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THE ANTIBACTERIAL PROPERTIES OF CONDENSED HETEROCYCLIC COMPOUNDS

Evsukova V.Y., Andreieva I.D., Kazmirchuk V.V, Maslyanchuk O.A.
Mechnikov Institute of Microbiology and immunology of AMS of Ukraine

The treatment of infectious diseases during many centuries has remained one of the most important problems of the medical science and practice. According to the World Health Organization (WHO) the infectious diseases and their complications are on the third place of the morbidity, mortality and incapacity patterns. Infectious diseases compose 25-60 % of the human morbidity [1].

The leading role in the prophylaxis and treatment of infectious diseases is played by antibacterial chemical compounds (antibiotics, sulphanilamides, diaminopyrimidines, hinolins, etc.) [2 - 11]. But along with the useful bactericidal or bacteriostatic activity, the treatment with antibacterial agents is often associated with multiple negative side effects – immunosuppressive activity, rapid inhibition of biochemical activity of intestinal microflora that is accompanied by significant disruption a intestinal microbiocenosis and dysbiosis development and requires specific corrective therapy, appearance of resistant pathogen strains, the risk of allergic reaction development [12 - 24].

On the background of the antibiotic therapy success aggressive microorganisms strains appear, that are resistant even to the new agents, especially in case of such pathogens as *Staphylococcus aureus*, *Klebsiella spp.*, *Pseudomonas aeruginosa*, *Acinetobacter spp*., etc. [2, 20 - 23].

The development of acquired resistance often is caused by accumulation of chromosomal mutations, inherited from generation to generation and then expressed in the phenotype [13 - 16]. But this property can also develop as a result of the transport of extrachromosomal genetic material (R-plasmids) from one bacteria to the other one. The exchange can occur among bacteria of the same species or interspecies transport can occur [23 - 26].

The infectious and pyoinflammatory diseases caused by resistant strains, are characterized by long disease course, they require hospitalization of the patients more often and they worsen the life prognosis and life quality of the patients [12, 17, 21, 27 - 34].

The spreading of antibiotics resistance, the absence of agents that are active towards the new pathogens and naturally resistant species, the unsatisfactory pharmacokinetics and side effects of presently existing remedies induce the search for new antibiotics and chemical preparations with antimicrobial activity and new ways and antibiotic compounds direct synthesis approach is being applied [16, 35 - 44].

According to the literature sources, from 1070 most widespread substances 661 (62 %) belong to the heterocyclic compounds [45 - 53]. Heterocyclic compounds are the organic compounds that contain a cycle with atoms of other elements (heteroatoms), most often – nitrogen, oxygen and sulphur, rarely – phosphorus, boron, silicon, etc. The diversity of heterocyclic compounds is very big due to the differences in the quantity of atoms in the cycle, nature, quantity and position of heteroatoms, the presence or absence of substitutes and condensed cycles and structural characteristics of heterocyclic ring [45].

The heterocyclic compounds play an important role in the vital functions of plants, animals and humans. The class of heterocyclic compounds contains such substances as plant chlorophyll, blood hemin, nucleic acid components, coenzymes, some amino acids (proline, triptophane,), almost all alkaloids, some antibiotics, vitamins and other medicinal agents [44 - 47].

Presently heterocyclic compounds of quinoline, isoquinoline, quinoxaline, indol and benzimidazole ranges are well characterized. The nitrogen analogs of the above mentioned compound classes are significantly less studied. Among them compounds extracted form natural objects, such as marine algae and organisms attract special attention. Particularly, such compounds as pyridoacridones and discohabdines have displayed significant antimicrobial activity [46, 52, 54].

Also cumarine synthetic derivatives and their heteroanalogs that remain poorly characterized until recently, are promising in terms of search for highly active compounds with antimicrobial activity [45].

It is known that the cumarine derivatives have diverse biological activity. In the natural surrounding cumarine and its derivatives are found both in free form and in glycosides. Herbs, orchids, pods of leguminous plants and citrus fruits contain these substances. The seeds of Dipteryx odorata and many other plants contain the parent compound cumarine. The physiologic activity of cumarine in the humans is very weak, but on the plant level it has considerable effect. Cumarine derivatives have more pronounced physiological activity [49] .

