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Quality Assessment of Active Substances that Demonstrate Sedative Effect of "Flegmen" Syrup

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I. Introduction

Amino acids are organic compounds which are considered material unity of all tissues of human body. They are responsible for metabolic processes and energy metabolism, ensuring the functioning of the body. Amino acids directly affect the state of the nervous system, regulating mental activity, mood and sleep [2,5]. A deficiency of even one building block can worsen a person's health and lead to serious biochemical and physiological disorders in the body. Therefore, amino acid supplements are best taken in all cases when you load yourself - physically or mentally, but cannot fill the increased need in a timely manner solely from food. There are three groups of amino acids that are replaceable, irreplaceable and conditionally essential [11, 12].

The deficiency of essential amino acids is compensated by the human body with plant foods, and in the case of medical indications, in the form of medicinal preparations containing these compounds. Many amino acids are not only of great physiological importance, but are highly effective pharmacological substances. Replaceable can be independently synthesized in the body. Essential ones are not synthesized on their own and enter the body with food. Conditionally essential amino acids can be synthesized independently in the presence of essential amino acids. There are several optimal periods for taking amino acids. During training, amino acids will help improve athletic performance, muscle growth and strength, as well as speed up recovery processes after exercise. During diets and drying, amino acids will help maintain muscles and health during forced starvation, as well as speed up the process of burning fat. IN periods of mental load of amino acids will increase intellectual productivity and relieve excessive psycho-emotional stress [9,10].

According to WHO, a significant part of the world's population suffers neuropsychiatric disorders during their lives. For the treatment of these types of disorders, sedative herbal preparations are often used, which is due to their wide range of action due to the presence of a complex of active substances in them, ease of use, ease of dosage, minimum contraindications and side effects.

With this in mind, from the plants most commonly used in the formulation of sedatives and having industrial stocks in the republic, namely, Regel's gooseberry, Turkestan motherwort, peppermint and licorice, we previously developed a collection and based on it a sedative syrup was obtained "Flegmen"[3,13].

Amino acids are an integral part of proteins, they perform one of the most important roles in the body. Almost all tissues are formed from them: skin, hair, ligaments, tendons. There are three types: replaceable, conditionally replaceable and irreplaceable. Non-essential amino acids are supplied to the body with food and can be synthesized in it. Essential amino acids must be supplied to the body from outside. Conditionally essential amino acids can be synthesized by the body from essential amino acids if necessary. There are twenty compounds in nature that form proteins. Non-essential amino acids include: glutamic acid, glycine, aspartic acid, serine, cysteine, tyrosine, alanine, proline. Essential amino acids are those amino acids that our body cannot produce on its own, they must be supplied with protein foods. Essential amino acids include: valine, isoleucine, leucine, threonine, methionine, lysine, phenylalanine, tryptophan, histidine. Conditionally essential amino acids include: arginine, tyrosine, cysteine. Each of them is responsible for a specific function [1,9,10].

As for the sources of obtaining biologically active substances, including amino acids, one of them is vegetable raw materials. In turn, it should be noted

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that biologically active substances of plant origin differ from synthetic compounds in that they are in plants in complexes easily absorbed by the body and biologically available concentrations [11,14]. Based on the above, this work, we decided to devote the study of one of the groups of such biologically active substances of the "Flegmen" syrup - amino acids in order to identify their possible participation in the manifestation of the sedative effect of the drug.

The purpose of the study was the study of the amino acid and mineral composition of the sedative syrup "Flegmen".

II. Experimental Part and Methods

To this end, we decided to review the methods for the analysis of amino acids in various objects (primarily in drugs) described in the literature. At the same time, it was established that there are currently many methods for determining amino acids in various objects. Among them, the most common are methods for the determination of amino acids by reverse-phase and cation-exchange High Performance Liquid Chromatography (HPLC), as well as electrophoretic methods. Considering the high prevalence and a number of advantages over other methods, we preferred HPLC in the choice of the amino acid analysis method. In particular, the improvement of HPLC technology and its wide practical application makes it possible to solve the problems of separation and quantitative determination of very small amounts (10 mg/kg and below) of analyzed components in complex objects. However, the absence of chromophore groups in most amino acid molecules requires a derivatization step when using this method. At the same time, various reagents have been proposed for pre- and post-column derivatization.

