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QUALIFICATION WORK

ON THE TOPIC: «DEVELOPMENT OF METHODS FOR DETERMINING THE ACTIVE SUBSTANCE IN THE DIETARY SUPPLEMENT "CALCIUM PANTOTHENATE" »

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ANNOTATION

The work is devoted to the development of a method for determining the active substance in the composition of a dietary supplement. The developed method was used for the qualitative and quantitative determination of calcium pantothenate in the dietary supplement "Calcium pantothenate". Research was conducted using chemical methods of identification - color reactions and Beilstein's test. Titrimetric method was chosen for quantitative determination. The work consists of an introduction, three chapters, a conclusion, a list of used literature of 50 titles. The content of the work is represented on 40 pages of typewritten text and contains 1 table, 9 figures and 8 conversion schemes.

Key words: calcium pantothenate, dietary supplement, active substance.

АНОТАЦІЯ

Робота присвячена розробці методики визначення діючої речовини у складі дієтичної добавки. Розроблена методика була використана для якісного і кількісного визначення кальцію пантотенату в дієтичній добавці «Кальцію пантотенат». Дослідження проводились з використанням хімічних методів ідентифікації - кольорових реакцій та проби Бейльштейна. Для кількісного визначення був обраний титриметричний метод. Робота складається з вступу, трьох розділів, висновків, списка використаної літератури, який складає 50 найменуваннь. Зміст роботи викладено на 40 сторінках машинописного тексту та містить, 1 таблицю, 9 малюнків та 8 схем перетворень.

Ключові слова: кальцію пантотенат, дієтична добавка, діюча речовина.

CONTENT

LIST OF ABBREVIATIONS

DS - dietary supplement

UkrPh - State Pharmacopoeia of Ukraine

EPh - European Pharmacopoeia

SPS - standard pharmacopoeial sample

API - active pharmaceutical ingredient

INTRODUCTION

Actuality of theme. Calcium pantothenate is a source of calcium ions. Calcium is called the king of all trace elements of the body. It is the basis of bones, teeth, nails, as well as an important component of the skin, connective tissues, muscles, and hair.

Our body contains this element 1.5-2% of body weight (no other element can "boast" such a quantity). 99% of calcium is concentrated in bones and teeth, responsible for their formation (from birth to 20 years) and strength throughout life. And only 1% is contained in blood and soft tissue cells. However, this one percent also plays an extremely important role: it ensures the normal course of biochemical processes in the body and affects the normalization of the immune system; serves to transmit impulses in the nervous system; provides the function of muscle contraction and rhythmic work of the heart; affects insulin secretion; has an anti-allergic effect.

It is used to treat neuralgia, eczema, allergies, polyneuritis and other diseases associated with metabolic disorders, as well as inflammatory processes. Participates in carbohydrate and fat metabolism, stimulates the formation of corticosteroids and is a component of coenzyme A.

In children, the deficiency of this trace element causes rickets (deformation of the bones, skull, spine, lower limbs), late eruption and replacement of (milk) teeth, caries, increased sweating, irritability, retardation in physical and mental development, and a tendency to convulsions.

In adults, lack of calcium in the body leads to the development of a very dangerous disease - osteoporosis (the density of bones decreases, as a result of which they become brittle and break). However, that is not all. Decreased memory, increased fatigue and irritability, poor sleep, dental disease, their destruction, etc. - continuation of the list of disorders due to calcium deficiency.

If a balanced diet cannot provide the need for calcium, then the use of special food products - dietary supplements, which are sources of this important element, can help.

Recently, their production and circulation have gained more or less popularity both in Ukraine and in the world. This also applies to dietary supplements containing calcium pantothenate as an active ingredient. However, the lack of complete regulatory and legal documentation regarding the methodology of quality control of dietary supplements leads to the fact that currently operators of the market of dietary supplements have a certain degree of freedom in terms of ensuring the quality and safety of such "special" products. Thus, in connection with the stable growth of the market of dietary supplements, the Ukrainian consumer is not protected from the falsification of this type of product. Therefore, the development of methods of identification and quantitative determination of the active substance in the composition of DS is an urgent problem in relation to establishing the quality of DS.

Since the beginning of the coronavirus pandemic, the use of dietary supplements among the population has become too widespread.

This is confirmed by the results of analytical research of the market of the leading company "Proxima Research" https://www.apteka.ua/article/589026 - the market of dietary supplements in Ukraine is growing confidently.

The volume of retail sales of dietary supplements in 2020 compared to the previous period increased by 25.8% in monetary terms, while medicines gave an increase of 7.9%.

According to Proxima Research, the growth of the market for dietary supplements is due to the increase in sales volumes in natural terms, the appearance of new products, price increases and a shift in consumption towards expensive products. Thus, the weighted average cost of one package of dietary supplements has increased by 68.4% since 2016 and is one of the most expensive categories of products in the "pharmacy basket".

That is, consumers are ready to buy dietary supplements, which are widely sold both in grocery stores and pharmacies. At the same time, being on the shelves of pharmacies, they actually began to compete with medicinal products, despite the fact that these are generally different product markets.

The aim of the study. Development of the method of qualitative and

quantitative determination of the active substance in the dietary supplement "Calcium pantothenate" produced by the company Quality Supplements and Vitamins "Life Extension", Inc. /USA/.

Objectives of the study. To achieve this goal, it was necessary to solve the following tasks.

■ to study literature data on methods of identification and quantitative determination of calcium pantothenate and summarize data on its pharmacological activity;

■ analyze various methods for identification and quantification of ingredients in the dietary supplement "Calcium pantothenate";

■ choose the conditions and develop a method of identification and quantification of calcium pantothenate in a dietary supplement, which would be characterized by reliability, efficiency, would be simple and would not require a lot of time for its use;

Research objects. The dietary supplement "Calcium pantothenate" produced by Quality Supplements and Vitamins "Life Extension", Inc. was selected as the object of the study. /USA/.

Subject of study. Identification and quantification of the content of potassium citrate in the dietary supplement "Calcium pantothenate".

Research methods. Reactions with glyoxalhydroxylamine solution (the appearance of a red color is observed as an analytical effect of the reaction), reaction with potassium ferrocyanide solution (the appearance of a white crystalline precipitate is observed as the analytical effect of the reaction), reaction with ammonium oxalate solution (the appearance of a white precipitate is observed as an analytical effect of the reaction, Beilstein's test (coloring of the flame in a yellow-hot color); reaction with a solution of copper (II) sulfate in an alkaline medium (as an analytical effect of the reaction, the formation of a blue complex is observed), reaction with a solution of ferrum (III) chloride (as an analytical effect of the reaction, the formation of a yellow color is observed), reaction of the formation of colored ferrum hydroxamate.

To determine the quantitative content of calcium pantothenate, the method of complexometric was chosen, which was carried out according to the pharmacopoeial method.

Practical significance of the obtained results. Given the extremely important importance of calcium pantothenate in the vital activity of the body, its determination and quantification still attracts considerable attention, including as part of an active dietary supplement (DS). Currently, there are many methods for determining calcium pantothenate, such as the complexometric method, the Kjeldahl method, IR-, UV-spectroscopy.

Який з методів слід використовувати в кожному конкретному випадку залежить від багатьох умов і повинен визначатись індивідуально.

The significant pharmacological value of calcium pantothenate in the composition (DS) requires the development of simple and expressive methods of their quality control for practical use.

Structure and scope of qualification work. The qualification work is structured traditionally, contains an introductory part, a review of the literature, an experimental section, general conclusions, a list of 50 used literary sources, laid out on 41 pages, contains 1 table, 9 figures, 8 schemes.

CHAPTER 1. BIOAVAILABILITY OF CALCIUM PANTOTHENATE AS A DIETARY SUPPLEMENT. (LITERATURE REVIEW)

1.1 Normative regulatory issues of active additives.

Recently, the production and circulation of special food products - dietary supplements have gained more or less popularity both in Ukraine and in the world. Although dietary supplements are not drugs, consumers actively use them to improve their overall health. Such positive trends in the promotion and sale of dietary supplements raise many questions for manufacturers, distributors and consumers. In particular, a significant group of issues concerns the quality of these products, the formation of the legal framework for regulation and state control in the sphere of circulation and import of such "special" products.

It should be noted that currently operators of the dietary supplements market have some freedom in terms of ensuring the quality and safety of such "special" products. Thus, in connection with the stable growth of the market of dietary supplements, the Ukrainian consumer is not protected from the falsification of this type of product.

On the one hand, the State Service of Ukraine for Food Safety and Consumer Protection is the guarantor of quality control of dietary supplements, however, since they are not medicinal products, certification, obtaining a conclusion of the state sanitary-epidemiological examination, preclinical study or conducting clinical trials no tests are required. Therefore, it is quite difficult to recognize fake or low-quality dietary supplements. Thus, when buying such products, any consumer should understand that checking the quality and effectiveness of one or another dietary supplement is a rather difficult task. That is why strengthening the level of regulatory regulation of operators of the market of dietary supplements will contribute to ensuring the quality of products and increasing the safety of the

population. Given the need to create regulatory documentation for the quality control of dietary supplements, the development of a methodology for determining the active pharmaceutical ingredient in a dietary supplement is an urgent problem.

