Rhodiola

Saratikov and Krasnov (1987) studied the properties of rhodiola as a mental and physical stimulant. Such stimulants work to prevent or delay exhaustion, improve the capacity for mental and/or physical work. The use of stimulants can be beneficial in certain disease states, and also in healthy individuals in the situations requiring prolonged and/or intensive physical or mental effort. The examples include athletes, air traffic controllers, emergency rescue personnel, etc.

Most synthetic stimulant drugs (e. g. phenamine derivatives) cause a variety of side effects, such as insomnia, palpitations, increased blood pressure, depression, anorexia, etc. Such stimulation is usually achieved via inadequately (in relation to the work required) and unsustainably increased catabolism and can lead to profound exhaustion and CNS inhibition [Bobkov et al, 1984], i. e. common synthetic stimulants usually have a significant negative phase.

On the other hand, certain plant-derived stimulants (such as ginseng, eleutherococcus, rhodiola, aralia, schizandra, leuzea, etc.) are characterized by very low toxicity, broad spectrum of uses, lack of negative phase or dependance even with prolonged use. Such stimulants can be called "energizers." While common stimulant drugs suppress natural exhaustion signals, the energizers delay the onset of exhaustion (via increasing reserves), but not suppress it its natural feedback.

The very first studies of rhodiola, conducted in mice in 1961-1962, showed rhodiola preparations to increase the holding time at a vertical pole and the swimming time [Marina and Prischep 1964] . Also, rhodiola tincture reduced the duration of barbital-induced sleep.

The toxicity of rhodiola is low. LD_{50} for the 40%-ethanol extract of rhodiola administered subcutaneously is 28.6 mg/kg [Saratikov and Krasnov, 1987]. Salidroside, a principal bioactive compound of rhodiola, does not produce adverse effects even at 1,000 mg/kg (which corresponds to 50 ml/kg of the extract). Oral administration of the rhodiola extract (1 ml/kg) or salidroside (20 mg/kg) to rabbits does not produce any changes in the body weight or behavior, and does not significantly alter ESR, hemoglobin, RBC or WBC. Subcutaneous or intravenous injection of salidroside (10-40 mg/kg) does not significantly affect arterial blood pressure.

Animal studies of the stimulant effects of rhodiola

In animal studies rhodiola preparations or derivatives were shown to significantly increase both dynamic and static work capacity [Aksenova 1968] (Table). Dynamic work capacity in mice was determined by the swimming time measurement, while static work capacity was determined by measuring the holding time at a vertical pole.

TABLE

Stimulant action of rhodiola preparations in mice under work load

Agent	Dose per 1 kg of body mass	Number of experiments	Endurance (time) under second* work load (M±m)	Increase in work capacity compared, to the control, %
Static work load				
Control	5 ml	21	35±4.8	
Rhodiola extract	5 ml	25	95±10.2**	173
Rhodosin	5 ml	12	93+9.7**	166
Salidroside	100 mg	21	80±10.8**	128
Dynamic work load				
Control	5 ml	10	8±1.1	
Rhodiola extract	5 ml	10	22±2.5**	175
Salidroside	100 mg	10	22±2.6**	175

* work load was applied before and 30 min. after the administration of rhodiola preparations

** the difference is significant compared to the control ($p<0.001$)

Rhodiola extract was shown to be more effective than eleutherococcus extract (at the same dose) in increasing the holding time at a vertical pole in mice: the former increased the holding time by 130% ($p<0.001$), and the latter - by 74% ($p<0.001$) [Marina et al 1983].

Studies of the stimulant effects of rhodiola in humans

The effect of rhodiola on mental work capacity was studied using proofreading test in heathy students [Aksenova 1968]. The students took a 5 minute proofreading test before and 1, 2, 3, 4, 6, 8, 24 hours after taking a rhodiola preparation (either 10 drops of rhodiola extract or 2.5 mg of salidroside) or placebo.

One hour after the administration of the rhodiola extract the number of mistakes (per 1,000 characters corrected) dropped by 56% compared to the control. This effects persisted for four hours, after which the number of errors increased but to a lesser degree than in the control. The number of characters read was by 5-7% higher than in the control.

