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QUALIFICATION WORK

on the topic**: DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF ANTIBACTERIAL CAPSULES**

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ANNOTATION

The qualification work proved the relevance of creating antibacterial capsules with ornidazole and yarrow extract. Based on the conducted physicochemical and pharmacotechnological studies, the rational composition of the capsules was substantiated. The physicochemical and technological parameters of the samples were determined using the appropriate methods.

The qualification work is presented on 42 pages, contains 4 tables, 13 figures, and a list of references of 33 items.

Key words: capsules, mixed infections, ornidazole, yarrow extract, technology

АНОТАЦІЯ

У кваліфікаційній роботі доведено актуальність створення капсул антибактеріальної дії з орнідазолом та екстрактом деревію. На основі проведених фізико-хімічних і фармако-технологічних досліджень обґрунтовано раціональний склад капсул. Фізико-хімічні і технологічні параметри зразків визначали за відповідними методиками ДФУ.

Кваліфікаційна робота викладена на 42 сторінках, містить 4 таблиць, 13 рисунків, список літератури з 33 найменувань.

Ключові слова: капсули, мікст-інфекції, орнідазол, екстракт деревію, технологія

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INTRODUCTION

Relevance of the topic. Preparations of 5-nitroimidazole group are highly active antimicrobials of a wide spectrum of action for systemic treatment of infections caused by anaerobic bacteria and protozoa.

At present, there is a tendency towards the growth of associated infectious-inflammatory diseases (mixt-infections) in the body, which develop through the joint influence of pathogens with different natures. Such associations with viruses, bacteria, chlamydia, protozoa (trichomoniasis), fungi, parasites are known.

Simultaneous exposure to multiple infections is a serious problem, especially during outbreaks. According to statistics, in almost one in ten cases, it is mixt infections that are detected.

Inflammatory processes remain an urgent problem in modern medicine. Despite a significant number of scientific studies and the introduction of the latest antibacterial agents, the frequency of inflammatory diseases does not tend to decrease.

The main spectrum of microorganisms that can cause inflammatory diseases are mainly microbial-protozoan-viral associates.

They are characterised by qualitatively new properties, clinical features and are not the sum of the pathological components of individual infectious components. Incorrectly selected drug, dose, regimen and duration of use, and patient negligence lead to chronic inflammation, periodic exacerbations, which leads to the search for ways to improve the effectiveness of inflammatory processes. In such cases, it is necessary to use of the most effective medicines.

Trichomonas, candidiasis, chlamydia, mycoureaplasma and viral infections can persist in the human body for life.

Undiagnosed trichomonas often leads to a lack of success in the treatment of other infections and are treated as reinfection.

The following drugs are widely known in the practice of doctors drugs such as tinidazole, metronidazole, trichopol.

But over several decades of their use the genetic modelling of new pools of trichomonads has occurred, which have developed protective mechanisms against the antiprotozoal effect of these agents. This prompted the search for and development of new reliable drugs.

The peculiarity of the new generation of ornidazole drugs is the presence of an active radical in their structure, which allows the drug to enter the cell by active and passive transport, selectively accumulating. Ornidazole contains an active radical with a chlorine atom. Under the influence of nitroreductases of anaerobic microorganisms (which are absent in aerobes), the following occurs reduction of the nitro group in the ornidazole molecule with simultaneous formation of free radicals.

Purpose and objectives of the study – to develop the composition and technology of a combined medicinal product in the form of capsules with antimicrobial action.

The task of the work is to conduct a literature review, a set of pharmacotechnological studies, the selection of excipients and the development of a rational technology.

Objects of study – powder of medicinal substance ornidazole, yarrow extract, excipients, mass for encapsulation.

Subject of the study – development of the composition and technology of antimicrobial capsules.

Research methods. In solving the problems set in the work, various technological, physical, physicochemical and analytical methods were used.

Structure and scope of the qualification work. The qualification work of 42 pages consists of an introduction, 3 chapters, including 4 tables, 13 figures and conclusions. The list of references includes 33 sources.

CHAPTER 1
RELEVANCE OF THE DEVELOPMENT OF ANTIBACTERIAL DRUGS

1.1 Peculiarities of the development of diseases caused by mixt-infections

Mixt-infection is a simultaneous infection with several pathogenic or opportunistic microorganisms (i.e. those that necessarily cause disease, or cause disease only when immunity is reduced, dysbiosis). For example, fungi of the genus Candida (which cause thrush), trichomonads, mycoplasmas, ureaplasmas, chlamydia can coexist in various combinations in the reproductive organs.

Peculiarities of the development of diseases:

- each microorganism can contribute to the clinical picture, the symptomatology of such diseases is diverse, which makes diagnosis difficult;
- the pathogens influence each other - trichomonads can absorb cells of other pathogens (chlamydia, gonococcus), preserving their viability and protecting them from the effects of drugs;
- it is difficult to select drug therapy in such a way as to effectively affect all available pathogens, correctly combine drugs, use them in the optimal sequence, and at the same time take care to prevent dangerous side effects for the patient.

There are currently over 20000 species of protozoa, of which almost 10000 species parasitise invertebrates and vertebrates. Up to 60% of the world's population is infested by intestinal parasites. Intestinal protozoan diseases are a major public health problem of public health worldwide, including parasitoses such as amoebiasis, giardiasis, trichomoniasis, etc.

These diseases can be accompanied by a severe clinical course and fatal outcome. Different species of intestinal protozoa can live in the body, depending on the severity

of the course of the disease. Symptoms of intestinal protozoa infestation may include diarrhoea, abdominal pain, nausea or vomiting, liver abscesses, colitis and depression.

Lamblia (Giardia lamblia) was considered a non-threatening intestinal parasite for humans, but after the pathogenicity of the intestinal pathogen was recognised different classes of drugs started to use.

Inflammatory diseases of urogenital organs caused by pathogenic and opportunistic microorganisms continue to be a serious problem due to the possibility of developing severe complications related to reproductive function. The social significance of the diseases under discussion is due to both reduced fertility and increased direct and indirect costs associated with reduced quality of life of patients.

A characteristic feature of the etiology of inflammatory diseases of the lower urogenital tract in recent years is the prevalence of mixt-infections (more than 67% of cases). Monocultures of aerobic and anaerobic microorganisms can be obtained very rarely, much more often microbial associations of different composition are isolated.

The pathological process caused by associations of microorganisms is not the sum of pathological components of individual infectious agents. Individual infections in an association are capable of acquiring new, as yet unexplored properties. The common features characterising the course of urogenital tract mixed infections are:

- high contagiousness;
- tendency to chronicity of the process;
- lack of persistent immunity;
- possibility of disease recurrence.

Mixed infection refers to a disease caused by two or more pathogens at the same time. The aggressiveness of the infectious agent depends on:

- the infectious dose of the pathogen;
- the pathogenicity and virulence of the pathogen strain;
- the presence of a mixt-infection.

The response of the macroorganism to the introduction of a pathogenic agent develops depending on:

- on the initial state of immunity (general and local);
- the presence of reinfection or relapse;
- premorbid background;
- physiological state of the epithelium of the urogenital tract.

The causative agents of inflammatory diseases of the pelvic organs and the urogenital tract can be both pathogenic and opportunistic microorganisms. Some of the most frequently detected pathogens are trichomonads, ureaplasmas and mycoplasmas.

Trichomonas vaginalis is a unicellular protozoan organism with the following properties:

- it’s virulence is enhanced by nucleic acids released from dead cells of the organism;
- affects almost exclusively the lower part of the human urogenital tract, mainly the areas of the mucous membrane covered with squamous epithelium;
- produces and temporarily fixes on its surface a soluble antigen that prevents it from damage by antibodies;
- ability to exist simultaneously in regular pear-shaped, flagellate, amoeboid, and globular forms;
- amoeboid parasites not only have adhesion to the cell surface, but also exhibit marked cytotoxicity towards epithelial cells;
- round spherical forms usually appear under unfavourable conditions or as a result of multiplication. These forms of trichomonads are usually not actively motile and are difficult to identify;
- the vegetative form of trichomonads rapidly transforms into a cystic form when exposed to pharmacological or chemical factors;

- the presence of an antichymotrypsin envelope and proteolytic enzymes that affect defence and ability to cross tissue barriers;
- TANK function, i.e. the ability of trichomonads to engulf, protect and transport other microbial and viral infectious agents into tissues in a viable state;
- changes in biological activity and mode of feeding, adhesive capacity and ability to reproduce depending on the predominance of hormones in the body.

In addition to trichomoniasis, the urogenital tract of men and women is often colonised by mycoplasmas/ureaplasmas. Most species of mycoplasmas (ureaplasmas) are not absolute pathogens. Sexually transmitted, under certain conditions they cause infectious and inflammatory processes in the urogenital organs, more often in association with other pathogenic or opportunistic microorganisms.

The urogenital tract is inhabited by: M.hominis, M.genitalium, M.fermentas, U.urealyticum.

M.hominis, M.genitalium, U.urealyticum species colonise the urogenital tract of men and women and are often the cause of non-gonococcal urethritis, vaginitis, pelvic inflammatory diseases.

The course of infectious processes is determined by the spectrum of pathogenicity factors of the microorganism and the immune status of the macroorganism. Pathogenicity of the pathogen is genetically determined and can be manifested by direct toxic (toxins, enzymes, metabolites) and indirect (potential) pathogenicity factors that provide adhesion, colonisation, persistence of the microorganism and have an adverse effect on cells.

The peculiarity of mycoplasma biology makes it possible to understand the reasons for different degrees of pathogenicity of these microorganisms. The main features of mycoplasmas are the absence of a dense cell wall and its precursors, exceptionally small cell size with simple organisation and minimal organelles, and the smallest genome among prokaryotes. Mycoplasmas approach large viruses in size.