The derivatives of cumarine-3-carboxylic acids are soporific agents. There is data concerning the study of antimicrobial activity of 2-iminocumarine-30carboxylic acid amides. The studies have shown that substances obtained as a result of such synthesis have bacteriostatic activity towards the standard strains of S.aureus and E.coli (minimum inhibiting concentration (MIC) amounted to 62 – 125 mkg/ml and 31 – 125 mkg/ml respectively) [51, 53].

In the middle of 90-s of XX century it was 150 since founding the chemistry of pyridine and around 70 years passed since the introduction of synthetic therapeutical agents with pyridine fragment into the treatment practice. At that time of the 1500 most well-known therapeutical agents that were applied in medicine, the agents of pyridine series composed about 5 % and the agents of piperidine series – 6 %. The pyridine series era came after the discovery of vitamine B_5. The determination of the simplicity of its structure at the beginning of the 20-th century – this natural compound with important biological activity consisted of 3-pyridine-carboxylic (nicotinic) acid – stimulated the synthetic research of pyridine derivatives for the development of artificial therapeutic agents. In the first decade since 1945 hydrazides of pyridine carboxylic acids, which have antituberculous properties, have emerged. In the 60 – 80 years of XX century series of neuroleptic, spasmolitic, antihypertensive and anti-

histaminic agents on the basis of pyrimidine have been developed. Up to the present day continuous search for new safe and more effective medicines with pyrimidine base for almost every branch of chemotherapy is being carried out [45, 55].

In the last few years several researches were carried out that were dedicated to the study of antibacterial properties of other antibacterial compounds, such as: hidrazones of quinolinates, methyl quinolinium derivatives, nitrogen- and ferrocontaining quinoline derivatives with ferrocenyl fragments. Also a study of activity among amides of 2-chlorine, 2-hydrazon – and 2-arylaminoacycholinic acids was carried out. It has been shown that the compounds of this synthesis have anti-inflammatory and analgesic activity [45, 55].

The pharmacological activity of acrydine group was studied on the case of C-substituted derivatives. This class of compounds contains such substances as acrychine and aminoacrychine that have strong antimalarial and antihelmynthic activity and also ryvanol, that manifests antimicrobial activity [46, 57].

It was established that all furopyrimidines have considerable antibacterial activity. It was also established that they are 3-8 times more active towards E.coli compared to the quinozol, (8-oxycholine), but the activity of both compounds towards S.aureus was the same [38, 39, 41].

There is virtually no data concerning N-substituted quinolinquinonimes. The activity of quinoid compounds with pyridine derivatives is known, but it the question whether N-arylsulphonil - substituted quinolonquinonimin compounds, that contain electophyl nucleus and nucleophil pyridine nitrogen atom, are stable or even actually existent remains to be resolved. From the practical point of view the study of the reactive capacity of quinolinquinonimes allows to obtain quinoline derivatives that have potentially high biological activity by direct modification of quinoid cycle [38, 45].

Due to the antituberculous activity the 4-pyridinecarboxylic (isonicotinic) acid derivatives have gained popularity. Until today many varieties of Mycobacterium tuberculosis have developed the resistance to the influence of considerable quantity of effective agents. At present it is necessary to apply combinations of several medicines for more successful elimination of the pathogen in the treatment of tuberculosis. Recently, several cases of resistance of some mutant mycobacteria to the complex agents that could contain up to 7 preparations. One of the most widely applied antituberculous agents is an 4-pyridincarboxylic acid derivative - izoniazid. The exact mechanism of its action is not known yet, but is is supposed that it can inhibit the enzyme responsible for biosynthesis of high fatty acids that compose the cell walls of mycobacteria. Fusarinic acid belongs to the derivatives of 2-pyridincarboxylic acid. It is a metabolite of Fusarium oxysporum and has antibacterial activity. That antibiotic inhibits dopaminehydroxylase and therefore blocks biosynthesis of neurohormone norepinephrine [58].

The aminopyridine group contains considerable quantity of biologically active derivatives. For example, suprastine has antihistamine activity. Triaminoderivative of phenazolpyridine is used as an analgetic. In the period from 1950 to 1960 a group of extremely important pyridinaloxydones was synthesized. These substances are applied as antidotes in case of phosphoorganic pesticides poisoning. Antidotes function according to the pharmacologic antagonism principle: they are able to deblock the cholinesterase due to the stronger interaction with phosphoorganic poison [45, 55].

