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QUALIFICATION WORK

on the topic

**DEVELOPMENT OF THE COMPOSITION OF RECTAL
SUPPOSITORIES WITH HOMEOPATHIC ARNICA TINCTURE**

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SUMMARY

The master's thesis proves the relevance of creating rectal suppositories with homeopathic arnica tincture for use in complex therapy of hemorrhoids. Based on the study of organoleptic, physicochemical and structural-mechanical parameters of suppository bases substantiated rational composition of rectal suppositories with homeopathic arnica tincture. Organoleptic, physicochemical and structural-mechanical parameters model samples were determined according to the relevant methods of the SPhU. Work set out on 42 pages, includes 9 tables, 3 figures, 76 references and 3 applications.

Key words: mountain arnica, homeopathy, suppositories, hemorrhoids.

АНОТАЦІЯ

У магістерській роботі доведено актуальність створення ректальних супозиторіїв з гомеопатичною настоянкою арніки для застосування в комплексній терапії геморою. На основі досліджень органолептичних, фізико-хімічних та структурно-механічних показників супозиторних основ обґрунтовано раціональний склад ректальних супозиторіїв з гомеопатичною настоянкою арніки. Органолептичні, фізико-хімічні та структурно-механічні параметри модельних зразків визначали за відповідними методиками ДФУ. Робота, викладена на 42 сторінках, містить 9 таблиць, 3 рисунки, 76 посилань та 3 додатки.

Ключові слова: арніка гірська, гомеопатія, супозиторії, геморой.

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INTRODUCTION

Actuality of topic. One of the important problems of modern medicine is diagnosis, treatment and prevention of proctological diseases. The last sometimes diseases of the rectum, including proctitis, proctosigmoiditis, hemorrhoids are becoming more common and do not tend to decrease. The reason for this is a sedentary lifestyle, irrational diet, bad habits such as alcohol, stress.

Hemorrhoids suffers from more than 10 % of the adult population of the planet, and the proportion of the total number of coloproctological diseases is about 40 %.

In this regard, the problem still remains relevant choosing tactics of treatment of this category of patients. Currently, despite a significant number of different pharmacological drugs with different mechanisms of action that available in the form of ointments and rectal suppositories, still remains open question about the choice of a drug, their sequence is unclear use in different phases of the process and the algorithm of combined application pharmacological agents [8, 39, 44, 52, 58, 70].

Drugs for local therapy of chronic and acute hemorrhoids and others diseases of the anal canal, as well as postoperative management of patients proctological profile may be suppositories, as their use allows to reduce the level of allergic reactions, to prolong the therapeutic effect, especially in the focus of inflammation, increase the rate of drug absorption substances and in some cases reduce the dose.

Suppositories containing active pharmaceutical ingredients anti-inflammatory, hemostatic and local anesthetic action, occupy one of main places in the treatment of patients with proctological pathology. However, them the range is still not wide enough [15, 18].

In recent years, there has been a growing interest in doctors, pharmacists and patients to a number of original areas of medicine, in particular homeopathy and homeopathic pharmacy. This is due to their advantages over allopathic medicine, namely: no side effects (subminimal doses of drugs deprived are used toxic and al-

lergenic effects on the body), most used medicines are products of natural origin, individual approach to the patient, as well as the possibility of combining homeopathic and other non-traditional methods (acupuncture, physiotherapy, aromatherapy, etc.). This is undoubtedly what makes homeopathy one of the first places in the health care system [25, 55, 56, 68].

Search for active pharmaceutical ingredients to expand range of drugs for topical treatment of hemorrhoids is relevant the task of modern pharmacy.

Some interest in addressing the use of homeopathic remedies represents mountain arnica (*Arnica montana* L.), which is widely used in phytotherapy and allopathy due to the content of: flavonoids, carotenoids, saponins, tannins, triterpene acids, bitters, mucus, organic acids, essential oils, etc. [5, 6, 7, 40].

In this aspect, arnica remains promising active pharmaceutical ingredient to create extemporaneous on its basis drugs, including suppositories for the treatment of hemorrhoids.

The **aim** of our research is theoretically and experimentally substantiate the composition of suppositories with homeopathic arnica tincture for the treatment of hemorrhoids.

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

- to analyze the literature on the prospects of application arnica in allopathy and homeopathy;
- to analyze the pharmaceutical market of Ukraine for natural drug's availability for the local treatment of hemorrhoids;
- to develop the technology of homeopathic arnica tincture;
- to study the physico-chemical parameters of the developed arnica tincture;
- theoretically and experimentally substantiate the composition of suppositories with homeopathic arnica tincture;
- to conduct physico-chemical, pharmaco-technological research of rectal suppositories.

Scientific novelty

The composition of suppositories with homeopathic arnica tincture for use in local therapy of hemorrhoids.

Theoretical and practical significance of the work

The theoretical and practical significance of the master's thesis is that the choice of suppository base was experimentally substantiated and the composition of the developed drug is proposed, which is possible to prepare in pharmacy and manufacture conditions.

Implementation of results

The main provisions of the qualification work are set out and discussed in the 3rd International scientific and practical conference “Innovations and prospects of world science” (November 4-6, 2021, Vancouver) and Scientific and practical conference with international participation, dedicated to the 100th anniversary of the National University of Pharmacy (September 10, 2021, Kharkiv). One abstracts of the report and one article have been published.

Structure and scope of qualification work.

Qualification work consists of an introduction, literature review (Chapter 1), the experimental part (chapter 2 and 3), general conclusions, references, appendices. The work is presented on 42 pages, includes 9 tables, 3 figure, 76 sources of literature and 3 appendices.

CHAPTER I.

PROSPECTS OF APPLICATION OF ARNICA IN HOMEOPATHIC AND ALLOPATHIC PRACTICE FOR TREATMENT HEMORRHOIDS

1.1. Arnica mountain, its chemical composition and use in allopathy and homeopathy

The medicinal substances that make up the group of enterosorbents are used in medicine for several millennia. Even in Ancient Egypt and Greece, charcoal was used inside for intestinal disorders or poisonings, externally for the treatment of wounds. Throughout many centuries, charcoal and gunpowder were sprayed with wounds wounded on the battlefield, and pounded coal was administered to patients with digestive disorders. In the XVIII cen. the sorbing properties of coal were described and *Lovits* theoretically substantiated the use of the enterosorption method, which for many years remained an important weapon in the struggle for human health [1].

Arnica in Greek means "sneeze" - ptarmica. Think that Dioscorides called it that, since the flowers and leaves of the plant cause sneezing. Later, the name was disfigured and the word "arnica" appeared. For another hypothesis, its generic name comes from the Greek word arnos - "lamb", for place of growth - in mountain meadows were used as pastures.

Species The name montana is Latin for "mountain". Arnica widely was used in Western Europe in the 11th century. Arnica mountain or Barannik mountain (lat. *Arnica montana*) - a species of the genus Arnica (lat. *Arnica*) of the family *Asteraceae* or *Compositae* (lat. *Asteraceae* or *Compositae*) - one of the largest families of dicotyledonous plants, widely distributed throughout the globe and represented in all climatic zones.

Arnica (*Arnica montana* L.) is a herb that grows predominantly in Siberia and Central Europe, as well as in the temperate climate of North America. Flowers plants are used in medicine [5, 40]. Perennial herbaceous plant 15-80 cm tall, cy-

lindrical. creeping horizontally branched rhizome up to 15 cm long and up to 1 cm thick, filiform dark additional roots. externally color roots are dark brown. The plant in the first year of life forms only a rosette of 6-8 large sheets, their length is 15 - 17 cm. In the second year of life arnica develops an upright, slightly branched stem at the top, covered with glandular hairs. At the base are 4-6 basal short petiolate, entire, obovate, pointed or obtuse leaves. Stem nine leaves (1-3 pairs) of arnica opposite, sessile, semi-amplex, oblong obovate or lanceolate, shortly glandular pubescent above, above dark green, and below - light green, naked. At the ends of the branches large (up to 3-8 cm in diameter) single inflorescences in the form of baskets with a hemispherical wrapper. The basket consists of two types of flowers: marginal yellow ligulate (about 20 pcs) and medium small (50 or more pcs) orange-yellow both tubular articles with a five-pronged corolla, in which instead of a calyx a bangs of hard bristles.

The fruit of mountain arnica is cylindrical, pubescent, narrowed towards the base, dirty gray, achene with bangs, 6-10 mm long. Bloom occurs in June - July, and fruit ripening in July - August. It mainly grows in the territory of Central and Western Europe from Carpathians to the Pyrenees, through forest meadows, forest edges, coniferous mountain meadows, and also beech forests and among shrubs. On personal plots it can be grow in the forest and forest-steppe zones of the European part. Mountain arnica listed in the Red Book [6, 40].