Thus, in the works of a number of researchers on a C18 column in the gradient elution mode with a methanol-phosphate buffer mixture with fluorimetric detection, glutathione, glutamylcysteine, and 16 amino acids were simultaneously determined using o-phthalaldehyde as a derivatizing agent. And in the works of a number of authors, naphthalenedialdehyde was used in the determination of desmosine, isodesmosine, and 17 other amino acids. 11-dansyl derivatives of amino acid isomers were separated (UV detection) on a β-cyclodextrin column using a mobile phase methanol–phosphate buffer (pH=6.5) [9, 10].

As you know, for each new drug, a specific analysis method should be developed for it. When developing an HPLC technique, in order to obtain reliable results, it is most important to find the optimal conditions for the analysis, the main of which is the choice of the mobile phase (the phase with the highest selectivity with respect to active substances), the column size, the type and size of the sorbent particles, and the elution mode (gradient or isocratic mode), detection method (conditions), standard, etc. All this, of course, requires appropriate research using various reagents and solvents, as well as a waste of time. However, when reviewing the literature, we came across the HPLC technique [6] used to determine similar substances in a similar object. This circumstance led us to the idea of testing this technique for our case, in order to establish its suitability for determining amino acids in "Flegmen" syrup and, if necessary, modifying it.

The object of the study was the "Flegmen"sedative syrup obtained on the basis of a plant liquid extract. The syrup obtained in this way is a thick solution of a light brown color, with a characteristic odor and a sweet, slightly icy taste [3,13].

The suitability of the chromatographic system was checked by the efficiency of the chromatographic column, the degree of separation of the peaks and the relative standard deviation.

Chromatography of the amino acids of "Flegmen" syrup and a standard mixture of amino acids with a known concentration was carried out sequentially under similar conditions. The results of the chromatographic analysis of the amino acids of the "Flegmen" syrup are shown in fig. one.

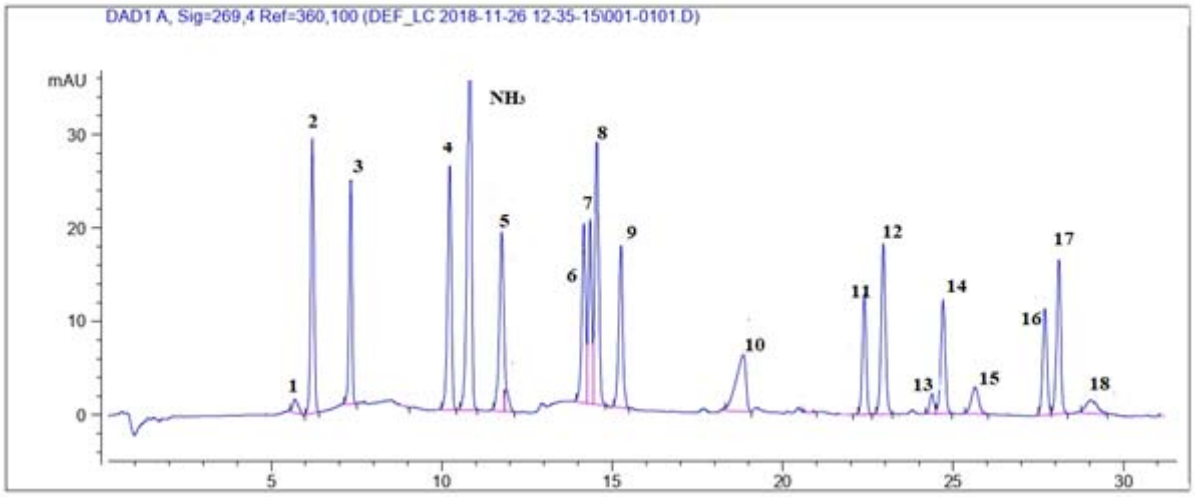

Fig. 1: Chromatogram of free amino acids of "Flegmen"syrup

1 - aspartic acid, 2 - glutamic acid, 3 - asparagine. 4 - serine, 5 - glutamine, 6 - histidine, 7 - threonine, 8 - glycine, 9 - arginine, 10 - alanine, 11 - tryptophan, 12 - methionine, 13 - tyrosine, 14 - valine, 15 - phenylalanine, 16 - isoleucine, 17-leucine, 18-lysine.

