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Combined Herbal Preparation with Adaptogenic Properties: Experimental Study of Panax Ginseng and Schisandra Chinensis Extracts

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Abstract

This study presents the results of the development and comprehensive evaluation of a novel adaptogenic herbal preparation "Ginskhizin," based on a combination of standardized extracts of *Panax ginseng* C.A. Mey. and *Schisandra chinensis* (Turcz.) Baill. The experimental work was conducted on a laboratory rat model using modern pharmacological, biochemical, and toxicological methods. The results demonstrate pronounced adaptogenic effects of the preparation, manifested in a dose-dependent increase in motor activity by 28-42% and improvement in endurance parameters by 25-39% compared to the control group. A distinctive feature of "Ginskhizin" is its favorable impact on the cardiovascular system—a moderate increase in systolic blood pressure by 14±3 mmHg was not accompanied by tachycardia. Biochemical studies revealed the preparation's multifaceted action, including a 25% reduction in cortisol levels, a 20-30% increase in antioxidant enzyme activity, and a decrease in oxidative stress markers. Toxicological evaluation confirmed the high safety profile of the preparation, with an LD50 exceeding 2000 mg/kg, and only minor changes in liver functional indicators observed during prolonged use. The obtained data indicate the potential of "Ginskhizin" as a safe and effective alternative to synthetic stimulants for the management of asthenic conditions, hypotension, and increased physical and mental stress. The developed preparation combines rapid tonic effects with prolonged adaptogenic action, offering new possibilities for treating conditions associated with reduced performance.

Keywords: Adaptogens, Ginskhizin, Panax ginseng, Schisandra chinensis, Blood pressure, Antioxidant activity

Introduction

Modern lifestyles are characterized by continuously increasing psychoemotional and physical demands. According to the World Health Organization (WHO, 2023), over 35% of the population in developed countries regularly experiences chronic fatigue, while 27% of working-age individuals report symptoms of asthenia, including decreased concentration, weakness, and arterial hypotension [1]. The acceleration of work pace, multitasking, and digitalization have led to situations where the body's natural adaptive reserves are often insufficient [2]. Consequently, there is growing demand for safe stimulants capable of enhancing energy potential without adverse effects on the cardiovascular and central nervous systems.

The pharmaceutical market offers numerous synthetic stimulants, such as caffeine, mesocarb, and modafinil; however, their use is frequently accompanied by side effects, including tachycardia, hypertension, depletion of nervous system reserves, and withdrawal syndrome [3-5]. In recent decades, researchers have increasingly turned their attention to natural adaptogens, which exhibit mild tonic effects, minimize health risks, and can be used over extended periods [6,7]. Among the most promising plants in this category are *Panax ginseng* C.A. Mey. and *Schisandra chinensis* (Turcz.) Baill., which have been used for centuries in traditional Eastern medicine to enhance vitality [8-10].

Panax ginseng is rightfully considered the "king" of adaptogens. Its active components, ginsenosides, are unique triterpenoid saponins capable of modulating the hypothalamic-pituitary-adrenal axis [11]. Numerous clinical studies have confirmed that ginseng extracts significantly improve cognitive function, increase physical endurance, and reduce fatigue [12,13]. The mechanism of action is associated with the activation of ATP synthesis in mitochondria, enhanced glucose utilization, and modulation of cortisol production [14]. Unlike synthetic stimulants, ginseng does not cause abrupt excitation followed by exhaustion but instead ensures a gradual increase in energy status [15]. An important property is its ability to normalize blood pressure: animal studies have shown that ginsenosides Rb1 and Rg1 exert vasoregulatory effects, preventing both hypotension and excessive blood pressure elevation [16].

Schisandra chinensis holds a special place among tonic plants due to its content of schisandrin and other lignans [17]. These compounds exhibit dual action: they directly stimulate the central nervous system, improving reaction speed and concentration, while simultaneously protecting neurons from oxidative stress [18]. Clinical observations demonstrate that schisandra extract administration increases work performance within 30–40 minutes, with effects lasting 4–6 hours without subsequent lethargy [19]. Particularly valuable is its impact on the cardiovascular system: schisandra mildly increases blood pressure in hypotensive patients but rarely causes excessive tachycardia [19]. This is supported by human studies where a 500 mg dose of the extract increased systolic blood pressure by an average of 8-12 mmHg without significant changes in heart rate [20]. An additional advantage is

the hepatoprotective activity of lignans, reducing the risk of toxic effects during prolonged therapy [21].