Thus a single dose of rhodiola preparations improves mental work capacity. It appears that mainly the quality of mental work is being affected. These data are similar to those obtained for such adaptogens as ginseng [Golikov 1961] and eleutherococcus [Brekhman 1968].

In a series of experiment Saratikov and co-workers [Saratikov and Krasnov 1987] studied the effects of rhodiola on the capacity for high intensity physical work. It was found that by the end of work, the group who were given rhodiola were less fatigued and their physiological characteristics (heart rate, blood pressure, coordination, hand grip strength, etc) were better than in the control group. Also, the recovery was faster in the group which received rhodiola. For instance, in 10 minutes after the end of work, heart rate in the rhodiola treated group dropped to 76 beats per minute (2.7 times) , while in the control group it decreased to 86 beats per minute (1.9 times). Similar results were obtained with the extracts of eleutherococcus, leuzea and ginseng.

Of interest is the study of the effects of rhodiola on cardio-vascular performance in 42 professional cross-country skiers aged 20-25 [Saratikov and Krasnov 1987]. The study was performed during training for 30 kilometer cross-country skiing races and 20 kilometer biathlon races. The athletes received 10 drops of rhodiola extract, 2 ml of eleutherococcus extract or a placebo 30-

60 minutes before a race. Rhodiola and eleutherococcus were shown to improve work capacity and post-race recovery as seen from the patterns of heart rate and blood pressure normalization following the test exercise challenge (Table). In addition, the athletes receiving the adaptogens finished the race faster and had better target-shooting results (statistically significant) than the control group. A post-race study of blood oxygen saturation in breath interruption tests revealed a better resistance to hypoxia and faster recovery in the skiers.

TABLE

Rate of heart rate and blood pressure normalization following the test exercise challenge in the skiers 24 hours after a 30 kilometer cross-country race.

Agent	Normalization time for heart rate after a test run				Normalization time for blood pressure after a test run			
	Before a race		24 hrs after a race		Before a race		24 hrs after a race	
	15 sec. run	3 min. run	15 sec. run	3 min. run	15 sec. run	3 min. run	15 sec. run	3 min. run
Control	1'48"	3'32"	1'58"	5'34"	3'28"	4'28"	4'4"	5'26"
Rhodiola extract	2'	3'25"	1'25"	2'02"	3'21"	3'57"	2'51"	3'02"
Eleuthero-coccus extract	2'	3'30"	1'45"	2'55"	3'20"	3'55"	3'	3'15"

Thus rhodiola preparations appear to be beneficial for improving work capacity, counteracting exhaustion and promoting recovery.

Biochemical mechanisms of the stimulant action of rhodiola

The effect of rhodiola on biochemical characteristics of muscular activity

In a large series of experiments in rats, Saratikov and co-workers [Saratikov and Krasnov 1987] studied biochemical mechanism by which rhodiola preparations improve physical work capacity and reduce exhaustion. The biochemical parameters studied included the content of ATP, ADP and creatine phosphate in the skeletal muscle; glycogen content in the muscle, liver and brain; blood glucose and pyruvate; lactate in the blood, muscle and brain; total blood lipids, phospholipids and free fatty acids. Also, the activity of the following enzyme systems was determined: succinate oxidase and cytochrome in the skeletal muscle and liver; phosphorylase in the muscle and liver; hexokinase in the muscle and brain; lipolytic activity in the adipose tissue.

It was found that in animals at rest rhodosin (a rhodiola preparation) does not significantly affect the content of ATP, ADP or glycogen in the skeletal muscle or the activity of the enzyme systems responsible for aerobic oxidation. On the other hand, rhodosin increased lactic acid content in the muscle by 66% and in the blood by 13% which appears to be the result of enhanced glycolysis fueled by liver glycogen. This suggestion is supported by the increase in muscle hexokinase activity by 59%, blood glucose elevation, decrease in the liver glycogen stores by 20% and increase in the activity of glycogen phosphorylase in the liver by 26%. A similar stimulation of glycolysis was reported for other adaptogens such as eleutherococcus and leuzea [Salnik 1970].

