RhodioPrime 6X：*Powered Adaptogen of the Vikings*

What is Rhodiola?

The Rhodiola family of natural herbaceous plants includes 96 different species, which are commonly known as arctic root, rosenroot, orpin rose, or golden root.[1-3] This herb is cultivated in the high-altitude, low-temperature areas of northern Europe and Asia and has been used for hundreds of years in China, Europe, North American, and by Vikings, who used it to increase endurance and physical strength.[2] In traditional Chinese medicine (TCM), it is often used to enhance vitality and to provide support when feeling fatigued[2]. In the 1960s, based on the results of numerous studies, Rhodiola was routinely incorporated in the Union of Soviet Socialist Republics as an adaptogen, as it was considered to exert energizing, balancing and stress resilience effects.[4] The plant may be used by healthy individuals to provide support during periods of fatigue and stress. Additionally, it has been employed occupationally to provide support for adverse environmental challenges, including extreme conditions such as high noise levels and low temperature, and in clinical practice to provide nutritional support for heart health, cognitive function, metabolic function, liver health, well-being and more.[5]

Since Rhodiola shows great potential with various capabilities, modern science is gaining more and more focus on it and especially on its extracts with a growing market for more effective formulations.

What is RhodioPrime 6X?

Although Rhodiola has been widely investigated as an adaptogen, its mechanism(s) of action have not been elucidated well. For example, Rhodiola plants contain a complex array of chemical components (e.g., salidrosides, flavonoids, polysaccharides, terpenoids), which makes it difficult to thoroughly reveal the herb's capabilities; thus, only after separating and analyzing the Rhodiola root's constituents were scientists able to unveil the herb's capabilities. While there have been at least 140 compounds isolated from the roots of the Rhodiola, it is said that salidroside is the main bioactive compound.[6]

RhodioPrime 6X is a Rhodiola extract with a salidroside content as high as 6%. As mentioned, salidroside is considered the main bioactive agent isolated from the roots of Rhodiola. Its chemical name is (4-hydroxy-phenethyl)-β-D-glucopyranoside and molecular weight is 300.3. Previous studies showed that salidroside has various biological effects, providing support for the cardiovascular system, nervous system, and liver,[7, 8] and it may also help promote cognitive function.[9] Its claimed benefits also include providing support for a healthy mood and feelings of well-being,[10] healthy antioxidant status,[11] healthy circulation and oxygenation [12, 13], anti-aging[14] and vibrant energy levels.[15]

What can RhodioPrime 6X do?

RhodioPrime 6X provides support for a range of overall health benefits including:

-Mental/Cognitive Support:

- Support for fatigue and stress management

- •Support for mood and feelings of well-being
- •Support for healthy BDNF levels
- •Support for feelings of anxiousness and stress
- •Support for healthy cognitive function

-Exercise and Physical Performance Support:

- •May help attenuate physical fatigue and promote performance
- •May help improve exercise capacity
- •May promote glucose uptake in skeletal muscle cells

-Antioxidant Support

- •Provides support for healthy antioxidant status

-Hormonal Support

- •Provides support for healthy estrogen metabolism

Highlights for Rhodiola Researches

1. Cognitive Support

The most important pathways by which Rhodiola (through salidroside) works as an adaptogenic is by promoting balance within the nervous system. Specifically, the herb has a profound relationship with the metabolism of neurotransmitters. There are five established biogenic amine neurotransmitters: the three catecholamines (e.g., dopamine, norepinephrine, and epinephrine), histamine, and serotonin, which regulate a variety of physiological functions, such as regulating cognitive abilities, mood, gut motility, the body's allergy and immune responses, and other biological processes.[16, 17] The two major enzymes involved in the catabolism of catecholamines are monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT).[18] Monoamine oxidases A and B (MAO-A and MAO-B), the two substrates of MAO, play central roles in neurotransmitter metabolism by metabolizing neurotransmitters in the brain. Research shows that the activity of these degrading enzymes may play a profound role in mood-related issues,[8] such as feelings of worry and anxiousness[9] and feelings of well-being,[10] as well as other cognitive concerns.[11] Hence, over the past several decades, there has been increased interest in natural products that may promote balanced MAO activity (and, therefore, healthy neurotransmitter activity) to provide cognitive and mental health support.