For medicinal purposes, arnica flower baskets are used. Raw materials are harvested during flowering in the second - third decade of June and early July in plants starting from the second year of life. At the beginning cut flower baskets at their very base, but without pedicels, leaving the rest of the peduncle no more than 1 cm long. Drying occurs in shade outdoors or in a well-ventilated area, for 7-10 days on paper or fabric, as well as in dryers at a temperature of 55 - 60°C. It is not recommended to turn over the raw materials during drying, as the baskets may crumble. You can store raw materials for 2 years when it is humidity is not more than 13 %.

Arnica flowers contain bitter dye arnitsyn up to 4 %, its main active ingredient. Arnitsyn is a mixture of 3 substances: arpidiol (arnidendiol), faradiol (isoarnidendiol) and a saturated hydrocarbon. in flowers also contains cynarin and essential oil in the amount of 0.04 - 0.07%. In addition, with flowers secrete an oil containing 56 % unsaponified substances, washing part of the oil is 50% represented by saturated acids; marked hydrocarbons, two resinous substances and a red lutein dye. As calcium and potassium salts, as well as organic acids: fumaric, malic and lactic.

Vitamin C content is about 21 mg/%. In addition, the content of tannins was noted in arnica flowers - 5%, inulin, proteins, fructose - 2.5%, other reducing sugars - 0.5%, sucrose - 1%, as well as various ballast substances [6, 7].

Arnica inflorescences also contain choline, alkaloids. In the roots of arnica contains unsaturated hydrocarbons, a small amount of phytosterols, as well as organic acids: isobutyric, formic, angelic and essential oils (up to 1.5% in fresh raw materials and 0.4 - 0.6% in dried), which is a light yellow liquid with a pungent, darkening odor. In the production of drugs use flower baskets and roots.

Preparations for internal and external use.

From the flowering heads of arnica, it has been used as a medicine for hundreds of years. Arnica was widely used in European folk medicine, and alcoholic tinctures were produced by early North American settlers for treatment of angina, as a febrile remedy, and also to improve blood circulation.

Homeopathic uses include the treatment of surgical or accidental trauma, use as an analgesic, and the treatment of postoperative thrombophlebitis and pulmonary embolisms [25, 56]. Arnica tincture is used for a number of conditions presented in Table 1.1.

The plant has a variety of pharmacological properties, since its flowers and roots contain substances of different chemical composition. In large doses, drugs made from arnica flowers have a calming effect and relieve convulsions [5, 6, 7, 40].

Table 1.1

The use of arnica tincture in medicine

Application method	Action
Internal	regulates bile secretion, lowers cholesterol; reduces reflex excitability of the brain; restores the nervous system after strokes; stops bleeding.
External	relieves inflammation of the gums and mouth; alleviates the effects of severe sunburn; restores normal metabolic processes in tissues with mild frostbite or burns; heals large wound surfaces.

Arnica flowers are able to reduce the reflex excitability of the brain, expand the cerebral vessels. That is why, in the recent past, arnica was used after cerebral hemorrhages in order to speed up recovery, functional state of the nervous system. In addition, tincture from the flowers of mountain arnica has a choleric effect. A big plus is the fact that with it no side effects have been reported in patients.

Medicines prepared from arnica roots have another effect. They stimulate the cardiovascular system, improve the nutrition of the heart muscles, increase coronary blood flow, dilating blood vessels [7].

In gynecological practice, tincture of arnica flowers is recommended as an effective hemostatic agent for uterine bleeding of various etiologies (in the postpartum period and with inflammatory diseases of the genital area), uterine fibromyoma with hemorrhagic syndrome. Arnica roots are used to prepare vasodilators, increase the amplitude of heart contractions and improve the nutrition of the heart muscle.

Due to the content of cynarine, it lowers the level of cholesterol in the blood. Arnica has been used externally for acne, bruises, sprains, and muscle pain. In addition, it has been used as a conventional anti-stimulant and CNS stimulant, and as

an antibacterial agent for abrasions and gunshot wounds. Arnica is also a component of hair tonics, dandruff treatment, perfumes and cosmetics. *A. montana* has been approved for external use in the Complete Monograph of the German Commission E, 2, 4, 5.

A number of flavonoid glycosides have been found in arnica (fig. 1.1.). Flavonoids (0.4 % - 0.6 %) include betuletol, eupafolin, flavonol glucuronides, hispidulin, isorhamnetin, luteolin, patuletin, spinacetin, tricine, 3,5,7, -trihydroxy-6,3', 4'-trimethoxyflavone, kaempferol, quercetin, kaempferol and quercetin derivative, jaceosidin and pectolinarigenin. Isomeric alcohols include arnidiol and foradiol [40].

Arnica terpenoids include arnifoline, arnicolide, and sesquiterpenes gelenalin (and their derivatives) and dihydrogelenalin. Gelenalin methacrylate pseudoguayanolide ester was isolated from the flowers. Number of sesquiterpene lactones varies greatly between species and geographical location, which complicates the standardization of preparations. The European Pharmacopoeia recommends a minimum sesquiterpene lactone content of 0.4% in *A. montana* preparations used as herbal medicine.

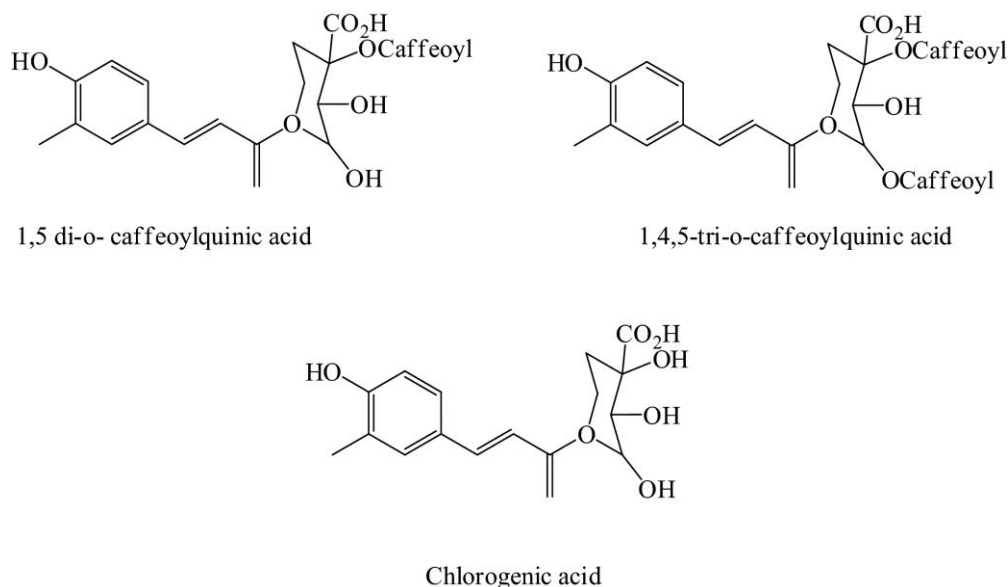


Fig. 1.1. Chemical formulas of biologically active substances

The amines of the plant are betaine, choline and trimethylamine. Coumarins include scopoletin and umbelliferon.

Carbohydrates such as mucus and polysaccharides (inulin) are found in arnica. Two homogeneous polysaccharides have been isolated, acid arabino-3,6-galactan protein and neutral fucogalactoxyloglucan. Further isolation of polysaccharides was carried out on a group of water-soluble acidic heteroglycans.

Volatile oils (0.3% - 1%) can be obtained from rhizomes and roots or parts of flowers and are used in perfumery. The composition of the oil includes thymol, its derivatives and fatty acids (for example, palmitic, linoleic, myristic, linolenic). The content of fatty acids in the essential oil of arnica was also evaluated. Other components found in arnica include arnitsyn compound, caffeic acid, carotenoids (alpha- and beta-carotene, cryptoxanthin, lutein), phytosterols, resin, tannins, lignans and anthoxanthin [5, 40]. The quantitative content of micro and macro elements in arnica inflorescences is shown in table 1.2.

Table 1.2

Quantitative content of micro and microelements in arnica inflorescences

Name of micro and macroelement	Quantitative content, mg/g
Potassium	19.30
Calcium	36.60
Magnesium	1.77
Iron	0.25
Manganese	35.50
Copper	4.50
Zinc	25.00
Cobalt	0.23
Molybdenum	0.08
Vanadium	1.76
Selenium	0.12
Lead	5.52
Nickel	3.28
Iodine	0.09

Arnica and its extracts are widely used in folk and homeopathic medicine for pain caused by arthrosis, tonsillitis, surgical interventions, bleeding, bruising, swelling after surgery, acne, boils, bruises, rashes, sprains.

Used part in homeopathic practice: for internal use rhizome with roots; for external use - a whole, fresh flowering plant.

Arnica Montana was introduced into homeopathic practice by S. Hahnemann in 1805. The action of Arnica was tested on 9 people, the data of the tests are in the volume of "Pure likology" [55, 56].