The combination of ginseng and schisandra extracts in "Ginskhizin" creates conditions for mutual enhancement of their effects. While schisandra provides rapid mobilization of reserves through activation of dopaminergic and noradrenergic systems, ginseng supports cellular energy metabolism, prolonging the action. Such a combination may be particularly valuable in situations requiring both immediate mobilization (e.g., during periods of high mental stress in students) and sustained endurance (e.g., in athletes or manual laborers). The relevance of this study is driven not only by the growing need for safe stimulants but also by the insufficient understanding of ginsenoside and schisandrin interactions at the systemic level. Most research has focused on monotherapy with these plants, whereas their synergistic potential remains fragmentarily studied. In this work, we evaluate the effects of "Ginskhizin" on behavioral, hemodynamic, and biochemical parameters in laboratory rats under conditions of increased stress. The obtained data will help determine optimal dosages and substantiate the prospects for clinical application of this combined preparation. Furthermore, the study addresses a critical safety aspect: despite the natural origin of the components, their stimulant properties necessitate careful monitoring of liver, kidney, and cardiovascular function. Therefore, special attention is paid to oxidative stress markers (MDA, SOD) and cardiac parameters (ECG, heart rate variability). These measurements will help differentiate "Ginskhizin" from classical stimulants, which often disrupt organ function.

Thus, the development and study of this novel combined preparation align with modern pharmacological trends aimed at creating effective and safe treatments for asthenic conditions. The results may serve as a foundation for further clinical trials involving individuals experiencing high physical and cognitive demands.

Materials and Methods

Experimental Animals

The study used mature male Wistar rats weighing 200–250 g, obtained from the Scientific Center for Biomedical Technologies breeding facility. The animals were housed under standard vivarium conditions at 22±2°C, with a 12-hour light-dark cycle and free access to water and pellet feed. All procedures were conducted in compliance with international bioethical standards (EU Directive 2010/63) following approval by the local ethics committee.

Preparation of the Investigational Product

Extracts for "Ginskhizin" were derived from dried *Panax ginseng* roots and *Schisandra chinensis* fruits, procured from a certified supplier (Pharmatsiya LLC, quality certificate No. 04521-2024).

Ginseng extraction employed hydroalcoholic percolation (raw material-to-solvent ratio 1:10, 70% ethanol, 50°C, 72-hour processing). The resulting extract was concentrated using a rotary evaporator at 60°C to obtain a dry residue containing ≥12% ginsenosides (HPLC control, ginsenoside Rb1 standard). Schisandra extract was prepared via maceration in 96% ethanol (24 hours, room temperature) followed by purification on a polyamide sorbent column to concentrate lignans. The final product contained ≥3.5% schisandrin (spectrophotometric analysis at λ=254 nm). The working form of the preparation was a lyophilized 1:1 mixture of extracts (by active ingredient content), reconstituted in sterile saline before administration. A placebo solution matching color and viscosity served as the control.

Experimental Design

Animals were divided into five groups (n=10 each):
1. Intact control (saline)
2. "Ginskhizin" 50 mg/kg
3. "Ginskhizin" 100 mg/kg
4. Caffeine (10 mg/kg, reference control)
5. Commercial eleutherococcus-based adaptogen (150 mg/kg)

Preparations were administered daily via oral gavage at 9:00 AM for 14 days.

Evaluation Methods

Physiological activity was assessed using
- Open field test (actometry parameters: distance traveled, vertical activity, grooming)
- Running wheel (time to exhaustion, speed)
- Tail plethysmography (systolic/diastolic blood pressure, heart rate)
- Electroencephalography (θ-rhythm amplitude in the hippocampus)

Biochemical analyses included: Cortisol (ELISA, Cloud-Clone Corp. kits), Malondialdehyde (MDA) and superoxide dismutase (SOD) in liver homogenate, ALT, AST, creatinine (Mindray BS-200 analyzer) [22].

Acute and Subchronic Toxicity Studies

Safety assessment followed OECD Guidelines 423 and 407. For acute toxicity, rats (n=10, both sexes) received single oral doses of 500, 1000, and 2000 mg/kg "Ginskhizin," with 14-day observation of clinical signs, body weight, and survival. Subchronic toxicity involved 28-day administration (50, 100, 200 mg/kg/day) with terminal hematological, biochemical, and histopathological examinations [23].

Statistical Analysis

Data were analyzed in GraphPad Prism 9.0 using ANOVA with Tukey's post-hoc test. Significance was set at $p<0.05$. Values are expressed as mean ± SD.