Identification and quantification of the amino acids contained in the study preparation was carried out by comparing the retention times and peak areas on the standard amino acid chromatogram with those on the amino acid chromatogram of the study preparation. Analysis of the obtained amino acid chromatograms of the test sample and the standard mixture showed the presence of several amino acids in the "Flegmen" syrup. The results of the analysis with names, chemical formula and amino acid content are presented in Table 1.

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Table 1

No.	Amino acid name	Chemical formula	Content μg/ml
one	Aspartic acid	$C_4H_7O_4N$	0.0240
2	Glutamine acid	$C_5H_9O_2N$	0.0840
3	Asparagine	$C_4H_8N_2O_3$	0.0044
five	Glutamine	$C_3H_7O_3N$	0.0124
6	Histidine	$C_4H_9O_2N$	0.0038
7	Threonine *	$C_6H_9O_2N_3$	0.0292
8	Glycine	$C_2H_5NO_2$	0.0543
nine	argenin	$C_2H_5O_2N$	0.0668
10	Alanine	$C_6H_{14}O_2N_4$	0.0418
eleven	tryptophan	$C_{11}H_{12}N_2O_2$	0.0218
12	Methionine *	$C_5H_{11}NO_2S$	0.0421
13	Tyrosine *	$C_9H_{11}NO_3$.	0.0112
fourteen	Valine *	$C_2H_5O_2N$	0.0177
15	Phenylalanine *	$C_6H_9O_2N_3$	0.0177
16	Isoleucine *	$C_6H_{13}O_2N$	0.0092
17	Leucine *	$C_6H_{13}NO_2$	0.0092
eighteen	Lysine HCl *	$C_6H_{14}N_2O_2$	0.0713
			0.5209

***** *Essential amino acids*

III. Research Results

According to the research data, "Flegmen" syrup contains 18 amino acids, which indicates a high biological value of the sum of amino acids of the studied liquid extract. Among the amino acids of the collection, glutamic acid predominates, which is used in the treatment of diseases of the central nervous system. From this it follows that the amino acids of the studied syrup can participate in the manifestation of the pharmacological activity of the syrup.

Further research was aimed at studying the mineral composition of "Flegmen" syrup.

Trace elements have been known for a long time, but only very recently they have been recognized

as substances necessary for Life. Trace elements are "food mainly for the endocrine glands", more precisely, for enzyme enzymes, since they are catalysts for vital processes. In the impact on the body, all microelements are interconnected and interdependent. Human needs for these "metals of life" are very individual. Minerals make up only 4% of the mass of the human body. Half of this amount is part of the solid parts of the body: bones, teeth, nails, hair, soft tissues. The rest is in the blood, in the intercellular and intracellular fluid.

70-80% of our body mass is water and gases soluble in it - carbon, hydrogen, nitrogen and oxygen, and most of all in our body oxygen is about 60% of body weight, carbon - about 17%, hydrogen - about 10%, nitrogen – only 3% [3].

Micro and macro elements control metabolic processes, maintain the physical and chemical integrity of cells and tissues by maintaining characteristic bioelectric potentials. It is microelements that play the main role in the activity of enzymatic processes necessary for life. That is why their deficiency, as well as excess, will immediately affect human health. It should be noted that the intercellular space contains mainly sodium and calcium, and inside the cells - potassium and magnesium. If the balance between them is disturbed, a person develops various diseases, accompanied by swelling. In this case, the balance should be maintained both between sodium and calcium, and between potassium and magnesium [2,12].