In homeopathy, Arnica is a remedy for bruises and various kinds of injuries, including birth and postoperative. Arnica quickly stops pain, stops bleeding, promotes the absorption of extravasates and the resorption of blood clots. Arnica is useful in the so-called trace diseases that have arisen after strokes, injuries, or any, even an ancient operation, which are the result of a concussion, expressed by persistent headaches. Arnica is also indicated for diseases resulting from overstrain of the heart muscle and skeletal muscles in athletes, wrestlers and athletes, especially with hypertrophy of the heart, which turns out to be shortness of breath, palpitations, general weakness. With hypertrophy of skeletal muscles when they have pain (myalgia). Arnica serves as an indispensable antiseptic in the postpartum period to prevent the development of sepsis. Rapid analgesic effect of arnica for external and internal use. Application indicate its selective effect on sensitive nerve cells. She considered to be a real vascular remedy, acting on the veins and arteries, and especially on capillaries. It is indicated for violation of cerebral circulation, with apoplexy, hypertensive crises, atherosclerosis of cerebral vessels.

Arnica is useful also in diseases of the gastrointestinal tract. It is prescribed from 3X to 30 dilutions. With bruises, postpartum and postoperative injuries after curettage of the uterus, prophylactically with the danger of habitual miscarriage, with various bleeding, acute thrombophlebitis, furunculosis is prescribed in 3X dilution every 1-2 hours, 5 drops or grainules [56].

With hypertension, varicose veins, hemorrhoids in 3, 6 and 30 dilutions 1-2 times a day with periodic breaks of 2-3 days. With angina pectoris - in 3X, or 6

distribution, depending on the response organism. Arnica is applied externally in a 3% solution as a wet dressing. In the absence of skin lesions, a wet bandage with arnica tincture is placed on the site of injury for anesthesia for 20-30 minutes. 5% and 10% arnica ointment is applied to cracked nipples [13, 14].

In allopathy, a tincture of mountain arnica flowers is used as a hemostatic agent for postpartum hemorrhages and bleeding associated with inflammatory diseases. It is used orally for various pathological conditions, atherosclerosis, myocarditis, cardiac angiospasm, hypertension, angina pectoris, internal bleeding, externally for lotions with bruises, abrasions, bruises, small wounds, boils, trophic ulcers, burns, frostbite [40].

Tincture of arnica flowers is also used externally in the form of lotions, diluting before drinking water in a ratio of 1:5 or 1:10 to avoid irritation.

Decoction of arnica flowers is used for rinsing the mouth with gingivitis, periodontitis, stomatitis.

In folk dermatology mountain arnica is widely used. Orally used for psoriasis, erythema nodosum and other infectious and allergic diseases with predominant inflammatory lesions of the blood vessels of the skin and subcutaneous tissue; externally for vitiligo, injuries with hemorrhages, bone fractures, etc. Arnica decoction is used for washing with dilated blood vessels, redness of the skin, oily and porous skin, as well as against dandruff and excessive sebum production, stimulating its growth, nest baldness, baldness and more.

Tincture.

Arnica tincture is a clear greenish-brown liquid with a peculiar odor, sharp, bitter taste. Prepared from finely chopped arnica flowers (1:10) on 70% alcohol. Take 30-40 drops per reception in water or milk as a hemostatic agent. Also has a choleretic effect.

Infusion of arnica flowers 10 g (3 tablespoons) of raw materials are placed in an enamel dish, pour 200 ml of hot boiled water, cover with a lid and heat in boiling water (in a water bath) for 15 minutes, cool at room temperature for 45 minutes, filter, squeeze, bring to the original volume with boiled water. Take 1 ta-

blespoon 3 times daily after meals in milk as a hemostatic and cholagogue. The infusion is stored in a cool place for no more than 2 days.

Mountain arnica juice. The juice is squeezed from flower baskets collected during full flowering. Take 30-40 drops with a spoonful of honey 2-3 times daily before meals. In small doses (10-20 drops with honey) has a tonic effect on the central nervous system, in large (40-60 drops) reduces its tone and prevents seizures [5, 7, 40].

1.2. Basic principles of homeopathic medicine

Homeopathy is a special form of regulatory therapy, the purpose of which is to influence the processes of self-regulation, to stimulate and normalize the body's defenses with the help of specific homeopathic medicines, selected strictly individually, taking into account the patient's reaction.

The word "homeopathy" comes from the Greek words *homios* - similar and *patos* - disease, ie "treatment that causes an effect similar to the disease itself" [55].

At present, no one needs to be convinced of the effectiveness of homeopathy, which has successfully withstood various restrictions and prohibitions. But the data homeopathies are mostly empirical observations, without a solid scientific basis. Therefore, the study of homeopathic remedies is extremely important [12, 68].

Homeopathy as a therapeutic therapy is based on four principles:

Principle of similarity (similar is treated by similar): the majority drugs, depending on the dose have two opposite effects on the body. The use of small doses of those drugs that in large doses in a healthy person cause phenomena similar to the clinical picture of the disease. This is the basic principle of homeopathy that was formulated by Hahnemann in 1796.

The principle of the study - this is the position of homeopathy, according to Hahnemann, is the need to study homeopathic remedies in large doses in a healthy person in order to identify side effects and, thus, establishing the pathogenesis of the drug. In addition to experiments on volunteers, an important source for drug

pathogenesis is the clinic of accidental and occupational poisoning. Pharmacological experiments on animals are of very little importance.

The principle of potentiation is a peculiar way of preparing medicines. Dynamicization or potentiation is the enhancement of the action of drugs in the process of their preparation by successive dilutions and shaking. Thus obtained dosage form has optimal therapeutic properties in the absence of side effects, so Hahnemann called its potency or dynamization (in translation - opportunity, ability).

The principle of small doses of medicines - homeopathic doses compared to the doses used in general medicine, are weak stimuli. The signals caused by them pass unimpeded into the nerve centers, without suppressing them, thus not suppressing the body's defenses.

Homeopathic doses are most effective in cases where the body is in a state of overexcitation and ceases to respond to strong stimuli.

The higher the degree of excitation of the body, the more effective homeopathic tool [55].

Homeopathic remedies are regulators of the body as they help restoration of self-regulation of an organism. Medical information derived from homeopathic medicine as an adequate weak stimulant for excited by the pathological process of the body causes a response in it, and work the affected organ is normalized [25].

Allopathic and homeopathic therapy cannot be considered in isolation from each other, as they are based on data from the same fundamental scientific and natural sciences (Table 1.3). The common goal of homeopathy and allopathy is the cure or improvement of a sick person with medication. They are also united by the main condition for achieving the goal, which states that treatment should be effective, safe and individualized. Methodological approaches that contribute to the goal in allopathy and homeopathy are radically different. This primarily concerns ideas about the nature of diseases and ways to cure them [55].

Unlike allopathy, which considers the elimination of the cause of the disease and its clinical manifestations (symptoms) to be the main factor of treatment, homeopathy recognizes the constitutional signs and reactions of a sick person as the

primary object of its teaching. Accordingly, homeopaths believe that "the patient is a disease that has become a person", and his symptoms are reactions of the body that are aimed at healing. Therefore, treatment is a process of displacing the disease from the body, and its main purpose is to enhance this process [56].

Table 1.3

Comparison of allopathy and homeopathy

Allopathy	Homeopathy
There is no individual approach to each patient. Excessive specialization. Referral of the patient from one deprives the specialist of another opportunities to observe the patient for a long time.	Individual approach to each patient.
Medicinal substances are tested on animals. Frequent complications and side effects drugs.	Medications are being tested on healthy people. Consists picture of the action of each drug means. No complications poisoning or side effects.
Medicines are mainly chemical, synthetic origin.	Medicines of natural origin: plants, minerals, insects, selection of animals, products diseases.
The main principle in treatment - suppression of symptoms.	The main principle in treatment - regulation, restoration dynamic equilibrium.
The patient's symptoms are adjusted to the pattern - the diagnosis. The drug is prescribed accordingly template, not including individual features of the patient's body.	Medicines are selected for each patient individually based on the law of similarity. There is an individual picture of the patient's disease, which then compared with the picture of the action of a drugs.

Homeopathic therapy takes into account an absolute set of properties of a sick person, determining its individuality: data on the etiology and the pathogenesis of all diseases that the patient suffered during his life, his constitutional and psychological characteristics, etc.

Homeopathic treatment of the same pathological processes in different patients can dramatically differ because it does not meet the basic characteristics of the disease, and features of the patient's body. Homeopaths consider development of a pathological process as a continuation of the constitutional properties of the organism and operate on the principle of "one patient - one disease". They also believe that the suppression of symptoms by allopathic drugs inhibits the function of the body's defenses, which may be the cause of formation of chronic diseases [25].

1.3. Hemorrhoids, classification and pharmacotherapeutic approaches of treatment

Hemorrhoids are a painful enlargement of the cavernous cavities of the venous rectal plexus. These cavities are filled with blood under stress, performing the function of a kind of "cushion" that protects tissues from traumatic action of solid fecal masses during the act of defecation [8, 21].

Hemorrhoids are an urgent problem of mankind, about 60 % of the world's citizens tolerate at least one episode of painful enlargement of hemorrhoids during his life. This percentage is much higher in the countries that are accepted as civilized [43-45, 53].