To ensure state control and regulation of dietary supplements, special legislation is in place in most countries. Organizations involved in the regulation of dietary supplements in the United States include

U.S. Food and Drug Administration, FDA;

Dietary Supplement Commission;

National Institutes of Health, NIH;

The US Congress, which approves laws and standards for the safety and regulation of dietary supplements;

House Committee on Energy and Commerce, Subcommittee on Health;

Senate Committee on Health, Education, Labor, and Pensions;

House Committee on Energy and Commerce, Subcommittee on Health.

In the European Union, there is a special regulation of dietary supplements, which provides for the registration and evaluation of the safety and effectiveness of dietary supplements before their release on the market. Organizations involved in the regulation of dietary supplements in the EU include

European Commission;

European Food Safety Authority;

Directorate-General for Health and Food Safety;

European Parliament;

Council of the European Union;

National regulatory authorities in each EU country, such as National Food Safety Agencies.

Ukraine also has its own legislation on dietary supplements, which regulates their production and sale on the market. Ukrainian legislation also defines the maximum permissible levels of active substances in dietary supplements and restrictions on their use. In particular, Ukrainian legislation provides that dietary

supplements cannot contain substances that are prohibited for consumption and must be safe for consumers.

Organizations involved in the regulation of dietary supplements in Ukraine include

State Service of Ukraine on Medicines and Drugs Control);

Ministry of Health of Ukraine;

State Sanitary and Epidemiological Service of Ukraine;

National Academy of Medical Sciences of Ukraine;

National Institute of Food Technologies;

Ukrainian Association of Producers and Suppliers of Dietary Supplements;

Ukrainian Association of Sport Nutrition;

Healthcare Committee of the Verkhovna Rada of Ukraine;

National Agency for Quality Assurance in Medicines and Medical Devices.

According to the requirements of the legislation, dietary supplements are subject to mandatory labeling. The product name, composition, dosage, recommendations for use, as well as the name and address of the manufacturer must be printed on the packaging of dietary supplements. It should also be stated on the package that the dietary supplement is not a substitute for full nutrition and cannot be used as the only source of nutrients.

1.2 Overview of the modern market of dietary supplements - sources of calcium.

The ideal way to get calcium, as with any nutrient, is through food. Dairy products such as milk, cheese and yogurt are the best and most obvious sources. One cup of low-fat plain yogurt contains 415 mg of calcium – more than a third of the daily recommendation for most age groups [1-3] .

Some non-dairy foods are also good sources of calcium, including: calcium-fortified orange juice, canned sardines with bones, firm tofu, canned

salmon with bones, calcium-fortified breakfast cereals.

The body also needs vitamin D to absorb calcium. A few foods naturally contain small amounts of vitamin D, such as canned salmon with bones and egg yolks. You can also get vitamin D from sun exposure.

But with insufficient calcium from eating only food, there is a need to use DS. Now there are many different products on the markets of Ukraine.

Today, calcium preparations in various combinations can be seen in any pharmacy for different groups of people. Everyone has the opportunity to purchase this vital element and take a health course [4].

DS for children:

U-cubes chewable calcium with D3 for children

(Children's calcium with D3) 250 mg/300 IU 120 candies

U-cubes chewable calcium with D3 for children (Children's calcium with D3) is a healthy chewable marmalade that can be used alone or in combination with U-Cubes chewable marmalade with multivitamins from Solgar. Each serving of Tapioca-Based U-Cubes with Vitamin D3 provides the pediatrician-recommended dose of vitamin D3¹... 600 IU (in each 4 chews) is 150% of the daily vitamin D3 requirement for children ages 4 and up ... and 75% of the daily requirement (300 IU in every 2 candies) for children aged 2 to 3 years. Vitamin D3 helps absorb calcium, which improves the health of bones and teeth. It also supports the health of the immune system [5-7] .

U-Cubes with calcium and vitamin D3 are made according to the Solgar method. This means it is made in small batches to ensure the highest quality. It's non-GMO and rigorously tested for safety and efficacy...but never tested on animals. Chewing candy with a great taste, suitable for children.

Producer: Bluebonnet Nutrition, USA Release form:

90 chewing candies

Age: 3+

Calcium Magnesium & Vitamin D3

90 chewy candies with vanilla frosting flavor

Calcium Magnesium & Vitamin D3 (Calcium Magnesium & Vitamin D3) helps to overcome this lack of nutrients due to the forms of calcium, magnesium, vitamin D3 contained in it, as well as super fruits and vegetables in the form of delicious chewing candies in the shape of animals [8].

Manufacturer: Nature's Plus, USA

Release form: 90 tablets

Age: 2+

Chewable Calcium for Kids (Chewable Calcium for Kids)

125 mg 90 tablets

Chewable calcium is a convenient form of calcium intake for children. Pleasant to taste and easy to use, chewable tablets are useful, especially for children.

Manufacturer: NOW Foods, USA

Release form: 100 chewable tablets

Age: 1+

Chewable calcium (Kid Cal) 200 mg 100 chewable tablets orange flavored

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1.3 Functions of calcium pantothenate in the life support of the human body

Calcium is called the king of all trace elements of the body. It is the basis of bones, teeth, nails, as well as an important component of the skin, connective tissues, muscles, and hair.

Our body contains this element 1.5-2% of body weight (no other element can "boast" such a quantity). 99% of calcium is concentrated in bones and teeth, responsible for their formation (from birth to 20 years) and strength throughout life. And only 1% is contained in blood and soft tissue cells. However, this one percent also plays an extremely important role:

Calcium is needed for the normal functioning of the human body. It is a key and vital mineral that performs many functions in our body [9-11].

Taking calcium pantothenate in the form of DD increases its bioavailability and is essential when its deficiency can lead to undesirable consequences.

Calcium is an "alkaline earth" metal belonging to the second group. A vital element not only for humans, but also for animals, fish, invertebrates and even plants. It cannot be said that everything around consists of calcium, but that a lot of it is certain.

For the human body, calcium is important not only as a building material for bone tissue, but also as an element that participates in the course of many processes and even regulates them.

Structural role of calcium. Almost all calcium in the human body (99%) is concentrated in bone tissue. Osteoblasts - cells from which bone is formed - secrete an alkaline enzyme that binds to calcium ions. Together, they form a non-organic compound - hydroxyapatite, which is a building block for the hard, "bearing" matrix of the skeleton. Even in a fully formed bone, cells are constantly being destroyed and formed anew. On average, the human skeleton is completely renewed every 10 years. Considering the fact that without calcium the construction of bone tissue is impossible, the need for this element persists throughout life.

At the same time, bone tissue is not only the main "consumer", but also the

main "depot" of calcium in the body. That is, it not only takes away, but also gives this element, if it is vital for other processes. Resorption (dissolution) of bone tissue is accompanied by the release of calcium ions into the blood, which bind to transporter proteins and are delivered to other organs and tissues [12-14].

Regulatory function of calcium. In addition to the fact that calcium forms the "building blocks" for the formation of bone tissue, it is also a catalyst for many processes. There are receptors on the surface of cell membranes that bind to calcium ions and, increasing or decreasing their concentration inside, make the cell respond to the "signals" of hormones, nerve impulses, etc.

So, with the help of this element, the following occurs: synthesis of ATP, transport of substances through cell membranes, passage of an impulse through the cells of the nervous system, hemostasis.

The element ensures the normal course of many vital processes. Without it, the narrowing and expansion of blood vessels, the transmission of nerve impulses, the contraction of muscles, the production of insulin and other hormones are impossible.

Calcium is essential, that is, it cannot be synthesized on its own and must come in the necessary amounts with food and water. The regulatory role of the element is more important than the structural one. Therefore, when the content of calcium ions in the blood falls below the normal level, the parathyroid hormone parathyrin, produced by the parathyroid glands, triggers the mechanism of calcium removal from the bones. This process is accompanied by softening and demineralization of bone tissue, which can lead to fractures and cracks [15].

In case of poisoning, the element enters the intestines in large quantities to neutralize the acidic environment and prevent a large loss of fluid. In critical situations, the body will extract calcium from the bone tissue and redirect it to the right point.

Can participate in the interaction between cells. In the structure of the cell

membranes of skeletal muscles and nerve fibers there are calcium channels, thanks to which the concentration of the substance in the cells can change rapidly. For example, if a nerve impulse stimulates the contraction of a muscle fiber, the channels open and calcium ions enter the cell. In it, they bind to an active protein, which, in turn, releases the substance from the storage vesicles.

The interaction of the substance with the protein tropinin-c initiates a cascade of reactions, as a result of which muscle contraction occurs. Then it is pumped outside the cell until the next activation.

The trace element is necessary for the stabilization of some proteins and enzymes. Activation of vitamin K-dependent coagulation factors in the coagulation cascade is also impossible without it [16-20].

1.4 Daily rates of calcium for different age groups.

Regional recommendations are the main documents used by residents of most countries when calculating daily consumption rates. For example, in Poland these are the recommendations "Normals of physiological needs in energy and food substances", and in Ukraine - "Normals of physiological needs of the population of Ukraine in basic food substances and energy" from 2017. Regarding calcium, the opinion of nutritionists and doctors coincides, therefore, the same norms are adopted almost all over the world, which are given below.