Rhodosin was also found to prevent or reduce certain metabolic shifts associated with intensive short-term work (15-min swimming) in rats. In the control animals, a 15 minute swim resulted in a 23% decrease in muscle ATP level and 44% drop in muscle creatine phosphate level. Also, there was a dramatic (103 and 95%, correspondingly) increase in muscle and blood lactate; and uncoupling of the processes of oxidation and phosphorylation (seen, for example, from the decrease in the quotient of oxidative phosphorylation). In the rhodosin treated animals, after a 15 min. swim, muscle ATP, ADP and creatine phosphate levels remained essentially unchanged, and the stimulation of anaerobic glycolysis is less dramatic. The latter can be explained, in part, by rhodosin activating glycolysis at rest. Also, rhodosin helped maintain the parameters of electron transfer and oxidative phosphorylation within the normal range. It appears that rhodosin promotes a faster and more efficient switch of the muscle to aerobic metabolism during intensive work. For instance, in rhodosin treated animals, there was an earlier mobilization of lipids from the adipose tissue and increase in free fatty acid levels, and, on the other hand, an increased uptake of lipids by the tissues.

Thus the ability of rhodosin to stabilize the levels of major energy-yielding substrates (ATP, creatine phosphate) during short-term work is probably due to the stimulation of aerobic energy production.

The administration of rhodosin also helps reduce metabolic changes during work of intermediate duration (2 hour swim in rats) and especially during prolonged work (5 hour swim) when the organism in near exhaustion. A five hour swim caused a significant decrease in the levels of ATP (by 15%), creatine phosphate (by 38%) and ATP/ADP ratio (by 39%) in the control animals, which indicates a depletion of energy reserves. There was also a decrease in the activity of respiratory chain enzymes and the consequent stimulation of glycolysis (an increase in lactic acid in the blood and muscle by 46 and 51% correspondingly; a drop in muscle and liver glycogen stores by 64 and 94% and a decrease in blood glucose level by 21%). These metabolic changes are similar to those seen in short-term intensive work, but in the latter case they resolve, at least partially, as the work continues and the metabolism readjusts to changed demands. Conversely, in the case of a prolonged, intensive work the above metabolic changes only intensify as the work progresses and can lead to a profound exhaustion and tissue damage. In the rhodosin treated animals, the levels of ATP and creatine phosphate, as well as ATP/ADP ratio did not fall (and even slightly increased) after a 5 hour swim. Rhodosin also prevented a drop in the activity of the enzymes of respiratory chain and a decrease in the efficiency of coupling of mitochondrial oxidation and ATP production. It should be noted that in a similar experiment a synthetic stimulant pyridrole failed to prevent a decline in the above metabolic parameter after a 5 hour swim.

It was suggested [Saratikov and Krasnov 1987] that metabolic shifts associated with exhaustion are in part due to disruption of mitochondrial membrane integrity, which results in a decreased proton gradient and uncoupling of mitochondrial oxidation and ATP production. Morphological studies indicated that rhodosin appears to preserve mitochondrial integrity during prolonged work, which may, in part, account for its ability to prevent exhaustion. This effect was not seen for pyridrole.

A number of studies demonstrated that rhodiola facilitates recovery from physical work. It was shown [reviewed in Saratikov and Krasnov 1987] that rhodiola preparations dramatically stimulate biosynthesis of protein and RNA in the muscle tissue during recovery period.

To conclude, one would note that many of the effects of rhodiola on muscular activity are similar to those produced by training.