Hydroxy- and hydroxymethyl derivatives of pirydine also are used as medicinal agents. To this class of compounds belong such agents as antisclerotic agent parmydine, vitamin B6 and antimalarial agent enpyroline [45].

Quinoline derivatives have an important place among antiparasitic agents. Most well known and effective remedy against malarial plasmodium is quinine – an alkaloid of cinchona tree bark. There are more than 20 alkaloids of chinchona tree, among which cynchonin is applied against tropical fever. The wide application of synthetic substances against malaria led to emergence of resistant strains of plasmodia (the malaria causative agent has no resistance to natural quinine). The first synthetic preparation was plasmochine (pamachine). In the 40-s of the previous century the most important derivative of all aminoquinolones, chlorochin (hingamine) was synthesized. It has found application not only in treatment and prophylaxis of malaria, but also in treatment of arthritis and lupus erythemathosus [34, 44].

The separate group of antiseptic, antibacterial and antifungal agents consists of 8-hydroxynolines. Xynosol is applied as an antiseptic for hand disinfection; also it is used for treatment of wounds and ulcers. Its 5-nitrogen derivative (5-NOK) is an effective antibacterial agent that is used in case of kidney and urinary tract infections. Disubstituted oxyquinolines – enteroseptol and quiniophon are applied in dyspepsia and acute intestinal infections treatment [15 - 17, 34 - 37].

At the end of 80-s of XX century synthetic antibiotics norfloxacine and ofloxacine, that display a wide range of antimicrobial activity, have emerged. They selectively inhibit DNA-hyrase and therefore disrupt the normal course of untwisting the circle double DNA spiral of pathogenic bacteria. In the last decades many thousands of similar fluoroquinolones were synthesized. In course of the study of the “structure-activity” relationship it was shown that an introduction of 1-cyclopropyl substitute rapidly enhances of the antibacterial activity of fluoroquinolones. Oxolinic and nalidixic acids were predecessors of fluoroquinolone antibiotics. These acids are highly antimicrobial substances, and oxolinyc acid is able to inhibit ДНК- hyrase more effectively than its analog nalidixic acid. The latter is used in the treatment of urinary tract infections. A natural antibiotic bruneomycin (streptonegrine) is used in chemotherapy of lympholeukosis and other malignant tumors. The structure of this antibiotic includes 4 –arylpyridine and quinolindionic fragments [7, 9, 10, 15 – 17, 40].

Pyrimidine cycle can be met in many agents with wide range of pharmacological activity. Compounds of this classes display antimicrobial and antiviral activity and besides are anti-HIV agents. Amine substitutes of pyrimidine have antimicrobial activity, for example, chloridine and trimetoprime. Trimetoprime is an antimicrobial

agent that inhibits the transformation of dihydrofolic acid into its tetraderivative. Not only antibacterial agents are found among aminopyrimidines. The absolute advantage of pyrimidine derivatives is their low toxicity. The wide range of pharmacological properties of preparations that contain a pyrimidine nucleus testifies for suitability of further purposeful search of new biologically active compounds [45, 49, 52].

In Ukraine the scientific development and research, dedicated to the determination of the antimicrobial activity of antimicrobial activite of new synthetis condensed heterocyclic compounds with pyridine fragment is almost absent. For the first time these compounds were developed and synthesized in National Pharmaceutical University in Kharkov in 2005. Our own research of substances with condensed pyridine fragment has revealed some active substances with antimicrobial activity against grampositive and gramnegative pathogenic microorganisms and Candida spp. fungi [59].

So, the review of domestic and foreign literature that condensed heterocyclic compounds synthesis and the study of their antimicrobial activity can lead to the development of promising antibacterial agents.

LITERATURE

1. WHO Global Burden of Disease project, 2002, version 1 : [Електрон. ресурс] . – Режим доступу: *http://www.who.int/*

2. Березняков, И.Г. Инфекции и антибиотики [Текст] / И.Г. Березняков. – Х.: Константа, 2004. – 448 с.

3. Сидоренко, С.В. Инфекции в интенсивной терапии [Текст] / С.В. Сидоренко, С.В. Яковлев. – М.: Бионика, 2003. – С. 5 – 16.

