



## Plant Oil-Based Dietary Supplement with Deer Antler Extract for Panic Attacks: A Clinical Study

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### ABSTRACT

Due to a recent increase in the number of people suffering from panic attacks, there is an acute need for a solution. Research data available suggests adopting a healthy diet to relieve or eliminate panic attacks. A plant oil-based dietary supplement with deer antler extract was tested for efficacy in treating panic attacks. Sixty participants, aged from 18 to 55, were involved in the clinical study. To assess the efficacy of the therapy, we monitored the autonomic nervous system dynamics, the hormonal changes, and the immune system and performed a comprehensive assessment of the autonomic nervous system and mental and emotional states. The study findings support the importance of nutrition and demonstrate the advantages of using dietary supplements for treating patients with PA.

It should be noted that the use of the developed supplement has a positive potentiated effect on the state of nervous, hormonal, immune regulation and bone tissue metabolism.

**Keywords:** Deer antler, Dietary supplement, Panic attack, Efficiency, Functional focus.

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### INTRODUCTION

The fast pace of contemporary life impacts every human being and induces significant neurophysiological changes. The first of the most evident reasons for these changes is an imbalanced diet that lacks essential nutrients and fails to provide adequate energy balance. Common nutrient deficiencies become the cause of alimentary diseases. Second, the Industrial Revolution is, on the one hand, beneficial to society, with its artificial intelligence and advanced digital technologies, automation of many production processes; while, on the other

hand, results in a notable worsening of the quality of life, with pollution and contamination, together with increased stress and anxiety. The third major reason is a viral attack that humankind experienced during the coronavirus outbreak, which affected the functioning of important regulatory systems such as the nervous and endocrine systems. As a consequence, the above-mentioned changes resulted in a massive increase in different autonomic nervous system (ANS) disorders, with a registered growth in the number of people suffering from regular panic attacks (PA).

Russian scientists define a panic attack as an extreme form of vegetative dystonia, with such symptoms as recurrent anxiety, breath shortness, pounding heart, and intense fear [1-5]. As for The International Statistical Classification of Diseases and Related Health Problems, recurrent and severe depressive disorders with psychotic symptoms are listed under the F33.3 code. Currently, approximately 40% of patients, who seek initial medical advice from general practitioners, show symptoms of PA. It should be noted that these patients represent the working-age population, and, thus, the problem requires prompt attention and an acute solution.

Recent research studies found that a combination therapy approach, that uses both medications and adaptogens, is one of the best ways to treat panic attacks. Adaptogens, such as deer antlers, are known to increase the body's nonspecific resistance to a wide range of harmful effects of a chemical, physical, and biological nature [6-11].

#### MATERIALS AND METHODS

A new plant oil-based dietary supplement that contains phospholipids and glycolipids extracted from the antlers of the Altai Maral was tested. Sixty participants, aged from 18 to 55, were selected and allocated into two groups (the main and control groups) of 30 people each. The participants of the main group were prescribed ten drops of the supplement to be taken sublingually before or with the morning meal daily for 4 weeks. The participants of the control group did not receive the dietary supplement. Upon the completion of the therapy, a clinical study was performed to assess the effectiveness of the new dietary supplement. A follow-up period of 2 weeks was set to record recurrent panic attacks.

The vegetative function was assessed using the Vane scale (a quantitative assessment developed by A.M. Vane, 2003). The assessment was carried out twice, four weeks before and four weeks after the treatment. The diagnosis of panic disorder was confirmed for the participants who demonstrated at least 4 of the symptoms.

The type of adaptive response was determined by calculating the percentage of lymphocytes in the leukocyte formula and segmented neutrophils, applying Goldberg's neutrophil-to-lymphocyte ratio [12].

A heart rate variability (HRV) examination was performed by registering short fragments of a standard record (cardiointervalogram). The following indicators were evaluated: index voltage; heartbeat frequency; variation range (to assess the effect of the parasympathetic nervous system on heart rate); heartbeat mode (to register humoral regulation of cardiac activity); the functioning of the cardiovascular center (heart rate and blood pressure via sympathetic and parasympathetic pathways); mode amplitude (to assess the effect of the sympathetic nervous system on heart rate).

