

ANNOTATION

of the theses on the topic "**Development of composition and technology of medicines based on substances derived "4*H*-pyrido[4',3':5,6]pyrano[2,3-d]pyrimidine**» for the degree of Doctor of Philosophy (PhD) in the specialty 6D110400 - Pharmacy by **Derbisbekova Uldan Batyrkhanovna**

Relevance of the research topic

One of the goals of health development program of the Republic of Kazakhstan "Densaulyk" for the years 2016-2020 is to ensure the modernization of the national health system, its efficiency and financial stability.

According to the WHO, despite the pace of economic development in all countries of the world, infectious diseases are among the priorities. About a quarter of Kazakhstan's adults suffer from various types of mycosis. Antimicrobial chemotherapy drugs are the main drugs used for the prevention and treatment of microbial genetic diseases. At the same time, the main negative phenomenon of antibiotic therapy is the constantly progressive resistance of microorganisms. The use of antimicrobials without a doctor's diagnosis is the main reason for the development of the stimulus's stability.

According to the recommendations of the WHO in order to ensure the strategic safety of the country's pharmaceutical production, it should be at least 20 % of the total pharmaceutical market. This figure is 10-12 %, and Kazakhstan pharmaceutical manufacturers produce generics based on simple drugs or imported substances. Therefore, the activation of the search for radically different molecules, without structural similarity with existing substances, is becoming increasingly important. The purposeful synthesis of new structures with antimicrobial and antifungal activity, in contrast to the search for composites of biological origin, allows to obtain significant amounts of derivatives for screening, which significantly increases the efficiency of the development. Since heterocyclic compounds remain the main source of new antimicrobial substances today, the search for active substances in a number of derivatives of condensed nitrogen-containing systems, in our opinion, is promising and relevant.

The purpose of the research

Development of the composition and technology of the dosage form based on the active substance of a number of 4*H*-pyrido derivatives[4',3':5,6]-pirano[2,3-d]pyrimidine with antifungal action.

Objectives of the research

1. Marketing analysis of antifungal drugs in the pharmaceutical market of the Republic of Kazakhstan.
2. Design development and screening of 4*H*-pyrido derivatives[4',3':5,6]-pirano[2,3-d]pyrimidine with antifungal action.
3. Synthesis of 2-(6-hydroxymethyl-9-methyl-2-aryl-5*H*-pyrido[4',3':5,6]pirano[2,3-d]pyrimidine-4-ilsulfonyl) acetamide in screening and design.
4. Evaluation of the quality of the synthesized substance and determination of storage conditions and terms.

5. Development of the composition and technology of the drug on the basis of the active substance.

6. Assessment of the quality of the drug and test for stability.

7. Study of biological activity and safety of the drug.

Objects of the research

The object of the study is a gel with antifungal action "Anticandid" (gel composition: substance piperidinil ethanol, carbopol, dimexide, propylene glycol, triethanolamine and purified water).

Method of research

Physical, physico-chemical, microbiological, technological, statistical, Pharmacopoeia and non-Pharmacopoeia methods were used.

Scientific novelty

For the first time, expedient synthesis of several derivatives N-aryl/alkyl-2-(6-hydroxymethyl-9-methyl-2-aryl-5H-pyrido[4',3':5,6]pyrano[2,3-d]pyrimidin-4-ylsulphonyl)acetamide, proven structure, the selection of the pharmacologically active substance with the most pronounced antifungal activity 2-(6-hydroxymethyl-9-methyl-2-(4-forfinal)-5H-pyrido[4',3':5,6]pyrano[2,3-d]pyrimidin-4-ylsulphonyl)-1-N-piperidinemethanol.

First developed optimal composition and rational technology of production of gel-based substances 2-(6-hydroxymethyl-9-methyl-2-(4-forfinal)-5H-pyrido[4',3':5,6]pyrano[2,3-d]pyrimidin-4-ylsulphonyl)-1-N-piperidinylidene with protivogribkovi action.

