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# Echinacea-Based Juice Processing and Study of its Quality Indicators

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**Abstract:- One of thepressing issues facing the sciencetists of pharmacy field in medicine is the preparation of complex syrups rich in a of biologically active substances for the treatment of the immune system diseases.**

**In recent years, Echinacea-based drugs have been successfully used in the immune system regulation. Especially in pediatric practice, Echinacea-based syrups are used as an optimal medicine. These remedy forms, namely syrups, are characterized by a high rate of absorption and excretionof the drug, affordability, painless administration and accurate dosing.**

**At present, the main taste regulated oral liquid medicines are syrups. Taking into account the expected advantages of Echinacea syrup, we decided to conduct research in this field.We have developed a formula for obtaining a drug rich in healing substances based on Echinacea using the following technology. First, echinacea roots were crushed and its extract obtained. Then the required amount of extractant was prepared in two versions: sucrose(saccharose ) solution and separately - sorbitol solution. The required amount of Echinacea extract was kept in a solution of saccharose and sorbitol. This allowed us to obtain 2 kind of syrups simultaneously: one for consumption by wide population (saccharose-based), the other one - sorbitol-based syrup for patients with glucose intolerance. The standardization indicators of both syrups, determined according to the State Pharmacopoeia, corresponded to the required standards.**

***Keywords:-*** *Echinacea, infection, syrup, technology.*

## I. INTRODUCTION

### *A. Echinacea medications in use in medicine*

*Echinacea*is a favorite remedy in homeopathy. The Indians living in America knew the healing features of *Echinacea* 100 years agoand called *Echinacea* plant "miracle flower", "sunset" and "precious flower". Homeopaths have established that its effect on the body is individual. This plant acts as an immunomodulator and is mainly used as an anti-cold remedy due to its anti-inflammatory components, *Echinacea* is a candidate agent for immunomodulation in the prevention and treatment of COVID-19 [1].Classical homeopaths used this plant both in microdoses and in higher concentrations after poisonous insect bites, as well as in pyoinflammatory processes. Echinacea may be used in homeopathy in blood infectious diseases, gangrene, and with skin purulent-inflammatory diseases as well. According to homeopaths, this plant exhibits the delectable effect in appendicitis, even peritonitis, releasing more pus from the body and draining it further into the abdominal cavity [2]. Echinacea has a wide spectrum of activity, due to which it is widely used in medicine for the treatment of infections of the upper respiratory tract and the common cold [3, 4]. Echinacea normalizes the restraint stress-induced reduction in splenic natural killer cell activity, as well as regulates the B-cells activity, increases the secretion of interleukins and shows the antifungal effect. Echinacea treatment increases the leanage of CD4+ and CD8+ T lymphocytes and restores serum cytokine levels, including interleukin-6 (IL-6), interleukin-10 (IL-10), and interleukin-17 (IL-17) [5]. Dapas B. et al revealed the up-regulation of IL-2 and IL- 8 mRNA levelsand the down regulation of the mRNA levels of the pro-inflammatory cytokines TNF-α and IL6 in lympho-monocytes under 10 ml of Echinacea syrup containing 100 mg of extract administered once a day for one month [6].Echinacea does not disrupt metabolism; reported side effects are generally minor, including stomach upset, nausea, and dizziness [7].*Echinacea*comprises the water-soluble immunostimulatory polysaccharides [8](4-O-methylglucuronyl arabinoxylans, arabino-galactans); the essential oils including borneol, bornyl-acetate, pentadeca-

8-en-2-on, germacrene D, caryophyllene epoxide; flavonoids (ferulic acid and its derivatives, methyl ester of chicory acid, 2-O-caffeoyl-3-O-feruloyl-tartaric acid, 2,3-O-diferuloyl tartaric acid, 2-O-caffeoyl tartaric acid); alkamides [5, 9]. Alkamides have been shown to possess stimulatory effects on phagocytosis due to which they are widely used for common colds [10].The scientists offer it as a potential of antioxidant and antibacterial agent in foods [11]. The antiinflammatory compounds of *Echinacea purpurea*were identified to inhibit prostaglandin E(2) production differed from other Echinacea species (*E. angustifolia, E. pallida, and E. Simulate*) involved in the transient receptor potential vanilloid 1 (TRPV1) receptor activation [12].

Below, the names of a number Echinacea-based drugs prepared, their effects, instructions for the preparation and use are presented.