For children. A growing body needs calcium especially acutely, and its deficiency is the most dangerous for babies. The norms are prescribed for children of different ages, so that in each period the child receives the required amount: babies from birth to 6 months - 200 mg/day; children from 6 to 12 months - 260 mg/day; children from 1 to 8 years old — 1000 mg/day; schoolchildren under the age of 18 — 1300 mg/day. Adolescents over the age of 10 should get the same amount of calcium as adults. It is especially important at any age to monitor the

level of vitamin D in the autumn-winter period, and to prevent its deficiency, to fill

the deficiency by taking supplements. Otherwise, even with proper calcium intake, it will not be available for the bone system, and its formation will be complicated [20-22].

1.5 Factors of effective intake of calcium pantothenate.

As for taking calcium preparations correctly, there are factors that determine how calcium preparations should be taken [22-25].

1. Type of calcium. Check the label to find out how much calcium a supplement contains. Calcium citrate can be taken with or without food. Calcium carbonate should be taken with food. Stomach acid produced when you eat helps your body absorb calcium carbonate.
2. The assimilation of calcium is very dependent on the food from which it enters the digestive system. Yes, some animal and vegetable fats (beef fat, palm oil) can bind to it and form insoluble soap-like compounds. In this case, calcium passes through the intestines in transit and is not absorbed at all.
3. In case of connection with oxalic acid (contained in coffee, rhubarb, beets, sorrel, etc.), crystals (oxalates) are formed, which can provoke the development of urolithiasis, and are also deposited in joints and intervertebral discs. That is why you should be especially careful when using calcium-containing products. It is important not to mix them with natural antagonists and to maintain time intervals between taking such food.
4. Total daily dose. Calcium is best absorbed when taken in smaller doses (usually less than 600 milligrams at a time). If taking 1000 mg of calcium per day, it is recommended to divide it into two or more doses during the day.
5. Medicines and supplements. Calcium supplements can interact with many prescription medications, including antibiotics, bisphosphonates, and high blood pressure medications. Avoid these foods while taking calcium because they can interfere with calcium absorption: caffeinated coffee, foods high in salt.

6. To absorb calcium, the body also needs vitamin D. It is formed in the human body when exposed to the sun.

   Entering the body with food, calcium can be absorbed through the walls of the duodenum or small intestine. This happens either passively - if an excessive amount is received - or actively - with the help of vitamin D, which increases the permeability of the intestinal walls to this element.

   Only up to 40% of the substance that enters the body can be passively absorbed, and 80-90% is absorbed with the help of vitamin D.

   It is especially important at any age to monitor the level of vitamin D in the autumn-winter period, and to prevent its deficiency, to fill the deficiency by taking supplements. Otherwise, even with proper calcium intake, it will not be available for the bone system, and its formation will be complicated [26].

1.6 Sources of calcium pantothenate.

Obtaining calcium pantothenate takes place in two directions:

1) Of natural origin

If you ask people on the street which products contain the most calcium, 9 out of 10 will answer - dairy products. This is a very common opinion, but it is not true. So, 100 grams of cow's milk contains 120 mg of calcium, and 760 mg in sesame halva. And all because sesame contains an excessive amount of this element - 975 mg/100 grams. But even this is not the leader, poppy seeds contain about 1500 mg/100 grams! And in general, many nuts, beans and greens surpass

milk in terms of calcium content.

It is found in large quantities in caviar, yeast, liver, egg yolk, and rice.

It would be possible, but then why do we drink this very milk from childhood, and lactic acid products are necessarily included in the menu of preschool institutions? After all, it is better to introduce nuts and legumes, halva into the diet.

The problem is that plant products rich in calcium are also rich in acids (phytic, oxalic), which prevent the assimilation of the mineral or form insoluble compounds with it. Some of the acid can be removed by soaking nuts or grains in drinking water. But even after that, the bioavailability of "vegetable" calcium will be lower than that of "milk". In addition, it is easier to include a few glasses of milk, a piece of parmesan or cottage cheese in the daily menu than, for example, 400 grams of parsley.

However, milk still has an affordable alternative. This is fish, or rather canned fish. The same sardines in oil in tomato will easily cover the daily requirement (100 grams contains up to 400 mg of Ca). There is especially a lot of substance in fish bones, after heat treatment they soften, so they are easy to chew and swallow. In addition, fish contains vitamin D and omega-3 acids, which are necessary for the cardiovascular system and the brain. If there is an opportunity to regularly consume high-quality seafood, it will be an excellent contribution to one's own health. The key word is "quality", because improper storage conditions, treatment with chemicals or high mercury content in fish will nullify all the benefits of such a diet.

Another source of calcium, often undeservedly forgotten, is water. In some regions, where the soil is rich in limestone, the calcium content of the local drinking water can reach up to 300 mg/100 grams. During the purification process, most of it is removed, but some producers of drinking water artificially saturate it with micro- and macroelements. The label must contain the composition, with a quantitative indication of anions and cations, in particular calcium [26-29].

2) Synthetic origin

Pantothenic acid was obtained in crystalline form in 1939 by Williamson. It is part of the coenzyme of vitamin A. According to its chemical structure, the acid is a derivative of the amino acid β-alanine H2N-CH2-CH2-COOH and α-,γ-dioxy-β,β-dimethyl-butyric acid, and the calcium salt D -(+)-α,γ-dihydroxy-β,β-dimethylbutyryl-N-amideβ'-aminopropionic acid - calcium pantothenate [30].

1.7 Side effects of excessive intake of calcium pantothenate

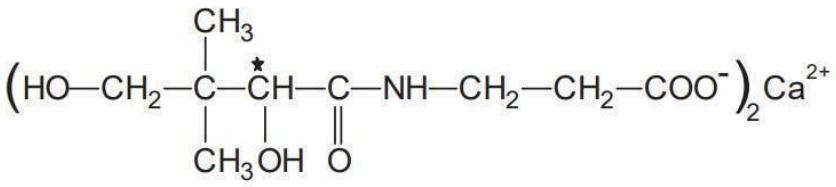
Possible side effects from excessive calcium intake [31]. Before taking DD "Calcium pantothenate", you should be aware of the side effects of excessive calcium intake, which include:

- Fasten
- Bloating and excessive accumulation of gasses in the intestines
- Risk of kidney stone formation
- Calcium can also reduce the absorption of some medications, including osteoporosis medications, thyroid medications, and some antibiotics.

Conclusions of chapter 1

1. An analysis of the literature on normative and regulatory issues of active supplements was carried out.
2. A review of the literature of calcium pantothenate, chosen as the object of the study, was conducted according to its physicochemical properties, methods of its use in medical practice.
3. The studied literary data allow us to draw a conclusion about the relevance of the development of new methods of analysis and the analysis of the possibility of applying existing ones specifically for the selected object of research.

CHAPTER 2. DETERMINATION OF THE ACTIVE SUBSTANCE - CALCIUM PANTOTHENATE



calcium salt of D-(+)-α,γ-dihydroxy-β,β-dimethylbutyryl-N-amideβ'-aminopropionic acid

In its pure form, the specified substance is a white powder, slightly hygroscopic, easily soluble in water, sparingly soluble in ethanol, practically insoluble in ether.

They are identified by the specific optical rotation of the aqueous solution, which should be in the specified interval, by the TLC method - the analysis of the chromatogram should prove: the spot of the sample solution of the test substance should be identical to the spot of the comparison solution in terms of position, color and Rf value, by the appearance of a blue color when adding of sodium hydroxide and a solution of copper (II) sulfate, by reaction with calcium.

Specific optical rotation is an indicator of the identity and purity of optically active substances. This is the optical activity caused by a layer of a substance with a thickness of 1 dm when converted to the content of 1 g of the substance in 1 ml of volume.

The specific optical rotation is the angle of rotation of the plane of polarized light (expressed in angular º) at the wavelength of the line of the sodium spectrum D (λ = 589.3 nm), measured at a temperature of t 20ºC, calculated for the thickness of the test substance solution layer of 1 dm in terms of on the content of 1 g of substance in 1 ml of solution.

When analyzing solid optically active substances, a solution of a known concentration (c, %) is prepared, poured into a polarimetric tube of length (l, dm.) and the angle of rotation (α) is measured on a polarimeter, and the specific optical rotation is calculated using the formula

:

$$[\alpha]_D^{20} = \frac{\alpha \cdot 1000}{1 \cdot c}$$

where c is the concentration of the solution, %.

Trial.

The tests are carried out with solution S, which is prepared by dissolving the test substance in water without carbon dioxide and bringing it up to the mark with the same solvent.

The appearance of solution S should be transparent and colorless.

The pH level of solution S must be within the specified range.

An admixture of 3-aminopropionic acid are investigated by the method of thin-layer chromatography, using silica gel as a substance for coating aluminum foil. Test solution: dissolve the test substance in water and bring it up to the mark with the same solvent. Tested solution: dilute the tested solution with water. Reference solution: Dissolve the standard pharmacopoeial compound calcium pantothenate in water. Comparison solution: dissolve 3-aminopropionic acid in water and bring to the mark with the same solvent. A sample of each solution is applied by capillary to the plate for chromatography separately. As a chromatography system using a mixture of water and ethanol in the ratio according to the methodology. After chromatography, the plate is dried in a stream of air and developed with a solution of ninhydrin. Heat Any spot corresponding to 3-aminopropionic acid in the chromatogram obtained with the test solution should not be more intense than the spot in the chromatogram obtained with the reference solution.

Chlorides. Solution S must meet the limit test for the content of chloride ions.

