An innovative technology for natural raw materials processing and phytocomplex production of a functional purpose

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Abstract. The main consumer vector of the food sector is positioned with functional products. Issues of providing the body with a complete, balanced diet are the determining factor in the formation of human health. Addressing women’s health issues is of particular relevance in the social policy of the state, since the health and development of the future generation as a whole depends on women’s health. The science-based prescription formula and innovative technology of the biologically active complex in the form of dietary supplements on a plant-based basis have been developed. Clinical trials on a representative group of women with premenstrual syndrome, conducted as evidence of its effectiveness. The developed phytocomplex contains synergistically active ingredients for nutritive and metabolic support of the female body during the period of hormonal imbalance. Phytoestrogens contained in herbal ingredients stimulate tissue receptors during menopause, triggering a response aimed at normalizing impaired functions. An innovative method of matrix tableting in the manufacture of dietary supplements provides a prolonged effect of biologically active substances with adjustable speed. The article shows that the developed form of dietary supplements is an effective treatment for premenstrual syndrome. In combination with the psychotropic drug Grandoxin, the dietary supplement leads to a significant improvement in all indicators of psychological testing, namely a decrease in the degree of depression, reactive anxiety, and a significant decrease in the indices of vegetative disturbances. Joint therapy has a more pronounced therapeutic effect. It completely suppresses or weakens the clinical manifestations of premenstrual syndrome. The developed formula of dietary supplement is well tolerated by patients and does not cause any side effects.

1. Introduction
The need of the contemporary market for healthy foods determines the need to develop innovative technologies for the processing of agricultural raw materials. The development of healthy food products is one of the key areas of contemporary nutrition. Threpsology is the science of nutrition for a healthy and sick person [1]. The basis of the production of such products is the use of centuries-old experience of scientific and traditional medicine [2]. Priority attention is paid to the development of specialized products, including dietary supplements, which are among the most effective and affordable methods of correcting nutrition and health, occupy an important place [3].

The development of new forms of specialized products with a direct influence on the maintenance of women’s health is of particular relevance. A person’s health and longevity are determined by balanced, wholesome nutrition of a woman during periods before pregnancy, pregnancy and lactation [4].
Today, food ingredients that have a direct effect on the metabolic processes of the female body are sufficiently studied [5], [6]. Their role in the correction of metabolic disorders and discomfort in different periods of life, especially in adolescence and menopausal periods, is studied.

2. Materials and Methods

Raw materials, semi-finished products, and prepared dietary supplements were used as materials. Generally available and special methods of researching the quality, safety of raw materials and finished products, their effectiveness and functional orientation were used.

Clinical studies were conducted on a representative group consisting of 108 patients with a premenstrual syndrome. The main group consisted of 54 patients aged 30-42 years who received supplements of 2 tablets per day with meals, in combination with the vegetotropic drug Grandoxin 50 mg 3 times a day. The control group took only Grandoxin in the specified amount. Patients were examined for all psychological test scores (Beck test depression, Spielberger test reactivity were studied). All patients were examined gynecologically, organic lesions of the female genitalia were excluded, an ultrasound examination of the abdominal organs, an ECG were performed. Field tests were performed at the General Surgery Clinic of the Siberian State Medical University (Tomsk, Russia) under the guidance of Doctor of Medical Sciences, Professor O. S. Popov. Our research was approved by the Committee on Human Ethics.

3. Research Results

The qualitative and quantitative composition of the prescription formula of a specialized product, based on the characteristics of raw ingredients and their active principles, is scientifically substantiated. Innovative dietary supplements tableting technology was developed. Clinical trials of dietary supplements were carried out to find evidence speaking in favor of effectiveness and functional orientation of the developed product.

3.1 Recipe

Formulation of innovative phyto formulas in the form of dietary supplements has been developed. Its ingredients exhibit synergistic properties in relation to the correction of metabolic disorders during periods of the menstrual cycle, preparation for pregnancy, various infectious and somatic diseases, and menopause. The composition of 1 tablet weighing 500 mg includes (mg): calcium carbonate - 100; Vitamin Premix - 49.2, which also includes vitamins (vitamin B3 - 3, vitamin B2 - 0.4, vitamin E - 2.75, vitamin A - 0.37, vitamin B5 - 2.1, vitamin D3 - 0.0025, vitamin B6–0.5, vitamin B1 - 0.5, vitamin H - 0.05, vitamin B12 - 0.00009); hops (cones) - 27.5; sodium ascorbate - 28.1 (vitamin C - 25); zinc oxide - 3.75 (zinc - 3); magnesium oxide - 25; manganese aspartate - 3.5 (manganese - 0.48); potassium iodate - 0.0625 (iodine - 0.037); sodium selenite - 0.0375 (selenium - 0.0171); chromium picolinate - 0.1 (chromium - 0.012); Alfalfa (herb) - 25; repyashok agrimony (herb) - 25; choline bitartrate - 15; inositol - 15; Angelica Sinensis - 15; potassium chloride - 10; iron sulfate - 10 (iron - 3.7); magnolavine (fruits) - 7.5; blessed thistle - 7.5; Damiana - 7.5; silicon dioxide - 5; lecithin - 5; lemon bioflavonoids of lemon - 5; bromelain - 5; L-cysteine - 4; L-methionine - 4; sublimated garlic - 4; ginseng (root) - 4; Cayenne pepper - 4; Ginkgo biloba extract - 2.5; para-aminobenzoic acid - 1.65; gammadinoic acid - 1.5; octacosanol - 1; royal jelly - 1.