4. Зузова, А.П. Инфекции полости рта и челюстно-лицевой области [Текст] / А.П. Зузова, А.С. Забелин, С.Н. Козлов, ред. Практическое руководство по антиинфекционной химиотерапии. – М.: Боргес, 2002. – С. 203 – 211.

5. Holzheimer, R.G. Antibiotic therapy in intra – abdominal infections – a review on randomized clinical trials [Text] / R. G. Holzheimer, H. Dralle // Eur. J. Med. Res. – 2001. – Supp. 30. - № 6 (7). – P. 277 – 291.

6. Bush, K. Antibacterial drug discovery [Text] K. Bush // Clin. microbiol. infect. – 2004. – Vol. 10 – Suppl. 4. - P. 10 - 17.

7. Антибактериальная терапия [Текст] / ред. Л.С. Страчунский, Ю.Б. Белоусов, С.Н. Козлов. – М., 2000. – С. 3 – 47, 85 – 90.

8. Козлов, Р.С. Антибактериальная терапия инфекций верхних дыхательных путей [Текст] / Р.С. Козлов // Здоров´я України. – 2008. - № 8 (189). – С. 31.

9. Рациональная антимикробная терапия [Текст] : рук. для практикующих врачей / Под ред. В.П. Яковлева, С.В. Яковлева. – М.: Литтера, 2003. - 1008 с.

10. Практическое руководство по антиинфекционной химиотерапии [Текст] / Ред. : Л. С. Страчунский, Ю. Б. Белоусов, С. Н. Козлов. - М. : Боргес, 2002. – 384 с.

11. Яковлев, С.В. Антибактериальная терапия осложненной пневмонии [Текст] / С.В. Яковлев // Consilium medicum. – 2001. - № 3(3). – С. 142 – 148.

12. Козлов, Р. С. Антимикробная резистентность Streptococcus pneumoniae в России : результаты проспективного многоцентрового исследования (фаза А проекта ПеГАС - 1) [Текст] / Р. С. Козлов, О. И. Кречикова, О. В. Сивая // Клин. микробиол. антимикроб. химиотер. – 2002. - № 3. – С. 267 – 277.

13. Беляев, А.В. Механизмы антибактериальной резистентности [Текст] / А.В. Беляев // Клиническая антибиотикотерапия. – 2003. - № 2(22). – С. 4 – 7.

14. Страчунский, Л.С. Состояние резистентности к антиинфекционным химиопрепаратам в России [Текст] / Л.С. Страчунский, Т.М. Богдонович, С.Н. Козлов, ред. Практическое руководство по антиифекционный химиотерапии. – М.: Боргес, 2002. – С. 32 – 39.

15. Березняков, И.Г. Резистентность к антибиотикам: причины, механизмы, пути преодоления [Текст] / И.Г. Березняков // Клин. антибиотикотер. – 2001. - № 4. – С. 18 – 22.

16. Березняков, И. Г. Резистентность к антимикробным препаратам: механизмы возникновения и клиническое значение [Текст] / И.Г. Березняков; Харьковская медицинская академия последипломного образования. - Х., 2006. – 72 с.

17. Березняков, И. Г. Резистентность к антибиотикам: причины, механизмы, пути преодоления [Текст] / И.Г. Березняков // Клин. антибиотикотер. - 2001. - № 4. - С. 18 – 22.

18. Яковлєв, С. В. Стратегия применения антибиотиков в стационаре [Текст] / С.В. Яковлев // Клин. антибиотикотер. - 2001. - № 5 – 6. - С. 3 - 10.

19. Felmingam D., Arakawa S. Resistance among urinary tract pathogens. Experience outside the USA// Clin. Drug Invest. — 2001. — V. 21, Suppl. 1. — P. 7 – 11.

20. Risk factors for the development of extended – spectrum β – lactamase – producing bacteria in nonhospilized patients [Text] / R. Colodner, W. Rock, B. Chazan et al. // Eur. J. Clin. Microbiol. Infect. Dis. — 2004. — V. 23. — P. 163 – 167.

21. Pathogens resistant to antimicrobial agents: epidemiology, molecular mechanisms and clinical management [Text] / K.S. Kaye, J.J. Engermann, H.S. Fraimow, E. Abrutyn // Infect. Dis. Clin. North Am. – 2004. – V. 18. – P. 467 - 511.

