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**MINISTRY OF HEALTH OF UKRAINE**
**NATIONAL UNIVERSITY OF PHARMACY**

**faculty for foreign citizens' education**

**department Technology of Drugs**

**QUALIFICATION WORK**

on the topic

# DEVELOPMENT OF THE COMPOSITION AND RESEARCH OF HOMEOPATHIC MEDICINES OF ROSEMARY

**Prepared by:** higher education graduate of group Phm17 (4.1d) - 06 English
specialty 226 Pharmacy, industrial pharmacy
educational program Pharmacy
Aimad NAJI
**Supervisor:** associate professor of higher education institution of department technology of drugs, PhD, associate professor Ganna YURIEVA
**Reviewer**: associate professor of higher education institution of department of Industrial drug technology, PhD, associate professor Natalia GERBINA

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## SUMMARY

The relevance of the development of homeopathic medicines of rosemary for use in the treatment of diseases of the nervous system is theoretically and experimentally substantiated in the master's thesis. Based on the results of experimental research, in particular organoleptic, physicochemical, pharmaco-technological, the technology of obtaining homeopathic tincture of rosemary D1 and homeopathic granules D3 is substantiated. The work is presented on 47 pages, includes 14 tables, 4 figures, 71 sources of literature.

*Key words:* rosemary, composition, technology, homeopathy, tincture, granules.



## АНОТАЦІЯ

У магістерській роботі теоретично та експериментально обґрунтовано актуальність розробки гомеопатичних препаратів розмарину для застосування в лікуванні захворювань нервової системи. На основі результатів експериментальних досліджень, зокрема органолептичних, фізико-хімічних, фармакотехнологічних, обґрунтовано технологію отримання гомеопатичної настоянки розмарину D1 та гомеопатичних гранул D3. Робота викладена на 47 сторінках, включає 14 таблиць, 4 рисунки, 71 джерело літератури.

*Ключові слова:* розмарин, склад, технологія, гомеопатія, настоянка, гранули.

## LIST OF ABBREVIATIONS

HM – homeopathic medicine

DF – dosage form

MT – matrix tincture

API – an active pharmaceutical ingredient

BD – basic drug

SPhU – State Pharmacopoeia of Ukraine

**CONTENTS**

# INTRODUCTION

**Actuality of topic.** Diseases of the nervous system are represented a wide and diverse space of pathology of various etiologies and symptoms. Neurological disorders are increasingly recognized as one of the main causes of death and disability worldwide. In 2020, the disease caused 2.22 million deaths. Neurological disorders are the fourth of the most common cause of death, accounting for 3.1% of the total fatalities. This is because the nervous system is extraordinary branched, and each of its subsystems is unique. Most often violations functions of the nervous system adversely affect the functions of other internal organs and systems [16, 17, 38].

It is known that the symptoms of neurological disorders can manifest themselves in different ways, very often, in particular in the form of motor disorders (paresis, paralysis, inability to move quickly, tremor), coordination disorders are also possible and speech, involuntary contractions of different muscle groups, tics, tremors. Also important symptoms of diseases of the nervous system are headaches (migraine), pain in the back and neck, arms and legs. Diseases of the nervous system may be manifested by epileptic seizures, tantrums, sleep disorders and consciousness, mental activity, behavior and psyche. Although modern medicine has a significant number of drugs, both synthetic and herbal origin, but most of them with long-term use, unfortunately lead to adverse reactions [18, 19, 26]. Therefore, the search for highly effective drugs is important with minimal side effects with prolonged use, which are not addictive. In this aspect, special attention is drawn homeopathic medicines, in particular rosemary preparations.

In homeopathic practice, this plant is used in the treatment of nervous diseases, including memory deficits, mental retardation, dizziness, headache, etc.

**The purpose and objectives of research**

The technology of homeopathic medicines has been experimentally developed rosemary for the treatment of diseases of the nervous system.

To achieve this goal it is necessary to solve the following **tasks**:

- to analyze the literature data about usage of rosemary as an API for the treatment of diseases of the nervous system;
- to consider the basic principles of homeopathy, its differences from allopathy;
- to analyze the approaches to homeopathic quality control of medicines;
- to develop the technology of homeopathic basic tincture of rosemary and study its organoleptic, physical, chemical and technological quality indicators;
- to develop the technology of homeopathic rosemary granules and to offer methods of quality control in pharmacies.

**Scientific novelty**

The technology of homeopathic medicines of rosemary and their quality indicators were studied.

**Theoretical and practical significance of the work**

The theoretical and practical significance of the master's thesis is that the technology of homeopathic medicines has been experimentally developed, including basic tincture and homeopathic granules of rosemary, as well as proposed methods of quality control in pharmacies.

**Implementation of results**

The main provisions of the qualification work are set out and discussed at 7th International scientific and practical conference “International scientific innovations in human life” (January 19-21, 2022, Manchester). Article has been published.

**Structure and scope of qualification work.**

Qualification work consists of an introduction, literature review (Chapter 1), the experimental parts (sections 2 and 3), general conclusions, references, appendices. The work is presented on 47 pages, includes 15 tables, 2 figures, 71 source of literature and 2 appendices.

# CHAPTER I.

# PROSPECTS OF THE DEVELOPMENT OF HOMEOPATHIC ROSEMARY MEDICINES

## 1.1. Application of rosemary in medicine

Rosemary was introduced from the Mediterranean. It is grown mainly in the Crimea and in the south of Ukraine, as an ornamental and essential oil plant. Rosemary is officially included in the group of medicinal plants in most countries of the world.

Evergreen, densely deciduous shrub 0.5-2.0 m high. The leaves are linear, opposite, sessile, leathery, 1.5-3.5 cm long and 2-4 cm wide, with edges curled down. The flowers are small, collected in dense inflorescences, coloring from dark purple to white [24, 27, 34].

Rosemary is a popular essential oil plant since ancient times. Its name comes from the Latin (sea dew) and was not given to it by chance: rosemary grows on the seashore, in splashes of sea foam. That is why the ancient the Greeks and Romans dedicated it to the foam-born Aphrodite (Venus) and believed that this wonderful plant can make a person happy, deprive evil dreams and preserve youth [28, 29]. Rosemary has long been a favorite spice in the Mediterranean. In regions with a warm climate, rosemary grows outdoors in one place up to 20 years old.

The chemical composition of rosemary is very rich and varied. The leaves of the plant have about 2.5 % essential oil, 1.2 % bitterness, 0.5 % alkaloids, tannins (5 – 8 %), flavones, β-sitosterol, amyrin, betulin, choline, resinous substances, wax, nicotinamide, nicotinic, ursolic, rosemary, glycolic and caffeic acids and minerals (up to 10 %). The essential oil contains pinenes (30 %), camphene (20%),

cineole (10 %), borneol (10-17 %), camphor (7 %), caryophyllene (up to 8 %), bornyl acetate (2 %), limonene, myrcene, pulegone, menthon [25, 34, 45].

Dried rosemary leaves are used to prepare various preparations and medicines. In addition, essential rosemary oil is squeezed out of the freshly harvested leaves. Rosemary is considered an antidepressant [62, 66-69], antispasmodic (ethereal butter); scarring agent [71]; antimicrobial agent; anti-inflammatory agent; carcinogen blocker and liver detoxifier; antirheumatic drugs (ointment with essential oil) [33, 40, 42].

In recent publications by world scientists, it has been recorded that rosemary is a promising source of anticancer molecules and is an enhancer of the bioavailability of anticancer drugs [32].

Rosemary has been used in folk medicine to relieve a number of ailments including headache, dysmenorrhea, abdominal pain, epilepsy, rheumatic pains, spasms, nervous agitation, memory enhancement, hysteria, depression, as well as physical and mental disorders, fatigue [41, 49, 50, 52] (fig. 1.1.).

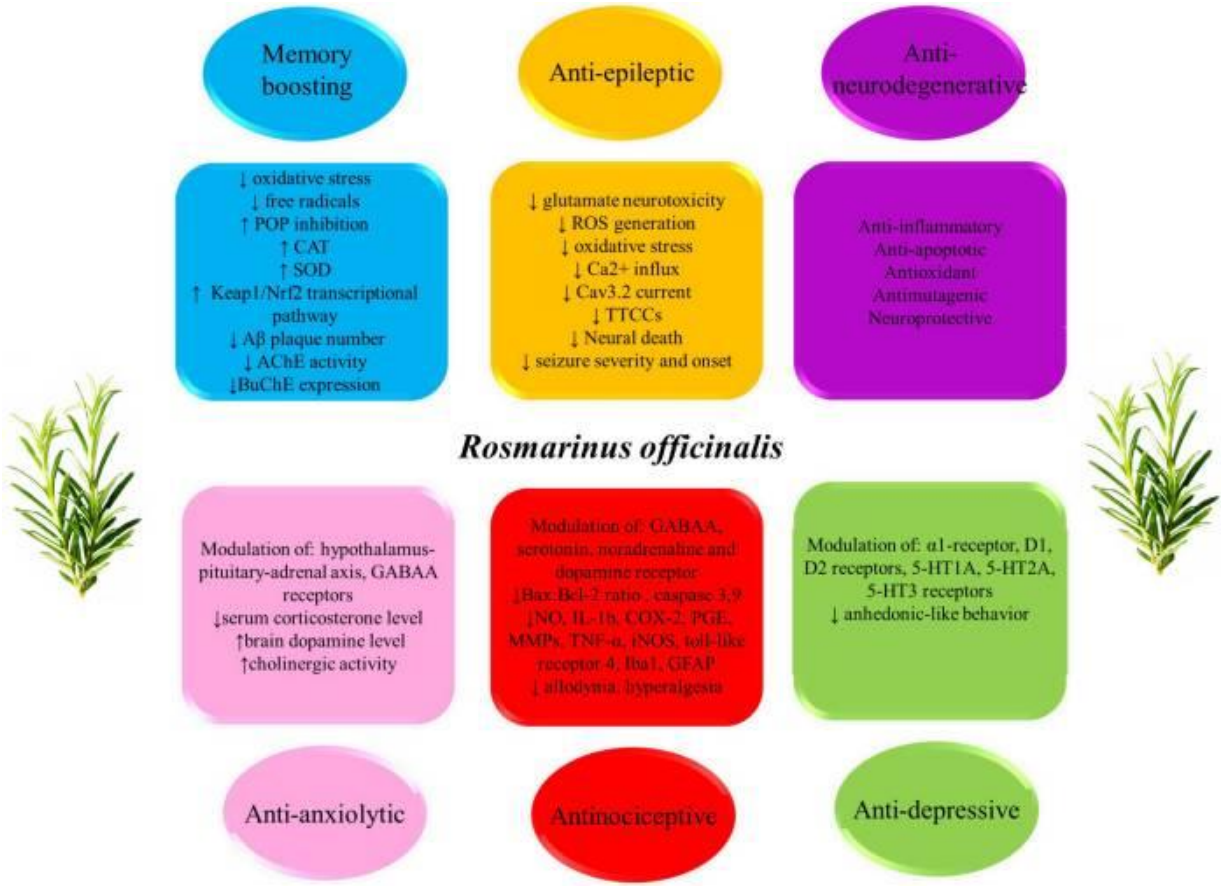
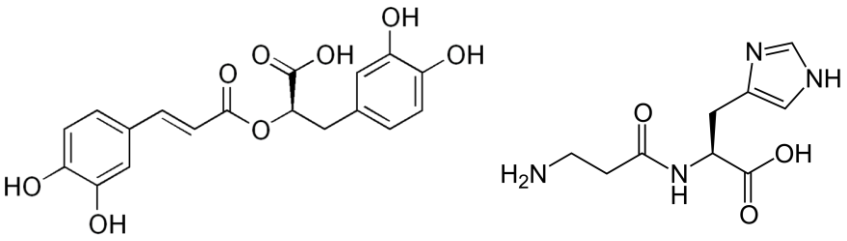