It should also be noted that the minerals contained in plants are divided into two groups: the first, called macroelements, includes potassium, sodium, calcium, magnesium, manganese, silicon, chlorine, phosphorus; plant ash contains at least hundredths of a percent of these elements; the second, called trace elements, include: iron, copper, zinc, iodine, barium, etc. Their content in the ash is thousandths of a percent. Accumulation of trace elements in plants is often selective: different types of plants grow in the same soil conditions, and only some of them are able to concentrate certain microelements [4,7,14].

The determination of the elemental composition was carried out using a highly sensitive multi-element analysis method - mass spectral with inductively coupled plasma (ICP - MS) [15]. As a result of the analysis, the presence of 57 mineral elements was established in the syrup. According to the results obtained, 2 elements (Br and K) were contained in concentrations from 100 to 1000 mg/kg, 2 elements (Na and Mg) ranged from 10 to 100 mg/kg, 2 elements (P and Fe) ranged from 1 to 10 mg/kg), and below 1 mg/kg 51 elements (Fe, Zn, B, Cr, Al, I, Sr, Mn, Cu, Ca, Sc, Ba, Mo, Ni, Li, V, Se, Sb, Zr, Sn , Nb, As, Co, Ga, Ag, Cd, Ta, Cs, Te,W, Tl, Bi, Re, Nd, Ce, Pb, Hf, Y, Gd, In, Sm, La, Er, Eu, Dy , Pr, Lu, Ho, Tm, Au, Hg, Pt)[102; pp.-206-213].resultsand study of the elemental composition of "Flegmen" syrup are presented in table 2.

Table 2: Elemental composition of "Flegmen" syrup

Element	Soda in μg/ml	Element	Sod-e in mcg/ml	Element	Soda - e in mcg/ml
Br	4015	Li	0.016	Nd	0.00018
K	2755	V	0.01	Ce	0.00018
Na	51.9	Se	0.011	Pb	0.00015
mg	16.5	Sb	0.005	hf	0.00013
P	1.96	Zr	0.003	Y	0.0001
Fe	1.41	sn	0.002	Gd	0.00007
Zn	0.22	Nb	0.0016	In	0.00007
B	0.16	As	0.0012	sm	0.00006
Cr	0.14	co	0.0011	La	0.00006
Al	0.12	Ga	0.001	Er	0.00006
I	0.125	Ag	0.0008	Eu	0.00005
Sr	0.11	CD	0.0007	Dy	0.0005
Mn	0.08	Ta	0.0007	Pr	0.00004
Cu	0.08	Cs	0.00055	Lu	0.00003
Ca	0.07	Te	0.0004	Ho	0.000019
sc	0.03	W	0.00046	Tm	0.00001
Ba	0.042	Tl	0.00035	Au	0.0000039
Mo	0.033	Bi	0.00033	hg	0.0000023
Ni	0.01	Re	0.00026	Pt	0.0000023

As the data in table 2 show, "Flegmen" syrup contains 57 elements. Of these elements, calcium, magnesium, potassium, sodium and chlorine, which are part of the cell in the form of ions, are vital. The listed elements are included in the group of macronutrients. Macronutrients in the syrup, the largest quantities are: bromine, potassium, sodium, magnesium, phosphorus, iron, zinc, boron, chromium. Elements found in syruphaving a positive effect on the vital activity of the organism, to a certain extent, contribute to an increase

in the pharmacological value of this medicinal vegetable syrup due to the combination with its main biologically active substances [10].