The scientific novelty of the research is confirmed by a patent for a useful model of the Ministry of justice of the Republic of Kazakhstan, "Pharmaceutical gel with antifungal action", №2239 from 15.09.2016 at the same time, a patent for inventions "Gel with antifungal action based on the substance piperidinylethanone", № 2017/0720.1 from 31.08.2017 was filed and a positive conclusion was adopted.

The main provisions of the dissertation research, submitted for defense:

- Results of marketing analysis of antifungal drugs in the pharmaceutical market of the Republic of Kazakhstan.

- Results of synthesis of 2-(6-hydroxymethyl-9-methyl-2-aryl-5H-pyrido[4',3':5,6] pirano[2,3-d]pyrimidine-4-ilsulfonyl) acetamide in screening and design.

- The results of evaluation of the quality of the synthesized substance and the determination of conditions and shelf life.

- Results of the development of the composition and technology of the drug on the basis of the active substance.

- The results of the evaluation of the quality of the drug and the stability test.

- Studying the biological activity and safety of gel "Anticandid" based on the substance of piperidinyl ethanone.

Practical significance of the study

Conducting the synthesis, derivatives of N-aryl/alkyl-2-(6-gidroksimetil-9-methyl-2-aryl-5H-pirido[4',3':5,6]pyrano[2,3-d]pirimidin-4-ylsulphonyl) acetamide, were synthesized active substance of piperidinemethanol.

Based on the substance of piperidineethanone was done in pharmaceutical-based gel.

We have made substance piperidineethanone, technological rules ready gel and a draft survey instrument.

Approbation of the research results

The main results of the research of the thesis: International scientific and practical conference "Actual problems of pharmacy and medicine" (Shymkent, 2015 y.); Management and marketing as a part of modern economy, science, education, practice: collection of scientific articles of the IV International scientific-practical Internet-conference (Kharkiv, 2016 y.); The Materials Sciences.-prakt. Conf. Quality management in pharmacy (Kharkiv, 2016 y.); Topical Problems of Modern Science and Possible Solutions: proceedings of the III International Scientific and Practical Conference (Dubai, 2016 y.); V scientific-practical conference with International participation "priorities of pharmacy and dentistry-from theory to practice" dedicated to the 25th anniversary of independence of Kazakhstan (Almaty, 2016 y.); V International scientific and practical conference (Kharkiv, 2017 y.); XII Scientific-practical conference of young scientists and students of TSMU Abuali ibni Sino with International participation dedicated to the "year of youth" (Dushanbe, 2017 y.); Social pharmacy: state, problems and prospects: mater. III Intern. sciences'.-prakt. Internet conferences (Kharkiv, 2017 y.); XI scientific and practical conference "quality Management in pharmacy" (Kharkiv, 2017 y.); 71st scientific-practical conference of students and young scientists with International participation "Actual problems of modern medicine" (Samarkand, 2017 y.); International scientific conference "Current research in the modern world" (Pereyaslav - Khmelnytsky, 2017 y.); WE are an International scientific and practical conference: Actual issues of science and practice of the XXI century (Nizhnevartovsk, 2017 y.); Young scientists-medicine: XVI scientific conference of young scientists with International participation (Vladikavkaz, 2017 y.); Science, technology, technology: modern paradigms and practical developments: collection of scientific works on the materials of the I International scientific and practical forum (St. Petersburg, 2017 y.).

Information about the publications

According to the results of research published 31 works, including: articles in international journals included in the database Web of Science Core Collection and Scopus - 3 (index $h-1$); articles in journals recommended by the Committee for control of education and science Ministry of education and science-8; articles and abstracts at international scientific conferences-9; articles and abstracts at scientific conferences with international participation and others-11; 1 patent for utility model № 2239 from 15.09.2016 y.

The scope and structure of the thesis

Research of the thesis includes introduction, literature review, research materials and methods, it consists of 7 sections of the study, conclusion, list of references and applications. The thesis is presented on 147 pages of typewritten

text in a computer set, contains 28 tables and 48 figures, the list of references including 292 sources. Attached are attachments from the letter A to the letter Sh.