**Fig. 1.1. Neuropharmacological properties of rosemary on nervous system**

The last, sometimes noticeable scientific interest is focused on the beneficial therapeutic properties of various types of rosemary extracts and its main components, such as carnosic acid, carnosol, rosmarinic acid, etc. (fig. 1.2) .




Rosmarinic acid Carnosine

**Fig. 1.2. Chemical structures of some constituents of rosemary (*Rosmarinus officinalis* L.)**

In traditional medicine, rosemary oil is recommended for use in pulmonary diseases, as well as gastric, anti-laxative, choleretic, diuretic and antispasmodic [5, 43, 4].

Rosemary preparations in the form of a decoction, infusion and alcoholic extract, as well as essential oil, are used for digestive disorders, vaginitis, and respiratory disorders diseases, varicose veins, pain in the heart, inflammation.

The use of an infusion of dried rosemary leaves led to a decrease in blood glucose levels in normoglycemic and diabetic patients and not a few toxic effects [56].

Rosemary oil stimulates the hair follicles and circulation in the scalp and thus may be helpful in premature baldness. Rosemary is also used for cosmetic purposes. The oil is useful for combating dandruff, promotes hair growth, and controls oily hair [6].

A noticeable therapeutic effect of rosemary is observed in neurasthenia, hysteria, sleepless, migraine, epilepsy, hypertension, vascular dystonia, dizziness, flatulence, impotence, chronic bronchitis, influenza and bronchial asthma [54, 55, 59, 60].

To date, rosemary officinalis is a part of many foreign-made combined preparations. Among them, preparations containing rosemary oil are the most common [15].

*Recipes with rosemary officinalis.*

An infusion of rosemary leaves is prepared by steaming one tablespoon of the herb with two cups of boiling water. After two hours, the infusion is filtered and consumed half a glass before meals three times a day. Also, this infusion is used externally in the form of douches, compresses and rinses.

For rubbing, an alcohol solution of rosemary oil is prepared. To do this, add 50 alcohol to 1 part of the oil.

Also, to prepare a bath, 200-250 g of dried rosemary leaves are poured into 2 liters of boiling water, then filtered and poured into a filled bath with a water temperature of 36-40 °C. Taking a bath lasts about 30 minutes [57].

In homeopathy, this herb was considered the best remedy for restoring memory disorders or getting out of forgetfulness (depending on the dose). Homeopathic remedies are prepared from a matrix tincture (MT) of the dried leaves of the plant [47, 37, 51].

The main clinical symptoms of rosemary preparations:

- ✓ disorders of falling asleep and sleep;
- ✓ errors of memory and perception;
- ✓ weakening of memory;
- ✓ headaches;
- ✓ noises in the head and ears;
- ✓ disorders of the menstrual cycle;
- ✓ dandruff, baldness;
- ✓ Violation of thermoregulation.

The main dosage forms of rosemary for internal use are homeopathic granules (D3, C3, C6 and above) and drops (D3, C3, C6 and above) [3, 4].

## 1.2. Basic principles of homeopathy

Homeopathic medicine,or homeopathy, is a form of complementary and alternative medicine that uses very small amounts of natural substances, which in higher amounts may cause a disease or symptom.

This branch of medicine came into being in the 19th century and was used frequently at the time. Interestingly, the first studies using homeopathic remedies were done on healthy volunteers - similar to many clinical trials done today.

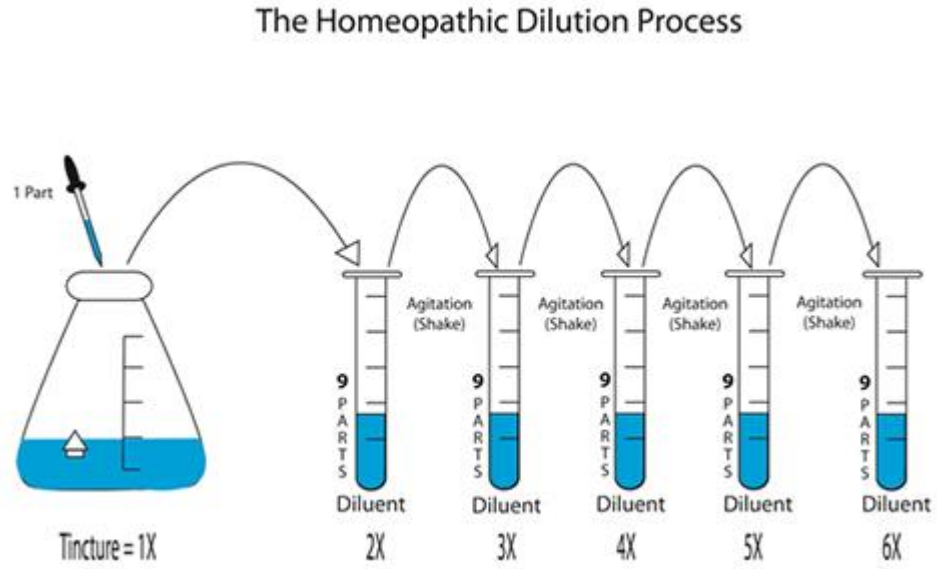
Homeopathy was developed by a German healthcare provider, Samuel Hahnemann, in 1807. He treated himself with a small amount of tree bark (cinchona bark) containing quinine, which is used to treat malaria. When he developed the symptoms of malaria, he came up with his law of "like cures like;" believing that drugs that cause specific symptoms can be used to cure the illnesses that cause those symptoms.

While the use of homeopathy has fallen off with the advent of newer conventional treatments, there are over 2,000 substances that have been utilized as homeopathic treatments.

The theory behind homeopathic medicine is that "**like cures like**" and that a substance that causes an illness in a healthy person might cure those symptoms in someone who is ill. It’s believed by practitioners of homeopathy that a small amount of the substance which causes a disease will stimulate the body to heal itself.

The thought is that diluting and agitating an ingredient activates the curative powers of the ingredient, thus enhancing its effect. Potency in homeopathic solutions is indicated by an D(X) or C.

- **D(X):** For every dilution, one part of an ingredient is mixed with two parts water. For example, a 1X potency would be a solution that is one part ingredient and 9 parts water.




- **C:** Potency may also be described with a C. A 1C solution refers to a solution that is one part ingredient and 99 parts water.


There are three main principles behind the practice of homeopathic medicine.

*The law of similars:* The law of similars refers to the "like cures like" theory noted above.

*The principle of the single remedy:* This principle holds that a single remedy should cover the physical, emotional, and mental symptoms of an illness combined.

*The principle of the minimum dose:* Only a small amount of substance is first used in a few doses, followed by an infinitesimal amount over time.

The term *homeopathy* derives from the Greek *homoion pathos*, which means 'similar suffering'. By comparison, the term *allopathy* which refers to orthodox (conventional) medicine, comes from *allos*, meaning 'different'.

Hahnemann believed that there was a vital force within everyone that was responsible for health and healing. Homeopathy is based on the concept of holism and the belief that every part of the body is connected; physical symptoms elicit a psychological response, likewise psychological symptoms result in functional and structural changes in the body. To treat a complaint, therefore, it is necessary to treat the whole person, not just the part or organ that is affected.

### 1.3. The main issues of quality of homeopathic medicines

Homeopathy is a system of medicine that was born in Europe at the end eighteenth century. Homeopaths use homeopathic remedies drugs that are prepared according to a clearly defined procedure, using substances of mineral, vegetable and animal origin [3, 4].

The technique of preparation of these drugs includes dilution of the original raw materials in aqueous-alcoholic solutions or other excipients, and also potentiation on different scales (Centesimal, Decimal, Fifty Millesimal). In some cases, breeding so large that it is almost impossible to find a single molecule of the original raw materials. The use of homeopathic medicimes (HM) is becoming common more in our time. With increasing use of HM and the rapid expansion of the world market, a major challenge for the authorities healthcare, the pharmaceutical industry and consumers are safety and quality of HM [10].

It is known that the safety of medicines, including homeopathic, in many ways depends on their quality. Requirements for quality control methods ready HM are more complex than for chemicals, especially in case of combined homeopathic.

In addition, the quality of HM depends on both the quality of the technological operations used during their production and the quality of raw materials.

High-quality medicines that meet high standards are guaranteed qualities necessary for the patient to be able to use them safely [7]. Today, this is becoming increasingly important as a result of the market globalization, most raw materials for the production of HM are of foreign origin. Therefore, ensuring the basic requirements for HM on at the international, national and regional levels is extremely important issues for consumer protection.

Over the last three decades, drugs of natural origin have been increasingly used. This is evidenced by data on the sale of phytopreparations around the world, and it is HM are the most commonly used among them. There is a large market for homeopathic products around the world. This is primarily due to the fact that HM contain very large dilutions (potencies) and API may not even be quantified in the drug. That is why it is believed that HM are safe and do not cause side effects [8].