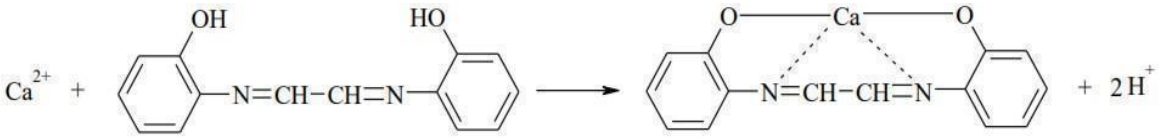
Heavy metals. Solution S must meet the limit test for the content of lead cations.

Losses during drying: determined after roasting in the oven.

2.1 Methods of determination of calcium.

1. A solution of glyoxalhydroxylamine in alcohol, a solution of sodium

hydroxide and a dilute solution of sodium carbonate are added to a neutral solution containing a calcium cation. The mixture is shaken with chloroform and water is added. The color of the chloroform layer is observed in red:



2. a) a solution of potassium ferrocyanide is added to a solution of a dietary supplement in acetic acid. The solution remains clear.

   b) a solution of ammonium chloride is added to the solution of the dietary supplement in acetic acid. A white crystalline precipitate is formed:

$$Ca^{2+} + 2NH_4{}^{+} + K_4[Fe(CN)_6] \rightarrow (NH_4)_2Ca[Fe(CN)_6]\downarrow + 4K^{+}$$

3. A solution of ammonium oxalate is added to the aqueous solution of the dietary supplement. A white precipitate is formed, insoluble in dilute acetic acid and ammonia solution, soluble in dilute mineral acids:

$$Ca^{2+} + (NH_4)_2C_2O_4 \rightarrow CaC_2O_4\downarrow + 2NH_4{}^{+}$$

$$CaC_2O_4 + 2H^{2+} \rightarrow Ca^{2+} + H_2C_2O_4$$

4. Beilstein attempt.

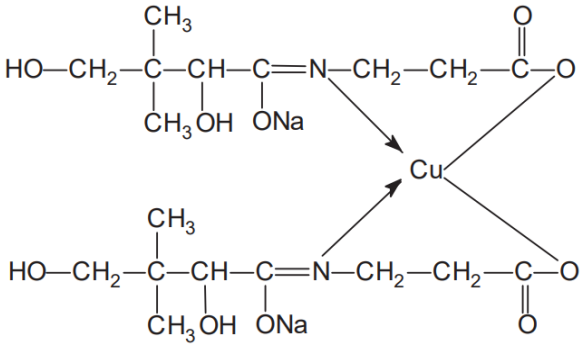
   The simplest preliminary test for the presence of a calcium cation in a substance is Beilstein's test. Calcium salt, moistened with hydrochloric acid and introduced into a colorless flame, colors it in a yellow-hot color.

   The loop at the end of a thin copper wire is heated until it stops coloring the flame of the spirit, let it cool without touching anything, collect a few crystals of the substance and carefully, from top to bottom, introduce it into

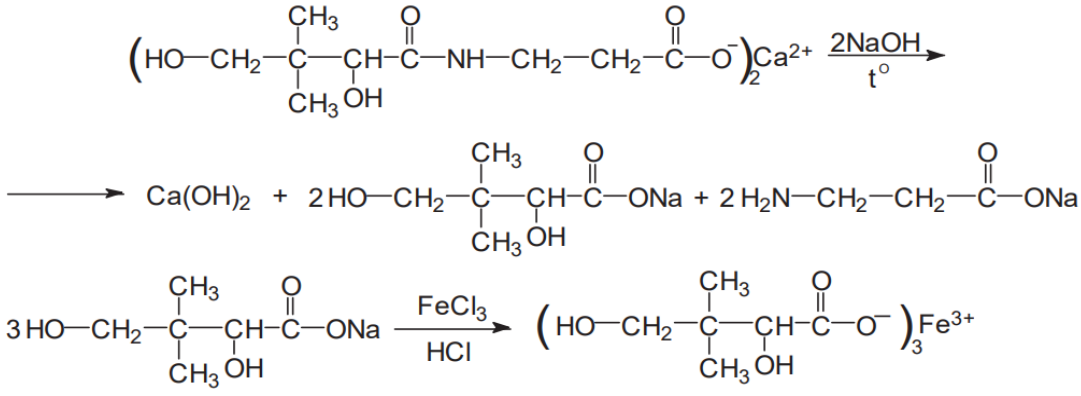
the colorless flame. In the presence of calcium cation, the flame turns yellow-hot.

2.2. Methods of determination of pantothenate.

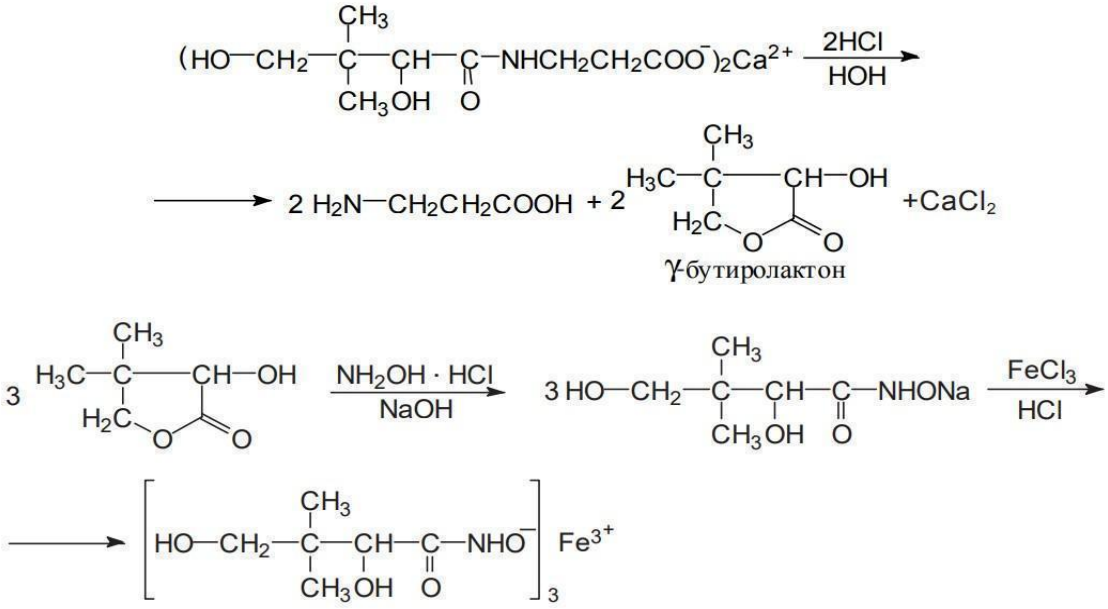
1. With a solution of copper (II) sulfate in an alkaline environment, the substance forms a blue complex (β-alanine):



2. The residue of α,γ-dihydroxy-β,β-dimethylbutyric acid is determined after alkaline hydrolysis. The substance is boiled with a solution of sodium hydroxide, after cooling it is acidified with hydrochloric acid and a solution of ferrum (III) chloride is added - a yellow color is formed:



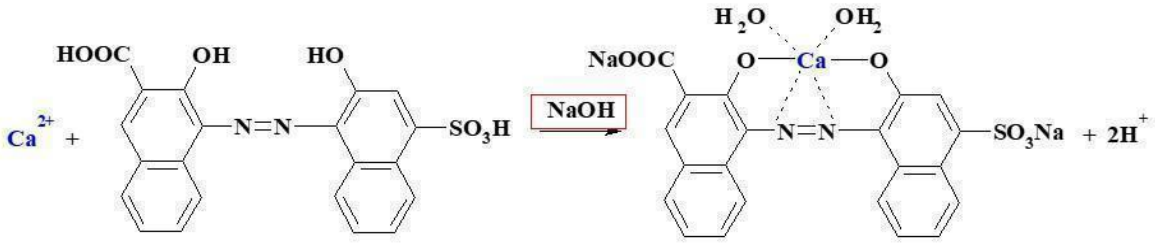
3.The reaction of the formation of colored ferrum hydroxamate (ester group):



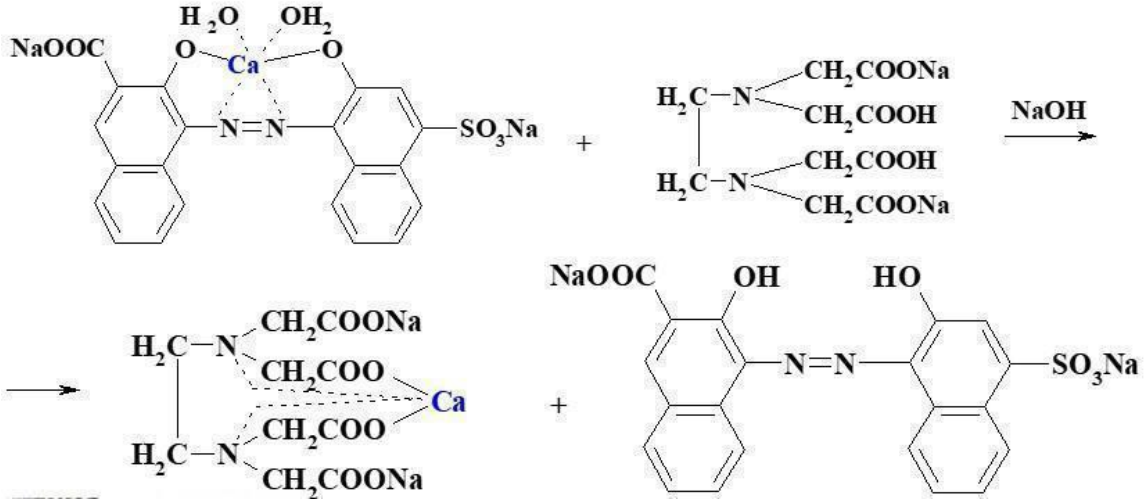
2.3. Quantitative determination of calcium pantothenate.

