#### Elements of herbal medicine strategy for children with frequent respiratory viral infections infections. Classic phytoadaptogens O.D. Barnaulov (N.P. Bekhtereva Institute of the Human Brain, Russian Academy of Sciences, St. Petersburg)

The strategy elements of phytotherapy for children with frequent respiratory viral infections.

# Classical phytoadaptogenes OD Barnaulov NP Bechterev Human Brain Institute RAS (St-Petersburg, Russia)

#### SUMMARY

Persistent stress contributes to the increase and aggravation of respiratory viral infections in children. Classical phytoadaptogens also have high stress-limiting properties. In this work, for the first time, a comparative assessment of the stress-limiting effect of pharmaceutical and promising phytoadaptogens for the introduction on the model of immobilization of immature rat pups is given. All studied drugs are more or less active. 4 representatives of the Araliev family are more active: ginseng, aralia, zamaniha, eleutherococcus. Representatives of other families are less active: leuzea, rhodiola, lemongrass. Preparations of ginseng and leuzea leaves are highly effective and promising for introduction into pediatrics. The widespread use of phytoadaptogens in traditional medicine to increase stress resistance has been experimentally confirmed.

Key words: phytoadaptogens, stress-limiting activity, ARVI, often sick children.

## RESUME

Persistent stress contributes to more frequent and complicated respiratory viral infections in children. Classical phytoadaptogens also have high stress-limiting properties. For the first time the comparative evaluation of the stress-limiting action of pharmacy and perspective phytoadaptogens on the model of immature rats immobilization was done. All studied preparations are more or less active. More active representatives of the Araliaceae family are: Panax ginseng, Aralia elata, Oplopanax elatus, Eleuterococcus senticosus. Less active are members of other families: Rhaponticum carthaimoides, Rhodiola rosea and Shizandra chinensis. Highly effective and promising for the introduction to pediatric formulations are leaves of Rhaponticum and ginseng.

Keywords: phytoadaptogen, stress-limiting activity, acute respiratory viral infection, frequently ill children.

The WHO resolutions defined the assimilation of experience, heritage of traditional and folk medicine as one of the priority directions of the development of scientific European medicine in the XXI century, which was perceived by domestic and foreign phytotherapists [12, 13, 14, 15, 18, 24]. The basic discipline of these medicines has been and remains herbal medicine (FT). While mastering and recognizing the achievements of scientific and European medicine in diagnostics and treatment, nevertheless, in China, Korea, Japan, Vietnam, India, Indochina, Tibet, Mongolia, Buryatia, Kalmykia, Iran, Tajikistan, a number of Arab countries for millennia dominated and traditional medicine is developing, especially FT. And the vast majority of humanity lives in these territories.

An example of the assimilation by domestic pharmacologists of the experience and arsenal of traditional medical systems long before the WHO resolutions and, as it were, in anticipation of them, can be the creation of a theory of the state of nonspecifically increased body resistance (SNPS),

the doctrine of adaptogens by the most talented Russian pharmacologist N.V. Lazarev and his school. At the initial stage, the goal was to increase resistance to infections [16.17]. From traditional medicine countries

In East Asia, the most frequently and effectively used plants were isolated and borrowed [9], some of which were called adaptogens. One of the first relatively fully experimentally and clinically studied phytoadaptogen was ginseng root [6, 10], the history of its use, in particular with the aim of maintaining health, preventing disease, goes back millennia [8, 22].

Single plant uses are rare in traditional medicine. So, for the purpose of health improvement, very rich people could afford to use a specially prepared tea from the root of wild-growing ginseng [8], but one of the principles of traditional medicine in Asian countries is the compilation of precisely multicomponent collections with the inclusion of a long ribbon of synergistically acting plants. M.A. Grinevich [9] gives such a typical collection, the use of which dates back more than 2000 years: Acantopanax divaricatus, Acantopanax giraldii, Acantopanax graciluslylus, Acantopanax henrii, Acantopanax leucorrhizus \*, Acantopanax nipponicus, Acantopanax ilaxantopus \* trifoliatus, Aralia palmata, Periploca sepium. 4 types are marked with an asterisk, which, relatively recently, botanists attributed to the genus Eleutherococcus. With the exception of Periploca sepium (family Asclepiadaceae), all plants belong to the Araliaceae family and are closely related to ginseng. Their roots in the above combination are still used in China and Japan (under the name Wujiapi) as a general strengthening, prophylactic agent [29].