However, there are some aspects of HM production that could lead to potential hazards. First, not all HM are prescribed in high dilution. Sometimes they may contain a concentrated matrix tincture made from sources of animal or vegetable origin. Second, HM are made from a wide range of natural or synthetic sources: minerals and chemicals, as well as plant materials, including roots, stems, leaves, flowers, bark, pollen, lichens, mosses, ferns and algae; microorganisms, including fungi, bacteria, viruses and parasitesplants; animal organs, tissues, secretions and cell lines. Human materials may include tissues, secretions, hormones, and cell lines. Some of these raw materials pose a potential hazard, even in high dilution.

Homeopathic remedies are based on the principle of high dilutions, and potentially active molecules (APIs) preserve the memory of the original substance. Therefore, the starting materials are homeopathic compositions and / or matrix

tinctures, which are subject to a process of sequential dilution and mixing to potentiation of the product with an inert carrier material (water, ethyl alcohol, glycerol, etc.) [20, 61].

From a safety point of view, it is important to note first that although homeopathic treatments often use ultra molecular dilutions of the starting material, there are also much lower dilution homeopathic remedies that contain molecules that may be active in biochemical sense. Therefore, although homeopathic remedies are generally considered safe when properly administered, toxicological aspects should not be neglected, especially when using low dilutions.

There are two major groups of potential hazards to HM, including those related to the origin of the materials and those related to the technological operations used to make the final drug [35].

They are used to prepare homeopathic remedies or their stocks / matrix tinctures of natural or synthetic sources, which are referred to in pharmacopoeial monographs or other normative documents. Contamination with pesticides and heavy metals is considered to be the main problem of danger from raw materials of plant origin. The content of toxic components in plant raw materials can vary significantly depending on the place and region of growth. The Good Manufacturing Practice (GMP) Guidelines, which cover the manufacturing process, premises, personnel, packaging and labeling, apply to HM as well as to conventional pharmaceuticals. Failure to follow these rules can lead to serious quality and safety problems, namely: incorrect identification, contamination of raw materials, cross-contamination or accidental contamination [20, 22].

The unique characteristics of the production of HM are a number of specific consequences that require specially qualified and experienced personnel. They must work with toxic materials, especially fresh raw materials prone to degradation and microbial contamination, as well as raw materials of animal origin, microorganisms, secretions, etc. The properties of HM can be compromised accidentally or intentionally by contamination of raw materials, excipients, fillers or packaging in which the dilution is carried out.

Where plant materials are used, all substances, including plant parts, exudates or processed materials, must comply with specific national quality standards and specifications, pharmacopoeial analytical requirements and monographs. Due to the complex and variable nature of plant material, in particular contamination by microbes, insects, pesticides, heavy metals, fumigants, toxins and radioactivity, adequate feedstock control, storage and processing is of particular importance. Manufacturers must strictly comply with the standards and regulations for determining the quality of raw materials, limit tests and additional tests [7, 11, 1223] (table 1.1).

Table 1.1

**Regulation on quality control of plant raw materials used in preparation HMs**

| | |
|---|---|
| Raw material identification | 1. Name;<br>2. Growth stage;<br>3. Part of the used plant;<br>4. Information about whether the raw material was processed or collected from the wild or the place of cultivation;<br>5. Comparison by manufacturer or recognized laboratory, illustrated sample description for macroscopic and microscopic characteristics, as well as the analytical determination of marker substances or standard substances (if any). |
| Limit tests | 1. Limit tests should be performed for:<br>• pesticides (agricultural and veterinary chemicals),<br>• heavy metals (if necessary, for metals such as lead, mercury, arsenic and cadmium),<br>• fungi, bacteria, fungal toxins;<br>• any other relevant contamination (eg by-products of the production of radiation products derived from ionizing radiation sterilization or residues from another decontamina- |

| | |
|---|---|
| | tion procedure).<br>2. Limit tests should be carried out on representative raw samples.<br>3. Limit tests and ranges must be in accordance with pharmacopoeial standards. |
| Additional tests | If necessary, tests are carried out to determine:<br>1. impurities;<br>2. total ash;<br>3. water content;<br>4. meaning of bitterness;<br>5. weight loss on drying;<br>6. contents of radioactive contamination. |

A clear description of the following characteristics must accompany each batch of raw materials, or justify its absence:

- used part/material;
- microscopic characteristics;
- identification tests;
- purity test;
- moisture/water content;
- determination of the content of toxic components (if any);
- method of preparation of uterine tincture.

Thus, the main approach of the regulatory authorities is to ensure the quality of HMs. Manufacturers, packers, labellers, importers and distributors of HMs or raw materials must comply with the requirements that include effective process control, analytical methods of analysis, storage conditions and sanitary conditions.

## CONCLUSIONS

1. Literature data on the characteristics and use of rosemary officinalis in medicine are summarized. The main groups of biologically active substances contained in this plant are considered, as well as the main recipes for the preparation of dosage forms with fresh and dried raw materials are proposed.
2. A comparative analysis of allopathic and homeopathic approaches in the treatment of patients was carried out. The advantages of treatment with homeopathic medicines based on the basic principles of homeopathy are presented.
3. The main approaches to the quality control of HMs, especially of plant and animal origin, are considered. Information on the mandatory quality control of the feedstock is summarized.
4. The expediency and prospects of the development of rosemary HM in the form of a matrix tincture and granules for the treatment of diseases of the nervous system have been proved.

# EXPERIMENTAL PART

# CHAPTER II

# OBJECTS AND METHODS OF RESEARCH

In the development of homeopathic medicines of rosemary - tinctures and granules intended for the treatment of nervous diseases, as API used dried rosemary leaves, which meets the requirements of the SPhU.

## 2.1. Objects of researches

The objects of research were dried rosemary leaves, tincture of rosemary D1, rosemary granules D3.

### 2.1.1. Characteristics of active substances

**Rosemary leaves** are a member of the genus Rosemary (*Rosmarinus*) of the *Lamiaceae family*, is a dense, evergreen, fragrant perennial plant. Rosemary is a powerful, highly branched shrub (90-200 cm high). The root system is well developed, it can penetrate 3-4 m deep. The old branches are woody, the bark is gray-brown in color. Young branches are covered with white felt, pubescent, tetrahedral. The leaves are oblong (2-4 cm), on a short petiole, wrapped inside. The outer surface of the leaf is dark green, and the underside is white, resinous. During the flowering period, pale blue small flowers appear. Rosemary leaves are harvested before flowering or during the flowering period of the plant. For this, young shoots are collected and dried, laying them thin in layers in well-ventilated rooms or outdoors in the shade. After drying, the leaves are separated from the stems and packed hermetically in glass containers. For faster separation of leaves from stems, dried raw materials are laid out in the sun for several hours. For artificial drying, it is necessary to provide a room temperature of 35-40 °C.

**Rosemary tincture D1** is a greenish-brown liquid, transparent with a smell of alcohol and a bitter taste.

**Rosemary D3 granules** are white spherical granules, odorless, sweet taste.

### 2.1.2. Characteristics of excipients

The following excipients were used to prepare the basic preparation of rosemary (matrix tincture) and homeopathic granules based on it: ethyl alcohol, purified water, sugar granules.

**Ethyl alcohol** (CAS No. 8001-79-4) is a clear, colorless liquid with a specific odor; store in a tightly closed original container with minimal contact with air, in a cool, dry and ventilated area away from sources of heat, open flame and protected from light.

**Purified water** (SPhU 1.1, p. 308-309) is a colorless, transparent liquid, odorless and tasteless, pH 5.0-7.0 (potentiometrically).

**Sugar granules** (Pills for homeopathic medicines) (SPU, type 2, 2, p.234) granules of spherical shape of white color or light yellow color, sweet taste without smell.

## 2.2. Methods of researches

Organoleptic, physicochemical, technological research methods were used in the course of the work.

**Appearance.** Determination of matrix tincture was performed on organoleptic parameters: transparency, color, odor, taste.

**Transparency** (SPhU, 1st ed., suppl. 2.2.1, p. 15). A test tube made of colorless transparent neutral glass with a flat bottom having an inner diameter of 15 mm to 25 mm was used. The determinations were performed in diffused daylight, looking along the vertical axis on a black background.

**Color** (SPhU, 1st ed., p. 2.2.2, pp. 15-17). Determined visually by comparing the color of the studied samples with purified water. The comparison was carried out in identical tubes of colorless transparent glass under diffused daylight light, viewing the samples horizontally against a white background.

**Relative density** (SPhU, 1st ed., p. 2.2.5, pp. 19-21). Method 1 (pycnometric method) was used to measure the density.

**Dry residue** (SPhU, supplement. 1, p. 2.8.16, pp. 63-64). The determination was performed with 5.0 ml of tincture.

**The alcohol content** (SPhU, supplement 1, p. 2.9.10, pp. 76-82) was determined pycnometric method.

**The number of sticky granules** is determined in the mass of a sample of 5.0 g of granules, weighed with an accuracy of 0.01 g.

**The number of granules of 1.0 g** is determined in the weight of the sample 5.0 g of granules, weighed to the nearest 0.01 g. Determination of the number of granules was performed on the basis of visual inspection in the weight of the sample 1.0 g of granules. Determine the weight of the sample 1.0 g of granules weighed to the nearest 0.01. The final value of the account of three samples. The number of granules in 1.0 g should be 28 - 30 pieces.

**The average weight of one granule** (mg) was determined after calculating the number of granules in the sample.

**Disintegration**. 10.0 g of granules are added to a volumetric flask of 100 ml, add 50 ml of water (t = 37 ± 20 C). Slowly shake the flask 1-2 times per second. Conduct at least three determinations.

**Bulk volume.** Determination is carried out according to the method of SPhU (1st ed., P. 2.9.15, p. 162).

**The content of extractives** in the base preparation was determined by evaporation in a water bath of a precise portion of the tincture, placed in a pre-weighed and dried for 60 minutes in a thermostat porcelain cup. Evaporation was performed for 30 minutes at $100^0$C in a thermostat to constant weight.

**The content of extractives** (X, %) was calculated using the formula:

$$X = (m_1 \times 100) / m$$

where: m - weight of the drug before drying, g;

$m_1$ - weight of the drug after drying, g.

**Capillary and capillary-luminescent analysis.** Strips 2 cm wide and 25 cm long were cut from filter paper of the same grade perpendicular to the texture of the paper and hung in a cylindrical glass vessel about 5 cm high and 3 cm in diam-

eter so that the ends of the strips touched the bottom. 5 ml of the test liquid was added to the vessel, placed in a moderately warm room, and after 24 hours the strips were dried and examined under daylight and UV light.

Identification of biologically active substances in tincture.