One of the widely used Echinacea medicinals are prostanorm tablets. A tablet contains st. john's wort herb, Centaurium umbellatum, licorice root, dry extract of *Echinacea Purpurea*root and tubers - 0.2 g.These tablets exhibit androgenic, anti-inflammatory, analgesic effectsand normalize diuresis. They havealso a bacteriostatic effect on gram-positive pathogen bacteria of Staphylococcus and Streptococcus strain[13]. A drug is effective when taken 1-2 tablets 3 times a day 30 minutes before meals or 40 minutes after, with the course of treatment 6-7 days.

Echinacea is also included in the plant collections used for joint pain, dysbacteriosis, alcoholic liver disease. For example, Jiang W et al state that *Echinacea purpurea* polysaccharides 80 provides effective supplementary support in preventing and treating alcoholic liver disease [14]. The following collections are used in the treatment of prostatitis, cystitis, inflammation of the urinary tract, urethritis: *Echinacea purpurea* root - 4 parts, broom grass ( *Thysanolaena* )- 1 part, black poplar (*Populus nigra*) shoots - 1 part, yarrow grass - 1 part, buckwheat birch grass - 2 parts, Coltsfoot (*Tussilago farfara*) leaves - parts, rosehip fruits- 3 parts[15, 16]

The remedy is prepared ex tempore, for which2 tablespoons of theseplants mixture are poured with water cup and boiled on low heat for 5 minutes, then kept for 4 hours. Taking 50 ml 3 times a day 30 minutes before meals exhibit healing effect.

Echinacea infusions also have a healing effect[17]. For preparation of infusion, a tablespoon of dry leaves, flowers and sprigs of *Echinacea* are pouredwith 0.5 liters of boiling water and incubate for 1 night in a thermos. 100-150 ml of infusion 3 times a day 30 minutes before meals helps to strengthen immunity. It is necessary to follow instructions for treatment course and take an Exinase infusion for 10 days with next5 days of break. After that, it is recommended to take 10 days of infusion and have another 5 days for break. If necessary, the treatment course may be repeated 3 times. Preparation of *Echinacea* is indispensable in the treatment of influenza. However, more often it is used for gastrointestinal diseases, including gastritis. This remedy eliminates headaches and improves appetite [14]. To prepare a fresh *Echinacea* preparation, a tablespoon of dry echinacea leaves in enamel bowl are poured with a cup of boiling water, soaked in a water bath for 15-20 minutes, and cooled. 1/3 cup 3 times a day before meals for 10 days removes pain symptoms in the body. After a 5-day break, the preparation should be takenanother 10 days; repeat this at least 2-3 times to complete a course of treatment.Echinacea oilis also used medicinally: root and leaf of *Echinacea* species contain volatile oils non-toxic that demonstrate significant anti-inflammatory and analgesic activities [18]; it is effective in the treatment of bronchitis, cervical erosion, trophic ulcers, tonsillitis [4]. For Echinacea oil preparation, 0.5 kg of freshly collected, washed and crushed *Echinacea*roots pour with 2.5 liters of unrefined vegetable oil and keep for 40 days; then filter through certain layers of cheesecloth.A tablespoon of Echinacea oil3 times a day 2 hours after meals is usedwith high efficacy for the treatment of tonsillitis and externally externally as the compresses.With sea buckthorn oil, it is effective in the gastric and duodenal ulcers in a 1: 1 ratio when used 2 tablespoons at bedtime for 7-10 days.

Echinacea also shows a good effect on general weakness. But increasing the plant dose causes a burning sensation in the mouth.The next widely used in medicine Echinacea-based remedy is Immunal, the international nameof wich is "*Echinacea Purpurea* juice" (*Echinaceae purpurae* herbae succus). It is aa concentrated *Echinacea Purpurea* extract referred to as immunostimulating agent. It contains 0.8 ml *Echinacea Purpurea* flowers juice in 1mlof 20% ethanol.This remedy also contains sorbitol 70% aqueous solution, less commonly known as a sugar alcohol glucitol, D-1,2,3,4,5,6-hexanehexol, which is a sweet, slightly yellowish liquid used in drugs as a flavoring agent, or plasticizer [19]. It is a white crystalline substance highly soluble in water and poorly soluble in alcohol found in seaweed, rowan (Sorbus aucuparia), plums, and starchy fruits. As for the pharmacological effect, this drug, as all rest Echinacea drugs, belongs to the family of herbal immunostimulants. The main active ingredients are caffeic acid derivatives (chicory acid and its esters) and polysaccharides (4-O-methyl-glucuron-arabinoxylan and arbino-rhamno-galactan) of *Echinacea Purpurea*enhancing thenon-specific protection of the organism.