Apart from neurotransmitters, the body also utilizes neuropeptides as messengers to carry out biological actions. Neuropeptide Y (NPY) is one of the most influential of these neuropeptides in terms of orexigenic (i.e., appetite stimulating) signaling,[19] controlling many of the cues and feelings associated with hunger. Moreover, as a neuropeptide widely distributed in the central and peripheral nervous system, NPY, which is referred to as a "stress-responsive" hormone, has also gained significant attention for its anti-stress and anxiolytic properties.[20] Additionally, NPY is associated with cardiovascular regulation, cognition, and modulation of neuroendocrine systems as well.[19]

As mentioned, studies have demonstrated that Rhodiola's biological properties are mainly attributed to salidroside, which has been shown to exert several adaptogenic functions.[21] Importantly, recent studies have shown that salidroside may exert positive actions within the nervous system,[22-24] in particular, providing support for healthy metabolism of β-amyloid

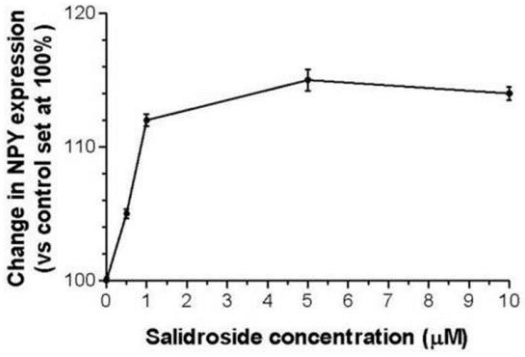
peptides *in vitro*[25, 26]and *in vivo*.[27] Additionally, numerous studies have shown that salidroside was able to influence the activity of MAOs [28, 29] and the expression of NPY [30, 31], and as a result, provide support for feelings of well-being, cognitive function, stress management and healthy appetite management.

MAO A and B inhibitory activities of *Rhodiola rosea* L. root extracts (at 100 μg/ml) and the bio-guided isolated compounds (at 10^{-5} M).

Sample	Inhibition (%)[b]	
	MAO A	MAO B
DCM extract	50.5 ± 0.1	66.9 ± 0.3
MeOH extract	92.5 ± 0.1	81.8 ± 0.3
Water extract	84.3 ± 0.8	88.9 ± 0.3
Fraction G-2	96.8 ± 0.2	81.4 ± 0.6
Fraction G-8	21.6 ± 0.2	88.5 ± 0.4
Salidroside (**1**)	–	35.8 ± 2.5
EGCG dimer (**2**)	43.1 ± 0.4	37.7 ± 0.5
Rhodioloside B and C mixture (**3**, **4**)	–	61.9 ± 3.0
Rosarin (**5**)	–	–
Cinnamyl alcohol (**6**)	27.7 ± 0.6	43.2 ± 1.5
Rhodiocyanoside A (**7**)	–	27.7 ± 4.8
Triandrin (**8**)	–	40.8 ± 3.5
Rosavin (**9**)	–	–
Tyrosol (**10**)	–	26.3 ± 0.7
Rosin (**11**)	–	–
Rosiridin (**12**)	16.2 ± 2.3	83.8 ± 1.1
L-Deprenyl[a]	36.0 ± 1.0	99.5 ± 0.2
Clorgyline[a]	100.0 ± 0.2	80.2 ± 0.9

[a] Reference compound.
[b] Inhibition lower than 15% was considered as inactive.

salidroside, but not rosavin, inhibits MAOB[32]



salidroside dose-dependently increases NPY expression[31]

1.1 Support for feelings of well-being and mood

An *in vitro* study performed at the University of Camerino showed that a single oral administration of a Rhodiola extract led to significant improvements in mood-related behaviors in mice, indicating the potential of Rhodiola to promote feelings of well-being.[33] Meanwhile, another study found that Rhodiola extract can help balance the activity of MAO enzymes, further demonstrating Rhodiola's potential for mood support.[32] In a double-blind, placebo-controlled human study, researchers found that 42 days of Rhodiola extract supplementation led to 65 to 70% improvements in feelings of well-being, indicating support for healthy mood states in the studied population.[3] On the whole, volunteers supplementing with Rhodiola extract saw significant improvements in their mood states compared to placebo.[3]

What's more, Rhodiola's main bioactive constituent, salidroside, has been shown to display a significant effect on mood.[34] According to a study carried out by Panossian et al., the effects of a Rhodiola extract administered to rats in doses of 10, 20 and 50 mg/kg on mood and feelings of well-being were greater than the effects of the standard of care; moreover, salidroside and tyrosol isolated from the roots of Rhodiola were found to exhibit the most favorable effects on mood[35]. The bottom line is that Rhodiola has shown promise in the area of mood support. The herb has gained increasing attention in the field of psychiatry, and additional research to evaluate its efficacy is ongoing.

Salidroside offers mood support	
At a Glance	
Publication	Zhu, L., et al., *Salidroside attenuates lipopolysaccharide (LPS) induced serum cytokines and depressive-like behavior in mice.* Neuroscience Letters, 2015. **606**: p. 1-6.
Study Design	Comparison
Participants	Mice
Duration	5 days
Intervention	Salidroside (12 mg/kg and 24 mg/kg) and fluoxetine (20 mg/kg) were administered intragastrically once daily for 5 days.
Control	Untreated mice
Key Findings	•Salidroside increased brain-derived neurotrophic factor •Salidroside decreased inflammation. •Salidroside decreased depressive-like behavior.

