Biologically active plant-based mixture for the prevention and complex treatment of bronchopulmonary pathology

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Abstract. The characteristics of the starting material and its active principles are given, which made it possible to scientifically substantiate the qualitative and quantitative composition of the prescription formula of a new specialized product. It is presented in the following biologically active additive form with directed functional properties, mg per one 0.6 g capsule: hydroxyl-cinnamic acids (kaftaric, chlorogenic, chicory), not less than 1.5; vitamin C – 60; rutine – 30; glycyrrhizic acid, not less than 2; zinc – 2.5; selenium – 0.0065. The hygienic quality of the developed product is shown, following regulated indicators of nutritional value defining its functional orientation are determined, mg/1 capsule: rutin – 30 (24-36); ascorbic acid – 60 (48-72); zinc – 2.5 (2.0 – 3.0); hydroxycinnamic acids, not less than 1.5; glycyrrhizic acid – 2.0. The regulated production parameters, which ensure the preservation of biologically active components of the formulation, are determined. The use of gelatin capsules allows combining prescription ingredients, protecting the contents from the effects of adverse factors, providing the necessary delivery speed to the target cell and localizing the action. Clinical trials of the effectiveness and functional properties of the developed product have been carried out by including it in the diet of children with acute respiratory diseases, such as bronchitis and pneumonia. The prescription of diet therapy provided an earlier return to normal life, cough and wheezing, swelling and hyperemia of the nasopharynx stopped faster. Research materials indicate the activation of immunity, increasing the body's resistance to infection. The results obtained indicate the advisability of including the phytocomplex in the complex therapy of considered patients, and also using it as a prophylactic for weakened children.

1. Introduction
The processing of raw materials aimed at the production of safe and healthy food is one of the main development directions of the food and processing industry. This area seems important not only from the standpoint of ensuring food security, but also preserving the health of the population [1,2,5]. This is especially important for specialized products, including biologically active food additives, which play an important role in correcting the nutrition and preventing common diseases, as evidenced by the results of numerous domestic and foreign studies [3,4]. Among the common pathologies, respiratory diseases clock in at one of the first places. Almost everyone and especially children suffer bronchopulmonary pathology annually [5-16]. This problem is exacerbated by an immunity decrease and the development of chronic immunodeficiency. Deterioration of the ecological situation of the environment (quality of water, food products, air composition, etc.) also adversely affects the health status. At the same time, frequent use of chemotherapy is undesirable, especially for children and the...
elderly. In this regard, developing the new types of specialized products, studying their effectiveness and functional orientation is relevant and timely.

2. Goal of research
Developing and defining the indicators of quality, effectiveness and functional orientation of a biologically active additive for treatment of children respiratory diseases in the acuity, as well as in the period of decaying exacerbation and as a factor in the prevention of bronchopulmonary pathology.

3. Research tasks
- to develop the recipe and production technology of a new specialized product in the form of a biologically active additive;
- to establish regulated quality indicators, including nutritional value, determining the functional properties of a biologically active additive;
- to conduct general clinical and radiological studies to confirm the diagnosis of children with bronchopulmonary diseases;
- to study the symptoms duration for acute respiratory diseases of children of different ages while taking a biologically active supplement and using traditional treatment.

4. Materials and methods
Extracts of plant materials – licorice root and echinacea, vitamins and minerals with synergistic functional properties, as well as laboratory and experimental samples of a specialized product were used as materials and objects of research.

Microbiological indicators were determined according to the requirements of current regulatory documents. Toxic metals and zinc were determined using a Varian 220A atomic absorption spectrometer, rutin was determined by UV spectrometry, the content of vitamin C, glycyrhizic acid and hydroxycinnamic acids (caftric, chlorogenic, chicory) by using liquid chromatography on a WatersW2996 chromatograph.

Effectiveness and functional orientation studies of the biologically active supplement were carried out with the participation of 20 patients of different ages and sex, 10 of them were inpatient and 10 in outpatient treatment.

Children in the hospital were distributed by age as follows: 3-7 years - 8 children; older than 7 years - 2 children.

Outpatient treatment was carried out in age groups: 1-3 years - 2 children; 3-7 years - 2 children; 7-14 years old - 6 children.

Eighteen of the 20 patients observed belonged to the group of frequently ill children, 9 had acute respiratory diseases, 3 were patients with bronchitis, 4 were patients in the midst of pneumonia, 4 patients had residual effects after diseases of the bronchopulmonary system.