The following pathogenicity factors of mycoplasmas are known:

- adhesins - play a crucial role in the development of the initial stage of the infectious process. Mycoplasmas are membrane parasites and are able to adsorb on various cells. Adhesion of ureaplasmas to human epithelial cells, erythrocytes and spermatozoa has been reported;
- endotoxins damaging epithelial cilia and human neutrophils have been described for M.pneumoniae. Endotoxins of urogenital pathogens are poorly studied;
- haemolysins. Moderate haemolytic activity has been described for M.genitalium. U.urealyticum haemolysins cause haemolysis of rabbit and guinea pig erythrocytes, but not of humans;
- arginine dehydrolases hydrolyse the amino acid arginine with the release of energy required by mycoplasmas;
- mycoplasmas, which degrade agrinin to ornithine with accumulation of ammonia, affect the pH of the vaginal secretion, which contributes to changes in the vaginal flora;
- only U.urealyticum has urease activity. Hydrolysis of urea produces ammonia, which has a toxic effect on target cells in the body;
- human IgA protease. U.urealyticum proteases cleave human IgA into 2 fragments. As a result of the proteases, immunoglobulins lose their ability to bind ureaplasma antigens and prevent infection;
- phospholipases. The phospholipase activity of U.urealyticum varies according to serotype. Phospholipases of some serotypes of U.urealyticum are thought to cause activation of prostaglandin synthesis during infection of the foetus and placenta, which may be the cause of spontaneous abortions, foetal abnormalities and pregnancy;
- glucose fermentation has been detected in M.genitalium and M.pneumoniae. Mycoplasmas fermenting carbohydrates (glucose) produce acidic

metabolites that sharply reduce the pH of the environment and have a destructive effect on epithelial cells. Thus, there is reason to believe that the enzymatic activity of mycoplasmas causes changes in the metabolism of cells - disrupts the metabolism and synthesis of amino acids and proteins.

The dominant factor determining the pathogenicity of mycoplasmas seems to be the ability to bind closely to the surface of eukaryotic cells, to enter into intermembrane interaction, in which the exchange of individual membrane components is possible. The pathogenic potential should include the ability to persist and multiply in the tissues of the macroorganism for a long time, as well as the ability to change the metabolism of infected cells, to disrupt the normal regulatory mechanisms of immunocompetent cells.

M.genitalium has been studied relatively recently, but among urogenital mycoplasmas, it is an undoubted pathogen by the totality and nature of pathogenicity factors. According to foreign literature, M.genitalium is considered a pathogenic species, and M.hominis and U.urealyticum are cofactors of diseases of the urogenital tract.

The criteria for prescribing etiotropic therapy for mycoplasma infection are:

- clinical manifestations of infectious-inflammatory processes of urogenital and other organs;
- the results of complex microbiological examination, including examination for the presence of pathogenic and opportunistic microorganisms;
- the degree of risk of upcoming operative or invasive manipulations;
- infertility associated only with mycoplasma infection;
- in pregnant women: obstetric and gynaecological history and the course of the current pregnancy.

The main principles of treatment of inflammatory diseases of the urogenital tract caused by mixt-infection (trichomonads, mycoplasmas/ureaplasmas) are:

- early diagnosis of the disease;

- etiological justification of antibacterial therapy taking into account;
- biological characteristics of the isolated microorganisms;
- microbial number;
- sensitivity to antibiotics and antimicrobials;
- peculiarities of synergistic and antagonistic interaction of the identified pathogens;
- problems of polypragmasy of simultaneously prescribed antibacterial drugs;
- adherence to the stage of anti-inflammatory therapy;
- administration of antitrichomonad therapy at the first stage of treatment;
- prescription of etiologically defined antibacterial drugs at the second stage of treatment;
- correction of immunological disorders in the body, normalisation of local immune defence indicators;
- examination and simultaneous treatment (if necessary) of all family members;
- simultaneous treatment of sexual partner(s);
- clinical, microbiological control of treatment effectiveness in 2 weeks - 1 month and clinical, microbiological and immunological control of the therapy in 3, 6 months.

The pharmaceutical market offers antiprotozoal and antibacterial drugs for the treatment of infections.

Trichomoniasis is considered one of the most common diseases of the urogenital tract. This infection has a so-called ‘cosmopolitan’ character.

In the world, according to WHO, trichomoniasis annually affects from 170 to 200 million people. The specific weight of this disease among all sexually transmitted infections is 25%.

Trichomoniasis often (according to statistics, 90% of cases) occurs in association with other infections: together with gonorrhoea, chlamydia, mycoplasmosis, ureaplasmosis, candidiasis.

In the treatment of patients with giardiasis and other protozoal diseases, nitroimidazole derivatives are used (metronidazole, tinidazole, secnidazole and ornidazole), benzimidazoles (albendazole, mebendazole), nitazoxanide, furazolidone, quinacrine, chloroquine and paromomycin.

The most commonly used drugs in the treatment of protozoal diseases in medicine and veterinary medicine are 5-nitroimidazoles. The drugs of this group are activated after penetration into the parasite and destroy microorganisms by means of release of toxic, partially reduced intermediates.

Tinidazole, secnidazole and ornidazole have a have a long half-life and treatment efficacy exceeds 90% with a single dose. Metronidazole has a short half-life and treatment efficacy exceeds 90% with a single dose.

Side effects of metronidazole have been reported in humans, such as anorexia, metallic taste, disulfiram-like effects, headache, dizziness, insomnia, irritability, neuropathy, seizures, rash, leucopenia, hepatitis and pancreatitis.

On the Ukrainian market one of the modern ornidazole preparations is ORGIL™ produced by Kusum Helthker, which has proven bioequivalence to the original ornidazole preparation. This means that ORGIL™ not only contains the same active ingredient at the same dosage, but also has the same bioavailability when administered at the same dosage, which makes it reasonable to expect a therapeutic effect comparable to that of the original drug.

Health care systems in both developing and developed countries are faced with the need to optimise financial costs and provide the population with high-quality and affordable medicines. ORGIL™ is just such a medicinal product.

Ornidazole, the active substance of ORGIL™, is a DNA-tropic agent with a bactericidal type of action. Ornidazole is active against Gram-negative and Gram-

positive anaerobic bacteria and protozoa: trichomonads, giardia, dysentery amoeba, balantidium, leishmania.

The spectrum of action against anaerobic bacteria includes Bacteroides spp., Fusobacterium spp., Eubacterium spp., Clostridium spp.; Peptococcus, Peptostreptococcus.

Another important aspect of the use of ornidazole preparations should be noted: to date, virtually no pathogens with developed resistance to ornidazole have been identified.

The problem of antimicrobial resistance is now becoming a global problem and is increasingly becoming a subject of research and discussion: for the patient, the risk of complications is increasing; for the physician, the risk of ineffective practice, ethical and psychological problems is increasing.

When developing ornidazole, which is not yet on the list of drugs to which resistance is developing, the already known disadvantages of other nitroimidazole derivatives were initially taken into account.

In terms of its pharmacological properties, ornidazole is a more advanced drug. This is due to the fact that ornidazole is characterised by better pharmacokinetic properties. Bioavailability of the drug when administered orally is high - 80-100%. This eliminates the need for widespread use of intravenous administration.

Ornidazole is slowly excreted from the body. Its elimination half-life from blood is 10-14 h. Maximum concentration of ornidazole in blood is observed in 3 h after its oral administration, and less than 15% of the ingested drug is bound to blood plasma proteins.

In course treatment the drug accumulates in the body. At the same time, high antimicrobial activity, good pharmacokinetic properties, slow excretion from the body allow in some cases of protozoal infections to treat with a shock dose only once, which excludes cumulative effect.

The therapeutic efficacy of ornidazole preparations has been confirmed by studies in many countries around the world. Ornidazole combines well with other groups of chemotherapeutic agents and in combination therapy can be used with beta-lactams (benzylpenicillin, cephalosporins), aminoglycosides, fluoroquinolones, macrolides, vancomycin, sulfonamides, co-trimoxazole.

Ornidazole is practically non-toxic, well tolerated by patients; the sensation of metallic taste when taking it is less pronounced than when taking metronidazole.

1.2 The role of phytotherapy in the treatment of bacterial infections

Currently, medicinal plants are increasingly being used as therapeutic agents for the treatment of bacterial infections. This is due to the fact that phytotherapy is well tolerated by patients, with virtually no undesirable effects.

Herbs are well combined with each other, they can be used simultaneously with any other methods of treatment, which has modern medicine, which allows much more effective and faster recovery.

In severe cases, the addition of medicinal plants to pharmacotherapy increases not only the effectiveness but also the safety of treatment, as they have a membrane-stabilising effect and with the fluid flow faster remove metabolites, toxins and cellular decay products from the body.

In some cases, when there are no signs of acute process, treatment with herbs can be the main type of therapy, it is indispensable in the recovery period and is used to prevent relapses of the disease in its chronic course.

The success of phytotherapy largely depends on the quality of products.

Some time ago, medicine was dominated by the notion that the most adequate way of treatment for many pathologies was monotherapy with the use of a single drug, the action of which was aimed at eliminating the main cause of physiological imbalance.

Such a concept took as a basis the existence of one main cause of pathology development and negated the influence of other factors, which in fact can have a significant impact on the development and clinical picture of the disease.

Nowadays, the world medical community realises the necessity of complex influence on many links of the pathological process.

The described approach, in particular, can be realised through the use of phytopreparations, since, as is known, plant extracts used in medicine initially contain a combination of active substances with synergistic effect.