The detected elements according to the degree of decrease in their content can be represented as the following series: Br> K> Na > Mg >P >Fe >Zn >B >Cr > Al> I> Sr > Mn= Cu> Ca >Sc >Ba>Mo>>Ni >Li >V >Se >Sb >Zr >Sn > Nb > As > Co > Ga >Ag>Cd= Ta> Cs> Te > W > Tl > Bi, >Re >Nd= Ce > Pb > Hf > Y > Gd=In >Sm> La > Er >Eu > Dy > Pr >Lu > Ho >Tm > Au > Hg= Pt

When determining the elemental composition of the syrup, special attention is paid to the content of toxic heavy metals - lead, cadmium and mercury, which the FAO and WHO Joint Commission on the Food Code (Codex Alimentaris) refers to the number of components subject to priority control in international food trade [8,9]. It is shown that the content of toxic heavy metals in the syrup is within the limits allowed by SanPin 0193-06[4]. Comparison of the concentrations of these metals in the studied preparation with their clarks showed that their content practically corresponds to uncontaminated territories, which indicates the environmental safety of raw materials.

Thus, for the first time by the ICP - MS method, the mineral composition of "Flegmen" syrup was determined, in which the content of 57 elements was found. Elements such as bromine, potassium, sodium, magnesium, phosphorus, zinc have been found, which have a pronounced sedative effect and have a beneficial effect on nervous tissue, restoring performance after emotional and physical stress. The data obtained allow us to conclude that the elemental composition of the syrup is very diverse and, accordingly, can have a complex effect. It has been established that the content of toxic heavy metals lead, cadmium and mercury does not exceed the permissible values, which indicates the environmental friendliness and safe use of the syrup in medical practice.

Also, from table 2 it can be seen that in the "Flegmen" syrup such elements were found that are involved in sedative activity.

Magnesium deficiency, even if not too great, can be the cause of heart disease. A serious lack of this mineral leads to disastrous consequences - as a rule, to heart attacks. Lack of magnesium leads to anxiety, fear, confusion, depression. Also, there is hyperactivity, nervousness, stepping from foot to foot, jumping gait, sharpness of movements. Loss of balance, dizziness, fainting, weakness in the arms and legs, blood pressure disorders, cold extremities. The trace element magnesium promotes the absorption of calcium. Bromine is involved in the regulation of the activity of the thyroid gland, as it is a competitive inhibitor of iodine.

The lack of bromine in food leads to insomnia, growth retardation and a decrease in the number of erythrocytes in the blood [2,11]. Phosphorus and bromine have a pronounced sedative effect and have a beneficial effect on the nervous tissue, restoring performance after emotional and physical stress [2,11,12].

Lack of iodine contributes to the development of Graves' disease (goiter). Children and adolescents require more iodine than adults. Iodine is used in atherosclerosis, treatment of syphilis in the tertiary period, inflammatory processes of the respiratory tract, chronic mercury and lead poisoning, to prevent and treat goiter [2,11]. Potassium iodide is prescribed for mastopathy of the mammary gland and other neoplasms in the endocrine glands. Iodine has a sedative (calming) effect on a person, increases mental abilities. Iodine is necessary for the synthesis of the thyroid hormone - thyroxine, as well as for the creation of phagocytes - patrol cells in the blood, which must destroy debris and foreign bodies. Phagocytes capture and digest microorganisms, defective cells.

Lithium prevents the development of neuropsychiatric diseases and has a positive effect on the treatment of schizophrenia [2,11,12]. Zinc deficiency is of exceptional importance, as it not only leads to underdevelopment of the nervous and reproductive systems, but is also deeply linked to immunodeficiency problems. T-lymphocytes in conditions of zinc deficiency are inactive.

Potassium is a very common mineral found in many foods. The best sources of potassium are plant products, especially dried fruits and berries, nuts, seeds, Jerusalem artichoke, potatoes, radishes, cabbage, green vegetables, oatmeal, beets, bananas, bread, currants, tomatoes. Symptoms of potassium deficiency are muscle weakness, heart problems and mental disorders. Low potassium intake can lead to sodium retention and high blood pressure. A potassium-rich diet has been linked to beneficial effects on cardiovascular health. The macroelement potassium is needed, first of all, for the transmission of nerve impulses, to maintain the acid-base balance of the blood, for normal carbohydrate metabolism, to ensure muscle contraction. Its need increases primarily with vomiting and prolonged diarrhea, with profuse sweating, with diuretics, with increased excretion of potassium in the urine, which can be caused, as well as excessive amounts of sodium, coffee, sugar and/or alcohol consumed, or low blood sugar levels. blood.