Due to caffeic acid derivatives of *Echinacea Purpurea* in the "İmmunal" drug, it destroys herpes and influenza viruses. Thus, the main mechanism of biologically active substances action in the preparation is as follows: the drug regulates the phagocytic activity of granulocytes and macrophages, as well as increases the number of lymphocytes in the human body, thereby destroying microorganisms.This drug increases the number of granulocytes, as well as activates the reductoendothelial system of the liver[20]. İt regulates the synthesis of T-lymphocytes and granulocytes, increases the activity of T-suppressors;regulates the synthesis of interferon. Due to all the effects mentioned above, it an antiviral, antibacterial and antifungal activities [21]. Active substances of a polysaccharide nature regulate cerebral circulation.Side effects of this medication include allergic reactions, skin rash, redness, swelling of the face, bronchospasm, dizziness, arterial hypotension. Thereat, this drug is contraindicated

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inthe tuberculosis, leukemia, collagenosis and other autoimmune diseases, multiple sclerosis, AIDS; with individual sensitivity to the components of the drug "Immunal", it is also not recommended.

Despite such a variety of drugs, there is an urgent need to develop easily digestible, quickly absorbed, not requiring a long time to prepare dosage forms from valuable medicinal raw materials in our fast-paced time. Undoubtedly, syrups are such forms, since they are easily digestible, well tolerated by both adults and children, easily dosed and exhibit an effect almost instantly[22]. For this reason, we have developed 2 syrups and tested their effects on volunteers before introducing them into manufacture[23].

## II. ECHİNACEA SYRUP PREPARATİON

### *A. Materials and methods*

For this, two syrups with *Echinacea* components were prepared in the Pharmaceutical Technology, Management and Economics Department laboratory.

| **100 ml of *Echinacea* syrup, composition I (for general population)** | **100 ml of *Echinacea* syrup, composition II (for diabetic patients)** |
|---|---|
| *Echinacea extract5,0* g<br>Sugar syrup 95 g | *Echinacea extract5,0* g<br>Sorbitol syrup 95 |

a) The technological process consists of the following steps:
First, obtaining *Echinacea* extract, preparation of sugar and sorbitol syrups, then mixing the echinacea extract with prepared syrups followed by filtration mixture to obtain a homogeneous mass, packaging and carrying out the quality standards of the resulting preparation.

b) Extractant preparation for obtaining Echinacea extract(maceration).
First,100 ml 5% *Echinacea* extract was obtained by the method of fractional maceration in a ratio of 1:5. We calculated the extractant required for extraction according to the formula V = V1 + PC, V = 100 + 20 x 2 = 140 ml. So, we need 140 ml of 40% extractant for extraction, i.e. to prepare 100 ml of Echinacea extract by fractional maceration in a ratio of 1:5, we first need to prepare 140 ml of a 40% extractant. We determine the amount of ethanol required for extraction using the formula:

$$X=V\cdot b/a =140\cdot 40/95=58,94 \text{ ml}$$

So, 58,94 ml of 95 % ethanol is required. Then we calculate the remaining amount of liquid (purified water) required to prepare 140 ml of 40% extractant. It is equal to 140-58.94 = 81.06 ml. Thus, we measured 58.94 ml of ethanol and 81.06 ml of distilled water into a beaker and stir.

c) Echinacea extract (maceration) receipt
Then, maceration is proceeded. To do this first, raw materials (20 g) were weighed on an analytical scale, put into a mortar and ground. For fractional maceration, the raw materials were put into 3 bottles in a ratio of 5:3:2.Thus, 10 g of raw materials were placed in the first flacon, 6 g in the second, and 4 g in the third, and closed. In the first flacon, 10 ml of 40% ethyl alcohol-based extractant was poured to 10 g of raw materials, mixed and kept for 4 hours, stirring constantly at ambient temperature with a closed neck. After completion of first step of the extraction process, another 40 ml of extragent was added to first flacon. Then the mixture was left for a day.