The very idea of phytotherapy is widely supported by the World Health Organisation – according to its experts, in the treatment of about 75% of patients it is advisable to use preparations of plant origin.

Use of phytotherapy at different stages of the disease.

During the initial stage of the disease, phytotherapy is the main method of treatment because of its mild action and low toxicity.

During the height of the disease, it can be used as a supportive method of treatment to increase the defences of the organism, enhance the effect of the main drugs and reduce their side effects.

In the period of recovery, phytotherapy again takes a leading place, especially in chronic diseases, as it can be used for a long time and is well combined with synthetic drugs.

It is necessary to prescribe medicinal plants individually, according to the indications, taking into account the age of the patient, realistically assessing the possibilities of phytotherapy, taking into account the possible intolerance of some plants.

It is recommended to take into account the form and nature of the course of not only the main, but also concomitant diseases.

At the initial stage of treatment is better to use individual medicinal plants or collections of 2-3 plants, and later - more complex composition. In addition, it is

advisable to carry out dietary correction with the help of ‘medicinal food’, food plants, the formation of the regime and background of the environment surrounding the sick child.

Therapy with medicinal plants requires a long period of application, especially in the chronic course of the disease.

In the treatment of chronic diseases a good effect is noted from preventive courses of phytotherapy, which are prescribed in periods of seasonal exacerbation.

In case of symptoms of intolerance to the herb (nausea, vomiting, itching, stool disorders), its use should be cancelled.

Plants that have bactericidal and bacteriostatic action, containing essential oils of the monoterpene group derivatives - cineole (leaves of sage, eucalyptus rod-shaped), aromatic essential oil group - thymol derivatives (herb thyme creeping and common); phenolic compounds - St. John's wort herb, calendula flowers.

Plants with anti-inflammatory action, containing tannins - oak bark, rhizome of lapchatka, rhizome of snake's throat, bloodwort, alder cones, etc.; plants containing essential oils, derivatives of azulene - flowers of chamomile apothecary and tongue-less; plants containing mucus - leaves of mother and stepmother, plantain, linden flowers.

CONCLUSIONS

1. An analysis of literary data on the relevance of the problem of increasing the incidence of mixed infections in the population has been conducted.
2. The pathogens of mixed infections have been considered.
3. Modern drugs for the treatment of mixed infections have been characterized.
4. The place of phytotherapy in the treatment of mixed infections has been determined.

EXPERIMENTAL PART

CHAPTERT II. OBJECTS AND METHODS OF RESERCHES

2.1 Objects of reserches

Ornidazole (drug master file «AARTI DRUGS LIMITED», INDIA) is a slightly yellowish crystalline powder, soluble in methanol and methylene chloride (Figure 2.1).

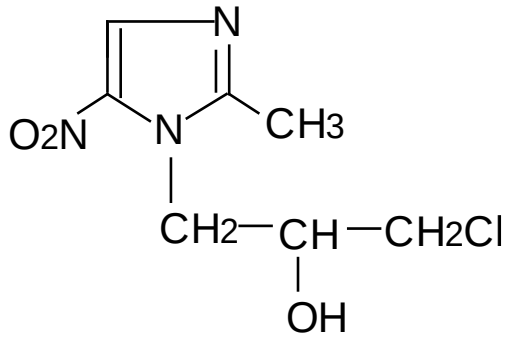

Figure 2.1. Structural formula of ornidazole

Yarrow (Achillea millefolium*)* dry extract (TC 20.4-42925937-001)

Yellow-brown powder easily soluble in hot water, polysorbate-80

Figure 2.2. Yarrow (Achillea millefolium*)* dry extract

2.2 Research methods

Pharmaco-technological properties, namely flowability, angle of natural repose, bulk volume and bulk density were studied using devices from the company "Pharma Test" (Germany). A Krüss MBL microscope was used to study crystallographic properties.

CONCLUSIONS TO CHAPTERT II

1. The objects of the study are described. The main properties of the ornidazole substance and yarrow extract are presented.
2. The methods of physical, chemical and pharmacotechnological research that were used in the work are indicated.

THE EXPERIMENTAL PART

CHAPTER III

EXPERIMENTAL VALIDATION OF THE COMPOSITION AND DEVELOPMENT OF CAPSULES TECHNOLOGY

3.1. Justification of the combination of active substances

At present, there is a tendency towards the growth of associated infectious-inflammatory diseases (mixt-infections) in the body, which develop under the joint influence of two or more pathogens of different nature.

Such associations with viruses, bacteria, chlamydia, protozoa (trichomoniasis), fungi, parasites are known. Treatment of the described infections presents a serious problem.

The largest share among the so-called mixed infections are sexually transmitted diseases (there are more than 20 of them) (trichomoniasis, chlamydia, bacterial vaginosis, genital herpes). They are characterised by a wide spread and a rather high incidence rate.

The main place among the listed sexually transmitted diseases is occupied by trichomoniasis. Its causative agent is Trichomonas vaginalis. There are more than 20 of their species and more than 120 strains of Trichomonas vaginalis.

Annually, about 120 million vaginitis caused by T. vaginalis are registered in the world, which exists in associations with other infections in about 90% of cases (23 - 40% of cases of inflammatory processes in the genitourinary sphere in men and 12 - 52% of cases in women). The cause of their occurrence is trichomonad infection.

For the treatment of associated mixt-infections, combination therapies that contain two or more antimicrobial agents are appropriate. This gives the patient a much better chance of success.

Combination preparations should be used in the treatment of mixed trichomonas-

bacterial infections. Examples include Meratin Combi (vaginal tablets Mili Healthcare, UK) containing only synthetic substances ornidazole, nystatin, neomycin sulfate, prednisolone, or Tiflox tablets (Norton International Pharmaceutical Inc., Canada) with ornidazole and ofloxacin. Unlike synthetic drugs, herbal remedies are also effective, but do not cause numerous side effects.

It is known that phenolic compounds of plant extracts containing flavonoids luteolin, isosalipurposide, apigenin and others exhibit antimicrobial, antifungal, antiparasitic and antiviral activity.

For the treatment of associated bacterial infections, we proposed a pharmaceutical composition in the form of capsules with yarrow extract and ornidazole.

Pharmaceutical development of the proposed composition is designed to enhance the expansion of the spectrum of action, as well as to increase the tolerability of the drug and reduce adverse reactions.

Phytopreparations are widely used in the complex treatment of many diseases. Rational is the use of dry extracts of plants with antimicrobial action for the treatment of associated mixt-infections. Yarrow extract is known to have antimicrobial properties against various groups of pathogenic microorganisms (Figure 3.1).

Figure 3.1. Yarrow Achillea millefollium

Common yarrow (Achillea millefollium) is a perennial herbaceous plant of the Aster family, 20-80 cm tall, with a thin creeping rhizome, from which shoots with rosettes of root leaves and flower-bearing non-branching stems branch off. Leaves are ordinary, lanceolate, twice- or thrice- (not to the very base) pinnately dissected.

Inflorescences are small numerous baskets, collected at the top of stems in complex shields. Tentacular flowers are 5, white, rarely pink; staminal flowers are 14-20. Seeds are flat, oblong, silvery grey. Flowering from June to October, seeds ripen in July-September.

Often grows along field margins, near roads, in forest belts and as a weed in vegetable gardens, orchards and fields; sometimes forms continuous thickets on deposits. Quite a large part of the medicinal raw material is harvested in the wild.

Herbs and flowers are used as medicinal raw materials. The herb is harvested during the flowering period of the plant by cutting off the tops of stems up to 15 cm long without rough, leafless bases or separately inflorescences with sickles, knives or secateurs.

Raw material is collected in dry weather, after drying dew. Yarrow is dried in the shade in the air, in well-ventilated rooms, spreading it in a layer of 5-7 cm on paper or cloth and periodically stirring. In good weather, it dries in 7-10 days. It can also be dried in dryers at a temperature of +40°C. The end of drying is determined by the brittleness of the stems.

Yarrow leaves contain vitamin K, methyl betaine (0.05%), essential oil (about 0.8%), formic, acetic and isovaleric acids, esters and alcohols; sesquiterpene lactones have been isolated from the inflorescences.

The essential oil is usually bright green in colour. Hamazulene (6-25%) is considered to be the most valuable component of the essential oil. In addition, the oil contains cineol, bornyl acetate, camphor, linalyl acetate, and others.

Yarrow herb contains essential oil (up to 0.8%), flavonoids (luteolin-7-glycoside, rutin), tannins and bitter substances, achillein, vitamin K, organic acids (acetic, formic,

isovaleric) and other substances.

The essential oil contains sesquiterpenoids: proazulenes (up to 25-30%, or up to 170 mg% in terms of dry raw materials) and achillein, a non-bitter sesquiterpene from the group of guaianolides, which are the precursors of hamazulene. Up to 40% of hamazulene was found in the essential oil samples, which gives it a blue colour.

Other sesquiterpenes are found in smaller amounts in yarrow essential oil: proazulene guaianolides achilicin (8-acetoxyartabsin), leucodin, mylefin, hermacranolide, as well as matricin, 2,3-dihydrodesacetoxymatricin, 8-hydroxyachilin, 8-acetoxyachilin, mylefolide (acetylbalchanolide), mylefolide, hermacrene D β-bisabolene, α-bisabolol, Δ-cadinene, 8-α-angeloxyartabsin, 8-α-tigloxyartabsin, balhanolide, leucomizine (deacetoxy matricarin), austricin (deacetyl matricarin), artilesin (matricarin isomer), artemisin, caryophyllene (10.1%) and azulene.