3.2 Production technology

The production technology consists of the following successive stages.:  

- **Raw material preparation.** Grinding of plant materials in a hammer mill, disinfection on the installation of the fluidized bed, sieved through a sieve with a mesh size of 1 mm is carried out;

- **Preparation of the mixture for granulation.** Joint dosing and pre-mixing of prescription ingredients with 1.5 kg of MCC M 12 (microcrystalline cellulose) occurs.

Then we proceed with sifting the mixture through a vibrating screen with a hole diameter of 1 mm,
grinding in a hammer mill, re-mixing occurs. Lumps and foreign inclusions should not be mixed. Mixing is carried out in a V-shaped mixer at the rate of 100 kg per 1 hour. The mixture homogeneity is checked by pressing the pestle on the surface; in this case, lumps and foreign inclusions should not be observed.

- **Preparation of wet and dry granules (extrusion).** For wet mixture granulation, a humidifier, namely 5% starch paste in the amount of 25%, is used. Granulation is performed on a horizontal granulator (extruder) press machine. The color uniformity of each granulate is checked, after which it is sent for drying with a temperature of the drying cabinet (65 ± 5 °C) to a residual moisture content of 4-6%.

- **Preparation of powder mixture.** Preparation is carried out by joint dosing of components. Sifting the powder mixture through a 1-mm vibrating screen, grinding in a hammer mill and re-sieving to avoid lumps and foreign inclusions is carried out. Mixing components is done in a V-shaped mixer for 1 hour at the rate of 100 kg of the mixture. Checking uniformity, the presence of lumps and foreign inclusions is done by pressing a pestle on the surface of the mixture.

- **Getting a mixture for tableting.** Dusting mixture and regranulate are placed in a V-shaped mixer and stirred at the rate of 100 kg per 1 hour. Quality control is carried out in accordance with the requirements of technical documentation by sending it to a testing laboratory.

- **Tabletting and dusting.** The mixture tableting takes place on a rotary tablet machine brand. The process is followed by controlling an average weight of the tablets every 30 minutes by weighing 20 tablets and individual specimens, weighing a similar amount. Deviations should not exceed ± 5%. The appearance is checked every 60 minutes by analyzing 10 tablets (the surface should be smooth and durable in the absence of dimples and sticking, chips, hillocks and lamination. Finished tablets are dedusted).

- **Film coating.** Suspension of dry film coating mixture is being prepared. For this purpose, the calculated amount of water were charged to the reactor-homogenizer and small portions, while running the stirrer, dry film coating mixture is added (stirred for 15 min), then it is homogenized for 10 minutes and filtered through a nylon filter with holes 0.315-0.45 mm. The reactor-homogenizer is connected to the installation for applying a film coating and spraying up to a mass of film coating of 3.5%; the weight of half-product is produced. The shelf life of the film coating solution is 24 hours at 20–25 °C and 7 days at 4–6 °C.

- **Evaluation of appearance and quality.** Examination of the finished product in appearance, its transfer to the testing laboratory for compliance with the technical documentation requirements. After receiving the research report, the finished product is placed in a container with the name, batch number, date of manufacture, operator signature on the label.

- **Packing, packaging, and storage.** 3 product packages are sent to a collection of arbitration samples. Packing and packaging is carried out according to the documented procedure.

### 3.3 Clinical trials

As a result of monitoring patients with premenstrual syndrome, improvement in clinical well-being was observed in the treatment process from the third day (namely, sleep improved, and irritability, tearfulness decreased, aggressiveness and headaches decreased), heart pain, fainting, hot flashes were absent, blood pressure returned to normal, dizziness decreased significantly. Tolerability of complex therapy was good; no side effects were noted.

Table 1 presents the dynamics of subjective and objective symptoms in patients with premenstrual syndrome of the main group and the control group. The data in Table 1 indicate that the dynamics of subjective indicators was more pronounced and reliable in the main group than in the control group.