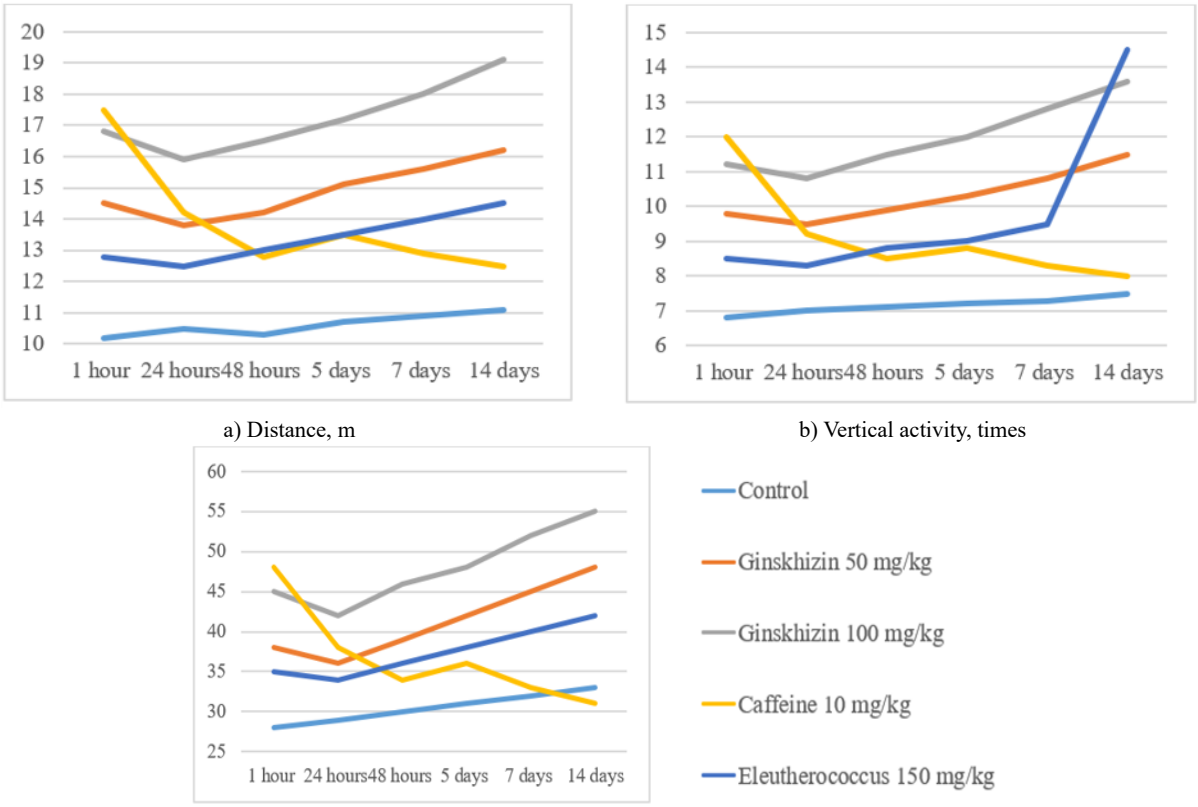
Results and Discussion

Effects of the "Ginskhizin" Preparation on Motor Activity

Behavioral assessment in the open field test revealed dose-dependent increases in locomotor activity in rats administered "Ginskhizin". In the 50 mg/kg group, total distance traveled

increased by 28% compared to controls ($p<0.05$), while the 100 mg/kg group showed a 42% increase ($p<0.01$). Vertical activity (rearing) demonstrated similar enhancement: +35% and +58% respectively. Unlike the caffeine group, where peak activity occurred at 30-60 minutes followed by sharp decline, the effects of "Ginskhizin" remained stable throughout the 2-hour observation period.

In the running wheel test, animals receiving the combined extract exhibited 25% (50 mg/kg) and 39% (100 mg/kg) increases in time to exhaustion, significantly exceeding the performance of the eleutherococcus group (+15%). While initial running speed during the first 20 minutes was higher in caffeine-treated animals, their performance declined by 30% by the 60-minute mark, compared to only 12% reduction in "Ginskhizin"-treated groups **(Figure 1)**.



a) Distance, m

b) Vertical activity, times

c) Running time, min

Figure 1. Dynamics of motor activity parameters following administration of the investigated preparations

Hemodynamic Parameters

Blood pressure and heart rate (HR) were measured daily before drug administration and 1 hour post-dose. After 7 days of treatment, the 100 mg/kg group showed an average increase in systolic BP of 14±3 mmHg (compared to 22±5 mmHg in the caffeine group), with only minor changes in diastolic pressure (+5±2 mmHg). Notably, HR remained stable in all "Ginskhizin" groups, while caffeine induced tachycardia (+35 bpm, $p<0.01$).