*Precipitation reactions for alkaloids*

A drop of tincture is placed on a glass slide. A second drop of reagent is applied (0.5 % picric acid solution, 1 % potassium permanganate solution, etc.). Then two drops are mixed with a glass rod and observed sediment formation.

*Color reactions for alkaloids*

Reaction with sulfuric acid: to 1 ml of tincture add 2 drops of sulfuric acid. Coloring is formed.

Reaction with nitric acid concentrated: to 1 ml of tincture add 2 drops of concentrated nitric acid. Coloring is formed.

Reaction with Erdmann's reagent, Frede's reagent, Mark's reagent: to 1 ml of tincture add 2 drops of the reagent. Coloring is formed. [12, 34]

*Identification reactions of amino acids and carbohydrates*

Reaction with ninhydrin

A few crystals of ninhydrin are added to 1 ml of the tincture and the mixture is heated in a water bath for 10 minutes. After shaking, a blue-violet color (amino acids) should form.

Reaction with 10% tannin solution

3 ml of tincture add 3 ml of 10% tannin solution. The mixture is shaken and left for 10 minutes. A haze should form, followed by precipitation (proteins).

Reaction with thymol

2.5 ml of tincture is added with 5 ml of concentrated sulfuric acid and 5 ml of a 5% alcohol solution of thymol. A red color should form after shaking (carbohydrates).

Reaction with resorcinol in concentrated sulfuric acid

3 ml of tincture is heated in a water bath for 10 minutes. Add a few crystals of resorcinol and 5 drops of concentrated sulfuric acid, heat to the formation of a

brown color solution. After cooling, 5 ml of purified water and 5 ml of 25 % ammonia solution are added. A yellow color with a pink precipitate should form (glutamic acid, fructose).

Reaction with resorcinol in hydrochloric acid medium: to 1 ml of tincture, add 2 ml of dilute hydrochloric acid and a few crystals of resorcinol, heat in a water bath. A yellow-brown color (fructose, glucose) should form.

Reaction with Felling's reagent: to 2 ml of tincture add 1 ml of concentrated sulfuric acid and place the test tube in a water bath for 5 minutes. Add 5 ml of Fehling's reagent and heat in a water bath at 100°C for 5 minutes.

An orange precipitate (polysaccharides) should form [10].

*Saponin identification reactions*

Reactions Lafon reaction

To 2 ml of tincture add 1 drop of 10 % copper sulfate solution, 1 ml of sulfuric acid and heat in a water bath. A blue-green color should form.

Reaction with chloroform

To 2 ml of tincture add 1 ml of chloroform and 5 drops of concentrated sulfuric acid. The organic layer should be orange in color.

Reaction with vanillin: to 2 ml of tincture add 1 ml of 0.5 % alcohol solution of vanillin, 3 drops of concentrated sulfuric acid and heat in a water bath. A yellow or red color should form.

Reaction with Erlich's reagent.

To 2 ml of tincture add 1 ml of the reagent. Has a pink color.

Reaction with formaldehyde in concentrated sulfuric acid.

To 2 ml of tincture add 1 ml of formaldehyde and 2 drops of concentrated sulfuric acid. A yellow color should develop slowly fading into pink color.

*Precipitation reaction*

To 1 ml of tincture add 4 drops of 10 % lead acetate solution. Precipitation is observed [24, 34].

*Identification reaction*

Reaction with reagent.

To 0.5 ml of concentrated hydrochloric acid, add 1 ml of tincture and 0.5 ml of the reagent, heat the mixture in a water bath. A green-blue color should form.

Reaction with Trim-Hil's reagent.

Add 0.5 ml of reagent to 1 ml of tincture and heat on a water bath for 2 minutes. [24].

*Identification reactions of tannins*

General precipitation reaction.

To 2 ml of tincture, add drops of 1 % gelatin solution until turbidity forms.

Precipitation reaction.

To 2 ml of tincture add 5 drops of formaldehyde solution in concentrated hydrochloric acid and heat in a water bath for 5 minutes. A precipitate should form.

Reaction with vanillin in sulfuric acid.

To 1 ml of tincture add a few drops of a 1 % solution of vanillin in sulfuric acid. A red color should form [34].

*Flavonoid identification reactions*

Reaction with sodium hydroxide: to 1 ml of tincture add 2 drops of 10 % sodium hydroxide solution. A yellow color should form.

Reaction of aluminum chloride: to 1 ml of tincture add 1 ml of 5 % alcohol solution of aluminum chloride. A yellow color should form.

Reaction of iron (III) chloride: to 1 ml of tincture add 3 drops of 1% alcohol solution of iron (III) chloride. A dark green or brown color should form.

*Polysaccharide identification reactions*

Reaction with ammonia solution: to 1 ml of tincture add 2 drops of ammonia solution. A dark yellow color (mucus) should appear.

Reaction with concentrated hydrochloric acid: to 1 ml of tincture add 2 drops of concentrated hydrochloric acid. A yellow-green color (mucus) should form.

Reaction with iodine solution: to 1 ml of tincture add a few drops of iodine solution. A yellow or brown color should form (cellulose).

Reaction with sodium hydroxide solution: to 1 ml of tincture add 2 drops of 10% sodium hydroxide solution. A yellow color should form (dextrin).

Reaction with Felling's reagent.

To 2 ml of tincture add 2 drops of an aqueous solution of copper sulfate (solution A) and 2 drops of solution B (potassium-sodium salt of tartaric acid). A blue precipitate should form (starch).

Reaction with α-naphthol in sulfuric acid.

To 1 ml of tincture add 2 drops of 20% alcohol solution of α-naphthol and 1 drop of concentrated sulfuric acid. A pink color (inulin) should form.

**Identification of excipients in granules.** Accurate weighing of 0.5 g of saturated granules is placed in a 50 ml beaker, 10 ml of water are added and stirred until the granules are completely dissolved. Reagents are added to 2 ml of an aqueous solution of granules and by color determine the content of biologically active substances.

Reaction with a cobalt chloride solution.

0.1 g of granules are dissolved in 3 ml of water, 1 ml of 1 M sodium hydroxide solution and 2-3 drops of 0.1 M cobalt chloride solution are added. Pink coloring should form.

Reaction with Felling's reagent: 0.1 g of granules are dissolved in 3 ml of water in a test tube. Add 0.5 ml of 1 M hydrochloric acid solution and place the tube in a water bath for 3 minutes. Add 3 ml of the reagent and heat at 100° C for 5 minutes. An orange precipitate (galactose, glucose, lactose) should form.

Reaction with ammonia solution

10.0 g of granules D3 are dissolved in 3 ml of water, 3 ml of 25 % ammonia solution are added and heated for 10 minutes. A yellow color should form.

Reaction with potassium hydroxide 5.0 g of granules D3 are ground in a mortar. 0.1 g of the resulting powder is added to a porcelain cup and 3 drops of a 2 M potassium hydroxide solution are added. Add a piece of solid potassium hydroxide. A yellow color should appear.

**Identification by TLC**

Qualitative determination of **sugars** was carried out by TLC using a Silufol plate [36].

For chromatographic determination, a mixture of solvents was used: n - butanol - acetone - water in the ratio (4:5:1). Chemically pure solvents were used to prepare the system.

To develop the plates, we used the treatment procedure with a 50% alcohol solution of thymol with concentrated sulfuric acid. The plates were heated in a thermostat at a temperature of 100°C. For the chromatographic determination of sugars contained in the tincture, 0.1 μl of 0.02 % aqueous solutions of fructose, glucose, sucrose, and lactose were used as a reference solution.

On the start line of the chromatographic plate, 0.1 μl or 0.2 μl of test solution are placed. Lifting height 10 cm. The plates were dried under draft in air. On the chromatogram of the tested solutions, pink spots were observed at the level of the reference solutions.

**Qualitative determination of phenolic compounds** was carried out by TLC in the solvent system: toluene - ethyl acetate - formic acid - water in the ratio (10:100:100:10).

To prepare the system, brand solvents chemically pure were used. To develop the plates, they were treated with a 10 % alcohol solution of aluminum chloride. The plates were heated in a thermostat at a temperature of 100°C.

For the chromatographic determination of phenolic compounds contained in the tincture, 0.1 μl of a 0.02 % standard alcoholic solution of caffeic acid and 0.1 μl of a 0.2 % solution were used as a reference solution rutin.

0.1 μl of the test solution was applied with pipettes to the start line of the chromatographic plate. Lifting height 10 cm. The plates were dried under draft in air. On the chromatogram of the test solutions, a bright yellow spot was observed at the level of the rutin reference solution and a bright blue spot at the levels of the caffeic acid reference solution [34].

Qualitative analysis of amino acids was carried out by thin-layer chromatography on Silufol plates.

To study the amino acid composition, a system of solvents was used: n-butanol – acetic acid – water (4:1:1). The ratio of solvents was taken in volume parts.

Solvents for the preparation of systems used brand chemically pure. For the detection of amino acids in the tincture, one-dimensional thin layer chromatography was performed in comparison with standard 0.1 % alcohol solutions of amino acids. Spots on the plates were applied with a pipette, 10 μl of tincture. The plates were dried under draft in air. The chromatogram was treated with a 0.2 % solution of ninhydrin in butane saturated with water and heated in an oven at a temperature of 100-105$^0$C for 10 min. To detect amino acids, their ability form purple and pink colored zones (proline - yellow) after treatment with the reagent was used [168].

Quantitative content of flavonoids was determined by spectrophotometric method [1].

The original test solution.

Place 10.0 g of tincture (exact portion) in a 100 ml conical flask, add 7.0 ml of 250 g/L hydrochloric acid solution, 70 ml of acetone and reflux for 1 hour in a water bath. Chilled the resulting solution is quantitatively transferred to a volumetric flask with a capacity of 100 ml with acetone and bring the volume of the resulting solution to the mark, mix.

20.0 ml of the resulting solution is placed in a separatory funnel, add 20 ml of water and extracted three times with ethyl acetate in portions of 15, 10 and 10 ml. All ethyl acetate extracts are placed in a second clean separatory funnel and washed twice with water in 50 ml portions. The water-washed ethyl acetate extract was filtered through a paper filter of 10 g of anhydrous sodium sulfate into a 50 ml volumetric flask. Wash the filter and separatory funnel with ethyl acetate, make up to volume with the solution in the flask.