Monoterpenoids include: α-pinene (3.3%) and β-pinene (2.4%), sabinene (3.1%), 1,8-cineole or eucalyptol (4.7-10%), pinocamphene (5.2%), menthol (5.6%), L-camphor (1.4%), as well as α-thujone, β-thujone, D-limonene, L-borneol, eugenol, santene, camphor, myrcene, carvone, α- and γ-terpinene, terpinolene, α-terpineol, ocimene X (cis), ocimene V (trans), p-cymene.

Yarrow herb contains alkaloids: achylein (0.05%), identical to betonitin, achycein, achylein, moshatin, stachydrine and L(-)-homostachydrine, trigonelline.

Yarrow contains tannins (up to 2.8%): tannins, sterols (mainly β-sitosterol, but also stigmasterol, campesterol, cholesterol, taraxasterol and pseudotaraxasterol), coumarins (0.35%), bitterness, resins, amino alcohol choline (up to 0.3%), biogenic amine betaine, amino acids, carotene, vitamins K and ascorbic acid (74.8 mg%), as well as inulin and other polysaccharides (up to 4.6%), which contain such monosaccharides as rhamnose, arabinose, xylose, mannose, glucose, galactose, ribose.

Yarrow herb contains up to 3% of flavonoids, mainly luteolin, luteolin-7-glucopyranoside, apigenin-7-glucopyranoside (cosmosin), as well as rutin, 5-hydroxy-3,6,7,4-tetramethoxyflavone, artemether, castein, quercetin, kaempferol, and

isorhamnetin glycosides.

Tannins, essential oil and sesquiterpene lactones provide anti-inflammatory, antimicrobial and desensitising activity. Phytoncides act bacteriostatically on Staphylococcus aureus and white staphylococcus and some species of streptococci.

High antifungal activity of the oil against the causative agent of thrush Candida Albicans, mycosis pathogens Trichophyton rubrum, T. mentagrophytes, T. mentagrophytes var. interdigitale, Microsporum canis, Aspergillus niger, etc. has been found.

The main properties that determine the internal use of yarrow: anti-inflammatory, vetrogonic, antispasmodic, wound-healing, blood purifying.

To conduct the experiment, first, a 10 % aqueous solution of the extract was prepared, and then its activity was studied by diffusion into agar. The results are presented in Figure 3.2.

From Fig. 3.2 shows that the yarrow extract powder has good antibacterial values against the given microorganisms.

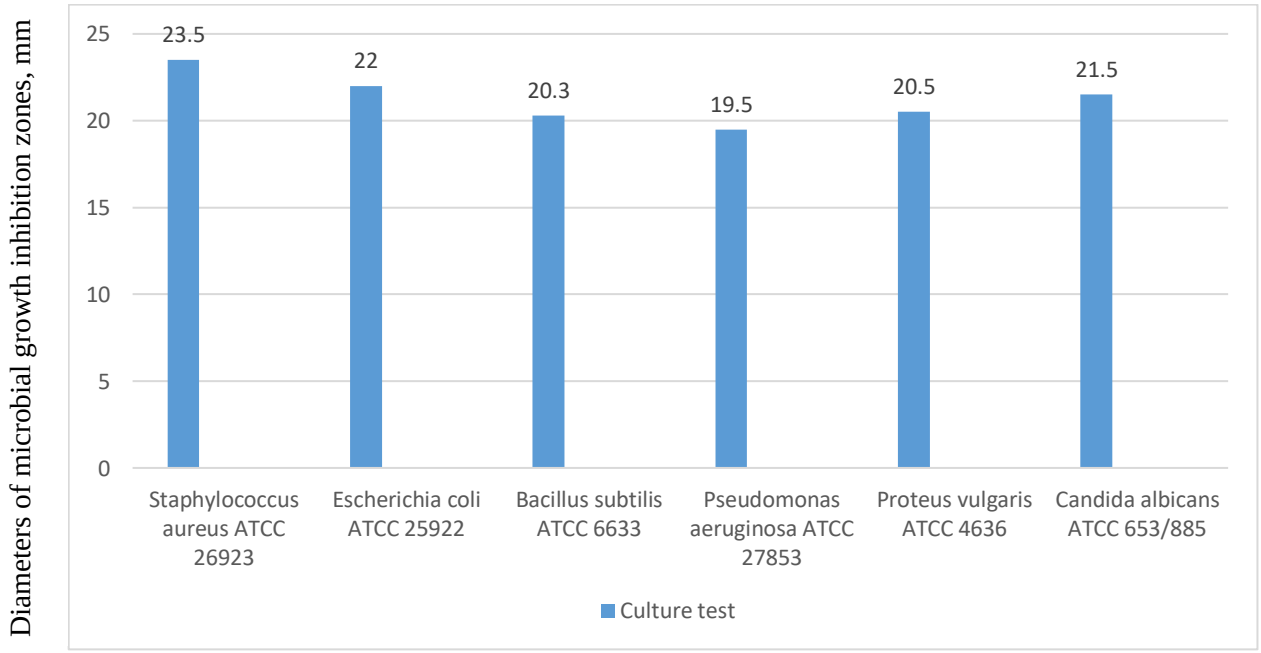

Figure 3.2. Antimicrobial activity of yarrow extract

Ornidazole is a C-nitro compound, which is 5-nitroimidazole, wherein in which the hydrogen atoms at positions 1 and 2 are replaced by 3-chloro-2-hydroxypropyl and methyl groups, respectively.

Ornidazole is used to treat protozoal and anaerobic bacterial infections. Ornidazole is a member of the imidazoles, C-nitro compound, secondary alcohol and organochlorine compound.

To determine the values of therapeutic doses of active substances for pharmaceutical development, the following samples were prepared:

1. composition No. 1:
   - ornidazole 0.25 g
   - yarrow extract 0.15 g
2. composition No. 2:
   - ornidazole 0.30 g
   - yarrow extract 0.1 g

The results of the antibacterial activity of the obtained samples are shown in Figures 3.3 and 3.4.

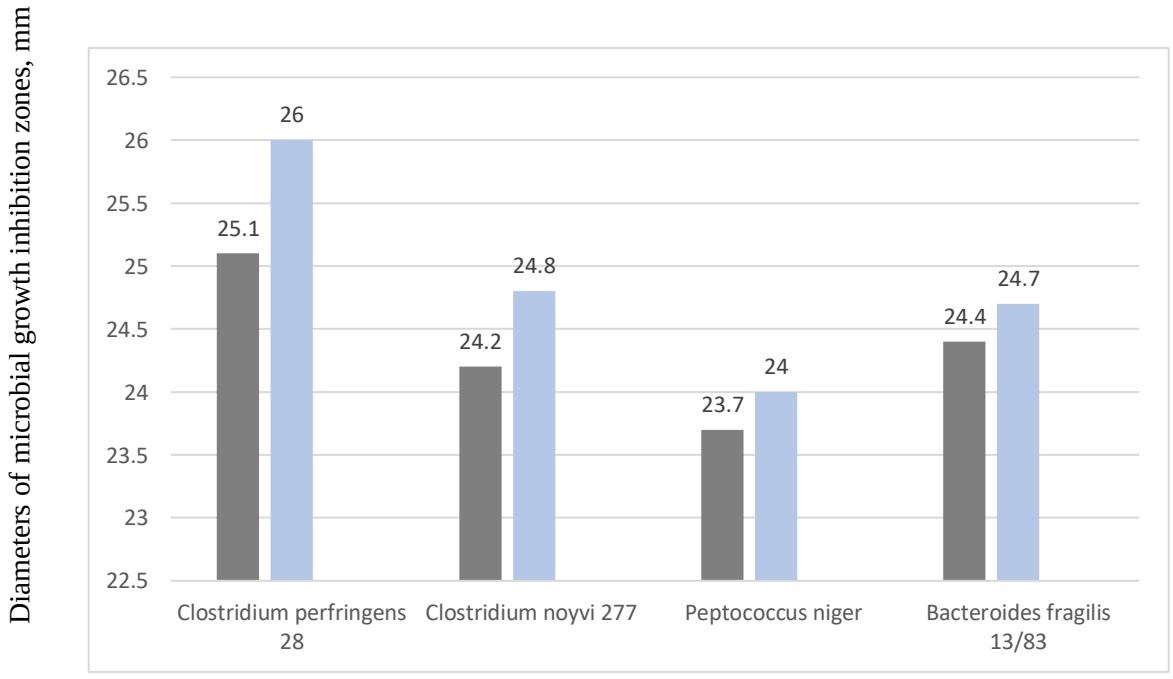

Figure 3.3. Antimicrobial activity of samples against anaerobic bacteria

Figure 3.3 shows the results of antimicrobial activity of the samples against anaerobic bacteria.

The test cultures were Clostridium perfringens 28, Clostridium noyvi 277, Peptococcus niger, Bacteroides fragilis 13/83.

Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Proteus vulgaris, Bacillus subtilis, Candida albicans were selected as test cultures.