1.2 Support for memory and cognitive function

Researchers found that oral supplementation with Rhodiola helped enhance memory in a dose- and time-dependent manner in healthy rats given a passive avoidance task.[36] Another animal study found that Rhodiola extract may help improve learning and retention after 24 hours. The study also showed significant improvements in memory tests after 10-day treatment with the same dose of the extract.[37] In a study performed at the University of Giessen, researchers assessed the efficacy of various Rhodiola extracts in a synaptic model of memory. Seven different Rhodiola extracts with different concentrations of rosavin and salidroside were obtained and studied. The study authors found that all variants were beneficial in terms of providing support for memory and cognition; furthermore, they found that the Rhodiola extracts containing both salidroside and rosavin promoted the best results. In simply comparing salidroside to rosavin, salidroside was more effective at lower concentrations, while rosavin was superior at higher concentrations.[38] However, in isolated studies, salidroside has several benefits on its own, but rosavins have failed to yield any conclusive advantages when used alone.[38] Along those lines, several studies have demonstrated that Rhodiola's biological properties in the central nervous system should be mainly attributed to salidroside, which has been shown to exert various adaptogenic functions; that is, salidroside seems to drive the most successful research. Both acute and consistent supplementation offers benefits;[39] for instance, a single acute dose of salidroside was also able to to provide support for memory and to help counteract feelings of overwhelm and despair in adult mice.[21]

Salidroside provides support for memory and healthy cognitive function	
At a Glance	
Publication	Jin, H., et al., *Therapeutic Intervention of Learning and Memory Decays by Salidroside Stimulation of Neurogenesis in Aging.* Mol Neurobiol, 2016. **53**(2): p. 851-866.
Study Design	Comparison
Participants	Adult mice at 4 months of age and old mice at 16 months of age
Duration	5 days
Intervention	Salidroside at different doses(1, 5, or 10 mg/kg per dose per day for 5 consecutive days)
Control	Untreated mice
Key Findings	Salidroside is effective against learning and memory decays via stimulation of CREB dependent functional neurogenesis in aging.

1.3 Support for feelings of worry and anxiousness

Numerous studies have reported that Robiola may provide support for feelings of stress and anxiousness by promoting a healthy balance of neurotransmitters, namely serotonin.[40, 41] For example, 10-20mg/kg of Rhodiola extract one hour prior to a light/dark exploration test was found to significantly, but not dose-dependently, improve mood- and stress-related behaviors in mice.[33] In another research study, supplementation with a Rhodiola extract for 10 weeks led to a significant reduction in feelings of anxiousness and related behaviors.[42] In an effort to better understand how Rhodiola achieves such effects, one study found that Rhodiola extract increased the protein content of the 5-HT1A receptor, which can help promote the production of serotonin.[40] In another study, researchers found that Rhodiola extract helped reduce the activity of the 5-HT3 receptor,[43] which is important considering this receptor is associated with increased feelings of worry and anxiety.[44] According to the two studies, it seems that Rhodiola is able to provide nutritional support that promotes healthy serotonin levels. Additionally, Rhodiola may

provide further support for stress-related feelings of anxiousness by helping balance the activity of serotonin receptors.

Salidroside provides support for anxious feelings	
At a Glance	
Publication	Palmeri, A., et al., *Salidroside, a Bioactive Compound of Rhodiola Rosea, Ameliorates Memory and Emotional Behavior in Adult Mice.* Journal of Alzheimer's disease : JAD, 2016. **52**(1): p. 65-75.
Study Design	Comparison
Participants	Adult mice
Duration	A single i.p. administration
Intervention	Salidroside was diluted in PBS and stored at –20°C. Immediately prior to use, salidroside aliquots were diluted to reach a 25 mg/kg concentration. Mice were individually weighted and then treated by intraperitoneal (i.p.) injections 10 min before the behavioral test.
Control	Untreated mice
Key Findings	A single i.p. administration of salidroside in mice enhanced memory and exerts an antidepressant, and anxiolytic effect

1.4 Provides support when feeling mental fatigue and stress

Whether it's at the end of a long day of work, following an exhausting training session or being "under the gun" of a stressful situation, we may occasionally find ourselves battling fatigue. As an adaptogen, Rhodiola shows great potential in this area, as it has been shown to provide restorative, body-balancing support for stress-related fatigue.[4, 45]