The optical density of the test solution was measured at a wavelength of 438 nm in a cuvette with a layer thickness of 10 mm

The content of the amount of flavonoids (X,%), in terms of quercetin calculated by the formula:

$$X = \frac{A_1 \times 100 \times 50 \times 25 \times m_0 \times 5 \times 1 \times 100}{m_1 \times 20 \times 10 \times 50 \times 20 \times 25 \times A_0},$$

where: $A_1$ is the optical density of the test solution, nm;

$A_0$ is the optical density of the standard solution, nm;

$m_1$ is the mass of sample tincture, g;

$m_0$ is the weight of a sample of quercetin standard sample, g.

*The original standard solution.*

20.0 mg (exact portion) of a standard sample of quercetin was placed in a volumetric flask with a capacity of 50 ml, 40 ml of acetone was added and dissolved by placing the flask in an ultrasonic bath for 5 minutes. The volume of the solution was adjusted to the mark with acetone and stirred. Place 5 ml of the resulting solution in a 20 ml volumetric flask and make up to the mark with acetone.

# CONCLUSIONS

1. Homeopathic raw materials were used as objects of study, such as: dried rosemary leaves, rosemary tincture D1, homeopathic granules D3.

2. Organoleptic, physical, chemical and technological research methods were used in the development of the homeopathic medicines of rosemary.

# CHAPTER III.
# DEVELOPMENT OF THE TECHNOLOGY OF HOMEOPATHIC MEDICINES OF ROSEMARY

## 3.1. Development of technology and research of homeopathic basic tincture of rosemary

### 3.1.1. Justification of the time of infusion of raw materials

Production and quality control of HMs is carried out in the world according to pharmacopoeias, in particular for Ukraine - according to the SPhU. Also, the use of Dr. W. Schwabe's guide and the German Homeopathic Pharmacopoeia is temporarily allowed for some HMs.

According to the manual, the preparation of basic preparations of rosemary is carried out using dried raw materials (rosemary leaves) according to method 4a, given in the SPU (1 ed.). Matrix tincture of rosemary D1 was made by maceration in the ratio (1:10) using alcohol ethyl 90% [37].

According to method 4a, the crushed raw material is mixed with a calculated amount of 90 % ethyl alcohol and kept at a temperature of 16ºC for 8 days at daily stirring, then the raw material is squeezed and defended for 8 days, after which the liquid is filtered.

In order to justify the time of infusion of raw materials, we made 5 samples of matrix tincture of rosemary with different infusion times (from 5 days to 9 days):

Sample 1 - 5 days of infusion.

Sample 2 - 6 days of infusion.

Sample 3 - 7 days of infusion.

Sample 4 - 8 days of infusion.

Sample 5 - 9 days of infusion.

Therefore, in order to determine the effect of maceration time on the physical and chemical parameters of the obtained tinctures, we studied their indicators, the results of which are shown in table 3.1.

Table 3.1

**Physical and chemical parameters of the matrix tincture of rosemary D1 depending on the time of infusion**

| **Indicators** | **Infusion time, days** | | | | |
|---|---|---|---|---|---|
| | **5** | **6** | **7** | **8** | **9** |
| Color | green-brown | | | | |
| Odour | tart, sweet, specific, weak | | | | |
| Taste | bitter, burning | | | | |
| Transparency | liquid is transparent, there are no mechanical inclusions | | | | |
| Ethanol content,% | 89.05 ± 0.50 | 88.80 ± 0.30 | 88.70 ± 0.30 | 88.10 ± 0.50 | 88.05 ± 0.30 |
| Relative density,kg/m$^3$ | 0.818± 0.002 | 0.819 ± 0.002 | 0.820 ± 0.002 | 0.821 ± 0.002 | 0.825 ± 0.002 |
| Dry residue,% | 3.62 ± 0.05 | 3.70 ± 0.05 | 3.77 ± 0.03 | 4.15 ± 0.05 | 4.16 ± 0.05 |
| Flavonoids content (%) in terms of quercetin | 0.032 ± 0.002 | 0.030 ± 0.003 | 0.033 ± 0.005 | 0.044 ± 0.002 | 0.045 ± 0.002 |

Notes: n = 5; P = 95%

As can be seen from the results of research, when infused for 5 -7 days there is a smaller amount flavonoids, and in the case of increasing the infusion time to 9 days, this figure does not change significantly.

The values of density and dry residue for the basic preparation of rosemary X1 are objective and are within acceptable limits. Thus, the results of the study jus-

tify the need to comply with these regimens of maceration in the manual, which is 8 days.

### 3.1.2. Technology of preparation of rosemary mather tincture in a pharmacy

On the basis of the conducted experimental researches and the received results we have developed technology of mather tincture of rosemary D1.

The first main stage of the technological process for all medicines is the preparatory work, in particular: preparation of the premises, auxiliary materials, equipment, packaging, API, excipients and solvents.

Production facilities where HM is manufactured must be wet cleaned with detergents and disinfectants. The floor should be washed at least once a shift, walls, doors - at least once a week. The ceiling is cleaned of dust once a month with the help wet cloth. All working surfaces of equipment, apparatus, small mechanization used in the technological process are subject to periodic washing and disinfection. Change of technological clothes and footwear should be carried out at least 2 times a week, and for needs - more often. Personnel hands should be treated before and during the work, but at least 3 times per shift.

In the manufacture of tinctures special attention should be given to the fact that all dishes must be thoroughly washed and dried. The glass from which the equipment is made and the work surfaces must not contain heavy metals and components that absorb or emit electromagnetic waves. At the beginning of each shift, the condition and cleanliness of the scales, as well as other small pharmacy inventory are checked.

The scheme of rosemary mother tincture technology in pharmacy is shown in Fig. 3.1.

The production of tincture consists of the following stages: preparation of medicinal plant raw materials of dried rosemary leaves, ethyl alcohol 90 %.

Conduct input control of raw materials in accordance with the relevant monograph of the German Homeopathic Pharmacopoeia and guidelines of Dr. Shwabe. Prepare 90 % ethyl alcohol from 96 % using tables.

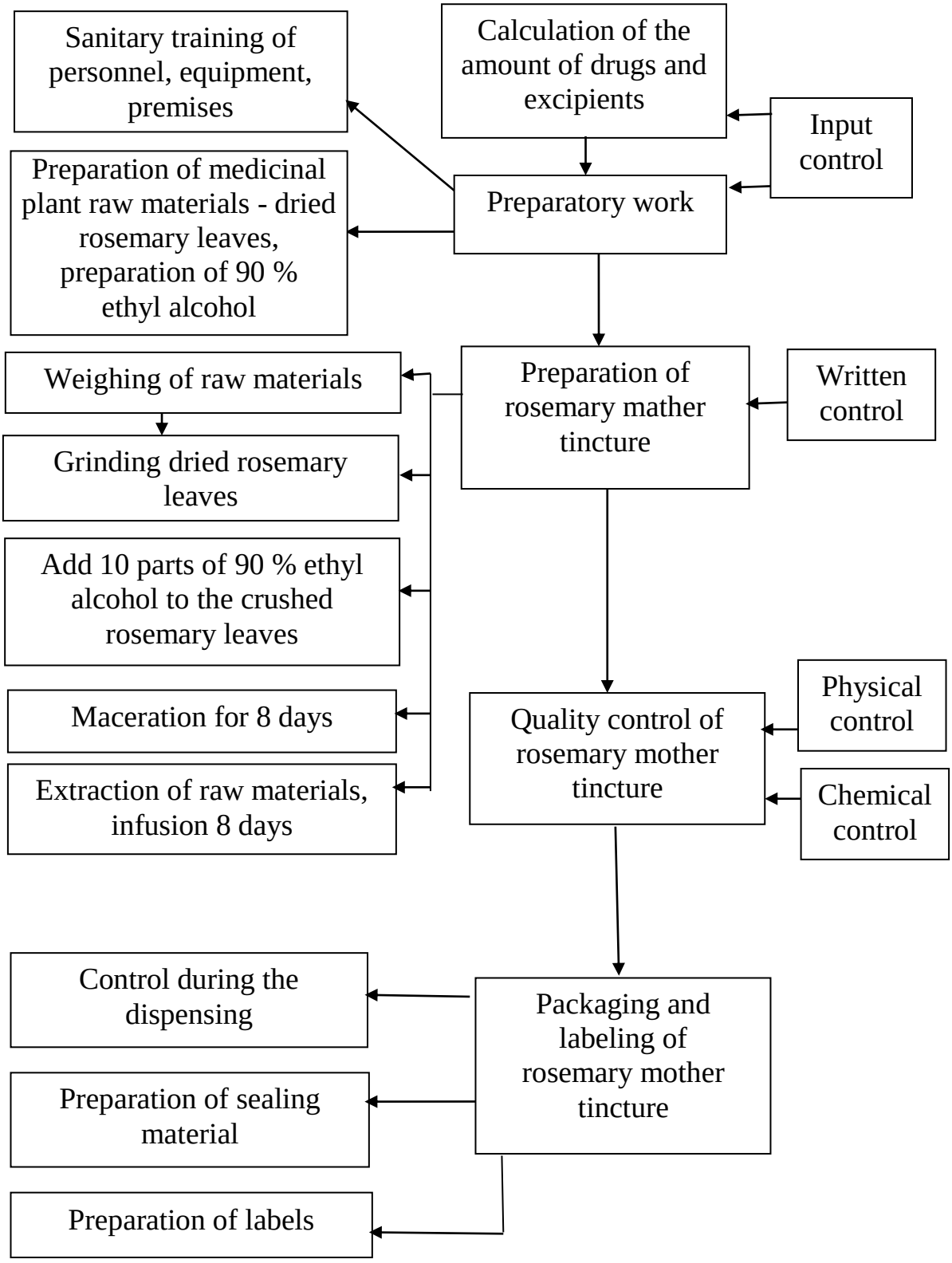



**Fig. 3.1. Scheme of rosemary mother tincture technology in pharmacy conditions**

**Preparation of rosemary mother tincture**

The tincture is prepared as follows: 10.00 g of dried rosemary leaves are weighed on a balance and transferred to a mortar. Grind thoroughly with a pestle. On a technical balance, pre-treated, weigh 100.00 g of ethyl alcohol 90 % (v/v) and transfer half into a mortar to the crushed raw material. Thoroughly mix the contents of the mortar, transfer to a dark glass bottle and wash off the remaining raw materials with the rest of ethyl alcohol.

The bottle is tightly closed with a cork and left for 8 days for maceration at room temperature, stirring daily. After that, the raw material is pressed through a press strainer and the resulting tincture is left for 8 days in a dark place, after which it is filtered, quality control is carried out and, accordingly, formalized.

**Quality control of rosemary mother tincture**

Quality control of tinctures is carried out in appearance, identification, determine the relative density, dry residue and concentration of ethyl alcohol.