22. Prevalence of antibiotic resistance in anaerobic bacteria: worrisome developments [Text] / D.W. Hecht // Clin. Infect. Dis. — 2004. — V. 39. — P. 92 – 97.

23. Mammeri, H. Bacteridal activity of fluoroquinolones against plasmid-mediated $Q_{hr}A$ – producing Escherichia coli [Text] / H. Mammeri, L. Poirel, P. Nordmann // Clin. Microbiol. Infect. – 2005. – V. 11. – P. 1048 - 1049.

24. Towner K. J. Mechanisms of acquired resistance. In: Greenwood D., editor. Antimicrobial chemotherapy. 4th ed. — Oxford, New York: Oxford University Press, 2001. — P. 145–155.

25. Towner, K. J. The problem of resistance [Text] / K. J. Towner // Antimicrobial chemotherapy / Eds: Greenwood D. – Oxford, New York: Oxford University Press, 2001. – P. 137 – 144.

26. Towner, K. J. Mechanisms of acquired resistance [Text] / K. J. Towner // Antimicrobial chemotherapy / Eds: Greenwood D. – Oxford, New York: Oxford University Press, 2001. – P. 145 – 155.

27. Динамика распространенности и чувствительности БЛРС - продуцирующих штаммов энторобактерий к различным антимикробным препаратам в ОРИТ России [Текст] / М.В. Эйдельштейн, Л.С. Страчунский, исследовательская группа РОСНЕТ // Клин. микробиол. антимикроб. химиотерап. – 2005. - № 7(4) – С. 323 – 336.

28. Fluit, A.C. Resistance integrons and super – integrons [Text] / A.C. Fluit, F. – J. Schmitz // Clin. Mscrobiol. Infect. – 2004. – V. 10. - P.272 – 288.

29. Turner, P.J. Trends in antimicrobial susceptibilities among bacterial pathogens isolated from patients hospitalized in European medical centers: 6-year report OF the MYSTIC surveillance study (1997 - 2002) [Text] / P.J. Turner // Microbiol. Infect.Dis. – 2005. – V. 51. – P. 281 – 289.

30. Felmingam, D. Resistance amond urinary tract pathogens. Experience outside the USA [Text] / D. Felmingam, S. Arakawa // Clin. Drug. Invest. – 2001. – V. 21. – Suppl. 1. - P. 7 – 11.

31. Trends in antimicrobial resistance in 1.968 invasive Streptococcus pneumoniae strains isolated in Spanish hospitals (2001 - 2003): decreasing penicillsn resistance in children's isolates [Text] / J. Oteo, E. Lazaro, F.J. Abajo, F. Baquero, J. Campos // J. Clin. Microbiol. – 2004. – V. 42. – P. 5571 – 5577.

32. In vitro selection of resistance in Haemophilus influenzae by amoxicillin-clavulanate, cefpodoxime, cefprozil, azithromycin, and clarithromycin [Text] / C.L. Clark, B. Bozdogan, M.R. Jacobs, P.S. Appelbaum // Antimicrob. Agents Chemother. – 2003. – V. 47. – P. 1017 – 1022.

33. Importance of local variations in antibiotic consumption and deographical differences of erythromycin and penicillin resistance in Streptococcus pneumoniae [Text] / C. Garcia-Rey, L. Aquilar, F. Baquero, J. Casal, R. Dal-Re // J. Clin. Microbiol. – 2002. – V. 40. – P. 159 – 164.

34. Horizontal transfer of par C and gyr A in fluoroquinoloneresistant clinical isolates of Streptococcus pneumoniae [Text] / M.J. Ferrandiz, A. Fenoll, J. Linares, A.G. De La Campa // Antimicrob. Agents Chemother. – 2000. – V. 44. – P. 840 – 847.

35. Qarcia-Rey, C. Antibiotic consumption and generation of resistance in Streptococcus pneumoniae: the paradoxical impact of quinolones in a complex selective landscape [Text] / C. Qarcia-Rey, J. E. Martin-Herrero, F. Baquero // Clin. Microbiol. Infect. – 2006. - V. 12. – Suppl. 3. – P. 55 – 66.