A double-blind and placebo-controlled study performed by Spasov et al, for example, examined the effects of 20 days of supplementation with 100mg Rhodiola extract in students during a stressful examination period. The result showed significant improvements in various indicators of acute, stress-induced fatigue, including cognition, mental clarity and physical fitness.[46] Furthermore, another placebo-controlled study examined the effects of Rhodiola supplementation (either 370 mg or 555 mg) in college-aged students. Utilizing a proprietary metric called an "anti-fatigue index," which measured multiple indicators of general lethargy, the researchers found that, compared to placebo, both levels of Rhodiola significantly improved mental and physical markers of fatigue.[47] Meanwhile, another trial found that supplementation with Rhodiola extract led to a significant improvement in the Pines' burnout score for participants dealing with stress-induced fatigue[48]. Another open-label trial with Rhodiola extract at 400 mg daily for 4 weeks showed general benefits on perceived stress (questionnaire), improvements in stress-induced social and work dysfunction, and reductions in fatigue.[49] Overall, these studies suggest that supplementation with Rhodiola extract is associated with improvements in mental fatigue associated with occasional stress.

To ascertain the mechanisms of action by which this adaptogen offers support for stress-related fatigue, one study examined some biochemical markers for evaluating anti-stress effects in rabbits subjected to restraint stress. The researchers found that both salidroside and extracts of Rhodiola were strong inhibitors of stress-induced p-SAPK/p-JNK, suggesting a potential association between the adaptogen's potential to support feelings of well-being as well as its positive effects on mental performance under stress.[50]

Salidroside provides support for mental fatigue and stress	
At a Glance	
Publication	Panossian, A., et al., *The adaptogens rhodiola and schizandra modify the response to immobilization stress in rabbits by suppressing the increase of phosphorylated stress-activated protein kinase, nitric oxide and cortisol.* Drug target insights, 2007. **2**: p. 39-54.
Study Design	Comparison
Participants	Male Chinchilla rabbits
Duration	8 days
Intervention	*E. senticosus* root extract –6.5 mg/kg, *R. rosea* root extract –1 mg/kg, *S. chinensis* berry extract –22 mg/kg; *B. alba* root extract –15 mg/kg, *P. ginseng* root extract –6 mg/kg, and salidroside –0.5 mg/kg.
Control	Untreated mice
Key Findings	Salidroside and extracts of S. chinensis and R. rosea were the most active inhibitors of stress-induced p-SAPK/p-JNK

1.5 May help promote healthy appetite management

There's evidence to suggest that Rhodiola may help promote healthy appetite

management and help provide support for cravings since there's a negative relationship between serotonin production and hunger and cravings.[51] In a stress-induced eating model using mice, researchers administered a Rhodiola extract one hour prior to feeding to see whether the treatment would aid with appetite management and food intake. They found that the extract significantly reduced food intake, noting that the active principle salidroside, but not rosavin, dose-dependently decreased eating under the test conditions[52], indicating that Rhodiola extracts may help curb appetite.

2. Support for Exercise and Physical Performance

Maintaining healthy energy levels is not only important in mental work settings but also in athletic performance. In 2004, a clinical trial tested the effect of four weeks of Rhodiola supplementation on exercise capacity. The two-phase study showed that Rhodiola extract significantly increased time to exhaustion and VO_2 max, suggesting that Rhodiola can benefit athletic performance by helping improve energy levels and providing support for exercise-related fatigue thus improving endurance exercise performance.[53] In another study, following supplementation with Rhodiola extract for 4 weeks, trained male athletes underwent a cardio-pulmonary exhaustion test and blood samples to evaluate exercise-related indications. The results showed that after an exhaustive exercise session, both lactate levels and parameters of skeletal muscle damage were reduced in participants who supplemented with Rhodiola when compared to the placebo-treated group. These results indicate that Rhodiola may enhance and optimize the ability to physical exercise.[54] An additional study found a reduction in creatine kinase and C-reactive protein after exhaustive exercise in healthy untrained volunteers supplementing with Rhodiola, when compared to placebo. These results demonstrate that Rhodiola extract may help mitigate the damage due to exhaustive exercise and also provide support for recovery from physical activity.[55] Since intense exercise increases oxygen consumption and may produce an imbalance between reactive oxygen species (ROS) and antioxidants, it may lead to oxidative stress. Another animal study evaluated the effects of salidroside on exhaustive exercise-induced oxidative stress in rats, and the results showed that salidroside was able to help raise exercise tolerance and increase the liver glycogen levels of the rats following exhaustive exercise. These results indicate that salidroside provides support for unhealthy levels of oxidative stress following exhaustive exercise.[56]

What's more, Rhodiola may be associated with an increased VO_2 max and time to exhaustion with a reduction of creatine kinase and C-reactive protein. Moreover, in another study, researchers showed that salidroside was able to activate AMPK in skeletal muscle cells and increase glucose uptake in a concentration-dependent manner.[57] This study also noted that insulin-induced glucose uptake was slightly enhanced with salidroside.[57] Thus it seems that, in terms of physical performance, apart from the generally "feeling less tired," Rhodiola may also contribute to promoting healthy energy levels by helping move nutrients to cells that need it.