**Packing and labeling of rosemary mother tincture.** The finished tincture is transferred into dark glass bottles with a capacity of 50 ml, sealed with a stopper and a lid. The label indicates the name of the medicinal product, dilution, weight and date of preparation.

### 3.1.3. Physical and chemical research of rosemary mother tincture

The next stage of our research was capillary analysis.

Capillary analysis of rosemary mother tincture D1 was performed according to the method of "Plan" at a temperature of $16^0$C and a relative humidity of 54 %.

The lifting length of the tincture was 104 mm; upper zone 25 mm - water transparent, light yellow; 20 mm - transparent zone of greenish-yellow color; lower zone 5 mm - greenish brown; 15 mm - brown area; 3 mm base - light brown.

The results of capillary analysis of the tincture are shown in table 3.2.

Table 3.2

**The results of capillary analysis of rosemary mother tincture D1**

| Zone and size | Coloring in daylight | Coloring in UV light |
|---|---|---|
| 1 zone - 2.5 cm | Light yellow, transparent | Green with blue manifestations, transparent |
| 2 zone - 0.4 cm | Greenish yellow, transparent | Greenish yellow, transparent |
| 3 zone - 1.6 cm | Brown-yellow, transparent | Light yellow, transparent |
| 4 zone - 0.5 cm | Greenish brown, opaque | Yellow, not transparent |
| 5 zone - 1.2 cm | Light - brown, not transparent | Light - brown, not transparent |
| 6 zone - 0.3 cm | Brown, not transparent | Brown, not transparent |
| Base - 0.3 cm | Light brown, not transparent | Light brown, not transparent |
| Length - 10.4 cm | | |

We have studied the main groups of biologically active substances (BAS), which are part of the tincture. For this purpose, qualitative reactions to the main groups of active substances, chromatographic and spectrophotometric methods of analysis were used.

With the help of well-known qualitative reactions, the presence of biologically active substances in the rosemary mother tincture D1, in particular, alkaloids, essential oils, tannins, was established. The results of the identification of alkaloids in the composition of rosemary tincture D1 are presented in table 3.3.

Table 3.3

**Identification of alkaloids in rosemary mother tincture D1**

| № | Reagent | Tincture D1 |
|---|---|---|
| Precipitation reactions | | |

| | | |
|---|---|---|
| 1 | Iodine reagent in saturated potassium iodide solution | ---- |
| 2 | Dragendorf's reagent | Yellow precipitate |
| 3 | 1% solution of potassium permanganate | White precipitate |
| 4 | Zonenstein's reagent | Yellowish-green precipitate |
| 5 | 0.5% solution of picric acid | Yellow precipitate |
| Specific reactions | | |
| 1 | Reagent - formaldehyde, sulfuric acid | --- |
| 2 | Erdman's reagent | Yellowish color |

The results obtained indicate the presence of alkaloids in the mother preparation of rosemary D1.

The results of the identification of tannins in the mother preparation of rosemary D1 are presented in table 3.4.

Table 3.4

**Identification of tannins in rosemary mother tincture D1**

| **№** | **Reagent** | **Tincture D1** |
|---|---|---|
| 1 | 1% gelatin solution. | White precipitate |
| 2 | 1% quinine chloride solution | White precipitate |
| 3 | 1% solution of formaldehyde in concentrated hydrochloric acid | White precipitate |
| 4 | 1% solution of iron chloride | Green color |
| 5 | Bromine water. | White precipitate |
| 6 | 1% solution of vanillin in an acidic medium | Brown-red color |

According to the obtained results of coloring it is established that tincture of rosemary D1 contains tannins.

The results of the identification of saponins in the composition of the mother tincture of rosemary D1 are presented in table 3.5.

Table 3.5

**Identification of saponins in rosemary mother tincture D1**

| № | Reagent | Tincture D1 |
|---|---|---|
| 1 | Formaldehyde in sulfuric acid conc. | Yellowish-pink color |
| 2 | 10% solution of lead acetate | White precipitate |
| 3 | Reaction with chloroform and sulfuric acid conc. | Yellow-orange color of the organic layer |
| 4 | Lafon's reaction | Blue-green color |
| 5 | Reaction with 0.5% solution of vanillin in sulfuric acid | Reddish color |

The data obtained indicate that the tincture contains saponins. The results of the identification of iridoids in the composition of the mother preparation of rosemary D1 are presented in table 3.6.

Table 3.6

**Identification of iridoids in rosemary mother tincture D1**

| № | Reagent | Tincture D1 |
|---|---|---|
| 1 | Reagent with hydrochloric acid | Greenish coloration |

According to the results, the tincture contains iridoids. The results of identification of sugars in the composition of basic drugs are presented in table 3.7.

Table 3.7

**Identification of sugars in rosemary mother tincture D1**

| № | Reagent | Tincture D1 |
|---|---|---|

| | | |
|---|---|---|
| Starch | | |
| 1 | Fehling's reagent | Dark green intense color |
| Dextrin | | |
| 2 | 10% sodium hydroxide solution | Yellow color |
| Cellulose | | |
| 3 | Iodine solution | Brown-yellow color |
| Mucus | | |
| 4 | Ammonia solution | Brown-yellow color |
| Inulin | | |
| 5 | Alcoholic solution of α-naphthol in sulfuric acid | Pink color |

The obtained results indicate that the mother preparation of rosemary D1 contains polysaccharides.

The results of the identification of flavonoids in the mother preparation of rosemary D1 are presented in table 3.8.

Table 3.8

**Identification of flavonoids in rosemary mother tincture D1**

| **№** | **Reagent** | **Tincture D1** |
|---|---|---|
| 1 | 10% sodium hydroxide solution | Yellow-orange color |
| 2 | 1% alcoholic solution of iron (III) chloride | Yellow color |
| 3 | 5% alcohol solution of aluminum chloride | Yellow color |

The obtained results of yellow coloring indicate that the basic preparation of rosemary D1 contains flavonoids.

Identification of phenolic acids also carried out in UV light for specific blue fluorescence.

To detect and identify phenolic compounds, we used the spectrophotometric method. The optical density of the studied tincture was measured on an SF-2000 spectrophotometer at a wavelength of 328 ± 2 nm; ethyl alcohol 90 % was used as a reference solution.

To determine the amount of phenolic acids, the UV spectrum of rosemary tincture was analyzed, as a result of which a match was found with the spectrum of rosmarinic acid (λ=327-330) (table 3.9).

Table 3.9

**Spectral characteristics of rosemary tincture D1**

| **UV spectrum** |
|---|
| maximum 328 ± 2 nm<br>shoulder λ = 327 – 330 nm |

As we can see, the presence of rosmarinic acid was reliably established in the studied tincture of rosemary D1.

Thus, the main groups of biologically active compounds (alkaloids, flavonoids, tannins, saponins, iridoids, polysaccharides) were found in the mother tincture of rosemary D1 using well-known qualitative identification reactions.

### 3.1.4. Chromatographic study of mother tincture of rosemary D1

Identification of biologically active substances in the homeopathic matrix tincture of rosemary X1 was also carried out using thin layer chromatography.

The first stage of our research was the choice of the optimal system of solvents for different groups of biologically active substances. We also used standard substances – "marker".

The determination of phenolic compounds was carried out with phenolic acid standards in a solvent system, in particular: chloroform-ethanol (4:1), butanol - acetic acid-water (4:1:2). After drying, the chromatograms were viewed under UV light and five to eight adsorption zones with blue and greenish-blue fluorescence

were observed. The adsorption zone of rosmarinic acid in the tincture was characterized by the highest luminescence intensity, which allows us to conclude that this compound predominates in the composition of the studied preparation.

The adsorption zones were compared with the adsorption zones of standard samples of phenolic acids. Thus, among the phenolic compounds, the presence of rosmarinic, caffeic and cinnamic acids were reliably detected in the composition of the studied tincture.

In order to identify alkaloids, we used a system of solvents: chloroform - ethyl alcohol (9:1); butanol - acetic acid (100:5).

Revealing reagent: Dragendorff's reagent, iodine vapor (respectively).

The length of the mobile phase was 11 cm.

Chromatograms were dried and processed with the appropriate revealing reagent, after which the results were analyzed in daylight and UV light.

Alkaloids were detected by the presence of brown-violet spots. Salts of alkaloids were converted to the state of bases. Identification of the spots obtained indicates the presence of alkaloids in the composition of the matrix tincture of rosemary D1.

To detect saponins, a solvent system was used: isopropanol - water - chloroform (30:10:5).

Identification of saponins in rosemary D1 tincture was determined by the presence of dark green spots with $R_f$ = 0.22 and 0.77.

For the identification of amino acids, a solvent system was used: ethanol - water (95:5).

Revealing reagent: 0.2 % alcohol solution of ninhydrin and heating for 15 minutes. Amino acids were identified by the presence of pink-violet or purple spots. The results of amino acid identification are presented in table 3.10.

Table 3.10

**Amino acid identification results**

| **Spot No.** | **$R_f$ value of** | **Color after treatment by** | **$R_f$ value of** | **Color "marker"** | **Amino acid-** |
|---|---|---|---|---|---|

| | tincture | reagent | “marker” | | “marker” |
|---|---|---|---|---|---|
| 1 | 0.14 | Purple | 0.12 | Purple | Ornithine |
| 2 | 0.18 | Light purple | 0.16 | Purple | Asparagine |
| 3 | 0.24 | Purple | 0.21 | Light purple | Arginine |
| 4 | 0.23 | Yellow-purple | 0.22 | Light purple | Aspartic acid |
| 5 | 0.28 | Purple | 0.26 | Purple | Glycine |
| 6 | 0.32 | Yellow-brown | 0.31 | Purple | Glutamic acid |
| 7 | 0.45 | Pink | 0.43 | Yellow-purple | Alanine |
| 8 | 0.62 | Pink-purple | 0.62 | Brown | Valine |
| 9 | 0.64 | Brown | 0.63 | Brown | Tryptophan |

According to the results, the homeopathic tincture of rosemary D1 had 9 spots, which had almost the same values of $R_f$ and color as the "marker".

### 3.2. Development of technology and physical and chemical research of homeopathic granules rosemary D3

Homeopathic medicines in Ukraine are prepared and their quality control is carried out according to the main standardizing document - SPhU (1st ed., 2nd ed.). According to the definitions of the European Pharmacopoeia (EPh 7.4 04/2012:2153 "Sugar granules (pills)" are drugs of solid consistency obtained from sucrose, lactose or other suitable excipients. They have adequate mechanical strength, which does not allow to crumble or disintegrate. They are intended to be saturated or coated with one or more rare homeopathic remedies.