The level of cytokines (Interferon-gamma (IFN $\gamma$ ), Interleukin 2 (IL2), Interleukin 4 (IL4), and Interleukin-1 beta (IL1 $\beta$ )) in supernatants was measured using a solid-phase enzyme-linked immunosorbent assay (Procon (Russia) and CytImmune (USA) kits were used).

The study was performed at 'ProfMed' scientific and research center of the Chair of Obstetrics and Gynaecology of Siberian State Medical University (Tomsk, Russia) and supervised by L.S. Sotnikova, Doctor of Medical Sciences, Professor.

#### RESULTS AND DISCUSSION

During diagnostic testing, the quantitative assessment of the patients revealed disorders of the ANS, as all the participants scored  $85.3 \pm 5.05$  points, which was 8 times higher than normal (normal values are fewer than 10 points). The average number of clinical manifestations of PA for the participants of the main group equaled  $10 \pm 2$ .

The data on the changes in the number of clinical manifestations of PA (before and after therapy) is presented in **Table 1**.

Upon the completion of the therapy, all participants of the main group demonstrated a decline ( $p < 0.05$ ) in the number of PA symptoms. It is important to note the complete relief of such manifestations as the fear of death and the feeling of losing control of the body.

No complaints or side effects related to the dietary supplement were recorded. The participants reported improvement in general well-being, mentioning (1) being better at managing emotional lability, (2) improved health and vitality, (3) and enhanced labor productivity. A comprehensive in-depth assessment of the

functional state of the ANS was carried out (Table 2).

**Table 1.** Tables should be placed in the main text near the first time they are cited

Clinical manifestations of PA	Main group (before therapy (n=30))	Main group (after a 4-week therapy (n=30))	Control group (n=30)
Trembling, chills	28	5*	0
Extensive sweating, cold sweats	14	3*	0
Heart palpitations, pounding heart, accelerated heart rate	22	6*	0
Nausea, bloated stomach	19	8*	0
Chest pain and/or discomfort	28	10*	0
Breath shortness, suffocation	19	4*	0
Fear of losing control and /or becoming mentally ill	12	2*	0
A feeling of being detached from the surroundings	10	2*	0
A feeling of being outside the body, a fear of losing control of the body	26	0*	0
Dizziness, unsteadiness, faintness, floating feeling	24	3*	0
Sleep disorder	30	8*	0
Numbness, a tingling feeling in hands and feet	22	4*	0
Confusion and lack of concentration	30	5*	0
Fear of death	28	0*	0

Note: \* - significant difference ( $P < 0.05$ ) when compared with the data before treatment

**Table 2.** Adaptive responses before and after therapy ( $X \pm m$ , p)

Adaptive response	Main group (before therapy (n=30))	Main group (after a 4-week therapy (n=30))	Control group (n=30)
Training	0	18*	30
Acute stress	14	2*	0
Chronic stress	16	10*	0

\*Note: 0 – no changes; 10 – pronounced changes

Upon the completion of the therapy, the number of participants with adaptive responses to training increased, while the number of participants experiencing stress and chronic stress declined ( $p < 0.05$ ).

During diagnostic testing, the Cerdo vegetative index amounted to  $44.2 \pm 2.32$  units, which indicated a predominance of excitatory influences in the activity of the ANS. The predominant sympathetic tone caused tension and deteriorated the adaptive capacity of the body, which was clinically manifested by symptoms of autonomic dysfunction and PA. Assessing the cardiointervalograms of the participants, we registered higher values for mode amplitude and stress index, as well as a larger variation range, when compared with normal values, which indicated increased sympathetic activity and decreased parasympathetic activity. The maximum sympatheticotonia was recorded among the participants aged from 35 to 45. The data

revealed the imbalance of the ANS divisions and the reduction in the adaptive capacity.

Having analyzed the data, we determined that the nutrition plans with dietary supplements contribute to adaptive responses and proper functioning of the ANS, help increase productivity, and improve adaptive responses.