At next step, 10 ml of alcohol extractant was added to 6 g of raw materials in the second (II) flacon for maceration, and kept for a day. After that, the extract from flacon I (45 ml) was filtered into this container II and stored for a day. Then, a new portion of the extractant (30 ml) was added to the treated plant material remaining in the first flacon.

Then 10 ml of extractant was added to 4g of raw material in flacon III and kept for maceration for a day, after which the extract (50 ml) from flacon II was filtered into flacon III, and the extract from flacon I (30 ml) was filtered into flacon II. The first flacon was no longer used.

At next step, a new portion of alcohol extractant (20) ml was poured to the second flacon and kept for a day. After this period, this extract (50 ml) from flacon III is filtered into a receiver. The extract from flacon II (25 ml) is again filtered into III and stored for the day.

After these procedures, the second flacon also was no longer used.At the end of that day, the next extract from flacon III was also filtered into a receiver (30 ml) and a new 20 ml of extractant added to the remaining extract in flacon III and kept for 4-5 hours. After this time, the final extract from flacon III was filtered into a receiver and flacon III was no longer used.

Combined in the receiver *Echinacea*extracts in a volume of 100 ml have been stored at a temperature of 8-10°C for 3 days. After this time, the extract was filtered through a moistened paper filter to remove accompanying ballast, after which the volume was brought to the required (100 ml) with 95% ethanol. The dry residue in the extract should be 2.9% at an alcohol concentration of 40%.

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*B. Sucrose syrup preparation*

To prepare sugar syrup (Syrupus sacchari), 36 ml of purified water was poured into a mortar, the mortar placed in a water bath, heated to 60-70 ° C. Sorbitol of 64 g of was weighed on an electronic scale, added to water in parts into a mortar with constant stirring. The mixture boiled for 5 minutes, then filtered through 3 layers of gauze. The resulting syrup is a light yellow transparent thick liquid.

*C. Sorbitol Syrup preparation*

The technological operation for sorbitol syrup preparation carried out similarly to that described above. First, 36 ml of purified water was poured into the mortar, and placed in a water bath, heated to 60-70°C. Then, 64 g of sorbitol was weighed on an electronic scale, added to that water in parts, continuously stirring, boiled for 5 minutes, then filtered into a beaker through a three-layer gauze. The resulting mixture was a clear viscous liquid.

At the next stage, sugar syrup was measured into a beaker of 95 ml, added 5% of Echinacea extract and mixed. Then the syrup was filtered into a sterile orange flacon, capped, and stored protected from light at room temperature. The product is a yellow transparent solution with a specific odor – this is a composition I.

Then 95 ml of sorbitol syrup was poured into a beaker, added 5% of Echinacea extract and mixed. The syrup was filtered into a sterile orange flacon, capped, and stored in protected from light place at room temperature.The resulting product is transparent liquid with a golden yellow color and a specific smell – this is a composition II.