TABLE

Comparison of the effects of rhodiola and training on muscular activity

Rhodiola preparations	Training
Increased ATP and creatine phosphate resynthesis	Increased ATP and creatine phosphate resynthesis
Increased glycogen content in the muscle, liver, and brain.	Increased activity of the key glycolytic enzymes (hexokinase, phosphofructokinase, pyruvate dehydrogenase, lactate dehydrogenase)
Less dramatic elevation of blood lactic acid and pyruvate	Less dramatic elevation of blood lactic acid and pyruvate
Increased activity of oxidative enzyme systems (NADH oxidase, succinate dehydrogenase, cytochrome)	Increased activity of oxidative enzyme systems (catalase, NADH oxidase, succinate dehydrogenase, isocitrate dehydrogenase)
Activation of proteases	Activation of proteases
Activation of aminoacyl-RNA synthetases	Activation of aminoacyl-RNA synthetases
Increased protein content in the muscle	Increase in muscle protein nitrogen
Accumulation of RNA in the muscle	Accumulation of RNA in the muscle
Earlier activation of lipid metabolism (increase in the transport and levels of free fatty acids and phospholipids; increased lipolysis)	Earlier activation of lipid metabolism (increase in the transport and levels of free fatty acids and phospholipids; increased lipolysis)
Better preservation of the structural integrity of mitochondria	Increased mitochondrial stability and resistance to swelling, increased mitochondrial density and protein content, increased number of cristae).

The effects of rhodosin on energy metabolism in the brain

Exhaustion is associated not only with the depletion of energy reserves in the muscle, but also with metabolic shifts in the brain. Saratikov and co-workers (1987) studied the effects of rhodiola on metabolic changes in the brain during intensive physical work. Short-term work produces only minimal shifts in the biochemical parameters of brain energy metabolism (ATP, ADP, creatine phosphate, glycogen). On the other hand, prolonged physical stress produces changes similar to those seen in the muscle. For instance, after a 5 hour swim in rats, brain levels of creatine phosphate were reduced by 10%, ATP - by 28% and ADP - by 18%; brain glycogen content decreased by 30% while lactic acid content increased by 27%. In mitochondria isolated from the rat brain, there was an uncoupling of the processes of oxidation and ATP synthesis and decrease in the activity of cytochrome and NADH oxidation systems. This appears to be due to the increased permeability of mitochondrial membranes, which leads to the disruption of the proton gradient. Apparently, rhodiola preparations prevent the above metabolic shifts by stabilizing mitochondrial membranes and thereby maintaining the efficiency of mitochondrial oxidative phosphorylation [Saratikov and Krasnov 1987]. Interestingly, a 5 hour swim was associated in rats with a decrease in the brain norepinephrine (by 26%) and dopamine (by 23%), which was prevented by the administration of rhodosin.

It should be noted that, as opposed to rhodosin, pyridrole (a synthetic stimulant) enhances biochemical changes occurring in the brain under a prolonged physical challenge.

The effects of rhodiola on the central nervous system

Russian scientists performed a number of studies of the effects of rhodiola on CNS [reviewed in Saratikov and Krasnov 1987]. Rhodiola preparations produced noticeable effects on electrical activity, neurotransmitter levels and other parameters in different brain structures. The effects of rhodiola preparations on CNS appear to be complex, with different areas or types of neurons being affected differently. It is not yet possible to conclude which of the many effects of rhodiola are responsible for its reported stimulant, antidepressant and stabilizing action on CNS.

The effects of rhodiola on the endocrine system

Saratikov and co-workers (1987) studied the effects of salidroside (10-12 mg/kg) and rhodiola extract (1 ml/kg) on the thyroid function in rats. The activity of thyroid was determined by I^{131} incorporation. It was found that both agents significantly stimulated thyroid function (Table). On the other hand, no statistically significant activation of the thyroid was seen in rats with surgically removed pituitary or cerebral hemispheres. It can be suggested, therefore, that the stimulation of the thyroid by rhodiola is largely indirect and occurs via CNS and hypothalamo-pituitary system.

In another series of experiments Saratikov and co-workers (1987) studied the effects salidroside of the adrenals and thymus during stress. A five hour swim in rats (moderate acute stress), was found to cause a significant increase in the blood level of 11-oxycorticosteroids (from 10.7 to 17.9 μg%) and a decrease in the content of ascorbic acid and cholesterol (by 31 and 39% correspondingly) in the adrenals. The thymus weight was decreased by 50%. A single dose of salidroside before a 5 hour swim prevented the increase in the level of 11-oxysteroids (it remained at 11.1), but did not prevent the decrease in the ascorbic acid and cholesterol content in the adrenals. Also, salidroside partially prevented thymus involution: the thymus weight decreased by only 28.8%.