36. Pankuch, Q.A. activity of fave quinolones, three macrolides and telithromycin against 12 Haemophilus influenzae strains with different resistant phenotypes [Text] / Q. A. Pankuch, Q. Lin, P.C. Appenlbaum // Clin. Microbiol. Infect. – 2005. – V. 11. – P. 1040 – 1044.

37. Sanders, C.C. Mechanisms responsible for cross-resistance and dichotomous resistance among the quinolones [Text] / C.C. Sanders // Clin. Infect. Dis. – 2001. – V. 32. – suppl. 1. – S. 1- 8.

38. Quinolone-resistant Haemophilus influenzae in a long-term care facility: clinical and molecular epidermiology [Text] / J. Nazir, C. Urban, N. Mariano et al. // Clin. Infect. Dis. – 2004. – V. 38. – P. 1564 – 1569.

39. Quinolones in 2005: an update [Text] / F. Van Bambeke, J. – M. Michot, J. Van Eldere, P.M. Tulkens // Clin. Microbiol. Infect. – 2005. – V 11. – P. 256 – 280.

40. Веретеинова, В. П. Фторхинолоны [Текст] / В.П. Веретеинова // Провизор. – 2002. - № 19. – С. 36 – 40.

41. Сидоренко, С.В. Роль хинолонов в антибактериальной терапии. Механизм действия устойчивость микроорганизмов, фармакокинетика и переносимость [Текст] / С. В. Сидоренко // РМЖ. – 2003. - № 2. – С. 12.

42. Фещенко, Ю. И. Фторхинолоновые антибактериальные препараты (общие сведения, клиническое применение). Лекция для врачей [Текст] / Ю. И. Фещенко, Ю. М. Мостовой. – Киев, 2002. – 26 с.

43. Roberts, R. B. Antimicrobial therapy. Антимикробная терапия (Рекомендации, 2008 г.) Часть I [Текст] / R. B. Roberts, B. J. Hartman, пер. Л. Бредневой // Клін. імунол. Алергол. Інфектол. - № 3 (14). – 2008. – С. 65 – 70.

44. Шкляєв, Ю.В. Синтез алкалоидов изохинолинового ряда [Текст] / Ю. В. Шкляев // Химия и компьютерное моделирование. Бутлеровские сообщения. – 2002. - № 7. – С. 21 – 34.

45. Избранные методы синтеза и модификации гетероциклов [Текст] : у 2 т. Т. 2 / Ред. В.Г Карцева. – М.: IBS PRESS, 2003. – С. 159 – 192.

46. Раевский, А.О. Моделирование связи «структура-активность» III. Системный физико-химический подход к конструированию биологически активных веществ [Текст] / А.О. Раевский, А.М. Сапегин // Хим.-фарм. журнал. – 1990. - № 1. – С. 43 – 46.

47. Финкельштейн, Е.Е. Исследование биологической активности структурных аналогов адамантана [Текст] / Е.Е. Финкельштейн, С.В. Курбатова, Е.А. Колосова // Вестник СанГУ. – Естественно-научная серия. – 2002. - № 4 (26). – С. 121 – 128.

48. Синтез, строение и противомикробная активность производных (3-метил-2-оксо-2,3дигидроимидазо[1,2-а]пиридин-3-ил) уксусной кислоты [Текст] / Н.В. Колотова, В.О. Козьминых, А.В. Долженко // Клин. мико-

биол. и антимикроб. химиотерапия. – 2002. – Т. 4. – Приложение 1. – С. 27.

49. Синтез и рострегулирующая активность в ряду производных N-пиридил-2,5-диметилпиперидин-4-онов [Текст] / С.К. Алимжанова, В.В. Черных, А.А. Тлеубаева, М.Ж. Турмуханова // International Scientific Conference "Chemistry, Chemical Engineering and Biotechnology", Tomsk, Russia, September 11 – 16, 2006. – Томск, 2006, 2006. – С. 191 – 192.

50. Майборода, Д.А. Синтез и изучение спектральных и фармакологических свойств 1-амино-4-(5-арилоксазомил-2)бутадиенов-1,3 [Текст] / Д.А. Майборода, Е.В. Бабаев, Л.В. Гончаренко // Хим.-фарм. журн. – 1998. - № 3. – С. 24 – 28.