- *Complexometric method*

Dissolve a precise amount of DD "Calcium pantothenate" powder in water. The resulting solution is placed in a conical measuring flask. Bring the volume of the solution up to the mark with water, add concentrated sodium hydroxide solution and chalcone carboxylic acid (indicator mixture). A solution of sodium edetate with a precisely known concentration is used as a titrant. The equivalence point is determined by the transition of the purple color of the solution to blue.



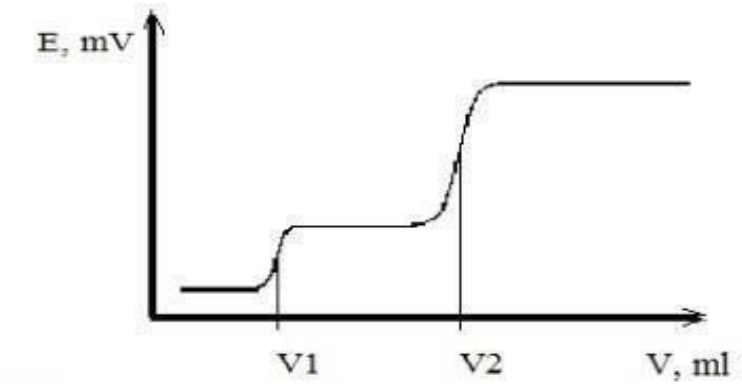
chalcone carboxylic acid



S=1

- *Method of non-aqueous acidimetric titration.*

The method of non-aqueous acidimetric titration with potentiometric determination of the end of the titration. The powder of DS "Calcium pantothenate" is dissolved in anhydrous acetic acid, titrated with a solution of perchloric acid with a precisely known concentration, determining the endpoint potentiometrically - the middle of the interval of the potential jump determines the fixation of the equivalence point.



1 ml of 0.1 M perchloric acid corresponds to 23,83 мг $C_{18}H_{32}CaN_2O_{10}$.

Calcium pantothenate must contain not less than 98.0% and not more than the equivalent of 101.0% bis[3-[[(2R)-2,4-dihydroxy-3,3-methylbutanoyl] calcium amino]propanoate], on a dry matter basis

.

Conclusions of chapter 2

1. Based on literature data, reliable, highly effective and economical methods of identification of calcium pantothenate were analyzed.
2. Chemical reactions for the identification of calcium pantothenate are based on reactions with a solution of glyoxalhydroxylamine (a red color is observed), a solution of potassium ferrocyanide (the solution remains transparent), with a solution of ammonium chloride (a white crystalline precipitate is formed), with a solution of ammonium oxalate (a white precipitate is formed), with a solution of copper sulfate (a blue color is observed), with a solution of ferric chloride (a yellow color is observed).
3. It was determined that experimental DS can be identified using the Beilstein test.
4. Based on literature data, reliable, highly effective and economical methods of quantitative determination of calcium pantothenate were analyzed: complexometry, non-aqueous acidimetric titration method with potentiometric fixation of the equivalence point.

CHAPTER 3. ANALYSIS OF THE ACTIVE SUBSTANCE IN THE DIETARY SUPPLEMENT "CALCIUM PANTOTHENATE"

3.1. Object of study.

Dietary supplement "Calcium pantothenate" produced by QualitySupplements and Vitamins "Life Extension", Inc. /USA/. GMO free. Pure powder, 200 g.

Expiry date: August 1, 2023

Available starting October 10, 2016.

Packaged weight: 230 g.

Dimensions: 2.9 x 2.9 x 5.2 in. (1 inch = 2.54 cm)

Product code: NW-014.

Manufacturer's description: powder containing a source of calcium ions. Participates in carbohydrate and fat metabolism, stimulates the formation of corticosteroids and is a component of coenzyme A.

Ingredients according to the manufacturer's statement: none. The production does not use yeast, wheat, gluten, soy, milk, eggs, fish, shellfish or tree nut ingredients. Conducted in a Good Manufacturing Practice (GMP) registered

facility that processes other ingredients that contain these allergens. Suitable for

vegetarians and vegans.

Manufacturer's Warning: For adults only. Before starting the application, you should consult a doctor. Keep out of the reach of children.

Manufacturer's recommendation: after opening the package, store in a dry and cool place, observing the expiration date.

Manufacturer's Disclaimer: The company always strives to be as accurate as possible in the images and information about its products. However, some changes made by manufacturers to packaging or ingredient lists may require some time before they are published. Keep in mind that even though sometimes the packaging of the products may change, this does not affect the quality and freshness of the products in any way. It is recommended that you carefully read the information on the packaging, warnings and instructions for use of the products before using them and do not rely solely on the information presented on the website. Please note that some of the product descriptions on our site are machine translated. This is done solely for your convenience. All such translations will be replaced by our linguists in the near future.

The active substance is calcium pantothenate (Calcii pantothenas). This is a chemical compound of API of synthetic origin.

Pharmacological group. A11H A31; D03A X04 — vitamins that promote wound healing.

Pharmacological effects. Calcium pantothenate (vitamin B5) stimulates the formation of corticosteroids. The substrate provides the synthesis of the acetylation coenzyme. As a component of coenzyme A, which ensures acetylation processes, it participates in carbohydrate and fat metabolism, the synthesis of acetylcholine, and corticosteroids. Optimizes the energy supply of the contractile function of the myocardium, improves regeneration processes.

Application. Polyneuritis, neuralgia; bronchitis; bronchial asthma; intestinal atony; eczema; trophic ulcers; burns; allergic reactions; toxicosis of pregnant

women; lack of blood circulation; abstinence syndrome (as part of combined

therapy).

3.2. Identification of the active substance.

The active substance is calcium pantothenate (Calcii pantothenas). This chemical compound is the calcium salt of pantothenic acid with the formula $C_{18}H_{32}CaN_2O_{10}$.(M.m. 476.53 g/mol), almost white powder.

Chemical name: calcium bis[3-[[(2R)-2,4-dihydroxy-3,3-dimethylbutanoyl] amino]-propanoate].

In the package of DS "Calcium pantothenate" there is an almost white fine crystalline powder without odor, easily soluble in water.

Specific optical rotation is an indicator of the identity and purity of optically active substances. The angle of rotation (α) was measured in angular degrees on a digital portable polarimeter.

at the wavelength λ = 589.3 nm of the sodium spectrum line D, temperature t = 20°C, in a polarimetric tube of length *l = 1 dm*, and the specific optical rotation is calculated by the formula:

$$[\alpha]_D^{20} = \frac{\alpha \cdot 1000}{1 \cdot c}$$

where c is the concentration of DS "Calcium pantothenate" solution, %.

Specific rotation of a 5% aqueous solution of DS "Calcium pantothenate"

+26,5. (+25,5 - +27,5).

Trial.

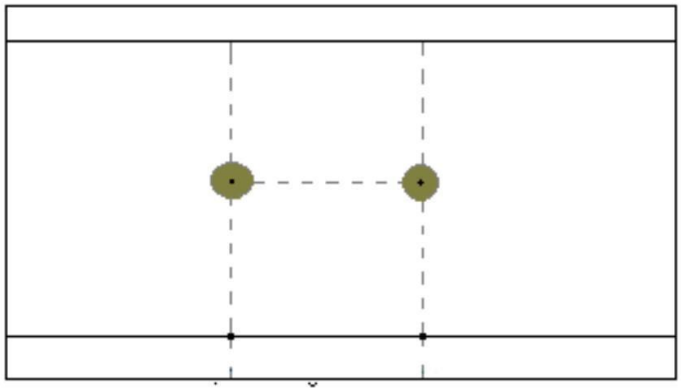
The tests were carried out with a solution of S DS "Calcium pantothenate".

Solution S DS "Calcium pantothenate". 2.50 g of DS "Calcium pantothenate" are dissolved in water without carbon dioxide P and brought to 50.0 ml with the same solvent.

The appearance of the solution S DS "Calcium pantothenate" is transparent and colorless.

pH of solution S DS "Calcium pantothenate" is 7,5. (6,8-8,0)

Determination of the impurity of 3-aminopropionic acid was studied by the method of thin-layer chromatography, using silica gel GR as a coating substance for the chromatography plate. Test solution (a). Dissolve 0.2 g of DS "Calcium pantothenate" in water P and bring to 5 ml with the same solvent. The tested solution (b). Dilute 1 ml of the test solution (a) to 10 ml of water R. Standard solution (a). Dissolve 20 mg of calcium pantothenate CRS in water P and dilute with it to 5 ml of solvent. Comparison solution (b). Dissolve 10 mg of 3-aminopropionic acid P in water P and make up to 50 ml with the same solvent. Apply 5 μl of each solution separately to the plate for chromatography. Observe how the process develops on a path of 12 cm, using a mixture of 35 volumes of water R and 65 volumes of ethanol R. Dry the plate in a stream of air and spray it with a solution of ninhydrin R1. Heat at 110 °C for 10 min. The spot corresponding to 3-aminopropionic acid in the chromatogram obtained with the test solution (a) is not larger and more intense than the spot in the chromatogram obtained from the reference solution (b) (0,5 %).