A different situation is seen during severe stress. In rats, a prolonged exhaustive swimming with load was associated with a 42.1% decline in plasma 11-oxycorticosteroids (down to 6.2 μg%), reduction in ascorbic acid and cholesterol content in the adrenals (by 46 and 42% correspondingly) and a dramatic involution of the thymus (by 59%). In prolonged, intensive stress, salidroside prevented a drop in the plasma 11-oxycorticosteroid levels and in the adrenal content of ascorbic acid, whereas thymic involution and a drop in adrenal cholesterol content were not affected by the agent. Also, salidroside increased total swimming time by 69%.

Thus antistress effects of salidroside appear to include reducing the intensity of the alarm phase and preserving adrenal function in prolonged stress. In short-term/moderate stress salidroside also provides some protection for the thymus.

The effect of salidroside on the accumulation of radioactive iodine in the thyroid
(average of 6-12 experiments)

Time (hrs)	Radioactivity of the thyroid (% of total radioactivity injected)								
	Intact animals			Animals with cerebral hemispheres removed			Animals with pituitary removed		
	Control	salidroside	p	Control	salidroside	p	Control	salidroside	p
2	11.7±1.5	13.2±0.3	0.33	10.7±0.5	9.5±0.3	0.12	4.8±0.2	5.6±0.4	0.214
24	8.8±1.1	13.3±0.6	0.044	4.6±0.8	4.8±0.3	0.41	2.2±0.4	2.7±0.2	0.28
48	7.5±0.8	11.6±0.6	0.001	2.9±0.9	4.1±0.2	0.21	2.0±0.2	1.8±0.1	0.38
72	6.5±0.8	9.7±0.6	0.044	1.7±0.5	2.4±0.2	0.21			

Rhodiola preparations appear to have significant effect on the reproductive system. Gerasimova (1966, 1969) studied the effects of rhodosin in mice. In sexually mature animals, rhodosin (2.5 ml/kg/day for 4 weeks) prolonged the heat time (from 1.3 to 2.8 days) and reduced the time between heats (from 3.8 to 2.2 days). Also, the animals receiving rhodosin had a statistically significant increase in the weight of uterine horns and ovaries (from 39,6±4.11 and 6.4±0.65 to 59.9±1.59 and 9.1±0.45 correspondingly). Most of the rhodosin treated animals also had an increase in the number of growing follicles and the cellular volume of the ova, and also an increased proliferation of the uterine epithelium. Thus rhodosin stimulates the secretory function of the ovaries and helps prepare the uterus for the zygote. It was found that the effect of rhodosin on the uterus requires mature ovaries (Table).

TABLE
The effect of rhodosin on the weight of uterine horns and ovaries (mg) in female white mice
(each value is an average for 10-12 animals)*

Group	Weight of uterine horns	Weight of ovaries
Sexually mature	39.6±4.11	6.4±0.65
Sexually mature+rhodosin	59.5±1.59	9.1±0.45
Sexually immature	24.0±7.79	7.4±0.43
Sexually immature+rhodosin	25.0±4.76	8.0±0.75
Ovariectomized	41.1±6.34	--
Ovariectomized+rhodosin	42.5±5.72	--

* rhodosin was administered to sexually mature animals for 4 weeks and to ovariectomized and immature animals for 3 weeks.

Komar and co-workers (1981) found rhodiola to have androgenic properties in fish.

The effects of rhodiola on the liver

Dubro and Solovyeva (1968 a, b) studied the effect of rhodiola on bile secretion in dogs. Rhodosin, at the doses 0.1-0.5 ml/kg, produced normalizing effect on bile secretion: in the animals with low secretion, it increased the secretion by 100-300%, whereas in hypersecreting animals, the secretion was reduced.