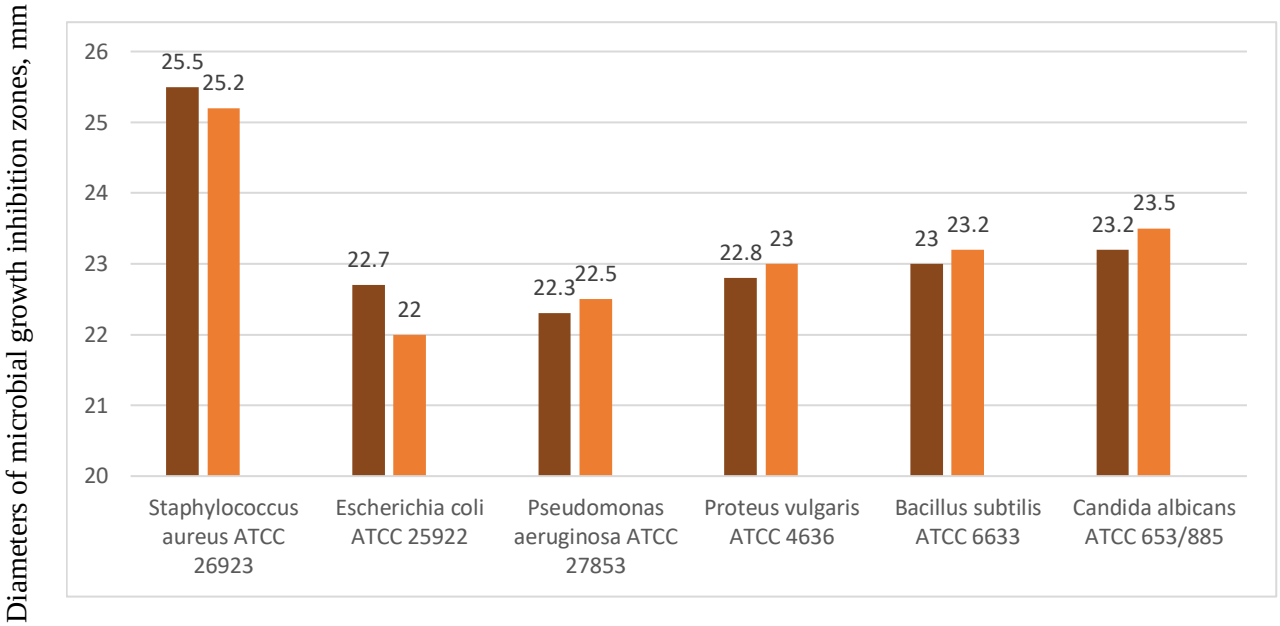

Figure 3.4. Antimicrobial activity of samples against aerobic bacteria and fungi

Figure 3.4 shows the results of antimicrobial activity of the samples against aerobic bacteria and fungi.

The obtained results show that the antimicrobial activity against anaerobic and aerobic microorganisms of composition No. 1 containing 250 mg of ornidazole does not differ significantly from composition No. 2 containing 300 mg of ornidazole.

Thus, experimental studies have shown that the plant substance of yarrow extract in combination with ornidazole extends the spectrum of antibacterial action of the pharmaceutical development to anaerobic and aerobic bacteria and fungi due to the

antibacterial properties of phenolic compounds and allows to reduce the concentration of ornidazole.

Thus, we proposed a combination of the main active substances: yarrow extract (0.15 g) and ornidazole (0.25 g).

3.2. Study of physicochemical and technological properties of ornidazole and yarrow extract

The research was carried out using the microscopy method. As a result of the experiment, it was found that the substance ornidazole is a finely dispersed powder. The crystals of the substance powder have an irregular anisodiameter prism shape with a basic size from 25 μm to 75 μm. Micrographs of ornidazole substance are shown in Figure 3.5.

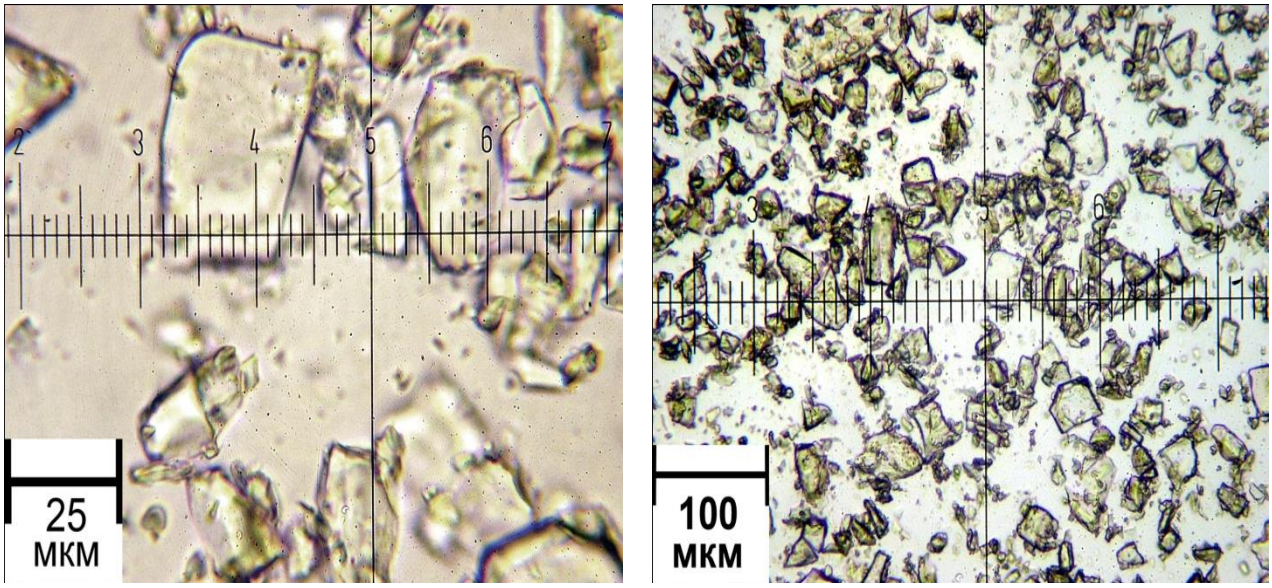

Figure 3.5 Micrographs of ornidazole substance at 600 (left) and 150 (right) magnification

The results of the crystallographic values showed that the irregular surface of the

powder particles would affect the fluidity value.

The results of the pharmacotechnological properties of ornidazole substance are described in Table 3.1.

Table 3.1

Pharmaco-technological properties of ornidazole substance powder

Parameters	**Units of measurement**	**Significance**
Bulk density	g/ml	0,57±0,01
Density after shrinkage	g/ml	0,82±0,01
Friability	s / 100 g of sample	59,10±1,50
Natural slope angle	grad	63±1,0
Carr Index	%	30,40±0,01
Hausner Index	-	1,44±0,01

Note n=5, P=95%

The results of the study of the crystallographic and pharmacotechnological properties of ornidazole powder showed that the powder of the substance has an unsatisfactory fluidity value.

Further research consisted of studying the properties of yarrow extract powder: crystallographic and pharmacotechnological. The crystallographic characteristics of the active ingredients have a direct impact on the technological features of the finished product.

Figure 3.6 shows a micrograph of yarrow extract powder particles.

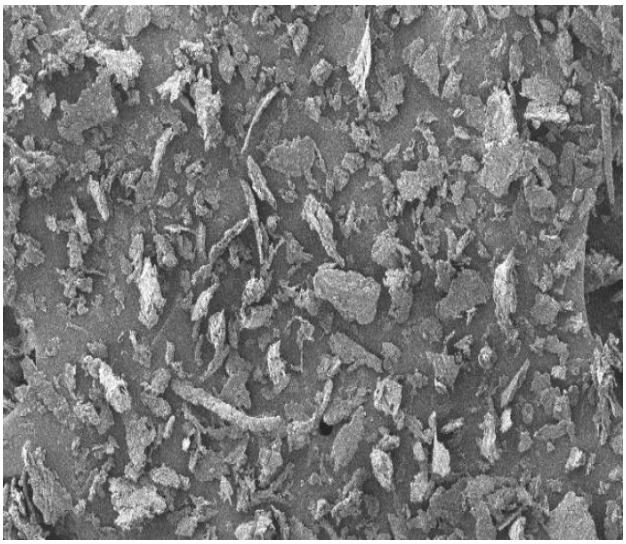

Figure 3.6. Micrograph of yarrow extract powder particles

As you can see from the figure the polydisperse particles of yarrow extract powder have irregularly shaped crystals, and the extract has a low fluidity value in terms of pharmacotechnological properties.

Table 3.2 shows the results of pharmacotechnological properties of yarrow extract powder.

Table 3.2

Pharmacotechnological properties of yarrow extract

Parameters	**Units of measurement**	**Significance**
Bulk density	g/ml	0,46±0,02
Density after shrinkage	g/ml	0,65±0,03
Friability	s / 100 g of sample	75,40±1,20
Natural slope angle	grad	68±1,5
Carr Index	%	27,30±1,0
Hausner Index	-	1,37±0,02

Note n=5, P=95%

When analysing the results of the pharmacotechnological properties of ornidazole and yarrow extract, it is advisable to use the technology of separate preparation of masses for encapsulation.

3.3 Selection of excipients

From the point of view of biopharmaceutical science, excipients in solid dosage forms should provide the appropriate pharmacological excipients in dosage forms should ensure proper pharmacological effect and pharmacokinetic parameters of the drug product.

It has been proved that excipients can significantly enhance the effect of drugs or reduce their activity, change the nature of action under the influence of various reasons. They can also enhance or delay the release of drugs.

Given the dose of ornidazole of 0.25 g and the unsatisfactory fluidity value, it is advisable to use the wet granulation method to obtain a mass with good technological properties.

For the correct selection of the humidifier, the moisture value was used, which is necessary for the formation of the granular mass.

The following substances were used as humectants: plasdon S 630, hydroxymethylpropyl cellulose, starch.

Solutions of the following concentrations were prepared: plasdon S 630 - 5%, hydroxypropylmethylcellulose - 1%, starch - 5%. Water was also used in the experiment.

The results of the experiment are shown in the Figure 3.7.

As can be seen from Figure 3.7, it is better to choose Plasdon S-630 solution at a concentration of 5 % as a humectant for ornidazole, because for the maximum value of granular strength, it is necessary to add a mass with the lowest percentage of moisture, namely 15 %.

For other samples, this value is higher and amounts to 18%, 22% and 25%, respectively.

