhodiola rosea have the potential to be used in the treatment of the above diseases, constituting an alternative to classic treatment methods. This allows the development of modern medicine and the use of substances naturally occurring in the plant. It is worth adding that Rhodiola rosea extracts are characterized by low toxicity and a high level of safety in their use. Based on the above, it can be concluded that the use of Rhodiola rosea is a potential therapy supporting the treatment of diseases of systems such as the cardiovascular system, nervous system and metabolic diseases. However, research on the effects of extracts obtained from Rhodiola rosea requires further in-depth study in order to minimize the negative effects of these substances.

Author's Contribution

Conceptualization: Marta Głąbień Methodology: Marta Głąbień, Aleksandra Rajewska Software: Anna Kuśnierz, Karolina Kusiak Check: Daria Aleksandrowicz, Olga Wieczorek Formal analysis: Marta Głąbień, Zofia Jakubczak Investigation: Marta Głąbień, Maria Weronika Zimniak Resources: Patryk Śliwiak, Aneta Kondratowicz Data curation: Daria Aleksandrowicz, Zofia Jakubczak Writing - rough preparation: Marta Głąbień Writing - review and editing: Marta Głąbień, Aleksandra Rajewska Visualisation: Marta Głąbień, Anna Kuśnierz, Karolina Kusiak Supervision: Olga Wieczorek, Aneta Kondratowicz, Maria Weronika Zimniak Project administration: Marta Głąbień, Aleksandra Rajewska, Patryk Śliwiak

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