Hepatoprotective activity of various rhodiola preparations during tetraiodocarbon poisoning was reported by Barnaulov and co-workers (1986).

Adaptogenic properties of rhodiola

Similarly to ginseng, eleutherococcus and other known adaptogens, rhodiola appears to enhance the organism's general resistance to a variety of adverse influences or conditions.

Rhodiola was shown to reduce toxic effects of varios drugs and chemicals. In particluar, it was shown to produce antihypnotic and antinarcotic action. Aksenova (1968), and Yelkin (1970) studied the effects of rhodiola and elentherococcus preparations on the onset of the drug-induced sleep. For most of the drugs and chemicals studied, rhodiola and eleutherococcus preparations reduced both onset time and duration of the drug-induced sleep (Table).

It was reported that the administration of rhodiola extract in mice (0.1 ml per animal for 10 days) increases LD_{50} for 40% ethanol from 24.1 to 56.2 ml/kg [Saratikov and Krasnov 1987]. Also, rhodosin was shown to dramatically reduce the toxicity of cholinesterase inhibitors. In rats who received 5 ml/kg of rhodosin, the acute poisoning with 750 mg/kg of chlorophos (an insecticide) resulted in a 26% mortality while in the control, the mortality was 73% ($p<001$) [Yelkin 1993]. It should be noted that rhodosin did not produce any changes in the cholinesterase activity.

In mice placed in the hermetic chamber, rhodosin produced a two-fold increase in the survival time ($p<0.001$), which, in part, appears to be due to the agent's ability to reduce the oxygen consumption by 10% [Khokhlov 1968].

In partially hepatectomized mice and rats, rhodiola extract (0.5 ml/kg for 14 days before the operation) increased mitotic index in hepatocytes by 84% [Netesa and Vstavskaya 1968].

TABLE

Antinarcotic action of rhodiola and eleutherococus preparations
[Aksenova 1968, andYelkin 1970]

Group	Dose (ml/kg)	Number of mice	Sleep onset time		Sleep duration	
			M±m	p	M±m	p
Sodium barbital (150 mg/kg)						
Control	5	23	33±4.5		237±25.6	
Rhodiola extract	5	39	38±4.6	0.42	133±22.8	0.002
Salidoroside	100	35	35±1.8	0.68	147±10.5	0.002
Gasoline (mg/l)						
Control	5	10	33±3.7		11±3.7	
Rhodosin	5	10	44±2.8	0.015	2±0.4	0.015
Eleutherococus extract	5	10	42±3.1	0.071	3.2±0.4	0.035
Acetone (mg/l)						
Control	5	17	32±1.1		5±1.2	
Rhodosin	5	17	33±1.0	0.48	6.0±1.2	0.54
Eleutherococus extract	5	17	34±1.3	0.27	5.3±0.7	0.84
Hexenal (70 mg/kg)						
Control	5	10	9±0.2		39±2.3	
Rhodosin	5	10	16±0.5	<0.001	21±0.6	<0.001
Eleutherococus extract	5	10	15±0.8	<0.001	20±0.9	<0.001
Chloral hydrate (300 mg/kg)						
Control	5	10	21±1.3		19±2.2	
Rhodosin	5	10	19±1.4	0.31	20±2.6	0.54
Eleutherococus extract	5	10	20±1.8	0.61	19±1.9	1.0
Ether (0.45 ml/l)						
Control	5	10	118±2.7		156±3.6	
Rhodosin	5	10	151±3.2	<0.001	118±1.6	<0.001
Eleutherococus extract	5	10	145±2.7	<0.001	127±3.7	<0.001

* In experiments with ether, time is in seconds,

** salidoroside in miligrams.

Note: sodium barbital, hexenal and chloral hydrate were administered subcutaneously; the ainmals were exposed gasoline, acetone, and ether vapors for 60 min., 50 min. and 5 min correspondingly.