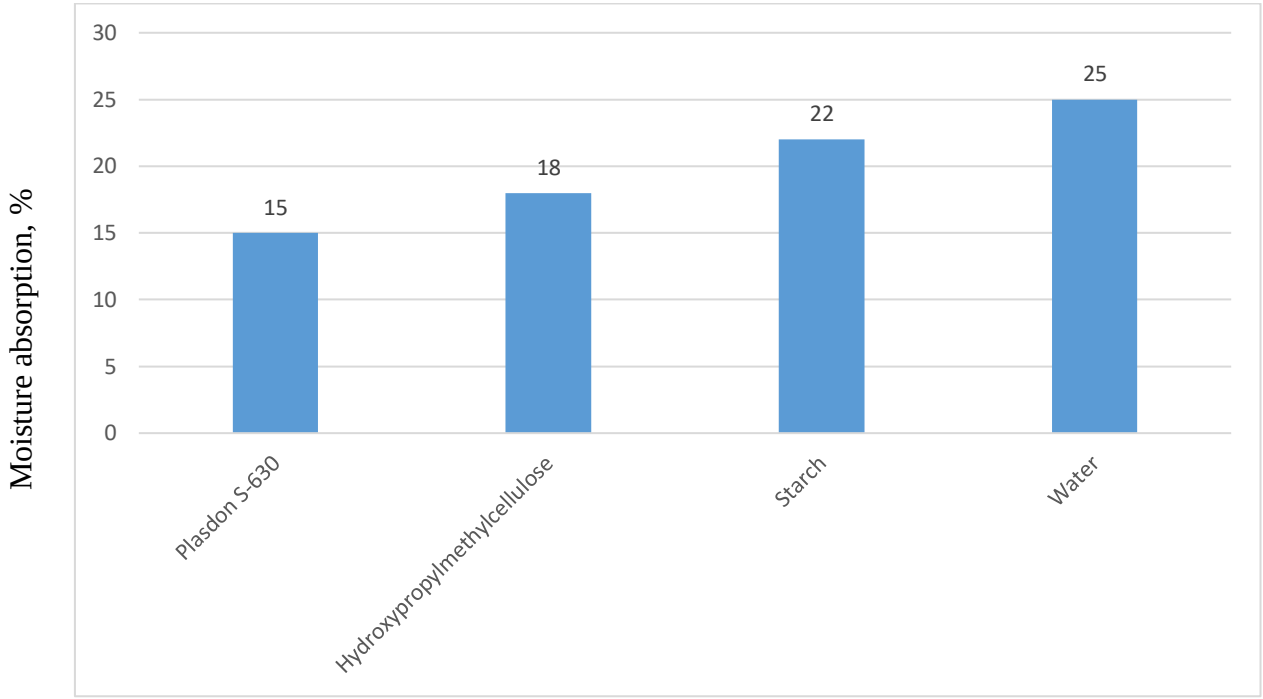

Figure 3.7. Choosing a humidifier

1 - plasdon S-630 solution 5%; 2 - GPMC solution 1%;

3 - starch glue 5%; 4 - water

Plasdone S-630 is a synthetic water-soluble copolymer of N-vinyl-2-pyrrolidone and vinyl acetate in the ratio of 60:40, to which trade names are as follows Copolyvidonum, Copolyvidon, Copovidon.

It is known from the literature that Plasdon S-630 gives the powdered mass more plasticity and improves solubility, as it has solubilising properties. This will increase the solubility of ornidazole and thus its bioavailability.

To improve the technological properties, such as the fluidity of the powder of the

yarrow dry extract substance, it is advisable to use moisture-activated granulation and various excipients (Figure 3.8).

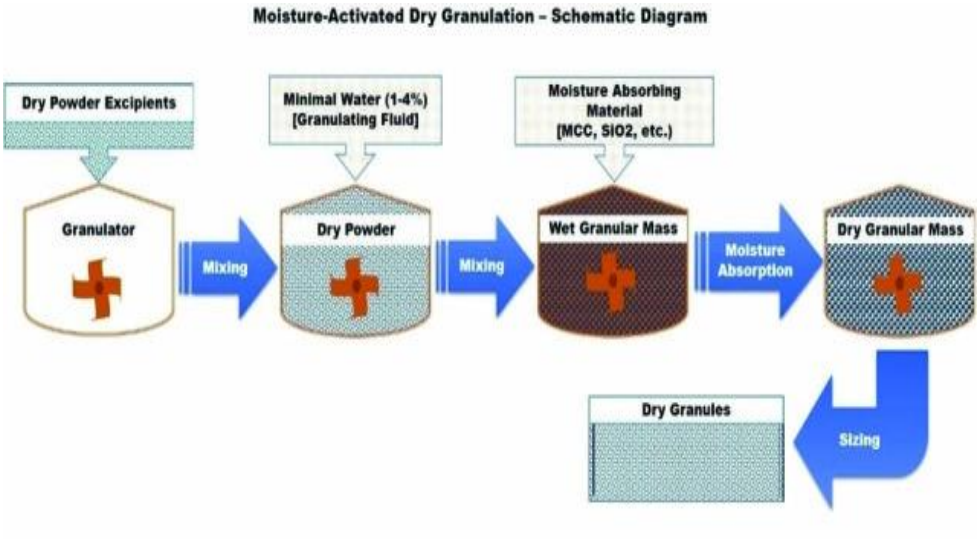

Figure 3.8. Granulation scheme

The technology of using moisture-activated granulation consists of the following stages:

Stage 1 "Agglomeration" combines the stages:

1) Mixing

2) Introduction of a "wetting" agent

Stage 2 "Moisture Sorption and Distribution" includes the steps:

1) Introduction of a "drying" agent

2) Addition of disintegrants and slip agents

Production of the finished granulate

A comparison of wet and wet-activated granulation is presented in Table 3.3.

Table 3.3

A comparison of wet and wet-activated granulation

Process conditions	**Wet granulation**	**Wet-activated granulation**
Amount of humidifier	20-50% by weight of the dry powder mixture	1-8% by weight of the dry powder mixture
Formation of pellets	It is advisable to use a granulator	Formed by stirring the powder mixture
Drying of pellets	Required	Not required
Appearance of the granules	Usually irregularly shaped	Small, rounded, with good processing characteristics
Fractionation stage	Required	Not required
Process efficiency	Long, requires sophisticated equipment	Economical, does not require sophisticated equipment, flows quickly

To obtain the yarrow extract granulate, 96% ethyl alcohol was used. During the granulation, a homogeneous mass of granules was formed (consumption of 8 ml per 100 g of the mixture).

The following substances from the group of fillers were tested to determine the flowability: PROSOLV® SMCCHD 90, MCC 101, and mannite.

PROSOLV® SMCC offers solutions to the problems often faced by conventional binder manufacturers: low bulk density, poor bulkiness, poor compactability, poor mouldability, disturbances of the binder manufacturers of conventional binders: low bulk density, unsatisfactory flowability, insufficient compressibility, poor adhesion and

sensitivity to lubricants.

Physical properties PROSOLV® SMCC:

- white, loose powder;
- high degree of whiteness;
- practically insoluble in water, acetone and anhydrous ethanol;
- chemically inert;
- high compressibility;
- excellent flowability;
- improved lubricity;
- improved mixing properties;
- specific surface area five times greater than that of conventional microcrystalline cellulose (MCC);
- the use of dust-free colloidal silicon dioxide increases the safety of personnel.

Co-treatment of MCC with colloidal silicon dioxide PROSOLV® technology favours a homogeneous distribution of colloidal silica particles throughout the product and on the surface of the MCC particles. Under low magnification, conventional MCC and silicified MCC are very similar in terms of size and shape.

However, at high magnification, electron microscopy reveals differences in the microstructure of PROSOLV® SMCC silicified MCC and conventional MCC.

Silicification makes the powder more friable. Consequently, it provides a much better friability of the powder compared to conventional grades of MCC. The particle size remains the same, which contributes to increased productivity due to higher tabletting speeds.

A photo of the powdered excipient PROSOLV®SMCC is shown in the figure Figure 3.9.

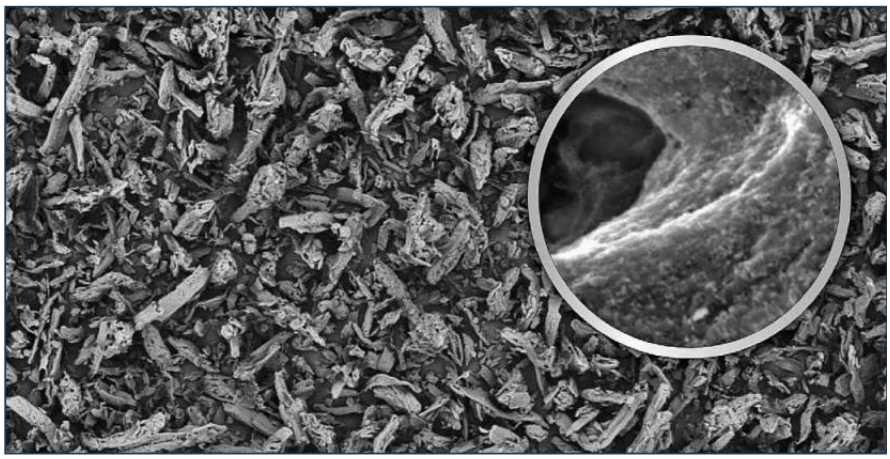

Figure 3.9. Photo of the excipient powder PROSOLV®SMCC

Compared to conventional MCC, the unique surface structure of PROSOLV® SMCC provides excellent mixture homogeneity and composition uniformity even for small doses of micronised active pharmaceutical substances.