Anatomically distinguish internal hemorrhoids – hemorrhoids distal (end) rectum, and external hemorrhoids when nodes are located outside in the area of the anus.

By the nature of the course of hemorrhoids is acute, associated with thrombosis of hemorrhoidal veins, and chronic - caused by constant overflow of stretched veins with blood.

Chronic hemorrhoids in women usually develop after the age of 30, with age the risk of developing the disease increases. Women suffer from hemorrhoidal varicose veins four times less often than men. However, the risk increases when the presence of the following factors:

- chronic constipation;
- prolonged sitting on the toilet;
- obesity;
- sedentary work, sedentary lifestyle;
- diseases with chronic cough;
- diseases of the pelvic organs.

A typical cause of acute hemorrhoids in women is pregnancy or childbirth. In such cases, adequate conservative treatment leads to the disappearance of the problem. However, if the therapy was untimely or careless, the disease becomes chronic.

Acute dilation of hemorrhoidal veins manifests itself in sharp pain, which becomes unbearable during defecation. In addition, pain can intensify during walking, as well as with increased intra-abdominal stress, coughing, laughing, hiccups [3, 4, 34, 39, 42,].

Another characteristic feature of the acute form of the disease - bleeding from dilated veins of the rectum. This symptom is manifested by fresh blood on the surface fecal mass.

Often hemorrhoids in women are combined with a crack in the anus. In such cases, blood stains on toilet paper and underwear after intercourse defecation appear even more often.

With chronic hemorrhoids, the pain is much weaker. Quite often the only signs of chronic pathology are itching around the anus and time from time blood appears on the surface of fecal masses.

Stages of development of internal hemorrhoids differ by the most objective symptom - the degree of dilation of varicose veins:

- I. The hemorrhoid is constantly in the intestinal cavity.

II. The knot falls out under tension and self-exercises back.

III. The patient has to fix the knot with his hands.

IV. One or more hemorrhoids are constantly outside and it is impossible to fix them.

At any stage, thrombosis of the dilated veins of the rectum may occur, in which case there is a pronounced pain syndrome characteristic of an acute attack.

With a long course of the disease, the risk of developing complications (anemia, neurasthenia, anal fissure, etc.) [50-52].

Diagnosis of hemorrhoids is carried out by a proctologist using finger research. Symptoms such as bleeding, pain, foreign body sensation in the rectum are found in cancer, as well as in other pathologies of the lower intestine. Therefore, the general list of examinations may include sigmoidoscopy or colonoscopy, as well as laboratory tests [66, 67, 74, 76].

At the final stage of diagnosis, a treatment strategy is chosen. Acute hemorrhoids are treated conservatively, while in the chronic form of the disease they turn to surgery, preferring minimally invasive methods of treatment [48, 54, 57-64].

The exception is cases when the operation is temporarily contraindicated. In women, this is pregnancy, the postpartum period, as well as situations where it is necessary to stabilize the general condition of the patient. Such a situation can occur in acute infections or exacerbation of severe chronic diseases [69-75].

Treatment of hemorrhoids.

Conservative treatment of painfully enlarged hemorrhoids should be carried out in a complex manner, influencing all factors contributing to the development of the disease. The stool should be normalized, because constipation and diarrhea equally injure the inflamed node. If the cause of hemorrhoids was an attack of diarrhea, every effort is made to heal from the disease, which caused a violation of defecation. Constipation is treated with a diet that includes a large amount of dietary fiber (prunes, dried apricots, oranges, apples). With persistent constipation, light laxatives (dufalac) are prescribed. In order not to irritate the intestines, spices, salt, vinegar, smoked foods, as well as carbonated drinks and alcohol. The pain in-

creases the spasm of the internal sphincter, which contributes to the stagnation of blood in veins. To relieve pain and spasm, warm baths with potassium permanganate or herbal decoctions are used.

Painkillers, antispasmodics, blood thinners, and drugs that promote tissue regeneration are prescribed as drug therapy. Preference is given to “local” therapy: ointments, creams, gels are used for the external location of the nodes, and suppositories for the internal location [3, 4, 21, 46, 47, 49].

1.4. Suppositories as a promising dosage form for hemorrhoid treatment

Today there are a large number of dosage forms used in such important fields of medicine as gynecology, proctology, urology, pediatrics.

Drugs can be introduced into the human body in different ways. Depending on the route of administration: the rate and completeness of drug entry into the body, the time of maintaining an effective concentration in blood plasma, the possibility of drug delivery to the site of action and, therefore, the presence or absence of therapeutic effect. Among the various methods of administration of drugs into the body of some interest in practical medicine are rectal and vaginal, which combine the benefits and features oral and parenteral [20-24, 33].

Dosage forms for rectal use are classified as follows:

- suppositories,
- capsules,
- solutions,
- suspensions and emulsions (in the form of enemas, microenemas or rectioles),
- powders and tablets for the preparation of rectal solutions and suspensions,
- mild drugs for rectal use (ointments, gels),
- foams (aerosols),
- rectal tampons.

The most common of all these dosage forms are suppositories, which are most often used for local or resorptive action of active pharmaceutical ingredients.

This dosage form is characterized by such advantages as:

- no side effects on the gastrointestinal tract;
- rapid onset of therapeutic effect, prolonged prolonged release of the drug;
- ensuring maximum interaction between the mucous membrane and API, without the detection of irritants;
- practically no allergic reactions;
- accuracy of dosing;
- lack of specific taste and smell characteristic of some substances;
- the possibility of use by patients with nausea and vomiting;
- the possibility of use in emergencies, as most API is rapidly absorbed in the large intestine and enters the systemic bloodstream directly through the middle and lower hemorrhoidal veins, as well as lymphatic pathways [1, 2, 15, 26].

It should also be noted that drugs in the form of suppositories are widely used in pediatric and geriatric practice, when it is difficult to oral and parenteral administration of drugs [9, 10].

Among the negative characteristics of suppositories are their thermolability, as most suppositories require special storage and transportation conditions, the possibility of premature removal of the drug from the injection site (leakage, defecation), unpleasant hygienic aspects of them application, as well as the negative compliance of some patients, because many patients are biased towards this LF, due to certain cultural traditions. Therefore, suppositories have many advantages and a minimum of disadvantages compared to other dosage forms [11, 17-19].

From the physicochemical point of view, suppositories are dispersed systems consisting of a base (dispersion medium) and drugs (dispersed phase). Such systems are complex multicomponent heterogeneous systems because they contain

one or more drugs substances dispersed or dissolved in a simple or complex base which may be soluble or dispersible in water.

The most popular drugs in the form of suppositories by gynecologists and proctologists. Therefore, in recent years, studies have focused on traditional areas of application of suppositories for the treatment of hemorrhoids, anal fissures, vaginitis of various etiologies [1, 2].

Suppositories are solid at room temperature dosed dosage form containing one or more active substances dissolved or dispersed in a suitable base, intended for administration into a body cavity and melted at body temperature. There are rectal suppositories, vaginal suppositories and sticks.

Suppositories are classified as:

1. By the nature of the action and localization of the pharmacological effect:

- suppositories of local (local) action: anesthetic, astringent, laxative, etc.;
- suppositories of general (resorptive) action: analgesic, antispasmodic, hypnotic, etc.

2. By input and geometric shape:

- rectal suppositories (*suppositoria rectalia*) are usually conical or torpedo-shaped and can be used both to provide local action and to achieve a systemic effect. Weight of one suppository from 1.0 to 4.0 g, children's - from 0.5 to 1.5 g; the maximum diameter should not exceed 1.5 cm;

- vaginal suppositories (*suppositoria vaginalia*) are mostly spherical (balls) or ovoid (ovules) and are usually intended for local action. The weight of one vaginal suppository is from 1.5 to 6.0 g;

- bacilli have a cylindrical shape with a pointed end and are inserted into the fistula, ear canal and urethra. The weight of the stick should be from 0.5 to 1.0 g, diameter not more than 0.2-0.5 cm

3. By method of manufacture:

- rolling off method,
- casting method,
- method of pressing.

4. By type of base:

- lipophilic,
- hydrophilic,
- diphtheria.

5. By type of dispersed system.

- homogeneous (if the drug is soluble in the base);
- heterogeneous (if the drug is introduced into the base by type of suspension or emulsion).

Suppositories must meet a number of requirements that ensure their quality, namely: uniform shape, hardness, homogeneity of mass; particle size; dissolution; disintegration; melting point or time of complete deformation of suppositories on lipophilic bases; homogeneity of the mass of dosage forms; identity and quantitative content of medicinal substances; homogeneity of drug dosage; microbiological purity [27-30, 32, 33, 38, 41]

CONCLUSIONS

1. As a result of the study and analysis of scientific information, the composition of biologically active substances contained in different parts of mountain arnica was studied, and a wide range of pharmacological actions of this medicinal plant material was considered.
2. The main approaches of homeopathy, its advantages over allopathy in the treatment of diseases are considered.
3. The main manifestations of hemorrhoids, classifications were studied in detail and the place of suppositories as a dosage form in their therapy was analyzed.