The data of a general clinical examination (blood and urine tests) and radiological materials were studied in order to confirm the diagnosis.

The control group consisted of 20 children with a similar pathology at the same age. A specialized product was prescribed for all children in the experimental group simultaneously with other medications and physiotherapy procedures traditionally used in this pathology.

The amount of biologically active additives prescribed to children 1-3 years old is 1:2 capsules 2 times a day, 1 capsule 2 times a day for 3-7 years old children, 1 capsule 3 times a day for 7-14 years old. The treatment regimen took 10-14 days. A specialized product was included in the diet and taken at 15-20 minutes before a meal.
5. Results and discussion
Biochemical properties of the starting ingredients are considered, which served as the basis for the scientific substantiation of the qualitative and quantitative formulation composition of the developed product (Table 1).

Table 1. Phytocomplex recipe composition.

| No | Name of the ingredients                                      | Content, mg in one 0.6 g capsule |
|----|---------------------------------------------------------------|----------------------------------|
| 1  | Echinacea purpurea extract                                   | 60                               |
|    | Oxycinnamic acids (kaftaric, chlorogenic, chicory), not less  | 1.5                              |
| 2  | Vitamin C (ascorbic acid)                                    | 60                               |
| 3  | Rutin                                                         | 30                               |
| 4  | Licorice root extract                                        | 20                               |
|    | Glycyrrhizic acid, not less                                   | 2                                |
| 5  | Zinc Asparaginate                                             | 13.4                             |
| 6  | Zinc                                                          | 2.5                              |
| 7  | Sodium Selenite                                               | 0.014                            |
| 8  | Lactose (milk sugar)                                         | 282.5                            |
| 9  | Polyethylene oxide (carrier)                                 | 24.1                             |
| 10 | Gum arabic (thickener)                                        | 10                               |
|    | Gelatin capsule (gelatin, glycerin)                          | 100                              |

The synergistic functions of recipe components made it possible to determine the functional orientation of the dietary supplement. The plant extract complex has a coating, anti-inflammatory effect. The active ingredients of licorice have antimicrobial, antihistamine, expectorant, diaphoretic, analgesic and restorative effects. The active substances of echinacea extract increase the cell activity of the immune system and stimulate the production of interferon, activating the nonspecific protective forces of the body. Vitamin C and rutin reduce vascular permeability and increase the body's resistance to viral and bacterial infections.

The technological process includes the following main stages:

Preparation of raw materials. Zinc asparaginate and ascorbic acid are sieved through an SGS-30 vibrating screen with a screen opening of 1 mm. The screenings are ground with a hammer mill MM-10 and re-screened;

Preparation of the preproduct 1. The required amount of water is dosed into the homogenizing reactor. The masses of echinacea extract, licorice extract, and instantgam BA are weighed according to the recipe and slowly added into the homogenizer reactor in small portions with the stirrer operating, stirred for 15 minutes, and then homogenized for 10 minutes with the stirrer switched on and the weighed quantity of pellets is loaded. The homogenizing reactor is connected to the granulator and the process of applying the prepared suspension to the pellets begins. After the application process is completed, the finished granules are unloaded. The uniformity of the suspension and the appearance of the granules, which are sieved through a 2mm sieve, are checked;

Preparation of the preproduct 2. The first portion of water is dosed into the homogenizing reactor. The weighed amounts of ascorbic acid, rutin, zinc asparaginate and the SS substrate are slowly, in small portions, filled into the homogenizer reactor with the working stirrer and stirred for 15 minutes. Then they are homogenized for 10 minutes (stirrer is on). A weighted quantity of pellets is loaded into the granulator. After that, the homogenizing reactor is connected to the granulator and the process of
applying the suspension to the pellets begins. The homogenizer is disconnected from the granulator and a second portion of water is poured into it. The weighed amounts of sodium selenite and the SS substrate are slowly, in small portions, filled into the homogenizing reactor and stirred for 15 minutes with working stirrer. Then they are homogenized for 10 minutes (stirrer is on). The homogenizer reactor is reconnected to the granulator and the suspension is applied to the same pellets. After the application process is complete, the finished granules are discharged.