DS solution "Calcium pantothenate" solution SFS calcium pantothenate

Chlorides. Dilute 5 ml of solution S DS "Calcium pantothenate" to 15 ml with water R and add silver nitrate solution. As an analytical effect of the reaction, we observe the appearance of turbidity of the solution. In parallel, we carry out this reaction with the reference solution. Meets the limit test for chlorides(200 ppm).

Heavy metals. 12 ml of solution S DS "Calcium pantothenate" does not exceed the limit (20 ppm). The test was carried out by preparing a standard using a standard lead solution (1 ppm Pb) R.

Losses during drying: 1,7 % was determined after roasting 10 g of DS "Calcium pantothenate" in the oven at105 °C./ Not more 3,0 % /

Devices and equipment.

Equipment: electronic balance, analytical balance, electric plate, muffle furnace, source of colorless flame - alcohol still, loop at the end of a thin copper wire, potentiometer, chromatography chamber, chromatography plates,

Dishes: test tubes, pipettes, burette, funnel, conical flasks, volumetric flasks.

Reagents: water P, ethanol P, ammonia solution P, 3-aminopropionic acid P, ninhydrin solution P, solution of 2 g/l glyoxalhydroxylamine P in alcohol P, diluted sodium hydroxide solution P, concentrated sodium hydroxide solution P, sodium carbonate solution P, chloroform P, acetic acid P, anhydrous acetic acid P, potassium ferrocyanide solution P, ammonium chloride P, solution of 40 g/l

ammonium oxalate P, hydrochloric acid, copper (II) sulfate solution in an alkaline medium, ferrum (III) chloride solution P.

Titrated solutions: 0,1 M perchloric acid solution; 0,1 M sodium edetate solution.

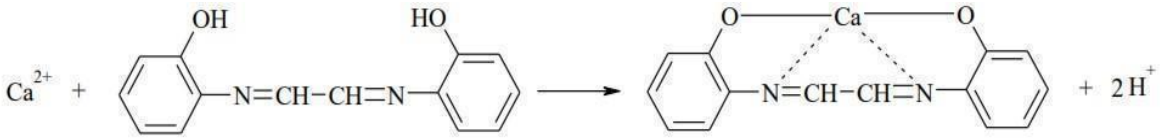
Indicators: chalcone carboxylic acid.

*Progress:*research was conducted according to pharmacopoeial methods.

3.2.1. Test for the authenticity of the calcium cation.

Method:

1. To 0.2 ml of a neutral aqueous solution of DS "Calcium pantothenate" add 0.5 ml of a solution of 2 g/l glyoxalhydroxylamine P in alcohol P, 0.2 ml of diluted sodium hydroxide solution P and 0.2 ml of sodium carbonate solution P. The mixture is shaken with 1 ml or 2 ml of chloroform P and add from 1 ml to 2 ml of water P - the chloroform layer acquires a red color:



2. a) dissolve about 20 mg of DS powder "Calcium pantothenate" in 5 ml of acetic acid P. Add 0.5 ml of potassium ferrocyanide solution P to the resulting solution. The solution remains transparent.

   b) about 20 mg of DS powder "Calcium pantothenate" is dissolved in 5 ml of acetic acid P. About 50 mg of ammonium chloride is added to the solution. A white crystalline precipitate is formed:

$$Ca^{2+} + 2NH_4^+ + K_4[Fe(CN)_6] \rightarrow (NH_4)_2Ca[Fe(CN)_6]\downarrow + 4K^+$$

3. 1 ml of 40 g/l ammonium oxalate P solution is added to 1 ml of an aqueous solution of DS "Calcium pantothenate" - a white precipitate is formed, insoluble in diluted acetic acid P and ammonia solution P, soluble in diluted mineral acids:

$$Ca^{2+} + (NH_4)_2C_2O_4 \rightarrow CaC_2O_4 \downarrow + 2NH_4^+$$

$$CaC_2O_4 + 2H+ \rightarrow Ca^{2+} + H_2C_2O_4$$

4. Beilstein attempt.

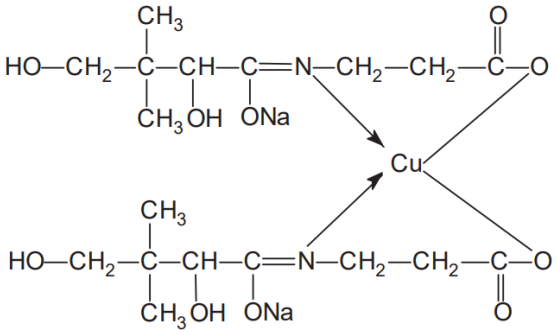
A loop at the end of a thin copper wire was baked until it stopped coloring the flame of the still. Let it cool without touching anything. Several crystals of DS "Calcium pantothenate" powder were collected, which had previously been moistened with hydrochloric acid and carefully, from top to bottom, introduced into the colorless flame of the alcohol.

The flame turns yellow-hot.

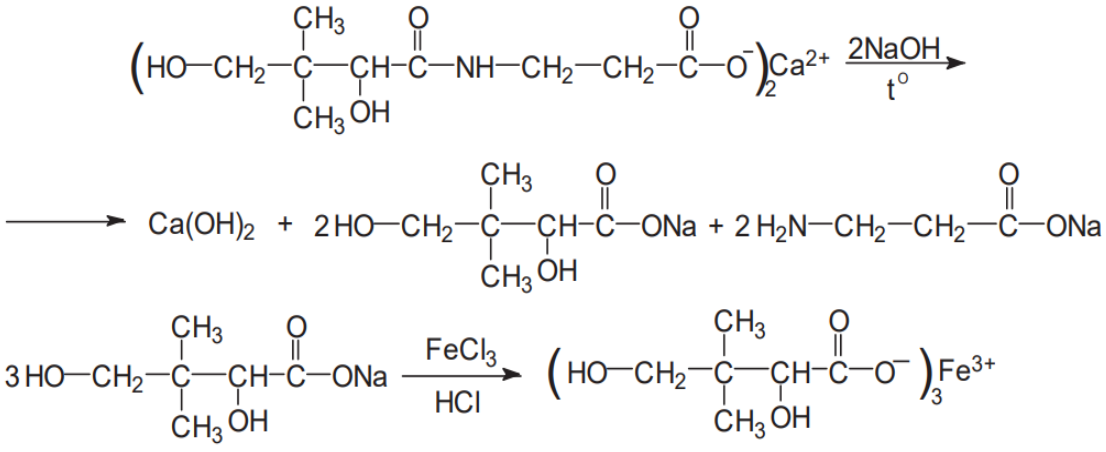
3.2.2. Test for the authenticity of pantothenate ion.

Method:

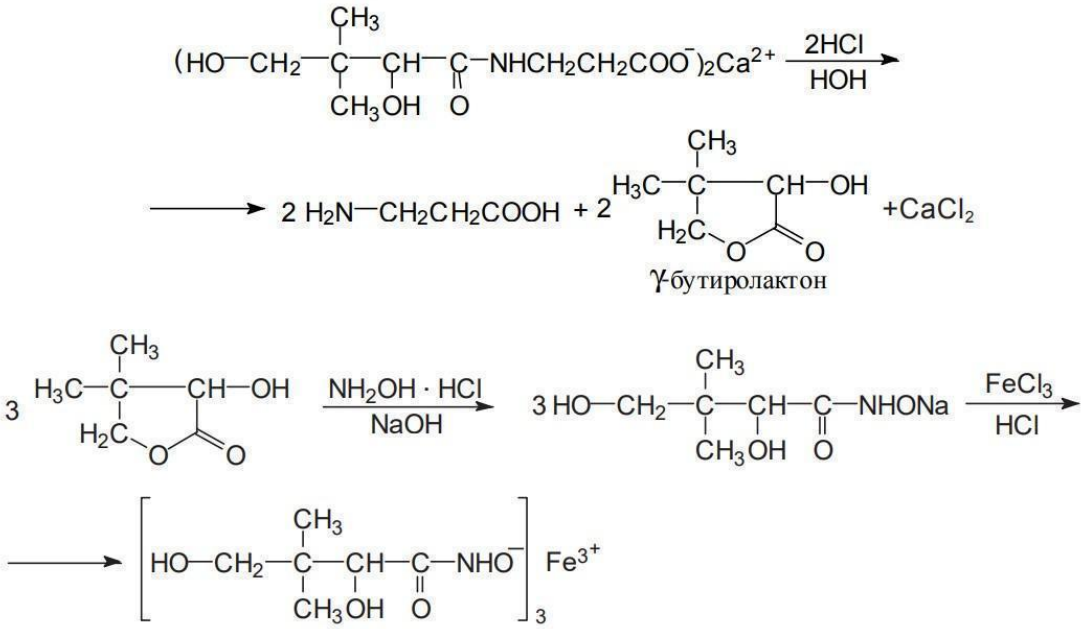
1. A solution of copper (II) sulfate P in an alkaline medium was added to 0.1 g of DS powder. The formation of a blue complex (β-alanine) was observed:



2. The residue of α,γ-dihydroxy-β,β-dimethylbutyric acid was determined after alkaline hydrolysis: 0.1 g of DS powder was boiled with sodium hydroxide solution P. The smell of amines is felt. They cooled in the air. After cooling, it was acidified with hydrochloric acid and added to a solution of ferrum (III) chloride P - a yellow color is formed:



3. The reaction of the formation of colored ferrum hydroxamate:



3.3. Quantitative determination of calcium pantothenate in the research object.

Method of non-aqueous acidimetric titration.