In the subjects of the main group, the frequency of complaints on weakness, fatigue, irritability decreased in 5 times; while dizziness, anorexia, headache decreased in more than 5 times. In single patients of the main group, migraine-like pain was noted, “hot” flashes significantly decreased. Analyzing the objective symptoms of patients in this group, we noted a significant decrease in the number of patients with high blood pressure, pulse lability, and subfebrile conditions.
Table 1. Dynamics of subjective and objective symptoms in patients with premenstrual syndrome of the main and control groups.

| Complaints                        | Group 1 (main) | | Group 2 (control) | | |
|-----------------------------------|---------------|---|-------------------|---|
|                                   | After treatment | % | After treatment | % | After treatment | % | After treatment | % |
| Weakness, fatigue                 | 54            | 100| 10               | 20 | 54            | 100| 20               | 40 |
| Excessive sweating                | 53            | 98 | 8                | 15 | 53            | 98 | 16               | 30 |
| Bulimia                           | 10            | 20 | -                | -  | 5             | 10 | -                | -  |
| Anorexia                          | 20            | 48 | 2                | 4  | 20            | 48 | 10               | 20 |
| Headache                          | 54            | 100| 10               | 20 | 54            | 100| 22               | 50 |
| Migraine-type headache            | 10            | 20 | 1                | 2  | 8             | 18 | 4                | 9  |
| Dizziness                         | 54            | 100| 8                | 15 | 54            | 100| 27               | 50 |
| Heart pain (cardialgia)           | 25            | 48 | 10               | 20 | 25            | 48 | 15               | 30 |
| Blood pressure (increase)         | 20            | 40 | 5                | 9  | 25            | 48 | 15               | 18 |
| “Hot” flashes                     | 40            | 80 | 10               | 20 | 35            | 70 | 18               | 35 |
| Numbness of the arms and legs     | 27            | 50 | 5                | 9  | 20            | 40 | 10               | 20 |
| Pulse lability                    | 20            | 40 | 10               | 20 | 25            | 48 | 12               | 24 |
| Increased libido                  | 10            | 20 | 1                | 2  | 8             | 18 | 4                | 9  |
| Low libido                        | 20            | 40 | 5                | 9  | 10            | 20 | 8                | 15 |
| Subfebrile condition              | 25            | 45 | 5                | 9  | 20            | 40 | 10               | 20 |
| Depression                        | 20            | 40 | 8                | 15 | 10            | 20 | 8                | 18 |

4. Discussion

The functional orientation of a specialized product is associated with the implementation of the physiological functions of phytoestrogens contained in extracts of ginseng, Damiana, Angelica Sinensis and hops.

Phytoestrogens are similar in chemical structure to estrogens; therefore, they are physiologically accessible to receptors in the body of women, thus playing an important role in correcting premenstrual syndrome. Phytohormones increase anti-stress function, affects the endocrine system, inducing the synthesis of its own estrogens, namely progesterone. In turn, the normalization of progesterone levels smoothes the symptoms of premenstrual syndrome, providing good physiological and psychological well-being.

During menopause, phytoestrogens provide a balance of calcium in bones, lower cholesterol levels. Separate properties of phytoestrogens provide a balance between excitation and inhibition of the nervous system, positively affecting the emotional state of a woman.

Included in the dietary supplements vitamins, minerals and amino acids control the normal level of
metabolism in the female body. In general, research results confirm these conclusions.

The innovativeness of technological solutions lies in the production of matrix tablet forms, a feature of which is the presence in the tablet of three types of granules with active substances that are released in the gastrointestinal tract in a certain order. Such a system is characterized by a prolonged nature of targeted release of biologically active substances with adjustable speed.

5. Conclusion

The use of dietary supplements in complex treatment in patients with premenstrual syndrome leads to clinical improvement of vegetative functions and all indicators of psychological testing. No side effects were noted, good tolerance to diet therapy is shown. Dietary supplements can be recommended in the complex treatment of premenstrual syndrome within a month. According to the doctor’s prescription, a further administration of the biocomplex is possible for 2-3 months in a maintenance dose, namely, 1 tablet per day.

The technology was tested at the “Art Life” enterprises, with the inclusion of dietary supplements in the Federal Register of the Russian Federation and the organization of mass production. The stability of the quality characteristics and competitiveness of a specialized product are guaranteed by the implementation of the System of Management in accordance with the standards of the ISO 9001, 22000 series and GMP rules.

6. Acknowledgment

The authors are grateful to the technology corpus of the company “Art Life” and the Department of General Surgery of the Siberian State Medical University for their advice and assistance in the work.

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