

## **ANNOTATION**

**to the dissertation for the degree of Doctor of Philosophy (PhD) in the specialty 6D074800 - Technology of pharmaceutical production of Abdambaev Daniyar Abduvalievich on the topic: "Chemical development of the biological active substance derivative of aryloxypropynyl piperidol and some carboxylic acids of adamantane"**

### **Relevance of the research topic**

Currently, in the country is being competed the implementation of the State Program for the Development of Healthcare of the Republic of Kazakhstan "Densaulyk" for 2016-2019. One of the objectives of the program is to improve the prevention and management of diseases. According to the SWOT-analyze of the program, one of the threats to health care is the emergence of new and the return of previously known infectious diseases. Therefore, infectious diseases are the socially significant problems both in the whole world and in Kazakhstan.

The infectious process is one of the most complex biological processes in nature, and infectious diseases are terrible, destructive factors for humanity, causing enormous economic damage. The number of known infections in science is increasing. If in 1955 there were 1062, then at present it is more than 1200.

The wide spread of infectious diseases and the development of resistance to existing antibiotics determine the relevance of the search for new antimicrobial agents among various classes of compounds, including derivatives of aryloxypropargyl piperidols and adamantane carboxylic acids. Because, in these series were found substances with extremely useful properties such as analgesic, local anesthetic, antispasmodic, antimicrobial, antiviral, and other activities. That is why research conducted in the field of synthesis, determination of biological activity and chemical development of new substances based on piperidine compounds and their various derivatives, are relevant.

### **The aim of research**

Chemical development of the biological active substance derivative of aryloxypropynyl piperidol and adamantane carboxylic acid.

### **Tasks of research**

1. Synthesis of derivatives of aryl-oxypropargyl piperidols and adamantane carboxylic acid.
2. Modification of the synthesized aryloxypropynyl- and adamantanecarbonyl piperidines in order to obtain water-soluble forms.
3. Establishing the structures of the synthesized compounds using modern physico-chemical methods of IR, UV,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy.
4. The study of antibacterial, fungicidal, antimalarial, antileyshmanial and antiviral activity of the synthesized compounds.

5. Determination of the structure-activity relationship of piperidine compounds and the selection of the most active compound for further development.

6. Standardization, determination of stability and acute toxicity of the selected compound.

7. Development of technological and instrumental production scheme of the active substance.

### **The object of research**

Naphthyloxypropargil piperidols, N-substituted adamantanecarbonyloxy piperidine derivatives, their hydrochlorides and complexes with  $\beta$ -cyclodextrin.

### **Scientific novelty**

The hydrochlorides of 1-methyl-4-adamantanecarbonyloxy piperidine and 1-hydroxyethyl-4-adamantanecarbonyloxy piperidine were synthesized for the first time. Also for the first time were obtained complexes of amides of adamantane of carboxylic acids with  $\beta$ -cyclodextrin.

The antimicrobial, antiparasitic, antiviral activity of the synthesized compounds was determined.

For the first time, work was carried out on the standardization, determination of the stability and acute toxicity of 1-benzyl-4-adamantanecarbonyloxy-piperidine hydrochloride.

### **The practical significance**

The results concerning the methods of synthesis of derivatives of aryloxypropyl piperidols and adamantane carboxylic acid their hydrochlorides and complexes with  $\beta$ -cyclodextrin, evidence of the structures of the obtained compounds and their biological activity allow us to recommend these compounds for further pharmaceutical development and widespread use. Among the synthesized compounds identified substances with pronounced fungicidal activity.

### **The provisions for the defense**

1. Synthesis of aryloxypropargyl derivatives of piperidol and adamantane carboxylic acid and their water-soluble forms in order to develop a new biological active substance.

2. Proof of the structure of the synthesized compounds by modern physicochemical methods of analysis.

3. Determination of the biological activity of the resulting compound.

4. Study of the structure-activity relationship in a series of piperidine compounds.

5. Technological scheme, results of determination of stability, acute toxicity and standardization of 1-benzyl-4-adamantanecarbonyloxy-piperidine hydrochloride.

### **Publications on the topic of the dissertation**

Based on the dissertation, 10 scientific papers were published, 5 articles of which in journals recommended by the Committee for Control in Education and Science of the MES RK, 4 publications in collections of international and foreign conferences, 1 article in the foreign journal Drug Invention Today included in the Scopus database.