

SYSTEMATIC REVIEW OF STUDIES PUBLISHED IN 2005-2025 ON THE ISSUES OF RUSSIAN COMBINED HERBAL PRODUCTS FOR IMPROVING PERFORMANCE

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Abstract. Introduction. Combined herbal preparations that include several standardized plant components and are positioned as means of multi-link action on fatigue and recovery processes are actively developing in Russia. Objective: to systematically summarize Russian studies from 2005-2025 on combined herbal preparations for improving performance. **Methods.** The studies on multi-component herbal compositions developed in Russia with indicators related to performance and endurance were included. The design, models, indicators and level of standardization were assessed. **Results.** The preclinical effects of the preparations “Tetrafiton”, “Kardekaim”, “Centafit”, “Leveton-P”, “Sport-Aktiv”, “Energodarin” are most fully documented. The advantage of the combined approach over mono-component regimens is recorded. **Conclusion.** Russian combined herbal preparations demonstrate consistent preclinical efficacy in validated models associated with improving endurance. Priority is given to compositions of three to five components with full analytical control and clinical protocols.

Keywords: physical performance, endurance, combined herbal preparation, adaptogens.

Introduction. Physical performance (PP) is interpreted as the integral ability of the body to perform muscular work of a given power and duration while maintaining key homeostatic constants [1]. The need for safe, legally permissible pharmacological agents that increase PP is especially great in elite sports, military medicine, and professions associated with extreme physical exertion.

In the late 1990s and early 2000s, an approach to combined herbal preparations based on standardized plant extracts was institutionally consolidated in Russia: the methodological guidelines of the Ministry of Health of the Russian Federation No 2000/63 set the framework for the standardization of extracts and the approval of combined compositions, the guidelines No 2000/154 clarified the terminology and scope of application of natural pharmacy in clinical practice. The earlier methodological guidelines of the Ministry of Health and Medical Industry of the Russian Federation dated 08.04.1994 on preclinical and clinical studies of natural preparations were also based on the regulatory framework, which created an evidence procedure for multicomponent compositions [2, 3].

The scientific argumentation of the synergism of components and the principles of designing a multicomponent herbal preparation (MHP) were reflected in the publications of Wagner and

Ulrich-Merzenich (2016). MHP is described as a targeted strategy for increasing the effectiveness and sustainability of action [4].

Modern Russian reviews emphasize that rational combinations of standardized extracts provide a multi-targeted profile of action and require strict analytical control of quality and dose dependence. At the same time, excessive polycomponentity worsens analytical control and reproducibility of batches [5-20].

For the purposes of improving PP, MHP is formed through the technologically controlled standardization of raw materials and finished forms, coordination of pharmacodynamics (metabolic and stress-limiting modulation, neuromodulation, microhemodynamics) [1-3, 9-12, 15, 16].

The objective of the study is to systematize and summarize research of Russian scientists dedicated to the development and study of the action of combined herbal preparations aimed at improving performance.

Methods and organization. This study is a systematic review based on the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement. The methodological approach included the following key steps: formulation of the research question, development of the search and selection protocol, establishment of inclusion and exclusion criteria,

assessment of the quality of the selected publications, synthesis and interpretation of the obtained data.

The review included Russian publications published between January 1, 2005 and August 31, 2025. The following types of documents were examined: peer-reviewed articles, dissertations and abstracts, patents, and official reports of scientific institutions.

To search for publications, the following key words and combinations were used: “combined herbal preparation”, “multicomponent herbal remedy”, “actoprotective activity”, “antihypoxic activity”, “physical performance”, “endurance”, “forced swimming”.

The following types of publications were excluded from the review: studies on monoextracts of herbal preparations, publications without data on the relationship with physical performance, reports with insufficient detail of composition, doses, or results, secondary retellings or reviews without reference to the original source, materials not related to multicomponent herbal compositions.

The systematic review was based on a comparative analysis of data extracted from Russian repositories and archival materials of scientific journals on the platforms of scientific electronic libraries CyberLeninka and eLIBRARY.RU, as well as on the official websites of journals and ROSPATENT databases.

Due to the expected heterogeneity of models, doses and duration of courses, quantitative meta-aggregation was not planned. A structured descriptive synthesis with a matrix by objects and outcomes was used: (1) compositions with a disclosed composition and a full set of preclinical markers; (2) compositions with a qualitatively described increase in endurance and stress resistance; (3) lines with a dissertation-patent base and safety data; (4) applied reviews in sports practice; (5) technological contours of standardization. The validity of the methods (forced swimming test, treadmill) was separately taken into account as a reflection of physical performance in animals, which is consistent with the practice of domestic preclinical publications [1-3, 9-12, 15, 16].

Results and discussion. More than 26 Russian sources were analyzed in 2005-2025: peer-reviewed articles from the Higher Attestation Commission list – 16, dissertations and abstracts – 6, patents – 2, methodological standardization publications – 2.