EXPERIMENTAL PART

CHAPTER II

OBJECTS AND METHODS OF RESEARCH

2.1. Objects of researches

2.1.1. Characteristics of active substances

To create a new drug, it was decided to take as an active pharmaceutical ingredient - arnica tincture, which was prepared from dried flowers according to the SPhU method 4a.

Arnica flowers (SPhU, 2.0 ed., p. 233) – *Arnica Montana L.* - Arnica mountain. Whole or partially broken, dried flowering baskets of *Arnica montana L.*

Content: not less than 0.40% m/m of the sum of sesquiterpene lactones, in terms of dihydrogelenaline tiglate and dry raw materials. The raw material has a fragrant smell. The opened basket reaches about 20 mm in diameter and about 15 mm in depth, has a stem (2-3) cm long. The involucre consists of (18-24) elongated-lanceolate bracts with pointed apices arranged in (1-2) rows: bracts about (8-10) mm long, green with yellowish-green outer hairs visible under dandruff. Bed baskets about 6 mm in diameter, convex, honeycomb and covered with hairs. Along its periphery are about 20 false flowers (20-30) mm long; the disc bed bears a large number of tubular flowers about 15 mm long. Ovary (4-8) mm long, crowned with bangs of whitish hairs (4-8 mm) long. There may be several brown achenes with or without bangs.

2.1.2. Characteristics of excipients

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).

Hard fat (type A). It is a homogeneous, solid, prickly mass from white to cream color, practically odorless, transparent in the molten state. Melting point - (34-36) °C.

Cacao butter. Cocoa butter has positive properties: it releases well the substances introduced into it, which have a pronounced melting point, has good plasticity, mixes well with various medicinal substances. It melts at a temperature of 30-34°C, turning into a transparent liquid.

Witepsol H 15. It is a solid, brittle mass at room temperature, melts easily at body temperature, tasteless and odorless white. Melting point 33.5–35.5 °C. Used as a suppository base. Compatible with many medicinal substances and quickly releases them, can be incorporated into 100% water, easily melts, pours, solidifies; characterized by pharmacological indifference and high stability.

2.2. Methods of researches

Determination of the **density** of arnica tincture was performed aerometrically method using a set of hydrometers.

Qualitative reactions of identification of biologically active substances:

To detect flavonoids:

Cyanidin test:

To 1 ml of tincture add 2-3 drops of hydrochloric acid P and 0.1 g magnesium powder, heated on a water heater for 3 minutes. A red color is formed.

Reaction with alkali solutions:

To 1 ml of tincture add 1-2 drops of 10% alcohol solution of sodium hydroxide. A yellow-orange color appears.

Reaction with ammonium hydroxide:

To 1 ml of tincture add 0.5 ml of 10% ammonium hydroxide solution. A yellow color appears.

Reaction from iron (III) chloride:

To 1 ml of tincture add 2-3 drops of 1% alcoholic solution of iron (III) chloride. A dark green or brown color is formed.

Preparation of 5% acetic acid solution:

5 ml of acetic acid P was placed in a volumetric flask with a capacity of 100 ml, the volume of the solution was adjusted to 70% with alcohol and mixed. The shelf life of the solution is 7 days.

Organoleptic control was carried out visually, evaluating the shape, color, size, uniformity of the suppository mass (the absence of inclusions, sparkles or pieces of the base in a longitudinal section).

The average weight of the suppository was determined according to the State Pharmacopoeia by weighing 20 suppositories with an accuracy of 0.01. Deviations in mass should not exceed $\pm 5\%$.

The melting point was determined by the open capillary method. To do this, the straightened suppository mass was placed in five glass low-melting glass capillary tubes (length 80 mm, outer diameter from 1.4 to 1.5 mm, inner diameter from 1.0 to 1.2 mm) to form a column about 10 mm high at each column. The capillary was placed in a refrigerator for 1 hour, then the melting point was determined using the device described in the State Pharmacopoeia of Ukraine. The melting point (average of five readings) was taken to be the temperature at which the test sample becomes liquid and begins to rise through the capillary tube. The melting point should not exceed 37°C .

Determination of the time of complete deformation.

We used a device consisting of a tube open from both capillary sides, metal stem and glass stem. The short end of the tube was closed with a stopper and filled with purified water at a temperature of $37\pm 1^{\circ}\text{C}$. A rod was lowered into the long end and the entire device was placed in a vessel with a stream of water at a temperature of $37\pm 1^{\circ}\text{C}$. Under rod a suppository was placed, previously kept on ice for 15 minutes, and a stopwatch was started. The time from the introduction of the suppository into the tube until the appearance of the rod at the bottom, the narrowing of the tube was taken as the time of complete deformation. Five parallel measurements were taken. The time of complete deformation should not exceed 15 minutes.

Determination of the dissolution time for suppositories on hydrophilic bases (PEO). To do this, one suppository was placed at the bottom of a 100 ml beaker containing 50 ml of purified water at a temperature of $37 \pm 1^\circ\text{C}$.

The beaker is shaken every 5 minutes so that the liquid and the sample acquire a rotational motion. The dissolution time was taken as the value from the moment placing suppositories in purified water until completely dissolved. The dissolution time should not exceed 1 hour. The determination of the pH of the aqueous extract from the suppositories was carried out by the potentiometric method according to the SPh XI ed. (1987, issue 1) [28] on the ionomers of the universal EV-74. An extract from suppositories was prepared according to the following procedure: one suppository weighing 1.5 g was placed in a flask with a capacity of 50 ml, 15 ml of purified water was added at a temperature of $60 \pm 5^\circ\text{C}$ and shaken thoroughly. After complete cooling, the resulting extract was filtered and the pH value was determined. Three parallel experiments were carried out.

Cooling temperature determination

The cooling temperature of the bases was determined using a Zhukov instrument. The base straightened at 50°C was poured into the device until it was filled by $\frac{3}{4}$ of its volume. The device was closed with a stopper through which a thermometer with a distribution of 0.1°C passes, installed in such a way that the mercury ball is located approximately in the middle of the mass of the base. The device was placed in a vessel with water at a constant temperature. With light periodic shaking, the straightened base was mixed until turbidity appeared, after which the base was allowed to cool without mixing. Thermometer readings were recorded every minute; the pour point was the temperature that the base maintained for some time during the solidification process.

Biopharmaceutical research on suppositories.

Biopharmaceutical studies on the release of flavonoids from suppositories were carried out in vitro by dialysis through a semi-permeable membrane. A cellophane film with a layer thickness of $45\ \mu\text{m}$ was used as a dialysis membrane. Dial-

ysis was performed in 70% ethanol in a TV 3-25 thermostat at a temperature of $40 \pm 1^{\circ}\text{C}$. Ethyl alcohol 70% was used as the dialysis medium.

Dialysate sampling was performed at 15, 30, 45, 60 and 75 minutes. The sample volume was 5 ml. The same amount of dialyzer was immediately replenished with dialysis medium. The taken samples were subjected to spectrophotometric analysis for content flavonoids in terms of rutin.

CONCLUSIONS

1. Arnica flowers and arnica tincture were used as the object of study in order to conduct further research on the creation of extemporaneous suppositories of hemostatic, anti-inflammatory action, as well as excipients.
2. When developing suppositories based on arnica tincture, organoleptic, biopharmaceutical and physico-chemical research methods were used.

CHAPTER III.

DEVELOPMENT OF THE COMPOSITION OF RECTAL SUPPOSITORIES WITH HOMEOPATHIC ARNICA TINCTURE

3.1. Technology of the preparation of homeopathic arnica tincture

Arnica tincture was prepared according to SPhU method 4a using the maceration method.

Technology for obtaining arnica tincture from dried raw materials.

10.0 parts of crushed plant raw materials of arnica (flowers) was poured with 100.0 parts of 60 % alcohol and left to infuse in a dark glass bottle at a temperature of 16 °C for 8 days with daily shaking.

The liquid was drained, the mass was squeezed out with a press strainer, both liquids were mixed and left for 8 days to settle in a dark place, after which the liquid was filtered through a paper filter. Obtained tincture of arnica is a dilution D1. Algorithm of tincture technology from dried plant raw material is represented on Fig. 3.1. The tincture was analyzed for organoleptic and physico-chemical parameters (Table 3.1).

Arnica tincture is a liquid of yellowish-brown color, peculiar smell, with a bitter taste, without mechanical inclusions. The content of medicinal substances in arnica tincture is 1:10. This tincture corresponds to the first tithe dilution and is a matrix tincture.

The color of arnica tincture is yellowish-brown tincture color, with a specific smell and bitter taste. The determination of color was carried out in daylight by placing a cuvette with tincture in front of a sheet of white paper and examining a 10 ml liquid layer content of extractives.

The dry residue was determined as follows: an accurately measured (25 ml) and accurately weighed amount of arnica tincture was evaporated on a water bath, which was placed in a pre-weighed porcelain cup. Then dried for 30 minutes in a thermostat at a temperature of 105°C.