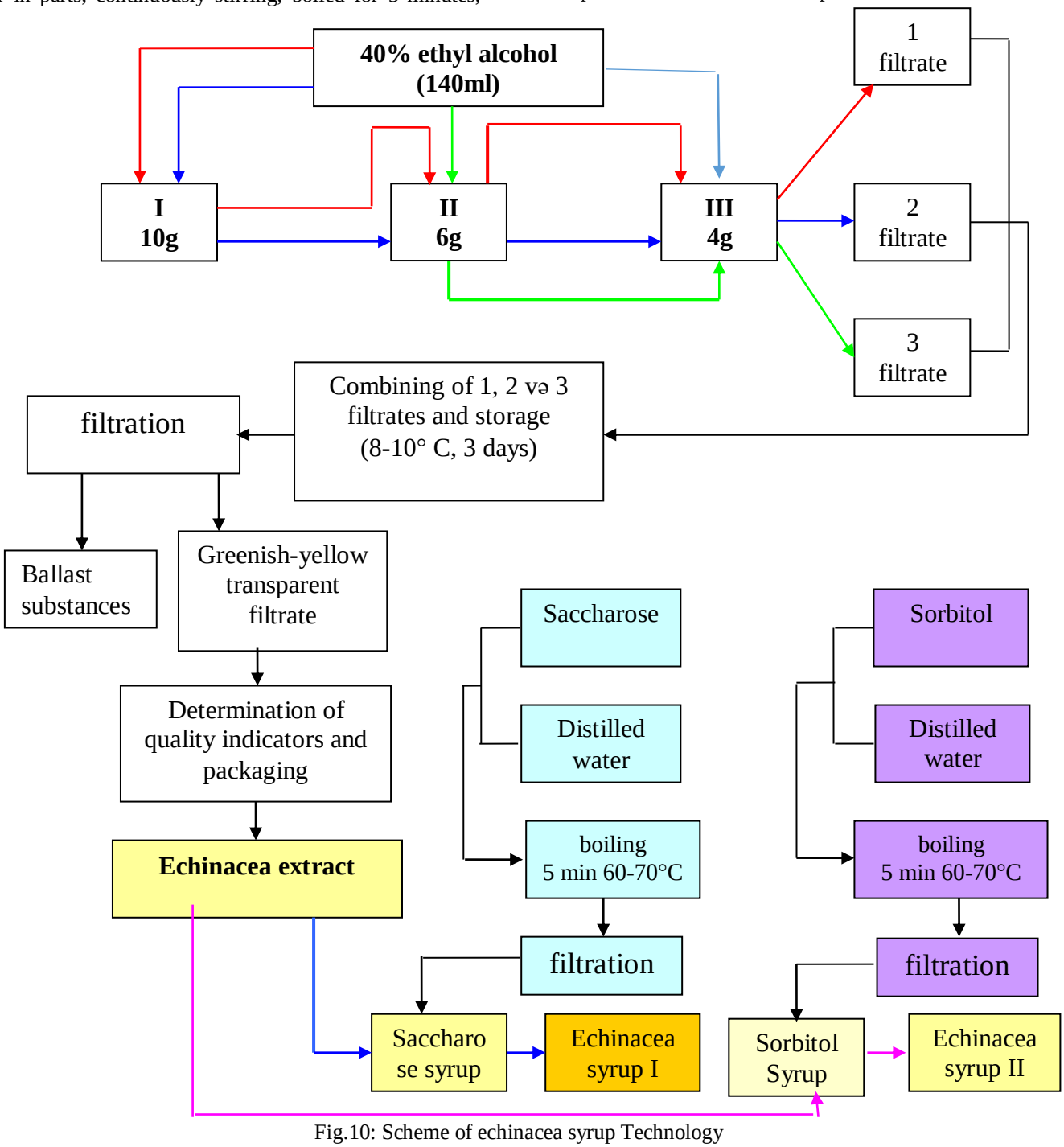


Fig.10: Scheme of echinacea syrup Technology

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The optic density, pH, refractive index, microbiological purity of I and II syrups and microorganisms availability were determined according to X and XI Drug Pharmacopoeia. The methods specified in the X and XI Drug Pharmacopoeia for the determination of syrup density in the aerometer, refractive index in the refractometer, pH in the pHmeter, and determination of active substances were broutht into requisition [1, 7].

The concentration of active substances were analyzed at the Analytical Expertise Center (AEC).

a) Determination of the refractive index in syrups.
The refractive index depends on the nature of the substance, the temperature at which the index is measured, the concentration of the solution, and the wavelength of light used to measure. The refractive index is determined using a refractometer, the index is calculated using the following formula:

$$X = \frac{n-n_0}{F}$$

where,

$X$ is the concentration of the solution,
$n$ is the refractive index of the solution,
$n_0$is the refractive index of the solution at standard temperature,
$F$ is a factor.

The determination were made on refractometers of the Abbe type, consisting of a collimating system and two prisms with a gap, in which the testing substance is placed. Refraction of light rays, i.e. refraction index, is carried out using prisms that have a high refractive index for the yellow sodium line; the refractive index is denoted $n_D$.The refractive index is usually determined at 20°C; when the temperature changes, it is indicated. Using a refractometer, you can quickly determine the amount of substance in the preparation with a high accuracy of ± 0.2%.

The determination of heavy metals in syrups was carried out as follows: 5 ml of the syrup was evaporated in a porcelain dish in a water bath to obtain a dry residue, then 1 ml of conc. sulfuric acidwere added, carefully burned and pierced. The resulting residue heated by adding 5 ml of a saturated ammonium acetate solution, filtered through an ash-free filter, washed with 5 ml of water, and the volume of the resulting filtrate adjusted to 200 ml.To 10 ml of the resulting solution we added 1 ml of diluted acetic acid, 1-2 drops of sodium sulfide, mixed, and after a minute compared with the color of the standard. 10 ml of the standard contains 0.0005% lead ions. To compare the resulting preparation with the standard, we added the same amount of sodium sulfide reagent to the obtained preparations (echinacea syrups A lead salt solution, depending on the concentration, forms a black or gray solution with sodium sulfide. Staining with a diameter of about 1.5 cm is observed on the upper part of the test tube with the test solution. The color formed in the test syrup solution should not be more intense than the color in the reference tube. In the standard solution, a gray color 6-8 cm thick is observed. With this standardization, the content of heavy metals in the our syrups does not exceed 0.001%.