Obtaining a mixture for encapsulation. The required amount of preproducts number 1 and number 2 are weighted, then loaded into a V-shaped mixer at the rate of 100 kg – 1 hour. The finished mixture for encapsulation is transferred to the quality control department in order to check the compliance with the requirements of technical documentation;

Encapsulation and dust removal. The resulting mixture is encapsulated using a Zanasi 40E automatic capsule machine. During encapsulation, the average weight of the capsules is checked every 30 minutes by weighing 20 capsules and the weight of the individual capsules by weighing 20 capsules in turn. Deviations of the average mass and masses of individual capsules should not exceed ± 5% of that indicated in the manufacturing process card.

Every 60 minutes, the appearance of the capsules is checked by examining 10 capsules. There should be no dents, scuffs, chips or jamming of the edges of the lid and body of the capsule (the capsule should be smooth and even along the vertical axis). Finished capsules are placed in a deduster and the dedusting process is carried out.

Before packaging, the appearance of the preproduct is checked and an average sample is taken to the quality control department. Ready-made capsules are weighed, placed in a container with an indication of the intermediate product on the name, quantity, batch number, production date and then transferred to the prepacking and packaging stage. The shelf life of the suspension for application on pellets is 24 hours. The encapsulation mixture is stored for no more than 15 days. With longer storage, changes in technological characteristics are possible.

An important advantage of the developed technology is that hard gelatin capsules provide the possibility of combining several incompatible biologically active substances in one capsule. The presence of a gelatin shell makes it possible to protect the contents from adverse factors, provides speed and localization of action.

It seems reasonable to describe the technology for obtaining extracts, given the modification of the extraction process and its importance in the formation of consumer properties of the developed products.

The extraction process begins with the control of raw materials, their identification according to the requirements of technical documentation and consists of the following main steps:

Obtaining the liquid extraction. The raw materials are placed in maceration tanks in an even layer of 40-50 kg to each tank, gratings are installed on the raw material layer to prevent its ascent, then fixed with clamps and the heating of the heat jacket is turned on. Demineralized water and sodium bicarbonate dissolved in it are used as the extractant, which is 8% of the dry matter content. The water is preheated to a temperature of 95°C and fed into the storage tank. For the first filling, the ratio of extractant to raw materials is 1:13, taking into account the absorption coefficient of the extracted raw materials, for the second filling the ratio is 1:10. The extraction time is 4 hours for each filling. The volume of extractant is controlled using a SGVK-15 "Agidel" counter. The resulting extract is pumped into distribution tanks. Control at the stage of obtaining liquid extraction is carried out by matching the name, quantity and series of raw materials to the process card taking into account the extraction time;

Condensing the liquid extract. The process is carried out in a vacuum-evaporator installation (VEI). The extract is continuously fed into the VEI using a vacuum. At the same time, the level of evaporated liquid should be at a height of not more than 10 cm from the upper edge of the boiling pipes, which is associated with the uniform VEI operation and less drop entrainment. It is necessary to monitor the readings of the vacuum gauges and the evaporation temperature when condensing the extract. The extract, concentrated to a solids content of at least 20%, is drained, filtered through a sieve into clean
tanks, weighed, labeled and fed to the drying area in a period not exceeding 24 hours with dry extract storage temperature of 5°C;

Obtaining the dry extract by spray drying. The drying and preheating temperature of the spray dryer is 90-95°C. After drying and blowing the dryer, the dry extract is unloaded and goes to the prepacking, packaging and labeling.

Adjustable technological parameters of production play an important role in shaping the quality characteristics of the products being developed.

Organoleptic, physico-chemical and microbiological studies of quality and safety during production and storage periods were carried out. The product was stored in a dry, dark place at a temperature of no higher than 25°C for 39 months.

Sanitary-hygienic and sanitary-toxicological safety indicators were determined after termination of considered period. The indicators correspond to the established standards.

Organoleptic characteristics, such as appearance, color, taste and smell were in accordance with the requirements of technical documentation. The content of vitamin C in one capsule was 55.3 ± 5.53, rutin – 32.1 ± 3, zinc – 2.6 ± 0.6, glycyrrhizic acid – 2.6 ± 0.3, hydroxycinnamic acids – 2.4 ± 0.24. Further storage should be considered inappropriate due to the appearance of extraneous taste. The materials obtained made it possible to establish regulated quality indicators, including nutritional value (Table 2).