Dry residue - 0.7042

Weight of 25 ml of tincture - 25.1500 g

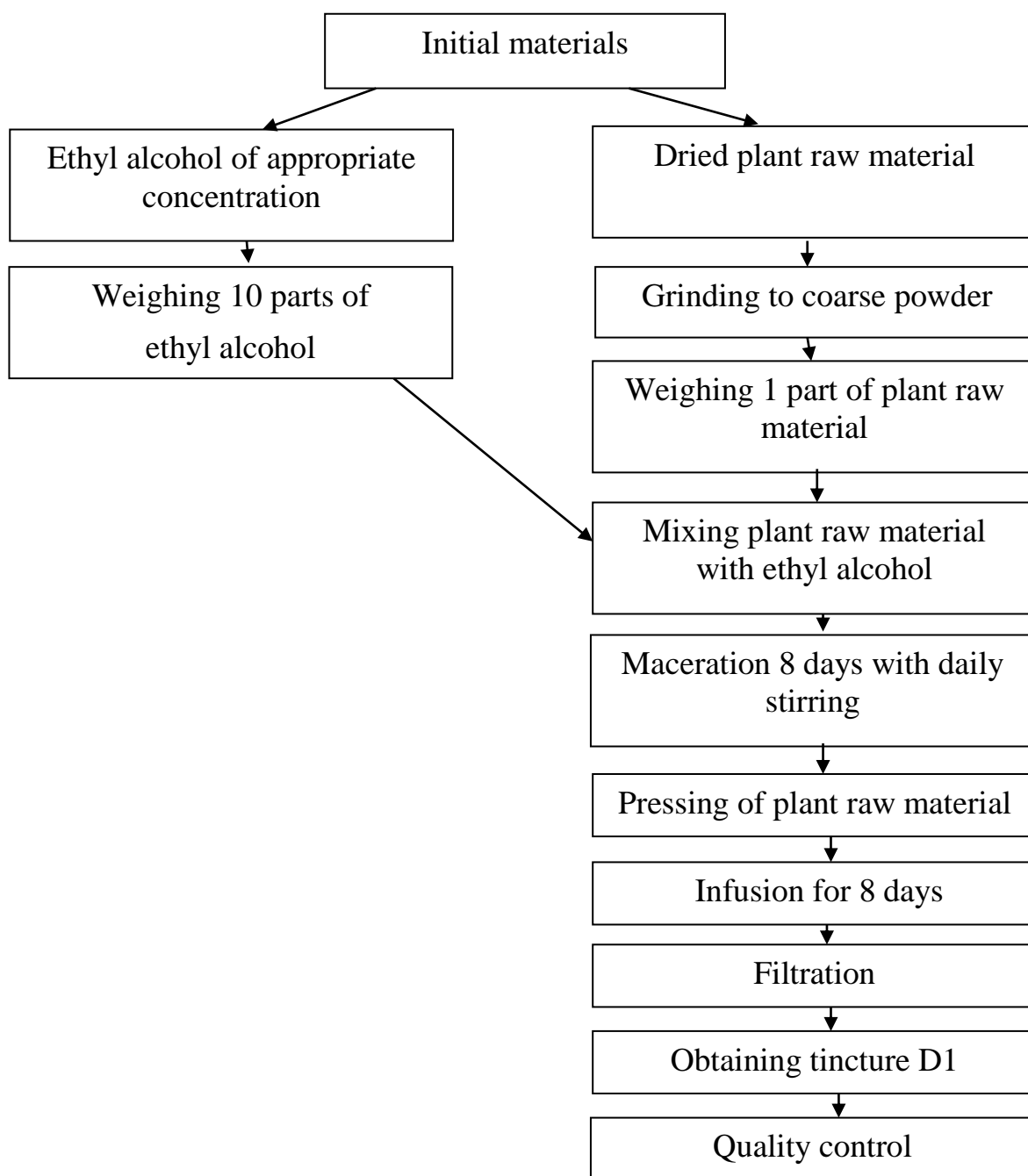


Fig. 3.1. Algorithm of tincture technology from dried plant raw material

The content of extractive substances: $(0.7042 : 25.1500) \times 100 = 2.8 \%$

Density.

Determination of the density of arnica tincture was carried out using a hydrometer. At temperatures above 17.5 °C. Index 0.0007 is added for each degree. The density of the tincture is 0.9041 kg/m³.

The content of ethyl alcohol was determined with an alcoholmeter; in tincture it is 59 %. The results are shown in table 3.1.

Table 3.1

**Organoleptic, physical and chemical indicators of homeopathic
arnica tincture D1**

№	Indicators	Observations
1.	Appearance	Yellowish-brown liquid
2.	Taste, smell	Bitter taste, specific smell
3.	Density, kg/m ³	0.9041
4.	Alcohol content, %	59 %
5.	The content of extractive substances, %	2.8 %

The main active ingredients in arnica flower tincture are flavonoids. The presence of these substances was confirmed by the following qualitative reactions:

- cyanidin test,
- with a solution of aluminum chloride,
- reaction with alkali solutions,
- with a solution of lead acetate,
- with a solution of iron chloride,
- with ammonium hydroxide solution.

Methods for conducting identification reactions are presented in chapter 2. The results of identification reactions for flavonoids are presented in Table 3.2.

Table 3.2

**The results of identification reactions for flavonoids in homeopathic
tincture of arnica D1**

№	Reaction	Observation	Standard
1.	With a solution of lead acetate	Yellow precipitate	Orange precipitate

2.	Cyanidin test	Pink color	Red or orange color
3.	With 10 % ammonium solution hydroxide	Pale yellow color	Yellow color
4.	With a solution of aluminum chloride color	Yellow color	Yellow-green
5.	1% alcohol solution iron (III) chloride	Green color	Dark green color
6.	10% alcohol solution sodium hydroxide	Yellow color	Yellow-orange color

As can be seen from the results of the table, the identification reactions gave colors that indicate the presence of flavonoids and the possibility of using these reagents to develop methods for quality control of arnica tincture.

3.2. Choice of the base for suppositories with homeopathic arnica tincture

To obtain suppositories with homeopathic tincture of arnica, we made model samples on lipophilic bases, which are most used in the composition of antihemorrhoidal suppositories of pharmacy and industrial production.

The concentration of arnica tincture per one suppository (1.5 g) was chosen on the basis of literature data in homeopathic practice and amounted to 0.25 g.

The traditional and classical basis for making suppositories in homeopathy is cocoa butter. The following were used as bases: witepsol H 15, solid fat, cocoa butter, and also a mixture of cocoa butter and beeswax (4:1). The compositions of model samples of suppositories are shown in Table 3.3.

Suppositories were prepared by pouring into detachable molds. The tincture was introduced into the base after its complete melting, the mixture was stirred and poured into molds lubricated with soapy alcohol.

The suppositories were cooled to complete solidification in the refrigerator at temperature $4\pm 1^{\circ}\text{C}$ for 60 min. After that, the suppositories were removed from

the mold. The mass of the suppository, set taking into account the volume of the pouring mold, is 1.5 g.

Table 3.3

Compositions of model samples of suppositories with arnica tincture

Components, g	Sample number			
	1	2	3	4
Arnica tincture D1	0.25	0.25	0.25	0.25
Witepsol H 15	up to 1.5	-	-	-
Beeswax	-	-	0.31	-
Cocoa butter	-	up to 1.5	up to 1.5	-
Solid fat	-	-	-	up to 1.5

The choice of base was carried out in terms of appearance and structural and mechanical properties. Biopharmaceutical studies have also been conducted to determine the degree of release of flavonoids. The results of the organoleptic control of the obtained suppositories are shown in Table 3.4.

Table 3.4

Indicators of organoleptic control of model samples suppositories with arnica tincture

Indicator	Sample number			
	1	2	3	4
Color	beige	beige	beige	beige
Smell	specific	specific	specific	specific
Homogeneity	Torpedo-shaped, homogeneous, glossy in section, inclusions are absent	Torpedo-shaped, homogeneous, matte, while incision, inclusions are absent	Torpedo-shaped, homogeneous, glossy in section, inclusions are absent	Torpedo-shaped, homogeneous, matte, while incision, inclusions are absent

As can be seen from the results, all samples of suppositories had characteristic torpedo-shaped, were homogeneous, had a beige color due to the presence of tincture.

In order to study the structural and mechanical properties was the melting temperature of model samples of suppositories and the time of complete deformation were studied. The results are shown in table 3.5.

Table 3.5

**Indicators of melting temperature and time of complete deformation
model samples of suppositories with arnica tincture**

Indicator	Sample number			
	1	2	3	4
Melting point (° C)	34.2 ± 0.4	35.5 ± 0.5	39.1 ± 0.5	33.2 ± 0.4
Time of complete deformation (min)	7.3 ± 0.5	7.4 ± 0.5	18.5 ± 0.4	4.9 ± 0.5

As can be seen from the results of the table, preference was given to the bases - cocoa butter and witepsol H 15, samples 1 and 2. The resulting suppositories were stored for 6 months.