The peak of interest in classical phytoadaptogens in Russia falls on the second half of the 20th century. Moreover, in a number of monographs, articles, bibliographic reviews, among their versatile, multidirectional medicinal properties, an increase in resistance to infections was also noted. It is explained by the many times proven immunomodulatory effect of phytoadaptogens, an increase in cellular and humoral immunity [11, 19, 30, 21, 26].

Particularly interesting is the direction of leveling by phytoadaptogens induced by persistent stress, extreme situations of immunosuppression, a decrease in the body's resistance to infections [1, 10, 17, 26], which is directly related to the topic of often and long-term ill children. The constellation of numerous stressful influences on children, especially those attending kindergarten and school, does not require detailed consideration and listing. Forced immobilization, lack of mobility, lack of adequate physical activity, positive emotions play a significant role among them. When establishing the stress-limiting properties of individual phytoadaptogens by single parameters [6, 7, 10, 26], there is no idea about their relative activity. However,

Purpose of the work: on the generally accepted model of immobilization stress in immature rat pups to give a comparative assessment of the stress-limiting activity of pharmaceutical and promising phytoadaptogens for the introduction.

## Material and research methods

A comparative assessment of the stress-protective properties of phytopreparations from the following plants was carried out:

1. Pharmacy 1:10 alcoholic tincture of the roots of Panax ginseng true Panax ginseng, this. Aralievs.

2. Tincture of leaves prepared according to the same technology by the method of repercolation Ginseng of true Panax ginseng, sem. Aralievs.

3. Pharmacy alcoholic extract 1: 1 of the roots of Eleutherococcus prickly Eleuterococcus senticosus was diluted 10 times with water to equalize the concentrations with tinctures of ginseng, sem. Aralievs.

4. Pharmacy alcoholic tincture 1:10 roots of Aralia high Aralia elata, family. Aralievs.

5. The same roots of Zamaniha high Oplopanax elatus, this. Aralievs.

6. The same, from the seeds of Schizandra chinensis Shizandra chinensis, fam. Lemongrass.

7. Alcoholic 1: 1 pharmacy extract of the roots of Leuzea safflower Leuzea carthaimoides (family Astrovye) was diluted with water to a concentration of 1: 10. Botanists have now adopted a different name that is not familiar to doctors and pharmacists: Rapontik safflower Rhaponticum carthaimoides (has a number of popular names: bighead, maral root).

8. Prepared tincture of 1:10 leuzea leaves, this. Astrovye.

9. Pharmacy alcoholic extract 1: 1 of the roots of Rhodiola rosea Rhodiola rosea (fam. Tolstyanka) were diluted with water to a concentration of 1:10.

All phytopreparations were dealcoholized completely by adding water to the original volume. Even the presence of 5–8% ethyl alcohol changes the behavior of animals. The drugs were administered through a tube into the stomach at a daily dose of 2.5 g / kg for 7 days before immobilization. The inadmissibility of subcutaneous, especially intraperitoneal (painful peritoneal syndrome) administration of herbal preparations was proved by us earlier [19].

Outbred immature rat pups weighing 85–100 g were immobilized for 17 h in plastic houses, putting them in a refrigerator for 1 h (5–7 °C). Without cooling, stress changes in immobilized burrowing animals are less pronounced. The classical Selye triad was registered [20]: the "melting" of the thymus and spleen, an increase in the mass of the adrenal glands, the erosion of the stomach was counted, grading them into small, dust-like and large (diameter more than 1.5 mm). The calculation of erosions is facilitated by the fact that they are stained with hydrochloric acid hematin, which makes the test easy to perform. In addition, the concentration in plasma of 11-OCS, glucose, non-esterified fatty acids (NEFA), and glycogen in the liver was determined by our earlier [1] conventional spectrophotometric methods. The results were accumulated for 6 sets, studying all compared herbal preparations in each setting. In each test, the drugs were ranked by activity, and then the total stress-limiting effect was compared in points. Lack of activity was assessed as 0 points. The results were processed statistically using the Fisher-Student's t test.