The method of non-aqueous acidimetric titration with potentiometric determination of the end of the titration.

Dissolve 0.180 g (exactly weighed) of DS "Calcium pantothenate" powder in 50 ml of anhydrous acetic acid P. Titration is carried out with 0.1 M perchloric acid, the equivalence point is fixed potentiometrically.

1 ml of 0.1 M perchloric acid corresponds to 23.83 mg of powder DS "Calcium pantothenate".

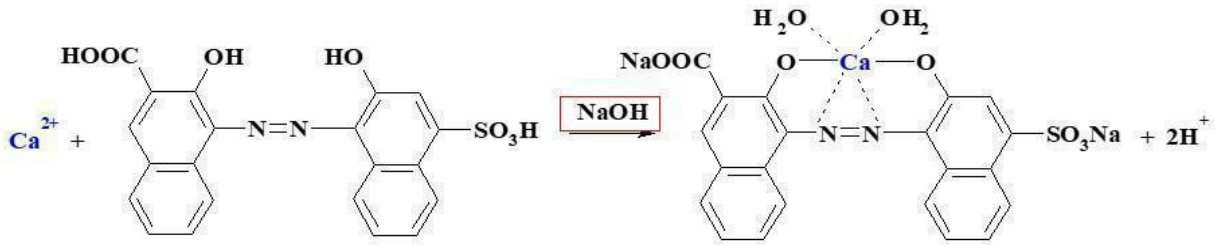
Calcium pantothenate contains not less than 98.0% and not more than 101.0% bis[3-[[(2R)-2,4-dihydroxy-3,3-methylbutanoyl]amino]propanoate] calcium, in terms of dry matter.

Complexometric titration method.

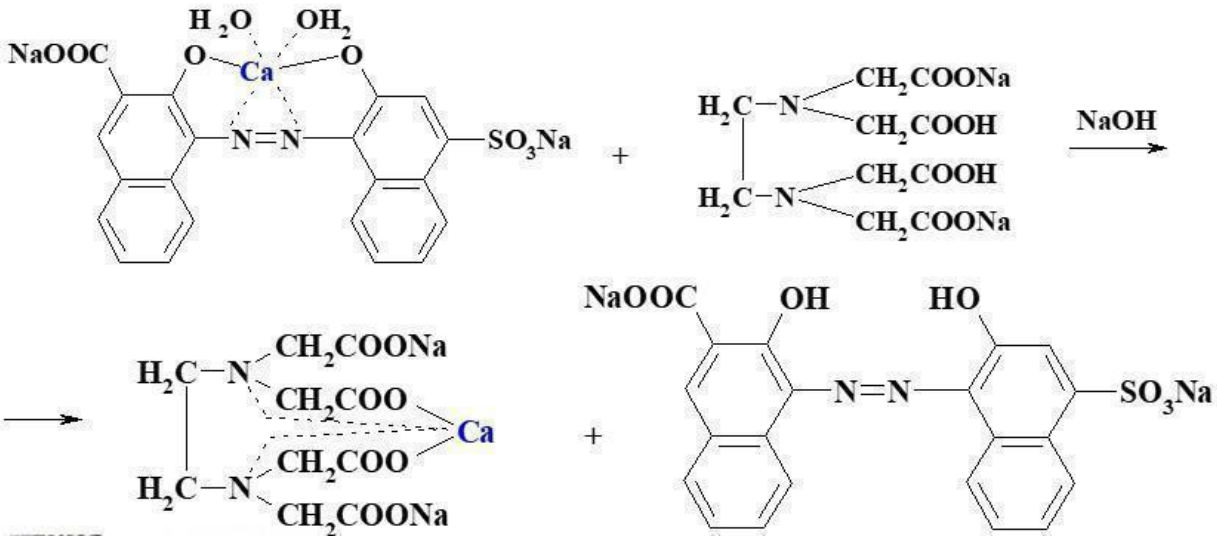
Quantitative determination of calcium pantothenate in the DS "Calcium pantothenate" was carried out by the complexometric method according to the pharmacopoeial method.

Method.

About 0.200 g (exact weight) of the research substance DS "Calcium pantothenate" manufactured by Quality Supplements and Vitamins "Life Extension", Inc. /USA/ is dissolved in 100 ml of water P. The resulting solution is placed in a conical flask with a capacity of 500 ml. Adjust the volume of the solution with water P to 300 ml, add 6.0 ml of sodium hydroxide solution of concentrated P, about 200 mg of chalcone carboxylic acid of the indicator mixture P and titrate with 0.1 M sodium edetate solution until the purple color of the solution changes to blue.



chalcone carboxylic acid



S = 1

The content of the active substance was calculated according to formulas:

$$T = \frac{C_{\text{sodium edetate}} \cdot S \cdot M_{\text{DS "Calcium pantothenate"}}}{1000} = \frac{0{,}1 \cdot 1 \cdot 476{,}53}{1000} = 0{,}047653\ (г/мл)$$

$$X,\% = \frac{V_{\text{sodium edetate}} \cdot K \cdot T \cdot 100}{m_{hint}} = \frac{4{,}20 \cdot 0{,}9989 \cdot 0{,}047653 \cdot 100}{0{,}1998} = 100{,}06\ \%$$

Statistical processing was carried out according to formulas;

Deviations are absolute = $m_{\text{factual}} - m_{\text{registered}}$

$$\text{Deviations are relative} = \frac{m_{\text{registered}} - m_{\text{factual}} \cdot 100}{m_{\text{registered}}}$$

General table of the results of the quantitative determination of the content of calcium pantothenate in the composition of the DS "Calcium pantothenate"

According to the results of the determination, the quantitative content of potassium pantothenate in DS is within the range of 98.00 - 101.00%, which meets the requirements of the European Pharmacopoeia. (APPENDIX A.)

Conclusion of chapter 3

A sample of DS "Calcium pantothenate" powder according to indicators: description, solubility, specific optical rotation, pH; impurities of 3-aminopropionic acid, chlorides, heavy metals; loss on drying, authenticity and quantification meet the requirements of the European Pharmacopoeia

GENERAL CONCLUSIONS

- Based on literature data, it was established that most of the known general methods for determining calcium pantothenate are based on reactions with a solution of glyoxalhydroxylamine (a red color is observed), a solution of potassium ferrocyanide (the solution remains transparent), with a solution of ammonium chloride (a white crystalline precipitate is formed), with an ammonium solution oxalate (a white precipitate is formed), with a solution of copper sulfate (a blue color is observed), with a solution of ferric chloride (a yellow color is observed).
- To determine the quantitative content of calcium pantothenate, the method of complexometric was determined to be the most effective.
- For the qualitative determination of calcium pantothenate, the methods developed for the pure substance were tested, which proved their ability to analyze calcium pantothenate as part of the studied dietary supplement.
- According to the selected methods, the identification and quantitative determination of calcium pantothenate in the composition of DD "Calcium pantothenate" manufactured by Quality Supplements and Vitamins "Life Extension" Inc. was carried out. /USA/, which is present on the Ukraine market.
- According to the results of the study, it was concluded that the sample of the substance in the composition of the DS "Calcium pantothenate" corresponds to the following indicators: description, solubility, specific optical rotation, pH; impurities of 3-aminopropionic acid, chlorides, heavy metals; loss on drying, authenticity and quantification meet the requirements of the European Pharmacopoeia for APIs.

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APPENDIX A

General table of the results of the quantitative determination of the content of calcium pantothenate in the composition of the DS "Calcium pantothenate"

№	***m_{hint}, g***	**V, ml**	**X, %**	***Deviations are absolute, g***	***Deviations are relative, %***
1	0,1998	4,20	100,06	0,0001	0,075
2	0,2100	4,41	99,00	0,0026	1,987
3	0,2102	4,65	99,85	0,0015	1,155
4	0,2104	4,14	99,99	0,0013	1,156
5	0,2112	4,26	99,87	0,0002	0,150

Ф А 2.2.1-32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department medicinal chemistry
Level of higher education master
Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
The Head of Department

Lina PEREKHODA
" 22 " August 2022

ASSIGNMENT
FOR QUALIFICATION WORK OF AN APPLICANT FOR HIGHER EDUCATION

Mahmoud KANISSI

1. Topic of qualification work: «Development of methods for determining the active substance in the dietary supplement "Calcium pantothenate"»,
supervisor of qualification work: Lina PEREKHODA, Head of Medicinal Chemistry Department, professor.
approved by order of the NUPh dated February 6, 2023 No. 35

2. Deadline for submission of qualification work by the applicant for higher education:
April 2023.

3. Outgoing data for qualification work: study of the state of scientific developments regarding the following issues; physicochemical methods in the pharmacopoeial analysis of the DS "Calcium pantothenate". Analysis of the suitability of existing methods and the development of a new method of identification and quantitative content of ingredients in DS "Calcium pantothenate".