During storage of suppositories made on the base of witepsol H-15, throughout the entire period of the study, no change in color, odor, uniformity, significant fluctuations in the values of the time of complete deformation, as well as the melting temperature of the suppositories, were noted. While storing suppositories in cocoa butter, a whitish coating (“graying”) appeared on the surface, fragility, which limited their shelf life to 6 months.

Subsequent studies on the choice of the optimal base concerned the biopharmaceutical indicator, namely the release of active biologically active substances from suppositories (flavonoids). For this, the method of dialysis through a semi-permeable membrane (*in vitro*) was used.

As a result of studies on the release of flavonoids *in vitro* experiments, it was found that the highest degree of release (%) is observed in samples based on

witepsol H15, which after 120 minutes is 82 %. Analysis of the data obtained showed that the base has a significant effect on the release of biologically active substances from the dosage form turn affects the therapeutic efficacy of the drug.

Based on the results obtained, for further research, the following composition of suppositories (g) was chosen:

Arnica tincture D1 - 0.25

Witepsol H15 - a sufficient amount to obtain suppositories weighing 1.5.

3.3. Structural and mechanical studies of suppositories with homeopathic arnica tincture

Samples of suppositories of the proposed composition were obtained in laboratory conditions. They were tested according to the following indicators: melting point, time of complete deformation, curing temperature.

The results of determining the melting and solidification temperatures of suppositories, as well as the time of complete deformation, are given in Table 3.6.

As can be seen from the data, the solidification temperature is lower than the melting temperature, which will make it possible to obtain candles by pouring under a favorable temperature regime. meets the requirements of the SPhU.

Table 3.6

The results of determining the melting temperature, solidification and time of complete deformation of suppositories

Series number	Melting point (° C)	Curing temperature (° C)	Time of complete deformation (min)
1	35.2	32.1	6.8
2	35.4	32.6	7.1
3	35.1	32.0	6.8
4	35.0	32.1	7.1
5	35.3	32.4	6.9

In addition, the following technology for the production of new extemporaneous suppositories with homeopathic tincture of arnica was developed, shown in Fig. 3.2.

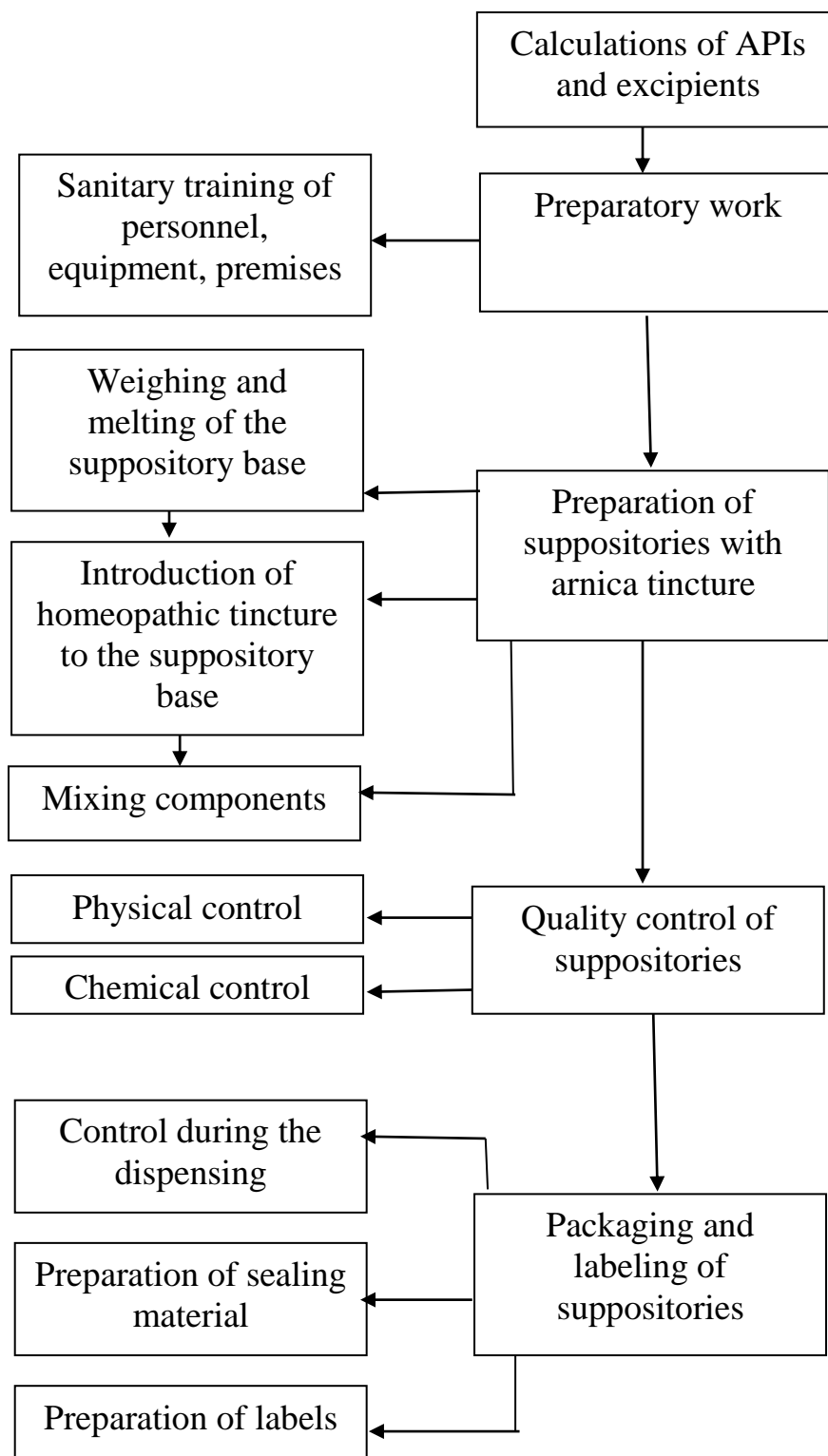


Fig. 3.2. Manufacturing technology of extemporaneous suppositories with homeopathic arnica tincture

Suppositories are wrapped in triangular-shaped parchment capsules and put into a cardboard box of 5 or 10 pieces.

Registration for the release must be done as follows: stick the prescription number, the label "External" indicating the name of the medicinal product, dose, number of suppositories and date of preparation; additional labels - "Keep in a cool place" and "Keep out of reach of children" must be applied.

CONCLUSIONS

1. The technology of homeopathic tincture of arnica from dried raw materials according to the SPhU method 4a and its main physical and chemical properties were investigated.
2. As a result of the organoleptic, physicochemical, structural-mechanical and biopharmaceutical studies, a rational basis was chosen for the development of antihemorrhoidal suppositories with homeopathic tincture of arnica, namely witepsol H 15.
3. Based on the research, a technology of rectal suppositories with homeopathic tincture of arnica has been proposed.

GENERAL CONCLUSIONS

1. Based on the analysis of literature data, the necessity of creating arnica suppositories for use in the complex therapy of hemorrhoids is substantiated.
2. Analyzed information about the properties of arnica, its use in allopathy and homeopathy.
3. The technology of homeopathic tincture of arnica has been developed and its physicochemical characteristics have been studied. The presence of flavonoids in the composition of the tincture was established.
4. Based on the study of the physicochemical and structural-mechanical properties of suppository bases, the rational composition of suppositories with homeopathic arnica tincture is substantiated.
5. The developed dosage form in the form of suppositories with homeopathic tincture of arnica can be recommended for expanding the range of antihemorrhoidal drugs.
6. Based on the results of the master's work, one article of the 3rd International scientific and practical conference “Innovations and prospects of world science” (November 4-6, 2021, Vancouver) and one abstract of the scientific and practical conference with international participation, dedicated to the 100th anniversary of the National University of Pharmacy (September 10, 2021, Kharkiv) have been published.

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APPENDIXES

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SCIENTIFIC AND PRACTICAL CONFERENCE
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PHARMACEUTICAL SCIENCES

UDC 615.454.21:615.322

THE CHOICE OF BASE FOR THE CREATION OF SUPPOSITORIES WITH A HOMEOPATHIC ARNICA TINCTURE

Cherkaoui Aya

Applicant for higher education

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Ph.D., Associate Professor

of Drugs Technology Department

Yarnykh Tetyana

D.Sc. (Pharmacy),

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Annotation: The urgency of creating rectal suppositories with homeopathic arnica tincture for use in complex therapy of hemorrhoids is proved. Based on the study of appearance, physicochemical and structural-mechanical parameters of the model samples the suppository base for the creation of rectal suppositories with homeopathic arnica tincture was selected. Organoleptic, physicochemical and structural-mechanical parameters of model samples were determined according to the relevant methods of the State Pharmacopoeia of Ukraine.

Key words: medicine, suppositories, suppository base, homeopathy, arnica.

One of the important problems of modern medicine is the diagnosis, treatment and prevention of proctologic diseases.