## Results and its discussion

The results are presented in table. 1. Registration of the Selye triad makes it possible to single out as the most active in preventing the "thawing" of the thymus preparations of leaves and roots of ginseng, which are already tinctures of leaves, roots of leuzea, aralia are significantly inferior in effectiveness. Inactive preparations of rhodiola, eleutherococcus, lemongrass. By the ability to prevent a decrease in the mass of the spleen, preparations of the roots of zamanikha, ginseng, aralia, leaves of leuzea and ginseng are in the lead. The preparations of Schisandra and Leuzea roots did not prevent a decrease in the spleen mass in comparison with the stressed control, but there were no significant differences with the most active preparations (intermediate position, tendency of activity). The preparations of ginseng, eleutherococcus, and leuzea leaves prevent the increase in the mass of the adrenal gland to the greatest extent. Schisandra, inactive in most parameters, reliably prevented an increase in adrenal mass in stressed rat pups. Preparations of the roots of aralia, zamaniha, leuzea, rhodiola are ineffective. In comparison with our earlier data on sexually mature male rats, the determination of the mass of the adrenal glands is the least informative test [1, 24]. Based only on it, it is possible to exclude from the range of stress-limiting drugs active in other tests.

Table 1

Comparative assessment of stress-limiting properties of classical phytoadaptogens

Группа, растение, часть его (количество животных)	Концентрация в крови			Масса органа мг/100 г				Количество эрозий желудка		
	НЭЖК мэкв/л	11-ОКС, мкг/0.1л	глюкозы, мМ/л	тимуса	селезен- ки	надпочеч- ника	гликоген печени, мг/100г	мелких	крупных	всего
Интактные (20)	$266 \pm 19^{*}$	$25,2 \pm 1,8^{*}$	$5,7 \pm 0,2^{*}$	$175\pm14^{*}$	$283 \pm 22^{*}$	$8,6 \pm 0,3^{*}$	$3,6\pm0,4^{*}$	0.	0*	0*
Контроль, стрессиро- ванные (20)	$453 \pm 21$	$37,9\pm2,5$	$8,7\pm0,4$	$98 \pm 9$	$235 \pm 21$	$11,5 \pm 0,7$	$0,8\pm0,2$	8,3 ± 1,4	$2,1\pm0,3$	$10,4 \pm 1,7$
Корень женьшеня (15)	$562 \pm 28^{*}$	$28,7 \pm 2,9^{*}$	$5,2 \pm 0,6^{*}$	$151\pm17^*$	$278\pm25^*$	$9,5 \pm 0,5^{*}$	$2,9\pm0,3^*$	$2,1\pm0,9^*$	0*	$2,1 \pm 0,9^{*}$
Лист женьшеня (15)	$505 \pm 32^{*}$	$24.4 \pm 3.1^{*}$	$6,1 \pm 0,6^{*}$	$162\pm16^*$	$271\pm22^*$	$9,8 \pm 0,6^{*}$	$2,7\pm0,3^*$	$1,3 \pm 0,4^{*}$	$0,5 \pm 0,1^{*}$	$1,8 \pm 0,6^{*}$
Корень элеутерококка (15)	$488 \pm 20^{*}$	$27.7 \pm 2.7^{*}$	$6,6 \pm 0,5^{*}$	$111 \pm 12$	$266 \pm 19^{\circ}$	$10,1 \pm 0,5^{*}$	$1,6\pm0,2^{*}$	$4,5\pm0,9^{*}$	$1.2 \pm 0.3^{*}$	$5,7 \pm 1,0^{*}$
Корень аралии (15)	$515 \pm 25^*$	$24,1 \pm 2,3^{*}$	$5,8 \pm 0,3^{*}$	$129 \pm 12^{*}$	$273\pm22^{s}$	$11,0 \pm 0,6$	$2,0\pm0,3^*$	$0,8 \pm 0,2^{*}$	0*	$0,8 \pm 0,2^{*}$
Корень заманихи (15)	$549\pm28^{*}$	$28,5\pm3,0^*$	$4,6 \pm 0,2^{*}$	$115\pm14^*$	$280 \pm 25^{*}$	$11,2 \pm 0,6$	$2,8\pm0,2^*$	$4.5\pm1.7^*$	$0,7 \pm 0,2^{*}$	$5,2 \pm 1,2^{*}$
Корень левзеи (15)	$502 \pm 31^{*}$	$29,1 \pm 3,2^{*}$	$6,9 \pm 0,5^{*}$	$119 \pm 12^{*}$	$260 \pm 12$	$11,0 \pm 0,5$	$1,6 \pm 0,3^{*}$	$6,5 \pm 1,1$	$1,7 \pm 0,3$	$9,2 \pm 1,5$
Лист левзеи (15)	$550 \pm 28^{*}$	$22,5 \pm 2,8^{*}$	$6,0 \pm 0,3^{*}$	$131 \pm 14^{\circ}$	$272 \pm 20^{*}$	$10,3 \pm 0,5^{*}$	$2,1 \pm 0,2^{*}$	$2,5 \pm 0,8^{*}$	$0.7 \pm 0.3^{*}$	$3.2 \pm 1.1^{*}$
Корень родиолы (15)	$471 \pm 19$	$35,2 \pm 2,7$	$6,5 \pm 0,5^{*}$	$108 \pm 9$	$265 \pm 22^{*}$	$11,2 \pm 0,5$	$1,8\pm0,2^*$	$7,6 \pm 1,4$	$0,8 \pm 0,3^{*}$	$9,4 \pm 1,6$
Семя лимонника (15)	$482 \pm 20$	$32,5 \pm 3,3^{*}$	$7,4 \pm 0,7^{*}$	$112 \pm 12$	$259 \pm 18$	$10,7 \pm 0,4^{*}$	$1,4\pm0,2^*$	$6,9 \pm 1,2$	$1,0 \pm 0,1^{*}$	$7,9 \pm 1,5^{*}$