4. Contents of the settlement and explanatory note (list of questions that need to be developed): physicochemical properties, production, metabolism, application, methods of identification and quantification, identification as part of a dietary supplement, quantification as part of a dietary supplement of calcium pantothenate.

5. List of graphic material (with exact indication of the required drawings):
1 table, 9 pictures та 8 schemes.

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Lina PEREKHODA, professor of higher education institution of department Medicinal Chemistry	March 2023	March 2023
2	Lina PEREKHODA, professor of higher education institution of department Medicinal Chemistry	April 2023	April 2023
3	Lina PEREKHODA, professor of higher education institution of department Medicinal Chemistry	April 2023	April 2023

7. Date of issue of the assignment:: « 22 » August 2022

CALENDAR PLAN

№	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1	Physico-chemical properties of calcium pantothenate (Literature review).	March 2023	**done**
2	Development of a method for the analysis of calcium pantothenate as part of DS.	March 2023	**done**
3	Development of methods for quantitative determination of calcium pantothenate in the composition of DS.	April 2023	**done**
4	Preparation of equipment and working solutions for the analysis of DS "Calcium pantothenate".	April 2023	**done**
5	Identification of the active substance in the DS"Calcium pantothenate".	April 2023	**done**
6	Quantitative determination of the active substance in DS "Calcium pantothenate".	April 2023	**done**
7	Generalization of the obtained results and conclusions based on the results of the work carried out.	April 2023	**done**

An applicant of higher education **Mahmoud KANISSI**

Supervisor of qualification work **Lina PEREKHODA**

ВИТЯГ З НАКАЗУ № 35
по Національному фармацевтичному університету
від 06 лютого 2023 року

нижченаведеним студентам 5-го курсу 2022-2023 навчального року, навчання за освітнім ступенем «магістр», галузь знань 22 охорона здоров'я спеціальності 226 - фармація, промислова фармація, освітня програма - фармація, денна форма здобуття освіти (термін навчання 4 роки 10 місяців та 3 роки 10 місяців), які навчаються за контрактом, затвердити теми кваліфікаційних робіт:

Прізвище студента	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
• **по кафедрі медичної хімії**				
Каніссі Махмоуд	Розробка методик визначення діючої речовини в дієтичній добавці "Кальцію пантотенат"	Development of methods for determining the active substance in the dietary supplement "Calcium pantothenate"	проф. Перехода Л.О.	проф. Баюрка С.В.

Підстава: подання декана, згода ректора

Ректор

Вірно. Секретар

Ф А2.8-47-110

ВИСНОВОК

Комісії з академічної доброчесності про проведену експертизу

щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

№ 112683 від «28» квітня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Каніссі Махмоуд, 5 курсу, Фм18(4,10д)англ-04 групи, спеціальності 226 Фармація, промислова фармація, на тему: «Розробка методик визначення діючої речовини в дієтичній добавці “Кальцію пантотенат”/ Development of methods for determining the active substance in the dietary supplement "Calcium pantothenate"», Комісія з академічної доброчесності дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,

професор  **Інна ВЛАДИМИРОВА**

2%

23%

Ф А 2.2.1-32-353

REVIEW

of scientific supervisor for the qualification work of the master's level of higher education of the specialty 226 Pharmacy, industrial pharmacy

Mahmoud KANISSI

on the topic«Development of methods for determining the active substance in the dietary supplement “Calcium pantothenate”».

Relevance of the topic. Given the extremely important importance of calcium pantothenate in the vital activity of the body, its determination and quantification as part of a dosage form still attracts considerable attention, including as part of an active dietary supplement (DS). The lack of methods for determining calcium pantothenate as an active substance in the composition of DS is a negative factor regarding the safety of use of DS present on the market of Ukraine, therefore the development of such a technique is very urgent.

Practical value of conclusions, recommendations and their validity. The actual goal of the qualification work of Mahmoud KANISSI was the development of a method for the qualitative and quantitative determination of calcium pantothenate in the DS "Calcium pantothenate" for use in the analysis of the quality of dietary supplements. In the course of the qualification work, Mahmoud KANISSI showed curiosity and interest in the analysis of a large amount of scientific literature on the subject of the qualification work. He managed to formulate questions, the answer to which had to be found in the literature, to identify the problems that arise in the analysis of dietary supplements.

Assessment of work. The work was performed at a high scientific level, the results obtained are reliable, the conclusions are logical and well-founded. The questions were successfully resolved.

General conclusion and recommendations on admission to defend. The qualification work of Mahmoud KANISSI in terms of its structure, level of scientific research, and practical value meets the requirements for qualification works and can be recommended for defense.

Scientific supervisor Lina PEREKHODA

«03» April 2023.

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Mahmoud KANISSI

on the topic«Development of methods for determining the active substance in the dietary supplement “Calcium pantothenate”».

Relevance of the topic. Recently, the production and circulation of special food products - dietary supplements have gained more or less popularity both in Ukraine and in the world. This also applies to dietary supplements containing calcium pantothenate as an active ingredient. However, the lack of complete regulatory and legal documentation regarding the methodology of quality control of dietary supplements leads to the fact that currently operators of the market of dietary supplements have some freedom in terms of ensuring the quality and safety of such "special" products. Thus, in connection with the stable growth of the market of dietary supplements, the Ukrainian consumer is not protected from the falsification of this type of product. Therefore, an urgent problem in relation to establishing the quality of DS is the development of methods for identifying the active substance in the composition of DS.

Theoretical level of work. The novelty of the obtained results lies in the development and justification of the possibility of using existing physicochemical methods for the identification of calcium pantothenate in a dietary supplement. The possibility of their use for the analysis of dietary supplements with calcium pantothenate has been confirmed.

Author's suggestions on the research topic. To develop methods for identifying the active substance in the dietary supplement, reactions with glyoxalhydroxylamine solution, potassium ferrocyanide solution, ammonium chloride solution, ammonium oxalate solution, copper sulfate solution, and ferric chloride solution were selected. The method of complexonometry was chosen for quantitative determination.

Practical value of conclusions, recommendations and their validity. As a result, new results were obtained regarding the method of determining the active substance in the composition of DS, suitable for practical use, which is characterized by reliability, efficiency, is simple and does not require a lot of time for its use. The developed technique was tested for the experimental determination of the active substance in the composition of DS "Calcium pantothenate", which is present on the market of Ukraine.

Disadvantages of work. Minor flaws and errors found in the text of the qualification work do not reduce the advantages of the work.

General conclusion and assessment of the work. The volume of experimental studies and their modern level, the analysis of the obtained data made it possible to solve all the tasks set in the work. The text of the qualification paper is well written, neatly designed, and the content meets the requirements for qualification papers. Mahmoud KANISSI's qualifying work can be recommended for defense.

Reviewer prof. Serhii BAIURKA

10 April 2023 p.

Ф А2.2.1-91-287

ВИТЯГ
з протоколу засідання кафедри медичної хімії
№ 10 від 21 квітня 2023 р.

ПРИСУТНІ:

проф. Ліна ПЕРЕХОДА, проф. Андрій ФЕДОСОВ, доц. Вадим ЗУБКОВ, доц. Ірина СИЧ, доц. Віталій ЯРЕМЕНКО, доц. Ілля ПОДОЛЬСЬКИЙ, доц. Наталія КОБЗАР, доц. Марина РАХІМОВА, доц. Маргарита СУЛЕЙМАН, ас. Олена БЕВЗ, ас. Ольга ВІСЛОУС

ПОРЯДОК ДЕННИЙ:

Звіт про стан виконання кваліфікаційної роботи здобувача вищої освіти іноземного факультету Фм18(4.10д))англ-04 групи (226 Фармація, промислова фармація освітньої програми Фармація) Махмоуда КАНІССІ на тему: «Розробка методик визначення діючої речовини в дієтичній добавці “Кальцію пантотенат”»

СЛУХАЛИ: доповідь здобувача вищої освіти фармацевтичного факультету Фм18(4.10д))англ-04 Махмоуда КАНІССІ на тему: «Розробка методик визначення діючої речовини в дієтичній добавці “Кальцію пантотенат”», керівник зав. каф. медичної хімії, д.фарм.н., проф. Ліна Перехода.

УХВАЛИЛИ: рекомендувати кваліфікаційну роботу Махмоуда КАНІССІ до офіційного захисту в Екзаменаційній комісії.

Зав. кафедри медичної хімії,
професор **Ліна ПЕРЕХОДА**

Секретар кафедри медичної хімії,
доцент **Марина РАХІМОВА**

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Махмоуд КАНІССІ до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Розробка методик визначення діючої речовини в дієтичній добавці "Кальцію пантотенат"»

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Махмоуд КАНІССІ у ході виконання кваліфікаційної роботи показав себе грамотним виконавцем, що вміє працювати з науковою літературою. Тема кваліфікаційної роботи є актуальною, а сама кваліфікаційна робота за своєю будовою, рівнем наукових досліджень, практичному значенню відповідає вимогам, що ставляться до кваліфікаційних робіт та може бути рекомендована до захисту.

Керівник кваліфікаційної роботи

_____ Ліна ПЕРЕХОДА

03 квітня 2022 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Махмоуд КАНІССІ допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувачка кафедри
медичної хімії

_____ Ліна ПЕРЕХОДА

21 квітня 2022 року

Qualification work was defended

of Examination commission on

« __ » of June 2023

With the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____ / Oleh SHPYCHAK /