51. Перепелкин, П.Ю. Создание на основе пиридинов соединений, обладающих вирулицидной активностью [Текст] / П.Ю. Перепелки, С.Л Желтухин., Н.Г. Кондрашина та др. // Сборник материалов международной конференции «Биотехнология и медицина». – Москва, 14-17 марта 2006. - С. 140.

52. Поройков, В.В. Компьютерное предсказание биологической активности веществ: пределы возможного [Текст] / В.В. Поройков // Химия в России. – 1999. - № 2. – С. 8.

53. Жингиету, Г. Основные принципы конструирования лекарств [Текст] / Г. Жингиету, В. Граник. – Кишинев, 2000. – 352 с.

54. Державна Фармакопея України [Текст] / Державне підприємство « Науково-експериментальний центр ». – Х.: РІРЕГ, 2001. – 556 с.

55. Першин, Г.Н. Методы экспериментальной химиотерапии [Текст] / Г.Н. Першин. – М.: Медицина, 1971. – С. 100 – 105.

56. Макац Е.Ф., Палій В.Г., Дабіжа С.І., Заріцький О.М. Порівняльна антимікробна активність антисептика декаметоксину та похідних хінолінового ряду //Вісник Вінницького держивного медичного університету. – 2002. – Т. 6, № 2. – С.308-310.

57. Крестецька С.Л., Драч М.І., Муамар Ківан Ахмед Спектр антимікробної активності гетероциклічних сполук нового синтезу // Вісник Вінницького державного медичного університету. – 2002. - № 2. – с. 297-298.

58. Михалев А.И., Конюшин М.Е., Колла В.Э. и др. Синтез и противовоспалительная активность 2-замещенных цинхониновых и 1,2,4-триазоло[4,3-а]хинолин-5-карбрновых кислот // Хим.-фарм. журнал. – 1997. –№ 2. – с. 33-34.

59. Evsukova, V.Y. Antimicrobial activity of synthetic derivates of condensed heterocyclic compounds with pyridine fragment [Text] / V.Y. Evsukova, I.D. Andreieva, V.V. Kazmirchuk, et al. // Annals of Mechnikov Institute. - N 1, 2009. – p. 14 – 18. - Online.- *www.imiamn.org/journal.htm.*

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THE ANTIBACTERIAL PROPERTIES OF CONDENSED HETEROCYCLIC COMPOUNDS

Evsukova V.Y., Andreieva I.D., Kazmirchuk V.V., Maslyanchuk O.A.

The review summarizes the data of domestic and foreign sources concerning antibacterial properties of condensed heterocyclic compounds of different groups. The prospect of direct synthesis of condensed heterocyclic compounds and the study of their antimicrobial activities in order to develop antibacterial agents on their basis is founded.

Key words: infectious diseases, condensed heterocyclic compounds, antibacterial activity.

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АНТИБАКТЕРІАЛЬНІ ВЛАСТИВОСТІ КОНДЕНСОІВАНИХ ГЕТЕРОЦИКЛІЧНИХ СПОЛУК

Євсюкова В.Ю., Андреєва І.Д., Казмірчук В.В., Маслянчук О.А.

Огляд підсумовує дані вітчизняних та закордонних літературних джерел щодо антибактеріальних властивостей конденсованих гетероциклічних сполук різних груп. Обгрунтовани перспективність цілеспрямованого синтезу конденсованих гетероциклічних сполук і дослідження їх протимікробних властивостей з метою створення на їх основі антибактеріальних засобів.

Ключові слова: інфекційні захворювання, конденсовані гетероциклічні сполуки, антибактеріальна дія

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АНТИБАКТЕРИАЛЬНЫЕ СВОЙСТВА КОНДЕНСИРОВАННЫХ ГЕТЕРОЦИКЛИЧЕСКИХ СОЕДИНЕНИЙ

Евсюкова В.Ю., Андреева И.Д., Казмирчук В.В., Маслянчук О.А.

Обзор обобщает данные отечественных и зарубежных литературных источников относительно антибактериальных свойств конденсированных гетероциклических соединений разных групп. Обоснованы перспективность целенаправленного синтеза конденсированных гетероциклических соединений и изучение их противомикробных свойств с целью создания на их основе антибактериальных средств.

Ключевые слова: инфекционные заболевания, конденсированные гетероциклические соединения, антибактериальное действие.