$$X_1 = \frac{D_1 \times 1000}{325,5 \times a} = \frac{0,347 \times 1000}{325,5 \times 7,4438} = 0,143\%$$

where 325.5 is the specific absorption value of pure rutin in alcohol at a wavelength of 362.6 nm under conditions of $E_{1cm}^{1\%}$; "*a"* is the amount of the testing syrup in the g.

b) Determination of the optic density of the resulting syrups
The syrup is placed in a 100 ml cylinder and a clean, dry hydrometer is carefully inserted into it. Density is determined by finding the liquid on the hydrometer scale according to the upper meniscus with an accuracy of 0.01.

c) Determination of the syrups pH.
The pH of the solution depends on the concentration of hydrogen ions in it. The State Pharmacopoeia provides colorimetric and potentiometric methods for determining pH. The colorimetric method is based on changing the color of indicators due to the hydrogen ions in the solution. We determined the pH with a potentiometer.

d) Determination of flavonoids in chinacea I syrup.
7.4438 g of Echinacea I (sucrose) syrup was dissolved in 10 ml of hot alcohol and filtered through a 4 № glass filter. The filter was washed twice with hot alcohol (10 ml each time), the combined filtrates were placed in a 100 ml flask. The resulting mixture was cooled and brought up to the volume required by the same alcohol. Then 5 ml of this alcoholic solution of Echinacea I syrup was placed in a 50 ml volumetric flask and again brought to the required volume with alcohol.The optical density of the resulting solution was measured in a cuvette of 1 cm at a wavelength of 375 nm ($D_1$) and 362 nm ($D_2$). The determination of flavonoids in sucrose-containing echinacea syrup was carried out according to the following formula:

e) Determination of flavonoids in echinacea II syrup (containing sorbitol).
6.6925 g of syrup was dissolved in 10 ml of hot alcohol and filtered through a 4№ glass filter. All subsequent stages of the determination of flavonoids are carried out according to the method above, and the amount of flavonoids was calculated using the following formula:

$$X_2 = \frac{D_2 \text{x} 1000}{325,5 \text{ x } a} = \frac{0,303 \text{ x } 1000}{325,5 \text{ x } 6,6925} = 0,139\%$$

| Compound | Description | Optical density, g/cm | Refractive index | pH | Number of flavonoids (rutin) | Microbiological purity |
|---|---|---|---|---|---|---|
| Echinacea syrup based on sorbitol | Thick liquid of golden color with a slightly specific odor and a sweet slightly cooling taste | 1,310 | 1,4209 | 4,76 | 0,143% | 1 g of the drug contains less than 500 aerobic bacteria; Enterobacteriaceae, Pseudomonas aeruginosa, Staphylococcus aureus are absent; fungi less than 50 |
| Sucrose Echinacea Syrup | yellow solid liquid, faintly specific odor, sweet, slightly refrigerating flavor | 1,245 | 1,4248 | 6,24 | 0,1390 | 1 g of the drug contains less than 500 aerobic bacteria; Enterobacteriaceae, Pseudomonas aeruginosa, Staphylococcus aureus are absent; fungi less than 50 |

Table 1: Comparative indicators of the sucrose- and sorbitol-based echinacea syrups quality

As follows from table.1, the optical density in the proposed sorbitol- and sucrose-based syrups of echinacea equal to 1.310 g/cm and 1.245 g/cm respectively; refractive index = 1.4209 and 1.4248; pH is equal to 4.76 and 6.24; and flavonoids (rutin) is 0.143% and 0.1390% respectively.

- **Clinical trials:** 109 patients participated in the study of Immunal action showed fewer winter season diseases.

## III. CONCLUSION

Its advantage over other agents in the treatment of infections lies in the absence of side effects, undoubtedly associated with all antimicrobial agents of chemical origin.

- **Conflict of interests:-** The authors declare that all the materials presented in the article are processed by them personally, and there is no conflict of interest regarding the publication of this scientific work.

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