Collection of the works from the reviewed time period demonstrates a stable direction of the effects of multicomponent phytocompositions aimed at improving physical performance. Regardless of the specific trade or laboratory name, we examined the combinations of plant components designed as agents with an actoprotective and antihypoxic, adaptogenic profile of action [1-26]. At the preclinical level, this was manifested primarily in an increase in the time to fatigue in the forced swimming test and, in some cases – in an increase in distance/power during load protocols on the treadmill.

The consistency of the effect's direction is supported by biochemical and physiological markers: a decrease in lactate and pyruvic acid concentrations, a decrease in the activity of creatine phosphokinase (CPK) and lactate dehydrogenase (LDG), an increase in the activity of superoxide dismutase (SOD) and catalase, and an increase in tissue adenosine triphosphate (ATP). This combination of signs indicates suppression of the hypoxic component of fatigue, stabilization of energy metabolism, and limitation of oxidative stress.

Below (table) is a sequential interpretation of the data obtained within each line of development, with a detailed analysis of the parameters: type of study, model/protocol, performance indicators, associated markers and observations. This allows for a comprehensive and objective analysis of the results, which is critical for the formation of substantiated conclusions and recommendations in the context of further research and practical application of the obtained data.

Comparison of the “Tetrafiton”, “Kardekaim”, “Centafit” lines, compositions with leuzea and cranberry meal, “Astragalus” and the “Ginseng with Astragalus” combined product reveals a common design logic: targeted combination of ecdysteroids, saponins, phenolic antioxidants and triterpenoids to cover metabolic and stress-limiting links of fatigue aimed at improving physical performance. In most series, course administration (7-14 days) was accompanied by an increase in endurance relative to the control data, which allows us to speak about the reproducibility of the effect between independent developments. At the same time, intensity of the effect varied due to differences in dosage, duration of the course and depth of standardization of the extracts, incomplete description of the methods of randomization and blinding [6, 7, 14-16, 24, 25].

Characteristics of the main lines of development of domestic multicomponent herbal preparations

Name of the drug	Type of research	Model or protocol	Performance indicator	Associated markers and observations	Sources
“Tetraphyton”	In vivo animal experiment	Rats, 7-day course, forced swimming test with an additional load	Increase in swimming duration relative to the control group	Increased adenosine triphosphate levels in skeletal muscle and myocardium; decreased lactic and pyruvic acids; increased catalase and superoxide dismutase; decreased activity of creatine phosphokinase and lactate dehydrogenase	[6, 7]
“Kardekaim”	In vivo animal experiment	Rats, forced swimming test; stress models	Increased physical endurance relative to the control group	Stress-protective activity in the immobilization stress model	[14-16]
“Centafit”	Dissertation complex of preclinical works	Models of intense exercise, hypoxia and stress	Increasing resistance to intensive loads (according to the text of the abstract)	Adaptogenic and antihypoxic effects; toxicological assessment presented	[9, 10, 18-19]
Composition of five plants (series of articles on actoprotection)	In vivo animal experiment	Rats, 7-day course, forced swimming test	Increase in swimming duration relative to the control group	Coordinated changes in energy and antioxidant markers	[7-9, 25]
Compositions “Adaptofit-28” and “Adapton-6”	Dissertations and abstracts	Models of physical and emotional stress	Increased overall resistance, including resistance to physical activity	Description of composition, doses and methods in dissertations	[26, 27]
Composition of leuzea extract and cranberry meal	In vivo animal experiment	Models of anabolic activity	Indirect relationship with performance through anabolic effect	Markers of anabolic action and their dynamics are described	[23, 24]
“Astragalus” and “Ginseng with Astragalus” (combined biologically active supplements)	In vivo animal experiment	Models of hypoxia and stress	Increasing resistance to hypoxia and stress	Antioxidant and adaptogenic effects	[27, 28]
“Energodarin”	In vivo animal experiment	Forced swimming test; comparison with individual components	The effectiveness of the combined approach is reported	Overall superiority over component monotherapies	[13, 25]

The demonstration of the advantages of combination over monotherapy deserves special attention: in a number of studies, a comparison of a complex formula with its separate components showed a more pronounced increase in the time to fatigue with an unchanged or better tolerability profile [13, 25]. This result is logically consistent with the concept of pharmacodynamic synergism and “kinetic cover”, which suggests mutual enhancement and stabilization of action due to

points of application separated by the mechanism and mutual influence on absorption, distribution and metabolism.

The “SportActive” technological line illustrates the role of standardization as a prerequisite for pharmacological stability [10-12, 25]. The presence of validated high-performance liquid chromatography (HPLC) for several marker compounds, quantitative control of phytoecdysteroids and auxiliary substances,

demonstration of inter-batch comparability allow us to link analytical quality characteristics with the stability of the biological response [10, 25].

Uniform safety protocols for all compositions are not presented, which limits meta-aggregation of data and requires unification of approaches to assessing toxicological endpoints at subsequent stages.