Recently, diseases of the rectum, in particular proctitis, proctosigmoiditis, hemorrhoids are becoming more common and do not tend to decrease. The reason for this is a sedentary, sedentary lifestyle, poor diet, bad habits such as alcohol abuse, stress. Hemorrhoids affect more than 10% of the adult population of the planet, and

CERTIFICATE

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**«ВІДКРИВАЄМО НОВЕ СТОРІЧЧЯ:
ЗДОБУТКИ ТА ПЕРСПЕКТИВИ»**

Матеріали науково-практичної конференції з міжнародною участю,
присвяченої 100-річчю Національного фармацевтичного університету

10 вересня 2021 р.
м. Харків

Харків
НФаУ
2021

CONTINUATION OF APPENDIX C

СЕКЦІЯ 3

**THE CHOICE OF THE BASE FOR THE CREATION
OF RECTAL SUPPOSITORIES FOR THE TREATMENT OF HEMORRHOID**

Aya Cherkaoui Eddahabi, Ganna Yuryeva

Scientific supervisor: Yarmykh T.

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Introduction. One of the important problems of modern medicine is the diagnosis, treatment and prevention of proctologic diseases. Recently, rectal diseases, in particular proctitis, proctosigmoiditis, hemorrhoids, are becoming more common and do not tend to decrease. The reason for this is a sedentary lifestyle, poor diet, bad habits such as alcohol abuse, stress. More than 10 % of the adult population of the planet suffers from hemorrhoids, and the proportion of the total number of coloproctological diseases is 40%.

Suppositories can be used as a medicine for local therapy of chronic and acute hemorrhoids and other diseases of the anal canal. It can reduce allergic reactions, prolong the therapeutic effect, especially in inflammation, increase the rate of drug absorption, reduce the dose (in some cases).

The search for active pharmaceutical ingredients in order to expand the range of drugs for topical treatment of hemorrhoids is an urgent task of modern pharmacy.

In this aspect, arnica (*Arnica montana* L.) is a promising active pharmaceutical ingredient for the creation of extemporaneous medicine, in particular suppositories for the treatment of hemorrhoids.

Purpose of the research. The choice of the base for the creation of rectal suppositories with homeopathic arnica tincture for the treatment of hemorrhoids.

Materials and methods. Arnica tincture was prepared from dried flowers in accordance with maceration method. As suppository base were used: Witepsol H15, solid fat, cocoa butter, as well as a mixture of cocoa butter and beeswax. Indicators of melting temperature of suppository samples and time of complete deformation were determined according to the methods of the State Pharmacopoeia of Ukraine.

Obtained results. The choice of the suppository base was carried out on the basis of appearance and structural and mechanical properties. Throughout the entire period of the study, no change in color, odor, homogeneity, significant fluctuations in the values of the time of complete deformation, as well as the melting temperature of suppositories made on the basis of Witepsol H15, was noted. The freezing temperature was lower than the melting point, which allows to obtain suppositories by pouring method at a favorable temperature.

Conclusions. Based on the obtained results, the suppository base - Witepsol H15 was selected for a further researches of biopharmaceutical indicators.

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**

Aya CHERKAOUI EDDAHABI

1. Topic of qualification work: «Development of the composition of rectal suppositories with homeopathic arnica tincture», 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: The purpose of the study is an experimental justification of the composition, the choice of suppository base for the development of rectal suppositories with homeopathic tincture of arnica, intended for use in the treatment of hemorrhoids. Object of researches: homeopathic tincture arnica D1, model samples of suppositories with arnica tincture.

4. Contents of the settlement and explanatory note (list of questions that need to be developed): - to analyze the literature on the prospects of application arnica in allopathy and homeopathy; -to analyze the pharmaceutical market of Ukraine for natural drug's availability for the local treatment of hemorrhoids; - to develop the technology of homeopathic arnica tincture; - to study the physico-chemical parameters of the developed arnica tincture; - theoretically and experimentally substantiate the composition of suppositories with homeopathic arnica tincture; - to conduct physico-chemical, pharmaco-technological research of rectal suppositories.

5. List of graphic material (with exact indication of the required drawings):

tables – 9

figures – 3

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

№ 3/II	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 _____ Aya CHERKAOUI EDDAHABI

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.	Шеркауи Иддахбі Айя	Розробка складу ректальних супозиторіїв з гомеопатичною настойкою арніки Development of the composition of rectal suppositories with homeopathic arnica tincture	доц. Юр'єва Г.Б.	доц. Степаненко С.В.

Підстава: подання декана, згода ректора.

Ректор

Вірно. Секретар



REVIEW

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

Aya CHERKAOUI EDDAHABI

on the topic: «Development of the composition of rectal suppositories with homeopathic arnica tincture»

Relevance of the topic. Declining quality of life contributes to an increase in morbidity among the population. In recent years, Ukraine has seen an increase in attention to non-traditional treatments, including homeopathy. The pharmaceutical market is replenished with new homeopathic remedies used by patients mainly for the treatment of chronic diseases, the share of which, according to the WHO, is constantly growing. Hemorrhoids is a disease that accompanied by varicose veins, inflammation of the veins in the rectum. Today it is one of the most common pathologies in the world. Suppositories for the treatment of hemorrhoids are the most effective dosage form that can successfully fight this disease. They have a local effect due to the rapid absorption of the active ingredient in their composition. Therefore, a promising area of modern pharmacy is the creation of extemporaneous homeopathic medicines for the treatment of hemorrhoids. The main goal of medical treatment is to control acute symptoms of hemorrhoids rather than to cure the underlying hemorrhoids. There are several modern drugs and traditional medicine used which are available in a variety of format including pill, suppository, cream and wipes. It has been experimentally established that flavonoids can increase vascular tone, reduce venous capacity, reduce capillary permeability, facilitate lymphatic drainage and have an anti-inflammatory effect. One source of flavonoids is mountain arnica.

Practical value of conclusions, recommendations and their validity. The obtained experimental material became the basis for the creation of a new drug based on homeopathic tincture of arnica - rectal suppositories, which will expand the range of herbal medicines for external use in the treatment of hemorrhoids.

Assessment of work. Qualification work in terms of theoretical and practical research fully meets the requirements for qualification work.

General conclusion and recommendations on admission to defend. Qualification work of Aya CHERKAOUI EDDAHABI can be submitted for defense to the Examination Commission of the National University of Pharmacy.

Scientific supervisor

Ganna YURYEVA

«12» of April 2022

REVIEW

for qualification work of the master's level of higher education,

specialty 226 Pharmacy, industrial pharmacy

Aya CHERKAOUI EDDAHABI

**on the topic: «Development of the composition of rectal suppositories with
homeopathic arnica tincture»**

Relevance of the topic. Today, the most common disease of the rectum, doctors consider hemorrhoids. After all, more than 40 % of patients who consult a proctologist, doctors diagnose hemorrhoids. 120-125 people out of every thousand population suffer from hemorrhoids. And every year the number of patients suffering from this disease is growing. Moreover, hemorrhoids have recently become significantly younger: most patients are people of working age. The choice of treatment for hemorrhoids depends on its stage or the nature of the complications. In conservative treatment, the main place is occupied by drugs of plant origin, which have analgesic and thrombolytic effects, improve the tone of cavernous vascular formations and blood microcirculation. One of the promising pharmaceutical ingredients are mountain arnica preparations.

Theoretical level of work. This work analyzes the literature on the modern use of arnica in allopathy and homeopathy, as well as information about its chemical composition and available pharmacological properties of mountain arnica. The main approaches to the choice of dosage form with arnica for the treatment of hemorrhoids are considered.

Author's suggestions on the research topic. The author proposes the technology of obtaining homeopathic tincture of arnica and substantiates the choice of excipients in the development of extemporaneous rectal suppositories based on it.

Practical value of conclusions, recommendations and their validity. On the basis of organoleptic, physicochemical and biopharmaceutical researches carried out by the author the choice of auxiliary substances in creation of suppositories of the combined action is proved.

Disadvantages of work. There are spelling and grammatical mistakes in the work.

General conclusion and assessment of the work. Qualification work of Aya CHERKAOUI EDDAHABI can be submitted to the Examination Commission for defense.

Reviewer _____

assoc. prof. Serhii STEPANENKO

«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 ЛЕВАЧКО-
ВА, 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 Айю ШЕРКАУИ ИДДАХАБІ з доповіддю
на тему «Розробка складу ректальних супозиторіїв з гомеопатичною настой-
кою арніки» (науковий керівник: доцент Ганна ЮР'ЄВА).

УХВАЛИЛИ:

Рекомендувати до захисту кваліфікаційну роботу.

Голова засідання

Тетяна ЯРНИХ

Секретар

Володимир КОВАЛЬОВ

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

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

Направляється здобувач вищої освіти Айя ШЕРКАУІ ЕДДАХАБІ до захисту кваліфікаційної роботи за галуззю знань 22 Охорона здоров'я спеціальністю 226 Фармація, промислова фармація освітньою програмою Фармація на тему: «Розробка складу ректальних супозиторіїв з гомеопатичною настойкою арніки».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Айя ШЕРКАУІ ЕДДАХАБІ 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 Айя ШЕРКАУІ ЕДДАХАБІ 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 /