Saturated homeopathic pills must meet the requirements of the article "Homeopathic saturated pills" (SPhU). In the production, packaging, storage and sale of granules for homeopathic medicinal products, measures must be taken to ensure

the necessary microbiological purity in accordance with the requirements of the article "Microbiological purity of medicinal products" (SPhU).

Method for the production of homeopathic granules.

In a glass transparent bottle with a volume of 50 ml (1.5 - 2 times more than the mass of granules), we weigh 20.0 g of sugar granules, add 0.2 g (6 drops) of 70% ethyl alcohol and a few shake the bottle once. Next, add 0.2 g (6 drops) of matrix tincture rosemary D1, cork the bottle with a cap wrapped in a parchment capsule and shake vigorously for 10 minutes. After that we pour out granules on a parchment capsule and air dry. Dried granules of rosemary D3 are placed in a dark glass bottle or a plastic container, close and leave in a dry, dark place at a temperature not exceeding $25^0$C. The scheme of the preparation of homeopathic granules are shown in figure 3.2.

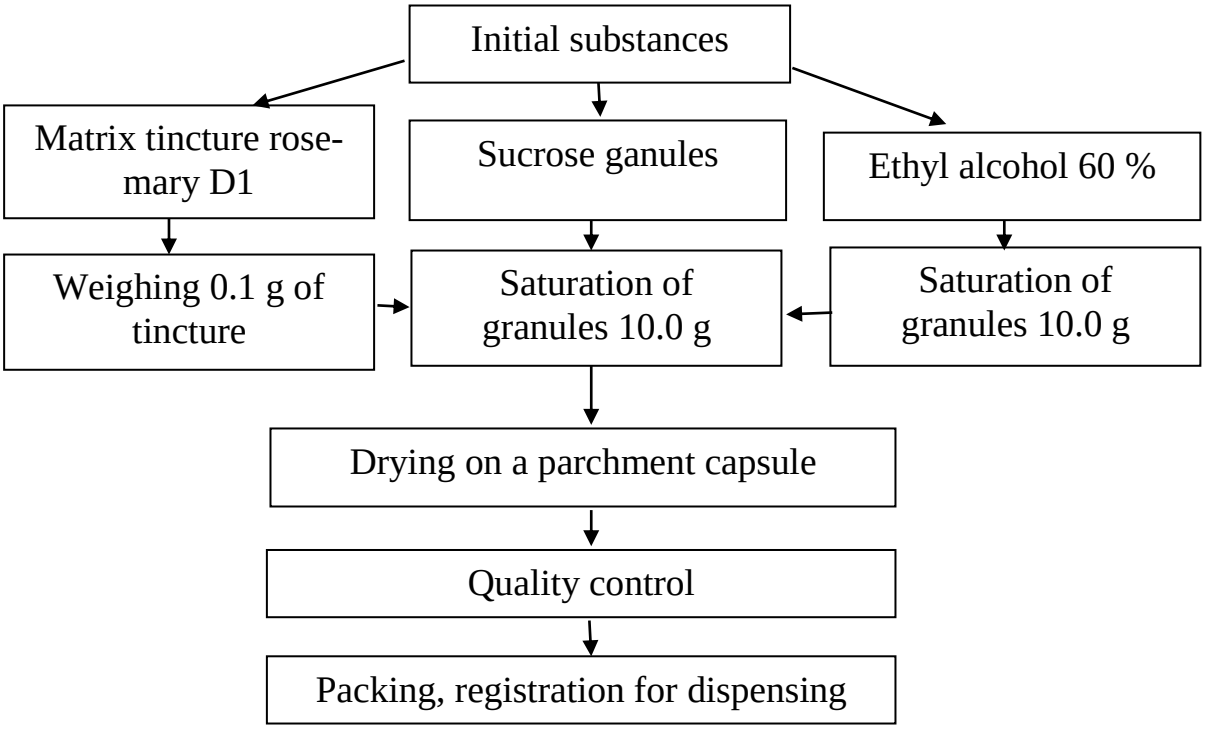



**Fig. 3.2. The scheme of technological process of preparation homeopathic granules rosemary D3**

Organoleptic and technological quality indicators obtained homeopathic granules of rosemary D3 are shown in table 3.11.

Table 3.11

Quality indicators of the obtained rosemary granules D3

| **Indicator** | **Observation** |
|---|---|
| Description | White spheres of sweet taste, spherical shape |
| Solubility | Easily soluble |
| Decomposition, min | 2.5 ± 0.5 |
| The number of sticky granules,% | 1.0 ± 0.5 |
| Bulk volume, g/cm3 | 0.78 ± 0.03 |
| Loss on drying,% | 1.25 ± 0.03 |
| The number of granules in 1.0 g, pieces | 30 ± 1 |

The obtained data testify to satisfactory organoleptic and technological indicators of the quality rosemary granules D3, which are within the permissible limits and meet the requirements of the State Pharmacopoeia of Ukraine (2nd ed. supplement 2, homeopathic pills are saturated).

The results of the identification reactions of the main groups of biologically active substances and excipients in the composition of homeopathic granules of rosemary D3 are presented in table 3.12.

Table 3.12

**Identification of sugars in the composition of rosemary granules D3**

| № | Reagent | Rosemary granules D3 |
|---|---|---|
| 1 | Cobalt chloride solution | Pink color |
| 2 | Fehling's reagent | Orange precipitation |
| 3 | Reaction with ammonia solution | Yellow color |
| 4 | Reaction with potassium hydroxide | Yellow color |

As can be seen from the data in the table, excipients in the composition of homeopathic granules can be determined using the above reactions, which are specific for the detection of sugars.

Determination of biologically active substances in the composition of the granules was carried out using colored reactions after evaporation of an aqueous solution of granules on a water bath. The results of identification reactions of different groups of biologically active substances in the composition of homeopathic granules of rosemary D3 are shown in Table 3.13.

Table 3.13

**Identification of biologically active substances in the composition of homeopathic granules of rosemary D3**

| № | Reagent | Rosemary granules D3 |
|---|---|---|
| | *Flavonoids* | |
| 1 | 10% alcohol solution of sodium hydroxide | Yellow color |
| 2 | 1% alcohol solution of iron chloride | Brown color |
| | *Saponins* | |
| 3 | 10% solution of lead acetate | Opalescence |
| | *Tannins* | |
| 4 | 1% solution of vanillin in sulfuric acid | Red color |
| | *Carbohydrates* | |
| 5 | Reaction with thymol | Red color |
| | *Mucus* | |
| 6 | Ammonia solution | Yellow color |

According to the results of research it is established that the granules contain the main BAS, namely: flavonoids, alkaloids, saponins, tannins, mucus, bitters, carbohydrates.

According to the obtained results, the proposed reactions can be used to identify the main groups of BAS and to assess the quality of the developed homeopathic granules. The obtained research results can be implemented in the work of homeopathic pharmacies in the development of complex homeopathic medicine, which include rosemary preparations.

## CONCLUSIONS

1. The effect of infusion time on the physicochemical and technological indicators of the quality of rosemary tincture has been studied. It has been established that the optimal infusion time is 8 days. This period is sufficient for the release of active substances from medicinal raw materials.
2. The technology of homeopathic matrix tincture of rosemary X1 was developed and the presence of the main groups of BAR in it, in particular, alkaloids, flavonoids, saponins, tannins, iridoids, was studied using the TLC method and well-known qualitative identification reactions.
3. Based on the results of organoleptic, physical, chemical and technological studies, a technology of preparation of rosemary granules D3 in pharmacy conditions has been developed. Methods for quality control of granules are proposed, they meet the requirements of the SPhU.

## GENERAL CONCLUSIONS

1. According to the results of the analysis of literary sources, it was found that the number of patients with diseases of the nervous system is constantly growing. Significant portion drugs for the treatment of these diseases are drugs of synthetic origin, which in most cases lead to side effects. actions.
2. The prospects for the development of safe homeopathic rosemary medicines for the treatment of patients with diseases of the nervous system are considered.
3. Analyzed information about the quality control of homeopathic medicines and the need to develop effective methods of quality control.
4. According to the results of the experimental studies, the optimal infusion time was established and the homeopathic technology of rosemary matrix tincture was developed, its organoleptic, physico-chemical characteristics were studied.
5. A technology for homeopathic granules of rosemary X3 based on matrix tincture D1 has been developed. Methods for controlling the quality of granules in accordance with the requirements of the SPhU have been proposed.
6. Based on the results of the master's work, article was published in the collection of materials of the 7th International scientific and practical conference “International scientific innovations in human life” (January 19-21, 2022, Manchester).

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# APPENDIXES

**APPENDIX A**

SCI-CONF.COM.UA

# INTERNATIONAL SCIENTIFIC INNOVATIONS IN HUMAN LIFE

## PROCEEDINGS OF VII INTERNATIONAL SCIENTIFIC AND PRACTICAL CONFERENCE JANUARY 19-21, 2022

## MANCHESTER 2022

**UDC 615.322:615.071:615.035:615.014.2**

# DEVELOPMENT OF THE TECHNOLOGY OF HOMEOPATHIC TINCTURE ROSMARINUS

**Naji Aimad**
Applicant for higher education
Drugs Technology Department
**Yuryeva Hanna**
Ph.D., Associate Professor of Drugs
Technology Department
**Herasymova Iryna**
Ph.D., Associate Professor of Drugs
Technology Department
National University of Pharmacy
Kharkiv, Ukraine

**Annotation:** The influence of maceration time on the quality indicators of rosemary mother tincture has been considered in this work. Rosemary dried leaves was chosen as an object of our research. Development of the technology of mother tincture on the basis of dried plant rosemary has been the purpose of our investigation. The physical and chemical indicators of homeopathic tincture *Rosmarinus D1* have been determinated.