Finally, PROSOLV® SMCC has 5 times more surface area, thereby improving the binding properties of MCC. This makes PROSOLV®SMCC the ideal choice for formulations with high dosage formulations for direct pressing and compacting.

Advantages

PROSOLV® SMCC creates unique technical and manufacturing advantages throughout the entire product life cycle, including:

- rapid formulation development;
- dust-free;
- high friability;
- stronger tablets due to better compressibility;
- less fillers required at lower dosages;
- smaller tablet size;
- improved mixing characteristics;
- better homogeneity;

- increased disintegration rate;
- increased production capacity.

The results of the experiment are shown in Figure 3.10.

The test results showed that the mass with PROSOLV® SMCCHD 90 has a flow value of 7 s/100 g of sample. For the other excipients, the flowability value with mannitol was 14 s/100 g of sample, and with microcrystalline cellulose 10 s/100 g of sample.

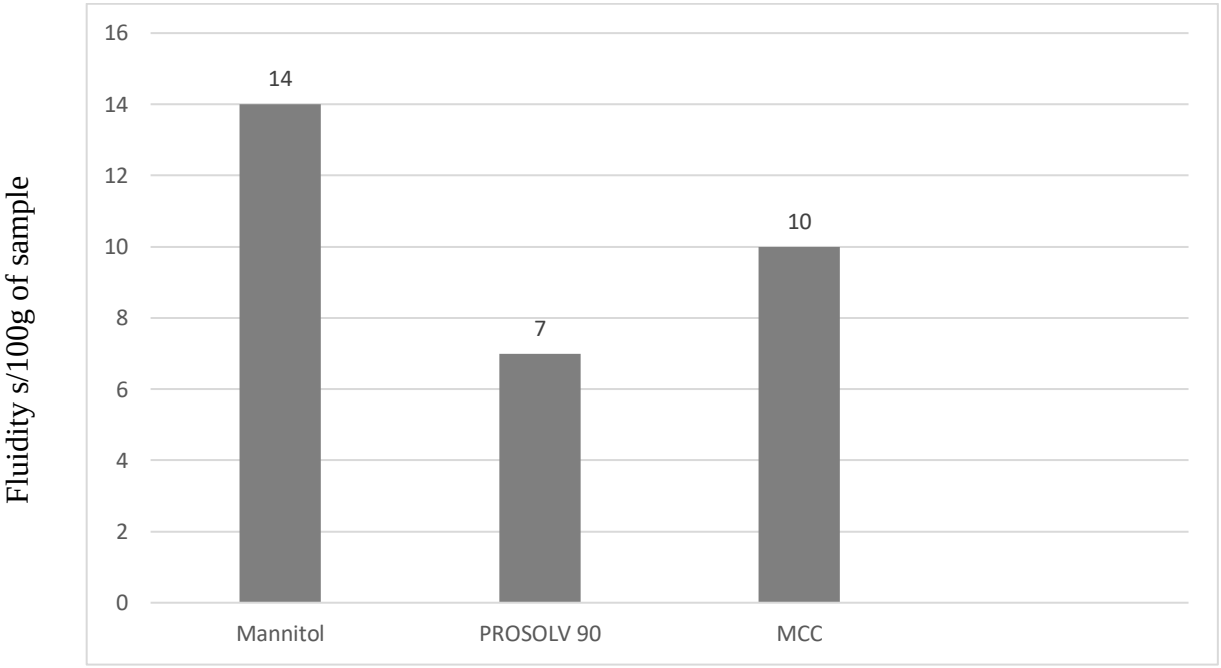

Figure 3.10. Comparative flow diagram for different fillers

The filler of the combined composition of PROSOLV®SMCC (98% MCC + 2% colloidal silicon dioxide) makes the capsule mass homogeneous and provides better fluidity compared to traditional MCC grades.

The colloidal silica particles are contained on the surface and in the pores of PROSOLV®SMCC, so the surface area increases almost 5 times.

Bulking agents are used to ensure the disintegration of the capsules. The

combined excipient CompactCel®MAB was selected for further experimental studies, as it has the properties of a leavening agent, a moisture regulator and a sliding agent.

A finely dispersed mixture of silica, calcium carbonate, microcrystalline cellulose and talcum powder called CompactCel®MAB (manufactured by Biogrund). This substance helps to avoid clumping of the encapsulated mass, ensures its homogeneity, homogeneity and manufacturability in production. We made capsule samples of the masses to determine the amount of CompactCel®MAB mixture. The results are shown in Figure 3.11.

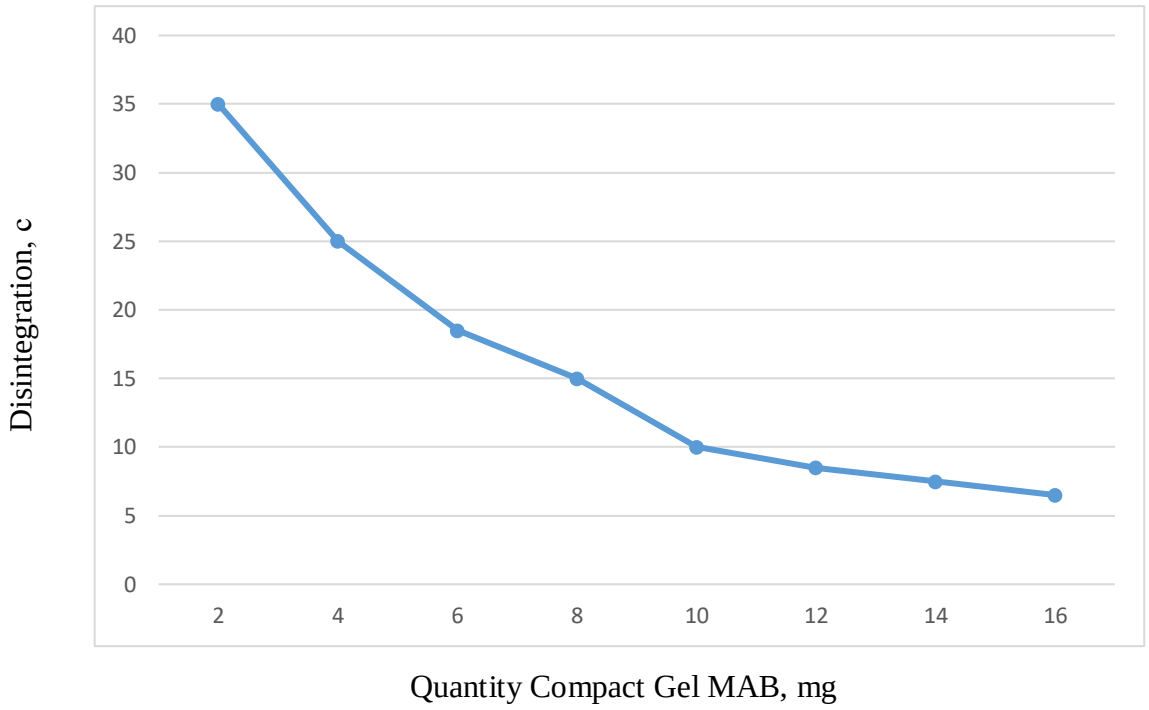

Figure 3.11. Effect of CompactGelMAB on capsule disintegration

The results allowed us to choose the amount of CompactCel®MAB 10 mg, which has good results in the disintegration test and is 10-11 minutes.

As a result of the research, the composition of the capsules was developed.

Table 3.4

Composition of capsules

Composition	g	%
Ornidazole	0,250	50,0
Yarrow extract	0,150	30,0
Plasdon S-630	0,005	1,0
PROSOLV®SMCC	0,085	17,0
CompactCel®MAB	0,010	2,0
Total	**0,500**	**100**

For the capsule mass, hard capsules No. 00 with a green lid and a white body were selected.

The capsule production process consists of the following process steps:

Stage 1. Preparation of raw materials
Stage 2. Preparing a humidifier
Stage 3. Production of mass with ornidazole
Stage 4. Preparation of mass with yarrow extract
Stage 5. Mixing, sieving and dusting of masses
Stage 6. Encapsulation
Stage 7. Packing capsules in blisters
Stage 8. Packing blisters into packs
Стадия 9. Packing packs in group packaging

CONCLUSIONS TO CHAPTERT III

1. In order to substantiate the composition and technology of the capsules, the main technological characteristics of the powders of the ornidazole substance and yarrow extract were studied.

2. To obtain granules with ornidazole, the wet granulation method was used.

3. To obtain a mass with yarrow extract, moisture-activated granulation and the combined excipient PROSOLV®SMCC were used.

4. The quantitative content of excipients for capsules with ornidazole and yarrow extract was conducted and substantiated.

CONCLUSIONS

1. An analysis of literature sources studying the problems of treating human protozoal diseases with drugs was conducted. Ornidazole is effective among antiprotozoal drugs on the pharmaceutical market.

2. For the treatment of associated infectious-inflammatory diseases (mixed infections), we have proposed a pharmaceutical composition in the form of capsules with yarrow extract and ornidazole.

3. Based on the obtained results of the pharmacotechnological properties of the substances ornidazole and yarrow extract, it is advisable to use the technology of separate preparation of masses for encapsulation.

4. Plasdon S-630 was chosen as a humectant at a concentration of 5%. To obtain a mass with yarrow extract, moisture-activated granulation and the combined excipient PROSOLV®SMCC were used.

5. To ensure the disintegration of the capsules, a finely dispersed mixture of powders of silicon dioxide, calcium carbonate, microcrystalline cellulose and talc called CompactCel®MAB (manufacturer Biogrund) was used.