Salidroside provides support for exercise and physical performance	
At a Glance	
Publication	Xu, J. and Y. Li, *Effects of salidroside on exhaustive exercise-induced oxidative stress in rats.* Mol Med Rep, 2012. **6**(5): p. 1195-8.
Study Design	Comparison
Participants	Rats
Duration	4 weeks
Intervention	Salidroside (25, 50 and 100 mg/kg, respectively) intragastrically (ig)
Control	Untreated mice
Key Findings	Salidroside was able to elevate the exercise tolerance and increase the liver glycogen levels of the rats following exhaustive exercise.

3. Other potential interactions

3.1 May provide support for healthy carbohydrate metabolism

The potential negative effects of unhealthy carbohydrate management has been associated with accelerated aging,[58] weight management issues,[58] and a variety of other health issues.[59] Carbohydrate metabolism concerns may stem from alterations in several pathways, including excessive accumulation of advanced glycation end-products (AGEs), which result from irreversible glycation of proteins.[58] Salidroside has been shown to support a reduction in AGE formation in an accelerated mouse aging model induced by D-galactose.[60] According to the study, salidroside helped mitigate increases in serum AGEs in some cases, and even more, the study found that salidroside may provide support for previous effects of AGEs in the neural and immune systems.[60]

Though the relationship between AGEs and carbohydrate management remains to be further elucidated, another study did highlight the potential effects of Rhodiola on healthy carbohydrate metabolism in mice. The researchers found that administration of salidroside resulted in a time- and dose-dependent effect on carbohydrate management.[61]

3.2 May promote organ health and function

Rhodiola may provide support for an array of body tissues and organs by way of its robust antioxidant capacity and by providing support for hypoxia.[62] Hypoxia, which simply refers to oxygen deprivation, can be potentially dangerous and have long-term health repercussions when out of balance and improperly timed.[63] Hypoxia inducible factor - 1 (HIF-1), a key regulator in the body's response to hypoxic conditions, can help activate numerous transcription factors that regulate oxygen delivery and metabolic functioning.[64] For example, HIF-1 appears to play a key role in the adaptive response to endurance exercise. Salidroside has been shown to promote healthy HIF-1 expression, which may, in turn, provide support for heart, liver, and kidney health and function.[64-66]

3.3 Support for healthy estrogen metabolism

There is evidence that Rhodiola extract may interact with the estrogen receptor without having any potentially negative estrogenic activity. Along these lines, Rhodiola has shown promise in providing support for complications associated menopause/perimenopause, such as fatigue, stress, feelings of well-being and cognitive performance.[67]

Recommend dosage for RhodioPrime 6X

Rhodiola has a very low level of toxicity with mild side effects and no known interactions with drugs and other ingredients.[68] In rat toxicity studies, the LD_{50} (lethal dose at which 50% of animals die) was calculated to be 28.6 mL/kg, approximately 3360 mg/kg of body weight.[69, 70]. Extrapolating that out to humans would equate to over 20,000 mg, depending on weight. With a suggested daily dose of 200 to 600 mg,[68, 70] reaching a dose that high is extremely unlikely.

One more thing to be added when taking Rhodiola supplements is that one should be wary of the possible inaccurate labeling. A meta-analysis based on the studies of 39 Rhodiola products from multiple suppliers found that 23% of them contained no rosavin, which is a key marker that distinguishes Rhodiola rosea from other species of Rhodiola. Additionally, the meta-analysis found that two of the products did not contain any salidroside, indicating that some manufacturers are adulterating their products with other species of Rhodiola plants.[71]