Studies by L.N. Shantanova et al. were conducted on rats, the weekly course and the forced swimming test with an additional load were applied [14-16, 29]. The 2018 publications showed a statistically significant increase in the time to fatigue relative to the control data against the background of the combined formula of the herbal preparation [20]. In the abstract of dissertation by Dimitrov (2019), parallel anti-stress effects are described [17]: biochemical profile of an increase in ATP in skeletal muscle and myocardium, increase in SOD and catalase activity, decrease in lactate, pyruvate, CPK and LDG. Numerical effect sizes in open versions of articles are presented in a limited way. The authors' contribution is the formation of a stable test protocol, reproduction of the effect in independent series. Conclusion: a combination of four standardized components demonstrates actoprotection in a validated model with good physiological consistency of markers; extended numerical reporting and clinical verification are needed.

The research of E.A. Alekseeva et al. covers the forced swimming test and immobilization stress models [6, 14-16, 28-29]. An increase in endurance relative to the control data and pronounced stress-protective activity are documented. A number of publications present the dynamics of antioxidant indices and indirect signs of energy stabilization. In public domain versions, the numerical values of the effect at the level of time to fatigue/distance are often not disclosed. Scientific contribution – demonstration of the relationship between actoprotection and the anti-stress component and the transfer of results between models. Conclusion: the direction of the effect is proven; unified quantitative reports and a standardized analytical passport of the composition are required.

A number of dissertation studies by B.A. Muruev confirms the adaptogenic and antihypoxic properties of the dry extract “Centafit” on models of intense exercise and hypoxia, with the inclusion of a toxicological

section [7-9]. The abstract indicates an increase in resistance to exercise, numerical data on the increase in time to fatigue in the public domain versions are limited [18]. The author's contribution is the validation of safety and tolerability in the studied doses, the formation of a basis for further standardization. Conclusion: technological fitness is above average due to the presence of toxicological sections; full-text quantitative results and comparable protocols of endurance tests are required.

Publications of 2018 (B.A. Muruev et al.) record an increase in swimming duration after a 7-day course in rats and consistent shifts in energy and antioxidant markers [6]. The contribution of the author groups is the demonstration of the reproducibility of the effect in parallel series and the linkage of *in vivo* results with biochemical panels. Conclusion: the actoprotective effect is confirmed in a validated model; accurate effect sizes and comparability of doses/schemes are required for interproject comparison.

Studies on the combination of leuzea extract with cranberry meal focus on the recovery and anabolic aspects [22, 23]. Preclinical data indicate positive dynamics of anabolic markers and acceleration of recovery after exercise; direct endurance tests in this line are limited. The authors' contribution is the expansion of the pharmacological base due to the anabolic circuit. Conclusion: development of comprehensive schemes of improving physical performance; the inclusion of validated endurance tests is required.

The line of phytocomplexes developed by Ya.I. Bilyach – “Energodarin” and “SportAktiv” – in a comparative experiment demonstrated the superiority of the combined formula over the monomodes of its components in the forced swimming test [10-13, 25]. The open access materials present the design and structure of the issue; detailed numerical tables are contained in the full text of the journal. Scientific contribution – empirical confirmation of the advantages of rational combination with equal duration of the course. Conclusion: the argument in favor of combination is confirmed; the next stage is clinical validation with objective metrics.

The technological and analytical series of works by Ya.I. Bilyach et al. formed a complete HPLC passport, provided quantitative control of phytoecdysteroids and potassium orotate and demonstrated inter-series comparability [10-13, 25]. In a preclinical model in rat swimmers, a 14-day course increased the time to complete fatigue

almost threefold relative to the control group data, which serves as a rare example of a rigid connection “quality → pharmacological response”. The authors’ contribution is the creation of a portable technological platform suitable for clinical translation. Conclusion: the standardization circuit is a necessary condition for the reproducibility and clinical verifiability of the actoprotective effect.

Analysis of the data set allows us to conclude that it is advisable to limit the number of components in the composition of drugs [5, 6, 13-25, 29]. Moderate compositions have a number of advantages, including a higher degree of standardization and better reproducibility of therapeutic effects. These properties are due to a smaller number of variables affecting the pharmacodynamics and pharmacokinetics of the drug, which contributes to more predictable and stable results when used in clinical practice.

Conflict of interest. The authors declare no conflict of interest.

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Conclusion. Russian combined herbal preparations demonstrate consistent preclinical efficacy. Independent randomized studies with objective performance metrics and universal biomarker panels, as well as widespread standardization of the composition are required to confirm clinical significance. The developers should focus on compositions of three to five plants with full analytical control of marker compounds and stable technology. It is important for clinicians and sports physicians to interpret preclinical data taking into account the lack of randomized clinical trials and to avoid extrapolations without any evidence. It is advisable for regulators to stimulate the registration of clinical protocols and open access to primary data arrays.

Further research will focus on clinical trials and validation of the effectiveness of herbal preparations in real-life conditions of use.

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