**Key words:** rosemary, homeopathy, medicine, mother tincture, technology.

Production and quality control of homeopathic medicines (HM) is carried out in the world according to pharmacopeias, in particular, in Ukraine - according to the State Pharmacopoeia of Ukraine (SPhU). It is also temporarily allowed to use the guidelines of Dr. Schwabe and the German Homeopathic Pharmacopoeia for certain HM. The preparation of rosemary basic medicine is carried out using dried raw materials (rosemary leaves) according to method 4a given in the SPhU (1st ed.) [1, 16-22]. Mother tincture of rosemary D1 was prepared by maceration method in the ratio (1:10) using 90 % ethyl alcohol. According to method 4a, the crushed raw material was mixed with a calculated amount of 90 % ethyl alcohol and kept at a

**APPENDIX B**


CERTIFICATE
is awarded to
Naji Aimad
for being an active participant in
VII International Scientific and Practical Conference
"INTERNATIONAL SCIENTIFIC INNOVATIONS
IN HUMAN LIFE"
24 Hours of Participation
(0,8 ECTS credits)
MANCHESTER
19-21 January 2022
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INTERNATIONAL SCIENTIFIC INNOVATIONS IN HUMAN LIFE
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MANCHESTER
19-21 JANUARY 2022

*F A 2.2.1–32-366*

**National University of Pharmacy**

Faculty for foreign citizens' education
Department Technology of Drugs

Level of higher education master

Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

**APPROVED**
**The Head of Department**
**Technology of Drugs**
**Tatyana YARNYKH**

"_18_" of June 2021

**ASSIGNMENT**
**FOR QUALIFICATION WORK**
**OF AN APPLICANT FOR HIGHER EDUCATION**

**Aimad NAJI**

1. Topic of qualification work: «Development of the composition and research of homeopathic medicines of rosemary», supervisor of qualification work: Ganna YURYEVA, PhD, assoc. prof.,

approved by order of NUPh from "17th" of February 2022 № 76.

2. Deadline for submission of qualification work by the applicant for higher education: April 2022.

3. Outgoing data for qualification work: Object of researches: rosemary, tincture of rosemary D1, granules rosemary D3

4. Contents of the settlement and explanatory note (list of questions that need to be developed): to analyze the literature data about usage of rosemary as an API for the treatment of diseases of the nervous system; - to consider the basic principles of homeopathy, its differences from allopathy; - to analyze the approaches to homeopathic quality control of medicines; - to develop the technology of homeopathic basic tincture of rosemary and study its organoleptic, physical, chemical and technological quality indicators; - to develop the technology of homeopathic rosemary granules and to offer methods of quality control in pharmacies.

5. List of graphic material (with exact indication of the required drawings):
tables – 15
figures – 2

6. Consultants of chapters of qualification work

| Chapters | Name, SURNAME, position of consultant | Signature, date | |
|---|---|---|---|
| | | assignment was issued | assignment was received |
| I Chapter | Ganna YURYEVA, ass. prof. of higher education institution of department Technology of Drugs | 18 June 2021 | 18 June 2021 |
| II Chapter | Ganna YURYEVA, ass. prof. of higher education institution of department Technology of Drugs | 10 September 2021 | 10 September 2021 |
| III Chapter | Ganna YURYEVA, ass. prof. of higher education institution of department Technology of Drugs | 5 December 2021 | 5 December 2021 |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

7. Date of issue of the assignment: 18 of June 2021

**CALENDAR PLAN**

| № з/п | Name of stages of qualification work | Deadline for the stages of qualification work | Notes |
|---|---|---|---|
| 1. | Analysis of literature data. Treatment of nervous system diseases, analyze of pharmaceutical market of homeopathic drugs and their dosage forms. | September – November 2021 | **done** |
| 2. | Researches of active substances and excipients | December 2021 – February 2022 | **done** |
| 3. | Justification of the results | March 2022 | **done** |
| 4. | Registration of qualification work | April 2022 | **done** |
| | | | |
| | | | |
| | | | |
| | | | |

**An applicant of higher education** _____ Aimad NAJI

**Supervisor of qualification work** _____ Ganna YURYEVA

**ВИТЯГ З НАКАЗУ № 76**

**По Національному фармацевтичному університету**
**від 17 лютого 2022 року**

1. нижченаведеним студентам 5-го курсу 2021-2022 навчального року, навчання за освітньо-кваліфікаційним рівнем «магістр», галузь знань 22 охорона здоров'я, спеціальності 226 – фармація, промислова фармація освітня програма – фармація, денна форма навчання (термін навчання 4 роки 10 місяців), які навчаються за контрактом, затвердити теми магістерських робіт:

| № з/п | Прізвище студента | Тема магістерської роботи | Посада, прізвище та ініціали керівника | Рецензент магістерської роботи |
|---|---|---|---|---|
| **по кафедрі технології ліків** | | | | |
| 1. | Наджі Аімад | Розробка складу та дослідження гомеопатичних препаратів розмарину Development of the composition and research of homeopathic medicines of rosemary | доц. Юр'єва Г.Б. | доц. Гербіна Н.А. |

Підстава: подання декана, згода ректора.

Ректор

Вірно. Секретар

*F A 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**
**Aimad NAJI**
**on the topic: «Development of the composition and research of homeopathic medicines of rosemary»**

**Relevance of the topic.** In Ukraine, as in the rest of the world, it is noted significant interest in finding safe, environmentally friendly, no side effects and addictive drugs of natural origin. This is due to the softness and complexity the action of biologi-cally active substances of herbal preparations, their good tolerance. Plants with several groups of BAS, the combination of which in their chemical composition expands and strengthens biological action and deserve special attention. In this question the application of homeopathic approach in the treatment of diseases is an actual. Homeopathy is the treatment of illness and injury with the smallest dose possible of substances that evoke symptoms similar to the ones being expressed by the patient. In classical homeopathy, there are many possible homeopathic treatments for nervous system diseases be chosen based on various specific details of the person seeking treatment. Homeopathic remedies, such as rosemary, can provide some relief during painful neurological attacks, sleep disturbances, and anxiety.

**Practical value of conclusions, recommendations and their validity.** The obtained experimental results are served as the basis for the creation of new homeopathic drugs based on rosemary, which will expand the range of medicines for the treatment of diseases of the nervous system based on a substance of natural origin and increase the effectiveness of treatment.

**Assessment of work**. The research methodology is based on the main technological and physicochemical principles reflected in the works of domestic and foreign authors. The study used a complex of organoleptic, physical -chemical and technological researches.

**General conclusion and recommendations on admission to defend.** The work was carried out at a high level, meets all requirements and can be submitted to the Examination Commission.

Scientific supervisor _____ Ganna YURYEVA

«12» of April 2022

*F A 2.2.1-32-356*

**REVIEW**

**for qualification work of the master's level of higher education,**
**specialty 226 Pharmacy, industrial pharmacy**
**Aimad NAJI**
**on the topic: «Development of the composition and research of homeopathic medicines of rosemary»**

**Relevance of the topic.** The modern rhythm of life forces us to adapt to many situations, to sacrifice time, sleep, energy and rest with the sole purpose - to have time for everything. Unfortunately, we can't do everything in time, and paying for this rush is too expensive - our health. The functioning of the body depends on the state of the nervous system, its coordinated and normal functioning. Symptoms of neurological disorders can manifest themselves in different ways, very often, in particular in the form of motor disorders, coordination disorders are also possible and speech, involuntary contractions of different muscle groups, tics, tremors. Diseases of the nervous system may be manifested by epileptic seizures, tantrums, sleep disorders and consciousness, mental activity, behavior and psyche. Although modern medicine has a significant number of drugs, both synthetic and herbal origin, but most of them with long-term use, unfortunately lead to adverse reactions. Therefore, the search for highly effective drugs is important with minimal side effects with prolonged use, which are not addictive. In this aspect, special attention is drawn homeopathic medicines, in particular rosemary preparations. In homeopathic practice, this plant is used in the treatment of nervous diseases, including memory deficits, mental retardation, dizziness, headache, etc.

**Theoretical level of work.** To generalize literary information about the modern state of nervous disease and usage of homeopathic medicines for this purpose.

**Author's suggestions on the research topic.** To carry out the complex of physical, chemical and technological researchers for development of the technology and analysis of homeopathic medicines rosemary.

**Practical value of conclusions, recommendations and their validity.** During this work, the literature data has been analyzed, the physical, physical-chemical, and organoleptic methods of research have been mastered. Results are of practical interest for the purpose to expand the range of domestic homeopathic medicines.

**Disadvantages of work.** There are spelling mistakes, technical errors in the work.

**General conclusion and assessment of the work.** Qualification work of Aimad NAJI can be submitted to the Examination Commission for defense.

Reviewer _____ assoc. prof. Natalia GERBINA

«19» of April 2022

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ**
**НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ**

**ВИТЯГ З ПРОТОКОЛУ № _10_**
«28» квітня 2022 року
м. Харків

**засідання кафедри**
**технології ліків**

**Голова:** завідувачка кафедри, доктор фарм. наук, професор Тетяна ЯРНИХ
**Секретар:** канд. фарм. наук, доцент Володимир КОВАЛЬОВ

**ПРИСУТНІ:** професор Олександр КОТЕНКО, професор Юлія ЛЕВАЧКОВА, доцент Марина БУРЯК, доцент Оксана Данькевич, доцент Ганна ЮР'ЄВА, доцент Вікторія ПУЛЬ-ЛУЗАН, асистент Світлана ОЛІЙНИК

**ПОРЯДОК ДЕННИЙ**

1. **Про представлення до захисту до Екзаменаційної комісії кваліфікаційних робіт другого (магістерського) рівня вищої освіти**

**СЛУХАЛИ**:
Здобувача вищої освіти 5 курсу групи Фм17(4.10д)англ-06 спеціальності 226 Фармація, промислова фармація Аімад НАДЖІ з доповіддю на тему «Розробка складу та дослідження гомеопатичних препаратів розмарину» (науковий керівник: доцент Ганна ЮР'ЄВА).
**УХВАЛИЛИ**:
Рекомендувати до захисту кваліфікаційну роботу.

**Голова засідання** **Тетяна ЯРНИХ**

**Секретар** **Володимир КОВАЛЬОВ**

*Ф А2.2.1-32-042*

# НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

## ПОДАННЯ
## ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
## ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Аімад НАДЖІ до захисту кваліфікаційної роботи за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Розробка складу та дослідження гомеопатичних препаратів розмарину».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

### Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Аімад НАДЖІ представив магістерську роботу, яка за об'ємом теоретичних та практичних досліджень повністю відповідає вимогам до оформлення магістерських робіт.

Керівник кваліфікаційної роботи

_____ Ганна ЮР'ЄВА

«12» квітня 2022 року

### Висновок кафедри про кваліфікаційну роботу

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

Завідувачка кафедри технології ліків

_____ Тетяна ЯРНИХ

«28» квітня 2022 року

Qualification work was defended

of Examination commission on

« ___ » of June 2022

With the grade _____

Head of the State Examination commission,

DPharmSc, Professor

_____ / Oleh SHPYCHAK /