Reference

1. Rohloff, J., *Volatiles from rhizomes of Rhodiola rosea L.* Phytochemistry, 2002. **59**(6): p. 655-61.
2. Panossian, A., G. Wikman, and J. Sarris, *Rosenroot (Rhodiola rosea): traditional use, chemical composition, pharmacology and clinical efficacy.* Phytomedicine, 2010. **17**(7): p. 481-93.
3. Darbinyan, V., et al., *Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression.* Nord J Psychiatry, 2007. **61**(5): p. 343-8.
4. Panossian, A., *Adaptogens: Tonic Herbs for Fatigue and Stress.* Alternative and Complementary Therapies, 2003. **9**: p. 327-331.
5. Xia, N., et al., *Schisandra chinensis and Rhodiola rosea exert an anti-stress effect on the HPA axis and reduce hypothalamic c-Fos expression in rats subjected to repeated stress.* Experimental and therapeutic medicine, 2016. **11**(1): p. 353-359.
6. Grech-Baran, M., K. Sykłowska-Baranek, and A. Pietrosiuk, *Biotechnological approaches to enhance salidroside, rosin and its derivatives production in selected Rhodiola spp. in vitro cultures.* Phytochem Rev, 2015. **14**(4): p. 657-674.
7. Song, E.-K., et al., *Hepatoprotective phenolic constituents of Rhodiola sachalinensis on tacrine-induced cytotoxicity in Hep G2 cells.* Phytotherapy Research, 2003. **17**(5): p. 563-565.
8. Wang, S., et al., *Protective effects of salidroside in the MPTP/MPP(+)-induced model of Parkinson's disease through ROS-NO-related mitochondrion pathway.* Mol Neurobiol, 2015. **51**(2): p. 718-28.
9. Zhu, L., et al., *Salidroside ameliorates arthritis-induced brain cognition deficits by regulating Rho/ROCK/NF-κB pathway.* Neuropharmacology, 2016. **103**: p. 134-42.
10. Yang, S.-J., et al., *Antidepressant-like effects of salidroside on olfactory bulbectomy-induced pro-inflammatory cytokine production and hyperactivity of HPA axis in rats.* Pharmacology Biochemistry and Behavior, 2014. **124**: p. 451-457.
11. Wang, X.-L., et al., *Salidroside improves doxorubicin-induced cardiac dysfunction by suppression of excessive oxidative stress and cardiomyocyte apoptosis.* Journal of cardiovascular pharmacology, 2013. **62**(6): p. 512-523.
12. Zhao, H., et al., *Inhibitory effects of salidroside on hypoxia-induced proliferation of rabbit pulmonary arterial*

smooth muscle cells. Journal of the Fourth Military Medical University, 2000. **21**(2): p. 186-189.

13. Zhang, W.-s., et al., *[Protective effects of salidroside on injury induced by hypoxia/hypoglycemia in cultured neurons].* Zhongguo Zhong yao za zhi = Zhongguo zhongyao zazhi = China journal of Chinese materia medica, 2004. **29**(5): p. 459-462.
14. Sun, L., et al., *The study on anti-senility experiment of diploid cells by Rhodiola sacha-linensis A Bor.* Chinese Journal of Gerontology, 2001. **21**(3): p. 225-226.
15. Li, M., et al., *Anti-fatigue effects of salidroside in mice⋆ ⋆Supported by the Foundation of the Gym Sport Bureau of Shanghai (04JT017).* Journal of Medical Colleges of PLA, 2008. **23**(2): p. 88-93.
16. Berger, M., J.A. Gray, and B.L. Roth, *The expanded biology of serotonin.* Annual review of medicine, 2009. **60**: p. 355-366.
17. Thangam, E.B., et al., *The Role of Histamine and Histamine Receptors in Mast Cell-Mediated Allergy and Inflammation: The Hunt for New Therapeutic Targets.* Frontiers in immunology, 2018. **9**: p. 1873-1873.
18. Paravati, S., A. Rosani, and S.J. Warrington, *Physiology, Catecholamines*, in *StatPearls*. 2020: Treasure Island (FL).
19. Beck, B., *Neuropeptide Y in normal eating and in genetic and dietary-induced obesity.* Philosophical transactions of the Royal Society of London. Series B, Biological sciences, 2006. **361**(1471): p. 1159-1185.
20. Reichmann, F. and P. Holzer, *Neuropeptide Y: A stressful review.* Neuropeptides, 2016. **55**: p. 99-109.
21. Palmeri, A., et al., *Salidroside, a Bioactive Compound of Rhodiola Rosea, Ameliorates Memory and Emotional Behavior in Adult Mice.* Journal of Alzheimer's disease : JAD, 2016. **52**(1): p. 65-75.
22. Zhang, S., et al., *Neuroprotection against cobalt chloride-induced cell apoptosis of primary cultured cortical neurons by salidroside.* Molecular and cellular biochemistry, 2011. **354**(1-2): p. 161-170.
23. Qu, Z.-q., et al., *Protective effects of a Rhodiola crenulata extract and salidroside on hippocampal neurogenesis against streptozotocin-induced neural injury in the rat.* PloS one, 2012. **7**(1): p. e29641.
24. Chen, T., et al., *Suppressing Receptor-Interacting Protein 140: a New Sight for Salidroside to Treat Cerebral Ischemia.* Molecular neurobiology, 2016. **53**(9): p. 6240-6250.
25. Li, Q.-Y., et al., *Salidroside attenuates hypoxia-induced abnormal processing of amyloid precursor protein by decreasing BACE1 expression in SH-SY5Y cells.* Neuroscience letters, 2010. **481**(3): p. 154-158.
26. Zhang, L., et al., *Neuroprotective effects of salidroside against beta-amyloid-induced oxidative stress in SH-SY5Y human neuroblastoma cells.* Neurochemistry international, 2010. **57**(5): p. 547-555.
27. Zhang, J., et al., *Salidroside attenuates beta amyloid-induced cognitive deficits*

via modulating oxidative stress and inflammatory mediators in rat hippocampus. Behavioural brain research, 2013. **244**: p. 70-81.