The macronutrient sodium is primarily needed for normal water exchange between blood cells and tissues, to maintain the acid-base balance in the body, to transmit nerve impulses, to ensure muscle contraction.

A profound lack of sodium can lead to coma and death. Excessive consumption of this macronutrient burdens the kidneys, causes edema (normal water exchange between blood cells and tissues is disturbed), can cause an increase in blood pressure, and leads to

excessive excretion of water and potassium in the urine (which, however, does not relieve edema). Dietary sodium deficiency usually does not occur. Acute deficiency can occur with profuse sweating in combination with the consumption of large amounts of non-sodium fluids, or as a result of vomiting and diarrhea. Symptoms are muscle cramps, lack of appetite, malabsorption of nutrients.

IV. Conclusion

Thus, as a result of the research, the amino acid and elemental composition of the "Flegmen" syrup was determined, while it was found that the syrup contains 18 amino acids and 57 macro and micro elements. Among the amino acids of the collection, glutamic acid predominates, which is used in the treatment of diseases of the central nervous system. Among the macronutrients, such elements as lithium, phosphorus, iodine, magnesium, bromine were found, which have a pronounced sedative effect and have a beneficial effect on the nervous tissue, restoring performance after emotional and physical stress. The data obtained allow us to conclude that the amino acid and elemental composition of the syrup is very diverse and, accordingly, can have a complex effect.

References Références Referencias

1. Abu Zaher Khaled, Zhuravlev N. S. Quantitative determination of the amount of flavonoids in the leaves of some species of the genus Rumex L. // Provisor- 2001.- No. 9.- P. 35-36.
2. Gorbachev V.V., Gorbacheva V.N. Vitamins, micro and macro elements. Directory. - Minsk: Book house "Interpres-service", 2002.-544p.
3. Sidametova Z.E., Olimov N.K. Establishment of quality standards for the sedative collection "Flegmen" // Pharmaceutical Journal. - Tashkent. - 2016. No. 3. - S.
4. Sanitary safety standards and nutritional value of food raw materials and food products (SanPin 0193-06). - Tashkent, 2006.
5. Samylina I.A., Yakovlev G.P. Pharmacognosy. – M.: GEOTAR Media, 2013. - P.53-54.
6. Rudenko et al. // Sorption and chromatographic processes. 2010. Vol. 10. Issue. 2 pp. 223-230.
7. Determination of the elemental composition of soils, soils and bottom sediments by atomic emission and mass spectral methods of analysis. – Industry methodology of III category of accuracy. - Moscow, 2009.
8. Olimov N.K., Normurodov A.S. Elemental composition of garlic powder//Pharmaceutical journal.- Tashkent, 2007.- No. 1.- P.50-51.
9. Olimov N.K., Aminov S.N., Normurodov A.S. Sarimsoq piyoz suvli va alcoholli extractlarining element tarkibi// Farmatsevtika jurnali.- Tashkent, 2008.- No.1.- B.26-28.
10. Normurodov A.S., Aminov S.N., Olimov.N.K. Amino acid composition of garlic powder // XIII Russian National Congress "Man and Medicine": Thesis report - Moscow, 2006. - P.566 .
11. Maznev N.I. The latest encyclopedia of medicinal plants. - Moscow: RIPOL classic: House, XX - I century, 2009.-621p.
12. Lovkova M.Ya., Rabinovich A.M., Ponomareva S.M. Why do plants heal? - M.: Nauka, 1990.-p.2.
13. Olimov NK, Sidametova ZE, and Abdullaev B. Sh. Sedative properties of the drug "Flegmen" on the basis of clinical-pharmacological tests // World Journal of Pharmaceutical Sciences ISSN- (Print): 2321-3310; ISSN (Online): 2321-3086.
14. J. Howenstine. Codex Alimentaris Ends Used in Agriculture. World Health Organization.-Jeneva, 1990.