Table 2. Regulated quality indicators of a specialized product.

| Indicator name          | Contents                                                                 |
|-------------------------|--------------------------------------------------------------------------|
| Appearance, color        | gelatin capsules containing yellow and brown pellets                      |
| Taste and smell          | Peculiar                                                                  |
| The average mass of capsules, mg | 600 (540 - 660)                                                          |
| The content of rutin, mg, in 1 capsule | 30 (24 - 36)                                                              |
| The content of vitamin C, mg, in 1 capsule | 60 (48 - 72)                                                              |
| The content of zinc, mg, in 1 capsule | 2.5 (2.0 – 3.0)                                                           |
| The content of oxycinnamic acids (kaftaric, chlorogenic, chicory), mg, in 1 capsule, not less than | 1.5                                                                        |
| Glycyrrhizic acid content, mg, in 1 capsule, not less than | 2.0                                                                        |

Shelf life is 3 years under the above-mentioned conditions with the necessary margin of 3 months.

The effectiveness and functional properties of the product have been proven in clinical trials by including a specialized product in the diet of frequently ill children with acute respiratory infections, bronchitis and pneumonia.

The effectiveness of diet therapy has been established already after 3-4 days from the start. All children showed normalization of well-being and positive dynamics in the manifestation of clinical signs of diseases. Catarrhal signs from the nasopharynx decreased, cough became less and more productive, wheezing in the lungs disappeared. On the 14th day after taking the biologically active supplement, an improvement in the clinical picture was noted both in the group of younger and older
children compared with the indicators of children in the control group (Fig. 1.2).

**Fig. 1.** The symptoms duration of acute respiratory diseases for 3-7 years old children while taking a biologically active supplement (BAS), days.

**Fig. 2.** The symptoms duration of acute respiratory diseases for 7-14 years old children while taking a biologically active supplement (BAS), days.
The prescription of a biologically active complex reduced the acute phase course of acute respiratory diseases due to activation of the immune system and a decrease in the clinical signs of the disease. Nasopharynx edema averagely stops 1.5 times faster than in the control group. As an effect of a biologically active supplement, cough stops by 17.21% faster, wheezing disappears by 21.38% faster, which indicates an increase in resistance and accelerated elimination of infection from the body while taking a biologically active supplement.

The tested product helps to increase the effectiveness of drug therapy, has a mild anti-inflammatory, antioxidant, adaptogenic and immunomodulatory effects.

Children in the control group received traditional treatment. It was noted that the positive effect for children taking the dietary supplement was more pronounced and earlier than for children who were on standard treatment. Especially noticeable was the significantly early disappearance of asthenia signs.

Children who received a biologically active supplement returned to normal life earlier, which allows recommending the developed product for treating the acute and chronic respiratory diseases, as well as for preventing the pathology of any localization.

Particular attention when considering infectious diseases of various etiologies is given to the immunomodulating properties of diet therapy. The most effective in this regard is Echinacea purpurea, which is part of a biologically active supplement. Polysaccharides have the most stimulating effect on immunity among all the chemical compounds of Echinacea, especially those with high molecular weight. The polysaccharide complex is capable of activating histogenic and hematogenous phagocytes, macrophages, enhancing the production of interferon, suppressing the allergic effect, increasing the number and activity of T-suppressors. Moreover, polysaccharides, together with flavonoids, potentiate the immunostimulating effect of each other. In addition to polysaccharides, chicory acid possesses immunomodulating properties, as well as other hydrophilic substances such as glycoproteins, alkaloids – betains and saponins, which stimulate the phagocytic activity of granulocytes and macrophages. Thus, the biologically active components of echinacea activate all parts of the immune response, potentiate the production of interleukin-1 by macrophages, induce the transformation of B-lymphocytes into plasma cells. They enhance antibody formation, cooperation of B- and T-lymphocytes, T-helper activity, have a pronounced anti-inflammatory effect, similar to the protective effect of the hormone - cortisone, which allows the body to cope with inflammatory and immune diseases.

6. Conclusions
The results indicate the advisability of including dietary supplements in the complex therapy of children with respiratory diseases, as well as the prevention of diseases for weakened children. A clinical effectiveness study of dietary supplements in children with pathology of the respiratory system showed good tolerance to the supplement, the absence of side effects, the rapid dynamics of the disease clinical symptoms when used.

The product has been tested and manufactured at enterprises certified in accordance with the requirements of international standards of the ISO 9001, 22000 series and GMP rules, which ensures stability of quality characteristics and competitiveness.

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