Upon the completion of the therapy, we assessed the severity of participants' psychopathological symptoms using a psychometric assessment and diagnostic scales. Both the central nervous system (CNS) and the ANS demonstrated improvement ( $p < 0.05$ ), with better emotional stability and lower asthenization. Half of the participants showed a satisfactory functional status of 8-10 points ( $p < 0.05$ ).

The orthostatic test revealed a significantly reduced reactivity of the sympathetic division of the ANS ( $p < 0.05$ ). Testing showed adequate activation of the parasympathetic division.

The impact of nutrition on the functional state of the ANS is demonstrated in **Table 3**.

**Table 3.** The functional state of the ANS before and after therapy ( $X \pm m$ , p)

Variables	Main group (before therapy (n=30))	Main group (after a 4-week therapy (n=30))	Control group (n=30)
The Cerdo vegetative index, c.u.	44.24±2.32	12.28±0.02*	2.23±0.04
Mode, sec	0.80±0.13	1.98±0.12*	2.46±0.27
Mode amplitude, %	78.27±3.01	40.10±1.25*	38.14±2.11
Variation range, sec	1.10±0.05	0.22±0.04*	0.28±0.02
Stress index, c.u	223.24±4.08	124.35±2.05	138.23±5.12

Note: \* - significant difference ( $P < 0.05$ ) when compared with the data before treatment

The evaluation of the HRV spectrum was performed after 4 weeks. According to the data of previous research studies, a four-week treatment period is sufficient for curbing panic attacks. Complex analysis of the hormonal status revealed statistically significant changes ( $p < 0.05$ ) in stimulated insulin and cortisol levels, while No changes in thyroid hormone levels or prolactin levels were registered.

Due to the adaptogenic property of the dietary supplement, over-activation of the sympathetic nervous system was suppressed; cortisol levels were normalized, which resulted in the normalized level of stimulated insulin. The data on the impact, the dietary supplement made on hormonal status, is presented in **Table 4**.

**Table 4.** Participants' hormonal status before and after therapy ( $X \pm m$ , p)

Hormones	Main group (before therapy (n=30))	Main group (after a 4-week therapy (n=30))	Control group (n=30)
Basal insulin ( $\mu\text{U/ml}$ )	12 [8:14]	10 [8:16]	2.7 - 10.4
Stimulated insulin ( $\mu\text{U/ml}$ )	32 [22:40]	14* [8:18]	2.7 - 10.4
Cortisol (nmol/l)	840	550*	150 - 650
Prolactin (mU/l)	590 [500:600]	535 [420:550]	109 - 557
TSH (mU/l)	3.6 [2.6:3.8]	3.4 [2.8:3.6]	0.4 - 4.0

Note: \* - significant difference ( $P < 0.05$ ) when compared with the data before treatment

We studied the relationship between biological stress regulation and somatic complaints. Early predictors of a predisposition to somatization are increased blood cortisol levels and reduced heart rate variability. These changes significantly reduce the body's resistance to typical psychosocial stressors. The interrelationship between the nervous, endocrine, immune systems, and mental spheres is the base of the psychoneurotic-neuroendocrine system. Almost all immune cells have receptors for hormones. Hormones can affect the immune system in two ways: directly, by binding to the receptors on the cell surface, or indirectly, by inducing dysregulation of cytokine production.

Cytokine balance is significant in modulating cellular responses in the brain in times of stress as well as during a panic attack. Cytokines influence the metabolism of neurotransmitters (serotonin, norepinephrine, dopamine, gamma-aminobutyric acid) and have a particular effect on the interaction between cells; they are important for the proper functioning of the immune, endocrine, and nervous systems. To evaluate the effect of the dietary supplement on cytokine balance, we studied spontaneous and phytohaemagglutinin (PHA)-stimulated production of TH1 and TH2 cytokines (**Table 5**).