Selye's triad includes erosive lesions of the gastric mucosa. This model is sometimes mistakenly interpreted as an experimental analogue of peptic ulcer disease, but erosion does not penetrate into the muscle layer and heal within 3-5 days. The most effective tincture of the roots of aralia, and after it preparations of roots and leaves of ginseng, leaves of leuzea. The preparations of the roots of rhodiola and leuzea did not reliably reduce the number of gastric erosions as one of the indicators of the stage of stress depletion. Due to the information content and simplicity of the test, it can be widely used for screening the antidestructive action of drugs [1].

Biochemical markers allow us to note the least activity of Schisandra in saving liver glycogen and preventing stress-induced hyperglycemia, and it was ineffective in mobilizing NEFA as an adaptive response. According to the hyperglycemia restriction test, the efficacy of all studied phytoadaptogens was established, which were arranged in descending order of activity in the following order: bait roots> ginseng  $\geq$  aralia  $\geq$  leuzea leaves  $\geq$  ginseng leaves  $\geq$  rhodiola roots  $\geq$  eleutherococcus  $\geq$  leuzea  $\geq$  schisandra seeds. Representatives of the Araliaceae family dominate in terms of antihyperglycemic activity, with the exception of Eleutherococcus, which is generally preserved in the distribution of plants in terms of their ability to prevent a decrease in the glycogen content in the liver, although all drugs were effective. We did not reliably mobilize NEZhK as an additional source of energy, allowing to conserve carbohydrate reserves, prolong the stage of resistance, preparations of rhodiola and lemongrass, which, in comparison with the above results, allows them to be classified as the least effective adaptogens. The same drugs did not restrict (Schizandra) or weakly restrict (Rhodiola) an increase in the 11-OCS level in blood plasma.

The ranking of alcoholic, dealcoholized extracts by points (mean ± confidence interval in brackets) allows, taking into account all tests, to arrange plants in descending order of stress-limiting activity in the following order: ginseng roots ( $76 \pm 1.2$ )> ginseng leaves ( $68 \pm 1.0$ )> Leuzea leaves ( $66 \pm 0.7$ ) = Aralia roots ( $66 \pm 2.2$ )> Zamanikha roots ( $56 \pm 2.2$ )> Eleutherococcus roots ( $35 \pm 1.7$ )> Rhodiola roots ( $17 \pm 1.0$ ) ≥ Leuzea roots ( $16 \pm 1.2$ )> Schisandra seeds ( $13 \pm 1.2$ ).