Similarly to other adaptogens, rhodiola preparations tend to normalize various physiological and biochemical parameters regardless of the direction of their deviation. For instance, rhodiola extract and salidroside improved both leukopenia and leukocytosis in rabbits [Zotova 1965, Aksenova 1968]; rhodiola preparations prevented the development of insulin-induced hypoglycemia and exhibited a weak hypoglycemic effect at high glucose levels [Kolmakove and Kutolina 1966]; rhodiola preparations also acted to normalize various biochemical parameters of energy production in the brain [Zimina and Khazanov 1984].

It should be noted that the removal of cerebral hemispheres, pituitary, adrenals or gonads reduces or eliminates many of the effects of rhodiola [Saratikov and Krasnov 1987]. Thus the agent's action appears to be dependant on functional CNS and endocrine system.

In animals studies, rhodiola preparations were shown to improve the course of some bacterial and viral infectious diseases [Saratikov and Krasnov 1987]. These results, however, are controversial and require further study.

Of particular interest is the antitumor and antimetastatic action of rhodiola. In a series of studies, Dementyeva and Yaremenko (1983, 1984) demonstrated that in mice with various types of implanted tumors, rhodiola preparations inhibited tumor growth by 40-75%. Furthermore, rhodiola significantly reduced the incidence of metastases - for some tumors 2-5- fold [Yaremenko and Dementyeva 1984]. One should also note that rhodiola was shown to reduce the severity of the side effects of chemotherapy.

Clinical studies of rhodiola

(brief overview)

The was a number of studies as to the usefulness of rhodiola for treatment and prevention of diseases. In most cases the doses used varied within a range of 5-25 drops of the extract three times a day. For this dose range, the were essentially no significant adverse reactions. Rhodiola preparations were not found to be habit forming.

In a number of studies, rhodiola extract was shown to be beneficial such conditions as nervous exhaustion, chronic fatigue, various types of neuroses, anorexia, irritability, chronic headaches, insomnia, and attention deficit [Krasik et al 1970 a,b; Saratikov et al 1965, Kaliko and Tarasova 1966]. This indicates that rhodiola produces a general improvement in mental and physical endurance and work capacity, and exerts a stabilizing effect on CNS.

Rhodiola extract was studied as a part of therapeutic regimen in psychiatric patients. It produced a significant improvement in the tolerance of antidepressant, neuroleptic and other drugs, dramatically reducing the incidence of adverse effects [Krasik et al 1970 a].

Bender and co-workers (1978) studied the effects of rhodiola in healthy volunteers aged 19-30. Rhodiola extract tended to normalize such physiological parameters as heart rate and blood pressure regardless of the direction of deviation.

Beneficial effects of rhodiola in the treatment of impotence were reported [Saratikov and Krasnov 1987]. Rhodiola extract was administered to 35 patients with erectile dysfunction and/or premature ejaculation at the dose 10-15 drops/day for three month. In 26 patients, there was an improvement of sexual function, normalization of the composition of prostatic secretions and increase in the urinary 17-ketosteroids.

Gerasimova (1970) studied the effects of rhodiola (5-8 drops of rhodiola extract twice a day for 4-6 weeks) in 40 women with primary (7 patients) and secondary (33) amenorrhoea. Restoration of normal menstrual cycle was observed in 25 women with secondary amenorrhea, 11 of whom became pregnant shortly thereafter.

On the basis of clinical studies, the following indications for rhodiola preparations were proposed [Saratikov and Krasnov 1987].

1) exhaustion in healthy individuals; chronic fatigue; recovery from infectious and other diseases and/or injuries.

2) improvement of mental work capacity; attention deficit; concentration difficulties; mental fatigue.

3) improvement of physical work capacity and endurance; acceleration of recovery from intensive physical strain.

4) mild neuropsychiatric conditions: neuroses (nervous exhaustion, depressive neurosis, obsessive-compulsive neurosis), some psychoses; male impotence.

5) as an adjunct to psychiatric treatments, to reduce the incidence or severity of drug side effects and, possibly, to enhance the effectiveness of psychoactive drugs (especially in schizophrenia patients).

6) in elderly, to enhance general activity.