**Table 5.** TH1 and TH2 cytokine production by peripheral blood cells: Spontaneous and PHA-stimulated ( $X \pm m$ , p)

Variables	Main group (before therapy (n=30))	Main group (after a 4-week therapy (n=30))	Control group (n=30)
IL - 1 $\beta$	Spontaneous, pg/ml	12128±6.87	79.97±532 ( $p < 0.05$ )
	PHA-stimulated, pg/ml	95.46±532	103.46±3.09
	Stimulation index, c.u	2.25±0.02	2.29±0.03
			50.91±3.09
			132.87±5.97
			238±0.05

	Spontaneous, pg/ml	2325±3.91	52.02±1.15 (p<0.05)	46.70±3.65
IL-2	PHA-stimulated, pg/ml	105.63±4.02	152.09±5.02 (p<0.05)	19630±8.42
	Stimulation index, c.u	1.98±0.02	5.52±0.03 (p<0.05)	438±0.08
	Spontaneous, pg/ml	11633±5.92	7933±3.79 (p<0.05)	58.89±334
IL-4	PHA-stimulated, pg/ml	23631±11.02	193.23±7.02 (p<0.05)	146.05±624
	Stimulation index, c.u	2.03±0.02	2.46±0.03 (p<0.05)	2.48±0.03
	Spontaneous, pg/ml	116.82±7.09	179.82±5.15 (p<0.05)	206.01±5.78
INF-γ	PHA-stimulated, pg/ml	123.09±5.57	207.42±624 (p<0.05)	25632±8.09
	Stimulation index, c.u	0.97±0.02	1.14±0.03	2.61±0.02

Note: \* - significant difference (P <0.05) when compared with the data before treatment

Activation of TH1 cells associated with the production of IL-1 $\beta$ , IL-2, and INF- $\gamma$  cytokines enhances cellular immunity. The humoral immune response is induced by the dominance of TH2 cytokines. When analyzing the cytokine production by blood mononuclear cells, we registered changes in the ability of immunocompetent cells to secrete cytokines.

Having assessed the IL-1 $\beta$  levels in mononuclear cells of the patients with PAs before the therapy, we recorded a significantly increased spontaneous secretion. After a four-week therapy with the dietary supplement, spontaneous secretion of IL-1 $\beta$  approximated to that of the control group. Levels of the PHA-stimulated production of IL-1 $\beta$  and the stimulation index were at reasonably comparable levels.

At the starting point of the trial, both the spontaneous and PHA-stimulated production of IL-2 was inhibited in the patients with PAs. The testing revealed a nearly restored IL-2 production after a four-week diet therapy.

Before the therapy, basal and PHA-stimulated production of IL-4 was documented as significantly higher than the reference values. Although the results obtained after a four-week therapy demonstrated a positive trend in the cytokine secretion by immunocompetent cells, it remained significantly different from the reference values.

Before the therapy, the evaluation of spontaneous and induced production of IFN- $\gamma$  by the mononuclear cells in patients with PAs revealed lower secretion. Since IFN- $\gamma$  is important for protection from viral infections, the data indicates a low immune response in patients with PA. After a four-week therapy, the synthesis of IFN- $\gamma$  by immunocompetent cells noticeably improved, although it remained lower than that of the control group.

The study findings indicate the importance of nutrition for spontaneous and PHA-stimulated production of IFN- $\gamma$ , IL-2, IL-4, and IL-1 $\beta$ . These cytokines are necessary for the proper functioning of the nervous and immune systems, ensuring stress resistance and resilience.

The two-week follow-up period included dynamic monitoring to record any re-current PAs. During the follow-up period, twelve out of thirty participants experienced panic attacks. After the therapy, PAs were less frequent and less severe and lasted from 10 to 20 minutes, 10±5 minutes on average.

## CONCLUSION

The study findings support the importance of nutrition and demonstrate the following advantages of using dietary supplements for treating patients with PA:

- Better stress resistance and resilience;
- reduced sympathetic tone and, therefore, the rebalanced ANS;

- Normalised stress hormones (reduced cortisol and stimulated insulin levels)
- stable cytokine balance (a steady production of key cytokines that affect the functions of the hormonal, nervous, and immune systems).

The combination of the ingredients used in the dietary supplement ensures the synergistic effect and helps to suppress the severity, frequency, and length of PAs. Analyzing the clinical study data, we can recommend the dietary supplement for effective prevention and therapy of panic attacks.

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