28. Vasileva, L.V., et al., *Beneficial effect of commercial Rhodiola extract in rats with scopolamine-induced memory impairment on active avoidance.* Journal of Ethnopharmacology, 2016. **193**: p. 586-591.
29. van Diermen, D., et al., *Monoamine oxidase inhibition by Rhodiola rosea L. roots.* Journal of Ethnopharmacology, 2009. **122**(2): p. 397-401.
30. Asea, A., et al., *Evaluation of molecular chaperons Hsp72 and neuropeptide Y as characteristic markers of adaptogenic activity of plant extracts.* Phytomedicine, 2013. **20**(14): p. 1323-9.
31. Panossian, A., et al., *Adaptogens stimulate neuropeptide y and hsp72 expression and release in neuroglia cells.* Frontiers in neuroscience, 2012. **6**: p. 6-6.
32. van Diermen, D., et al., *Monoamine oxidase inhibition by Rhodiola rosea L. roots.* J Ethnopharmacol, 2009. **122**(2): p. 397-401.
33. Perfumi, M. and L. Mattioli, *Adaptogenic and central nervous system effects of single doses of 3% rosavin and 1% salidroside Rhodiola rosea L. extract in mice.* Phytother Res, 2007. **21**(1): p. 37-43.
34. Zhu, L., et al., *Salidroside attenuates lipopolysaccharide (LPS) induced serum cytokines and depressive-like behavior in mice.* Neuroscience Letters, 2015. **606**: p. 1-6.
35. Panossian, A., et al., *Comparative study of Rhodiola preparations on behavioral despair of rats.* Phytomedicine, 2008. **15**(1): p. 84-91.
36. Getova, D.P. and A.S. Mihaylova, *Effects of Rhodiola rosea extract on passive avoidance tests in rats.* Central European Journal of Medicine, 2013. **8**(2): p. 176-181.
37. Petkov, V.D., et al., *Effects of alcohol aqueous extract from Rhodiola rosea L. roots on learning and memory.* Acta Physiol Pharmacol Bulg, 1986. **12**(1): p. 3-16.
38. Dimpfel, W., L. Schombert, and A.G. Panossian, *Assessing the Quality and Potential Efficacy of Commercial Extracts of Rhodiola rosea L. by Analyzing the Salidroside and Rosavin Content and the Electrophysiological Activity in Hippocampal Long-Term Potentiation, a Synaptic Model of Memory.* Frontiers in pharmacology, 2018. **9**: p. 425-425.
39. Jin, H., et al., *Therapeutic Intervention of Learning and Memory Decays by Salidroside Stimulation of Neurogenesis in Aging.* Mol Neurobiol, 2016. **53**(2): p. 851-866.
40. Mannucci, C., et al., *Serotonin involvement in Rhodiola rosea attenuation of nicotine withdrawal signs in rats.* Phytomedicine, 2012. **19**(12): p. 1117-24.
41. Chen, Q.G., et al., *The effects of Rhodiola rosea extract on 5-HT level, cell proliferation and quantity of neurons at cerebral hippocampus of depressive rats.*

Phytomedicine, 2009. **16**(9): p. 830-8.

42. Bystritsky, A., L. Kerwin, and J.D. Feusner, *A pilot study of Rhodiola rosea (Rhodax) for generalized anxiety disorder (GAD).* J Altern Complement Med, 2008. **14**(2): p. 175-80.
43. Panossian, A., et al., *Synergy and Antagonism of Active Constituents of ADAPT-232 on Transcriptional Level of Metabolic Regulation of Isolated Neuroglial Cells.* Frontiers in neuroscience, 2013. **7**: p. 16-16.
44. Kennett, G.A., et al., *Anxiolytic-like actions of the selective 5-HT4 receptor antagonists SB 204070A and SB 207266A in rats.* Neuropharmacology, 1997. **36**(4-5): p. 707-12.
45. Darbinyan, V., et al., *Rhodiola rosea in stress induced fatigue--a double blind cross-over study of a standardized extract SHR-5 with a repeated low-dose regimen on the mental performance of healthy physicians during night duty.* Phytomedicine : international journal of phytotherapy and phytopharmacology, 2000. **7**(5): p. 365-371.
46. Spasov, A.A., et al., *A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of Rhodiola rosea SHR-5 extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen.* Phytomedicine, 2000. **7**(2): p. 85-9.
47. Shevtsov, V.A., et al., *A randomized trial of two different doses of a SHR-5 Rhodiola rosea extract versus placebo and control of capacity for mental work.* Phytomedicine, 2003. **10**(2-3): p. 95-105.
48. Olsson, E.M., B. von Schéele, and A.G. Panossian, *A randomised, double-blind, placebo-controlled, parallel-group study of the standardised extract shr-5 of the roots of Rhodiola rosea in the treatment of subjects with stress-related fatigue.* Planta Med, 2009. **75**(2): p. 105-12.
49. Edwards, D., A. Heufelder, and A. Zimmermann, *Therapeutic effects and safety of Rhodiola rosea extract WS® 1375 in subjects with life-stress symptoms--results of an open-label study.* Phytother Res, 2012. **26**(8): p. 1220-5.
50. Panossian, A., et al., *The adaptogens rhodiola and schizandra modify the response to immobilization stress in rabbits by suppressing the increase of phosphorylated stress-activated protein kinase, nitric oxide and cortisol.* Drug target insights, 2007. **2**: p. 39-54.
51. Curzon, G., *Serotonin and appetite.* Ann N Y Acad Sci, 1990. **600**: p. 521-30; discussion 530-1.
52. Cifani, C., et al., *Effect of salidroside, active principle of Rhodiola rosea extract, on binge eating.* Physiol Behav, 2010. **101**(5): p. 555-62.
53. De Bock, K., et al., *Acute Rhodiola rosea intake can improve endurance exercise performance.* Int J Sport Nutr Exerc Metab, 2004. **14**(3): p. 298-307.
54. Parisi, A., et al., *Effects of chronic Rhodiola Rosea supplementation on sport performance and antioxidant capacity in trained male: preliminary results.* J Sports Med Phys Fitness, 2010. **50**(1): p. 57-63.