The analysis of the use of the studied adaptogens in traditional medical systems and folk medicine prepares to some extent for the perception of ginseng as the "king" of adaptogens, in which not only the roots, but all parts of the plant are used [8]. The identification of the highest activity in representatives of the Araliaceae family, a number of which is closed by Eleutherococcus, is essential. The experience of collecting the roots and leaves of leuzea allows us to assert that there can be no "maral root" as such, since the maral eats the aerial part during the rut [23], but it is not able to dig up the roots and separate them from the ground. Therefore, the result of the superiority of leaves over roots is not accidental. This is essential for practice. Leuzea and ginseng leaves are much easier to harvest in large quantities over several years than roots. Their high efficiency is quite compatible with environmental considerations. The use of leuzea and rhodiola ("golden root") is largely aimed at correcting the reproductive sphere, which, however, does not diminish their importance as adaptogens not only with a lag in sexual development in older children, but development in general, an increase in resistance to ARVI, other damaging agents and influences [1, 12, 19]. Finally, the least effective lemongrass, which also has adaptogenic properties, is better known as a stimulant, a kind of doping that allows "without food and rest to drive the animal on the trail" [4], which obliges the herbalist to specifically assess the need to use or exclude it.

Systematically using classical phytoadaptogens in combination with other plants in the preparation of multicomponent personalized preparations for the treatment of children (mainly in the prepubertal period, 9-16 years old) exposed to ARVI, for the prevention of colds, we focus on the demonstrative effect of such phytotherapy, which allows over time in most children, sharply reduce the frequency of ARVI, the severity and duration of episodes, and in some cases, completely prevent them. The effectiveness, strategy and tactics of TF of frequently ill children are presented by us in a number of publications [2, 3, 5]. Phytoadaptogens, their combinations are indicated for those who often suffer from acute respiratory viral infections, stress-vulnerable, weakened, asthenic, quickly fatigued, as well as suffering from other so-called concomitant diseases (neuroses, chronic fatigue syndrome, viral hepatitis, cholecystitis, gastritis, recurrent cystitis, pyelonephritis, obstructive bronchitis, allergies, chronic tonsillitis, etc.). For an accurate personalized selection of phytoadaptogens, other medicinal plants and methods of therapy, careful diagnostics are required, worked out in traditional medical systems [27, 28, 25], whose experience also confirms the need for widespread use of adaptogens in the treatment of children (and adults) suffering from frequent ARVI, bronchopulmonary diseases. The use of phytotherapy methods, classical adaptogens in the complex treatment of children sharply raises the bar for the therapeutic effect. other medicinal plants and methods of therapy require careful diagnostics, developed in traditional medical systems [27, 28, 25], whose experience also confirms the need for widespread use of adaptogens in the treatment of children (and adults) suffering from frequent ARVI, bronchopulmonary diseases. The use of phytotherapy methods, classical adaptogens in the complex treatment of children sharply raises the bar for the therapeutic effect. other medicinal plants and methods of therapy require careful diagnostics, developed in traditional medical systems [27, 28, 25], whose experience also confirms the need for widespread use of adaptogens in the treatment of children (and adults) suffering from frequent ARVI, bronchopulmonary diseases. The use of phytotherapy methods, classical adaptogens in the complex treatment of children sharply raises the bar for the therapeutic effect.

#### conclusions

1. The first experimental comparative assessment of stress-limiting the activity of classical phytoadaptogens for a number of morphological and biochemical parameters in immature rat pups made it possible to establish that all the studied drugs are more or less effective. The most active are representatives of the Araliev family: ginseng, aralia, zamaniha, eleutherococcus. Representatives of other families are inferior to them: leuzea, rhodiola, lemongrass.

2. High stress-limiting activity was shown by tinctures that are not used today. ginseng and leuzea leaves, which creates prospects for practice to expand the arsenal of effective phytoadaptogens.

3. A characteristic feature of phytoadaptogens is their ability to limit stress-induced hyperglycemia, release of 11-OCS, preserve the content of glycogen in the liver, mobilize additional energy resources in the form of non-esterified fatty acids.

4. Prolongation of the stage of resistance, limitation of the destructive stage of depletion manifests itself in the ability of phytoadaptogens to reduce the number of gastric erosions, to limit the "melting" of the thymus and spleen, to prevent the depletion of liver glycogen.

5. Experience in the use of classical phytoadaptogens in the treatment of frequent and long-term sick children allows us to note their high efficiency.

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Barnaulov, O.D. Elements of herbal medicine strategy for children with frequent respiratory viral infections. Classical phytoadaptogens / O.D. Barnaulov // Traditional medicine. - 2015. - No. 3 (42). - S.52-56.

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