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APPENDIXES

Ф А 2.2.1-32-366

National University of Pharmacy

Pharmaceutical faculty
Department of Industrial Technology of Medicines and Cosmetics
Level of higher education master
Specialty 226 Pharmacy, industrial pharmacy
Educational and professional program Pharmacy

APPROVED
The Head of the Department
of Industrial Technology of
Medicines and Cosmetics

Olena RUBAN
«26» of September 2024

ASSIGNMENT
FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Ahmed BOUSSAOULA

1. Topic of qualification work: «Development of the composition and technology of antibacterial capsules», supervisor of qualification work: Vita HRYTSENKO, Doctor of Pharmacy, Professor approved by order of NUPh from "27th" of September 2024 № 237

2. Deadline for submission of qualification work by the applicant for higher education: May 2025.

3. Outgoing data for qualification work: medicinal substances: ornidazole, yarrow extract, excipients: components of the capsule mass

4. Contents of the settlement and explanatory note (list of questions that need to be developed): literature review, objects and methods, experimental part, references

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

tables – 4, pictures – 13

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Vita HRYTSENKO, professor of higher education institution of the Department of Industrial Technology of Medicines and Cosmetics	26.09.2024	26.09.2024
2	Vita HRYTSENKO, professor of higher education institution of the Department of Industrial Technology of Medicines and Cosmetics	21.10.2024	21.10.2024
3	Vita HRYTSENKO, professor of higher education institution of the Department of Industrial Technology of Medicines and Cosmetics	03.02.2025	03.02.2025

7. Date of issue of the assignment: «26» September 2024

CALENDAR PLAN

№	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Topic selection	September 2024	**Done**
2.	Literature data analysis	September-November 2024	**Done**
3.	Conducting experimental research	October 2024-January 2025	**Done**
4.	Work design	February-April 2025	**Done**
5.	Submission of finished work to the commission	May 2025	**Done**

An applicant of higher education _____ Ahmed BOUSSAOULA

Supervisor of qualification work _____ Vita HRYTSENKO

ВИТЯГ З НАКАЗУ № 237

По Національному фармацевтичному університету

від 27 вересня 2024 року

Затвердити теми кваліфікаційних робіт здобувачам вищої освіти 5-го курсу Фм20(4,10д) 2024-2025 навчального року, освітньо-професійної програми – Фармація, другого (магістерського) рівня вищої освіти, спеціальності 226 – Фармація, промислова фармація, галузь знань 22 Охорона здоров'я, денна форма здобуття освіти (термін навчання 4 роки 10 місяців), які навчаються за контрактом (мова навчання англійська та українська) згідно з додатком № 1.

Прізвище, ім'я здобувача вищої освіти	Тема кваліфікаційної роботи		Посада, прізвище та ініціали керівника	Рецензент кваліфікаційної роботи
по кафедрі промислової технології ліків та косметичних засобів				
Буссаула Ахмед	Розробка складу та технології капсул антибактеріальної дії	Development of the composition and technology of antibacterial capsules	проф. Гриценко В.І.	проф. Семченко К.В.

Ректор

Вірно. Секретар

ФА2.8-03-317

ВИСНОВОК

експертної комісії про проведену експертизу
щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

«06» травня 2025 р. № 331123396

Проаналізувавши кваліфікаційну роботу здобувача вищої освіти Буссаула Ахмед, групи Фм 20 (4,10д) English -2, спеціальності 226 Фармація, промислова фармація, освітньої програми «Фармація» навчання на тему: «Розробка складу та технології капсул антибактеріальної дії / Development of the composition and technology of antibacterial capsules», експертна комісія дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
проректор ЗВО з НПР,
професор **Інна ВЛАДИМИРОВА**

Ф А 2.2.1-32-353

REVIEW

for qualification work of the master`s level of higher educftion, specialty 226 Pharmacy, industrial pharmacy

Ahmed BOUSSAOULA

on the topic: «Development of the composition and technology of antibacterial capsules»

Relevance of the topic. Mixt-infection is a simultaneous infection with several pathogenic or opportunistic microorganisms (i.e. those that necessarily cause disease, or cause disease only when immunity is reduced, dysbiosis). The development and creation of new effective drugs for the treatment of mixt-infections remains the priority task of modern medicine and pharmacy. The optimal dosage form for the treatment of mixt-infections are capsules. Therefore, the development of highly effective drugs in this dosage form is relevant.

Practical value of conclusions, recommendations and their validity. Based on the analysis of literature data the author selected the active pharmaceutical ingredients - ornidazole and yarrow extract. In the course of pharmaco-technological research the composition and technology of antibacterial capsules for the treatment of mixt-infections were substantiated.

Assessment of work. The successful solution of tasks enabled the author of the qualification work to achieve the goal and obtain practical and theoretical results. The work was done at a sufficient scientific level, which indicates the author's ability to work with literary sources, analyze, systematize and generalize the experimental data obtained.

General conclusion and recommendations on admission to defend. The qualification work of Ahmed BOUSSAOULA meets all the requirements for qualification works and can be presented for defense at the Examination Commission of the National University of Pharmacy.

Scientific supervisor _____ Vita HRYTSENKO

«13» May 2025

Ф А 2.2.1-32-356

REVIEW

for qualification work of the master`s level of higher educftion, specialty 226 Pharmacy, industrial pharmacy

Ahmed BOUSSAOULA

on the topic: «Development of the composition and technology of antibacterial capsules»

Relevance of the topic. Today, the spread of mix-infection is gaining momentum. Pharmacological correction of these pathological conditions is an urgent problem in modern medicine. The presence of mixed infections in the human body leads to a sharp deterioration in the quality of life. As a result, many patients are faced with a choice of treatment.

Theoretical level of work. The author has studied and worked out the methods of pharmaco-technological research and has shown an adequate level of mastery of the theoretical provisions and the topic of the work. The material is presented logically and consistently.

The author's suggestions on the topic of research. As a result of this research, the author proposed the composition of active ingredients and excipients, justified the technology of antibacterial capsules and described the stages of the technological process of their production.

Practical value of conclusions, recommendations and their validity. Based on the results of the pharmaco-technological research the author has justified the composition and technology of antibacterial capsules. The material of the experimental studies is presented logically and consistently, the results are structured. The validity of the

results is confirmed by a significant amount of research and statistical methods of their processing.

Disadvantages of work. There are incorrect expressions and grammatical errors in the work.

General conclusion and evaluation of the work. The qualification work of Ahmed BOUSSAOULA based on the results of research and the volume of the experiment performed can be presented for defense at the Examination Commission of the National University of Pharmacy.

Reviewer _____ professor Kateryna SEMCHENKO

«15» May 2025

Ф А2.2.1-91-287

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ВИТЯГ З ПРОТОКОЛУ № 12
«16» травня 2025 року
м. Харків
засідання кафедри
промислової технології ліків та косметичних засобів

ПРИСУТНІ: проф. Рубан О.А., проф. Бобрицька Л.О., проф. Гриценко В.І., проф. Кухтенко О.С., проф. Сліпченко Г.Д., проф. Ковалевська І.В., доц. Криклива І.О, доц. Ніколайчук Н.О., доц. Січкар А.А., доц. Безрукавий Є.А., доц. Манський О.А., доц. Солдатов Д.П., доц. Кутова О.В., доц. Трутаєв С.І., ас. Пономаренко Т.О.

ПОРЯДОК ДЕННИЙ:

1. Обговорення кваліфікаційних робіт щодо їх представлення до захисту в Екзаменаційній комісії НФаУ.

СЛУХАЛИ: здобувача вищої освіти 5 курсу групи Фм20(4,10д)англ-02 Ахмед БУССАУЛА про представлення до захисту в Екзаменаційній комісії НФаУ кваліфікаційної роботи на тему: «Розробка складу та технології капсул антибактеріальної дії» (Керівник: д.фарм.н. Віта ГРИЦЕНКО).

В обговоренні кваліфікаційної роботи брали участь проф. Рубан О.А., проф. Ковалевська І.В., доц. Криклива І.О.

УХВАЛИЛИ: рекомендувати до захисту в Екзаменаційній комісії НФаУ кваліфікаційну роботу здобувача вищої освіти фармацевтичного факультету групи Фм20(4,10д)англ-02 Ахмед БУССАУЛА на тему: «Розробка складу та технології капсул антибактеріальної дії».

Голова
Завідувачка кафедри ПТЛ та КЗ **Олена РУБАН**

Секретар **Антоніна СІЧКАР**

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Ахмед БУССАУЛА до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю226 Фармація, промислова фармація
освітньо-професійною програмою Фармація
на тему: «Розробка складу та технології капсул антибактеріальної дії»

Кваліфікаційна робота і рецензія додаються

Декан факультету _____ / Микола ГОЛІК /

Висновок керівника кваліфікаційної роботи

Здобувач вищої освіти Ахмед БУССАУЛА у процесі роботи розглянув сучасні підходи до лікування мікст-інфекцій, провів аналіз препаратів для їх терапії та довів актуальність створення нового лікарського засобу у формі капсул антибактеріальної дії. Автором обґрунтовано оптимальний склад і технологію одержання капсул. Ахмед БУССАУЛА допускається до захисту кваліфікаційної роботи в Екзаменаційній комісії Національного фармацевтичного університету.

Керівник кваліфікаційної роботи

_____ Віта ГРИЦЕНКО

«13» травня 2025 року

Висновок кафедри про кваліфікаційну роботу

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

Завідувачка кафедри
промислової технології ліків та косметичних засобів
_____ Олена РУБАН

«16» травня 2025 року

Qualification work was defended

of в Examination commission on

« ____ » ___of June_____2025

With the grade_____

Head of the State Examination commission,

DPharm Sc. Professor

_____ / Volodymyr YAKOVENKO /