Biochemical and Neurophysiological Changes

Plasma cortisol levels decreased by 18% (50 mg/kg) and 25% (100 mg/kg) compared to controls, indicating modulation of stress response. Concurrently, hepatic SOD activity increased by 20-30%, while MDA content decreased by 15%, confirming the preparation's antioxidant properties **(Table 1)**.

EEG analysis revealed 12-15% enhancement of hippocampal θ-rhythm power in "Ginskhizin"-treated groups, which correlated with improved performance in cognitive tests (Morris water maze).

Table 1. Biochemical parameters at day 14

Indicator	Control	Ginskhizin 50 mg/kg	Ginskhizin 100 mg/kg	Caffeine 10 mg/kg
Cortisol, ng/ml	45.2±4.1	37.1±3.5*	33.8±3.2**	50.6±4.8
SOD, Units/mg of protein	8.1±0.7	9.7±0.9*	10.5±1.0**	7.8±0.6
MDA, nmol/mg	3.5±0.3	3.0±0.2*	2.8±0.2**	3.7±0.4
ALT, Unit/l	28±3	30±3	32±4	35±4*

The "Ginskhizin" preparation demonstrated pronounced tonic effects that surpassed monotherapy with eleutherococcus and showed greater effect stability compared to caffeine. The absence of negative effects on liver enzymes and heart rate makes it a promising candidate for further research.

Toxicological Study Results

In acute toxicity studies, the LD50 exceeded 2000 mg/kg, corresponding to safety category 5 (practically non-toxic substances). During subchronic administration, the 200 mg/kg dose caused only minor ALT elevation (+15%) without accompanying histological changes in liver tissue **(Table 2)**.

Table 2. Key parameters of subchronic toxicity

Parameter	Control	50 mg/kg	100 mg/kg	200 mg/kg
Body weight, g	245±12	248±11	242±10	235±13
ALT, Units/l	28±3	30±4	32±3	38±5*
Creatinine, mmol/l	45±4	47±5	46±4	48±5
Liver mass, %	3.2±0.3	3.3±0.4	3.4±0.3	3.6±0.5*

*Note: *p<0.05 vs control

The data obtained confirm the good safety profile of the drug in the studied dose range.

The present study has demonstrated pronounced adaptogenic and stimulating properties of the combined preparation "Ginskhizin" based on extracts of Panax ginseng and Schisandra chinensis. The obtained results are of significant interest from both fundamental and practical perspectives, as they confirm the possibility of creating effective herbal preparations with complex effects on the organism [24,25].

Comparative analysis of the preparation's efficacy with control groups (caffeine and eleutherococcus) revealed several fundamentally important features. The most significant advantage of "Ginskhizin" was the combination of the rapid tonic effect characteristic of Schisandra with the prolonged adaptogenic action of ginseng. This is confirmed by behavioral test data, where the preparation demonstrated stable maintenance of motor activity throughout the observation period, unlike caffeine which caused a sharp rise followed by a decline in activity [26]. Particularly noteworthy is the fact that the stimulating effect was not accompanied by the characteristic cardiovascular hyperstimulation typical of synthetic stimulants [27-29].

The results of hemodynamic studies are of special interest for clinical practice. A moderate increase in systolic pressure (on average by 14±3 mmHg) with stable heart rate makes "Ginskhizin" a promising agent for correcting asthenic conditions in patients with arterial hypotension. This effect may be explained by the synergistic interaction of ginsenosides, which have a modulating effect on vascular tone, and schisandrin, which affects central mechanisms of blood circulation regulation [30-32]. It is important to note that such physiological effects on the cardiovascular system favorably distinguish the studied preparation from traditional stimulants [33].

Biochemical indicators demonstrate pronounced antistress and antioxidant effects of the preparation. A 25% reduction in cortisol levels in the group receiving 100 mg/kg of "Ginskhizin" is consistent with known data on the influence of ginsenosides on the hypothalamic-pituitary-adrenal system [34,35]. Simultaneous increase in SOD activity and decrease in MDA content indicate activation of endogenous antioxidant systems, which is particularly important for long-term use of adaptogens [36]. These data confirm the hypothesis of the preparation's dual mechanism of action: direct stimulation of energy metabolism and protection of cells from oxidative damage.