55. Abidov, M., et al., *Extract of Rhodiola rosea radix reduces the level of C-reactive protein and creatinine kinase in the blood.* Bull Exp Biol Med, 2004. **138**(1): p. 63-4.
56. Xu, J. and Y. Li, *Effects of salidroside on exhaustive exercise-induced oxidative stress in rats.* Mol Med Rep, 2012. **6**(5): p. 1195-8.
57. Li, H.B., et al., *Salidroside stimulated glucose uptake in skeletal muscle cells by activating AMP-activated protein kinase.* Eur J Pharmacol, 2008. **588**(2-3): p. 165-9.
58. Campos, C., *Chronic hyperglycemia and glucose toxicity: pathology and clinical sequelae.* Postgraduate medicine, 2012. **124**(6): p. 90-97.
59. Mouri, M.I. and M. Badireddy, *Hyperglycemia*, in *StatPearls*. 2020: Treasure Island (FL).
60. Mao, G.-X., et al., *Protective role of salidroside against aging in a mouse model induced by D-galactose.* Biomedical and environmental sciences : BES, 2010. **23**(2): p. 161-166.
61. Li, F., et al., *Protective effect of salidroside from Rhodiolae Radix on diabetes-induced oxidative stress in mice.* Molecules (Basel, Switzerland), 2011. **16**(12): p. 9912-9924.
62. Li, X., et al., *Salidroside stimulates DNA repair enzyme Parp-1 activity in mouse HSC maintenance.* Blood, 2012. **119**(18): p. 4162-4173.
63. Sekhon, M.S., P.N. Ainslie, and D.E. Griesdale, *Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model.* Critical care (London, England), 2017. **21**(1): p. 90.
64. Movafagh, S., S. Crook, and K. Vo, *Regulation of hypoxia-inducible factor-1a by reactive oxygen species: new developments in an old debate.* Journal of cellular biochemistry, 2015. **116**(5): p. 696-703.
65. Zhu, Y., et al., *Salidroside protects against hydrogen peroxide-induced injury in cardiac H9c2 cells via PI3K-Akt dependent pathway.* DNA and cell biology, 2011. **30**(10): p. 809-819.
66. Ouyang, J.-F., et al., *In-vitro promoted differentiation of mesenchymal stem cells towards hepatocytes induced by salidroside.* The Journal of pharmacy and pharmacology, 2010. **62**(4): p. 530-538.
67. Eagon, P.K., et al., *Evaluation of the medicinal botanical Rhodiola rosea for estrogenicity.* Cancer Research, 2004. **64**(7 Supplement): p. 663-663.
68. Panossian, A., G. Wikman, and J. Sarris, *Rosenroot (Rhodiola rosea): traditional use, chemical composition, pharmacology and clinical efficacy.* Phytomedicine : international journal of phytotherapy and phytopharmacology, 2010. **17**(7): p. 481-493.
69. Kurkin, V. and G.J.J.M.P. Zapesochnaya, *Chemical composition and pharmacological characteristics of Rhodiola rosea.* 1985. **1985**: p. 1231-445.
70. Khanum, F., A.S. Bawa, and B. Singh, *Rhodiola rosea: A Versatile Adaptogen.* Comprehensive reviews in food science and food safety, 2005. **4**(3): p. 55-62.

71. Booker, A., et al., *The authenticity and quality of Rhodiola rosea products.* Phytomedicine, 2016. **23**(7): p. 754-762.