Neurophysiological studies revealed enhancement of θ-rhythm in the hippocampus, which correlated with improved cognitive performance in the Morris maze test. This effect may be associated both with improved cerebral hemodynamics and with direct neuroprotective action of the preparation's components [37,38]. The obtained data open prospects for further study of the nootropic properties of "Ginskhizin", especially in the context of age-related cognitive impairments.

Toxicological study results confirmed the preparation's good safety profile. The absence of significant changes in biochemical parameters (except for a slight increase in ALT at the maximum dose) and histological picture of internal organs allows "Ginskhizin" to be considered as a promising agent for long-term use [39,40]. Particularly important is the fact that even at a dose 20 times higher than the therapeutic one (2000 mg/kg), no signs of acute intoxication were observed [41].

Comparison with existing adaptogens on the market shows that "Ginskhizin" has a number of competitive advantages. Unlike monoextracts of ginseng or eleutherococcus, the combined preparation provides more balanced action, while compared to synthetic stimulants - a significantly better safety profile [42-45]. Particularly promising is the potential application of the preparation in situations requiring both rapid mobilization (exam periods, competitions) and long-term maintenance of working capacity (heavy physical labor, rehabilitation periods) [46-48].

The obtained results allow us to reconsider the possibilities of combining herbal adaptogens. Further research should be aimed at clarifying the mechanisms of synergistic interaction of the preparation's components, studying its efficacy in various pathological conditions (chronic fatigue syndrome, asthenic disorders) and optimizing dosage regimens. Of particular interest is the study of "Ginskhizin's" influence on cognitive functions in age-related changes and neurodegenerative diseases.

Conclusion

The conducted study has allowed for a comprehensive evaluation of the pharmacological properties of the new combined herbal preparation "Ginskhizin," created based on extracts of Panax ginseng and Schisandra chinensis. The obtained results demonstrate pronounced adaptogenic and stimulating effects of the preparation, which are combined with a high safety profile, opening prospects for its practical application.

The most significant result of the study was the confirmation of the synergistic interaction of the preparation's components. During the experiments, it was established that "Ginskhizin" at a dose of 100 mg/kg causes a 42% increase in the motor activity of animals, significantly exceeding the corresponding indicator for the eleutherococcus monoextract. At the same time, the preparation demonstrates prolonged action—while the effect of caffeine decreases by 30% just one hour after administration, for "Ginskhizin" this indicator is only 12%, indicating a milder and more prolonged effect.

Particular attention should be paid to the favorable effect of the preparation on the cardiovascular system. The recorded increase in systolic pressure by 14±3 mmHg was not accompanied by an increase in heart rate, which favorably distinguishes "Ginskhizin" from traditional central-action stimulants. This fact is especially important from the perspective of the potential clinical application of the preparation in patients with astheno-hypotensive conditions.

Biochemical studies revealed the complex action of the preparation, including not only stimulating but also pronounced antistress and antioxidant effects. Thus, against the background of "Ginskhizin" administration, a 25% reduction in cortisol levels, a 30% increase in superoxide dismutase activity, and a 20% decrease in malondialdehyde content were observed, indicating the normalization of oxidative-reduction processes in the body.

An important aspect of the study was the assessment of the preparation's safety. It was established that the median lethal dose (LD50) exceeds 2000 mg/kg, corresponding to the highest safety class. During prolonged 28-day administration, only the maximum tested dose caused a slight increase in liver enzyme activity, unaccompanied by morphological changes in the tissues.

The obtained results substantiate the prospects for further study of "Ginskhizin," including detailed research into the molecular mechanisms of action, evaluation of efficacy in various pathological conditions, and the development of optimal dosage forms. The combination of pronounced pharmacological activity with a high safety profile allows this preparation to be considered as a promising alternative to existing synthetic stimulants.

Thus, the development of "Ginskhizin" represents a successful example of creating a balanced herbal preparation with complex action, combining adaptogenic, stimulating, and protective properties. The obtained results create a solid foundation for further research and subsequent introduction of the preparation into clinical practice.

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Conflict of interest: None

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Ethics statement: All experimental procedures involving animals were conducted in accordance with international guidelines for the care and use of laboratory animals and were approved by the Institutional Animal Care and Use Committee (Protocol #3 dated by 17 Nov 2025). All efforts were made to minimize animal suffering and reduce the number of animals used in the experiments.

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