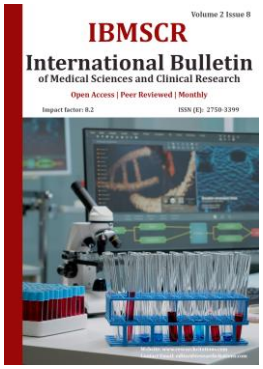


RELEVANCE AND PROBLEMS OF THE SEARCH FOR MEANS WITH A SPECTRUM OF ANTIMICROBIAL ACTION BETWEEN NATURAL AND SYNTHETIC SUBSTANCES

Phayzullaeva Zamira Rakhmatovna
fz1392fz@gmail.com
Khodjaeva Muattar Asadullaevna
Tashkent Medical Academy.
Tashkent Pharmaceutical Institute
https://doi.org/10.5281/zenodo.7854364

Abstract. This analytical article presented the results of the analysis of literature published on prestigious bases on the antimicrobial activity of biologically active substances. At the same time, the research carried out on the epidemiology, relevance of the occurrence of resistance from the ratio to drugs with existing antibacterial activity is fully explained and we express our deep gratitude to the authors for this information. The results of the analysis of literature data on the antimicrobial activity of natural and synthetic structured substances were also discussed in search of highly effective anti-microbial agents. Thus, the results of the research carried out can be concluded from the analysis as such. In itself, hetero ring-preserving compounds have high activity under in vtiro conditions, requiring in vivo studies based on them. The antimicrobial activity of biologically active substances obtained on the basis of plants is relatively unstable, which makes them the need for modifications.

Keywords. Medicinal plants, antimicrobial activity, new antimicrobial drugs, problems, *Staphylococcus aureus, Pseudomonas aeruginosa,* AMR.

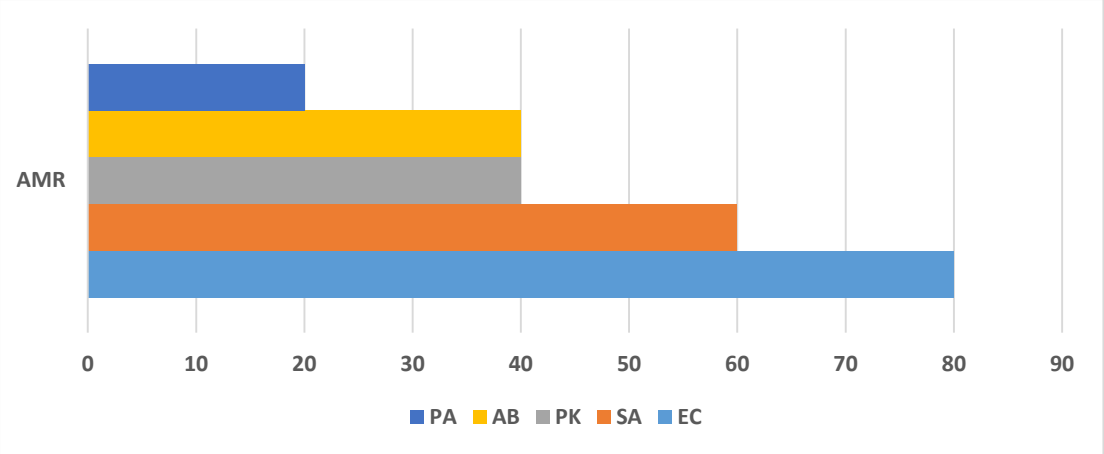
Relevance. Antimicrobial resistance of bacterial pathogens is a global problem, leading to high morbidity and mortality in the clinical setting. Today, there are pathogens resistant to existing antimicrobial drugs and an increased incidence of them. The rapid development of drug-resistant bacterial and fungal infections has required global efforts to find a new generation of drugs with high activity against them. Specifically these bacteria include gram-positive *Staphylococcus aureus*, which is a potent causative agent of nosocomial infections, Bacillus subtilis causes burns, food poisoning, and catheter-related infections. In immunocompromised patients, however, *Clostridium sporogenes,* which is mainly associated with pleuropulmonary infections, as well as other Gram-positive bacteria such as *Pseudomonas aeruginosa*, usually affect urinary tract, burns, and injuries. It is also *Escherichia coli*, a common cause of diarrhea, urinary tract infections, food poisoning, and sepsis [1-4]. Compounds with natural structures or compounds derived from medicinal plants can provide new, simple approaches to the fight against pathogenic bacteria. It is worth noting that in order to solve the most important problem of increasing the resistance of microorganisms to modern antibiotics, there is a need to research new antimicrobial compounds or extracts with synthetic structures. This leads to the need to identify and isolate new biologically active compounds, mainly from medicinal plants, with the help of standardized modern analytical measures. It is known that antimicrobial compounds with natural structures are increasingly attracting commercial attention as harmless additives for the purpose of labeling synthetic food preservatives. Chemical biodiversity of plants is a valuable potential source. Among them, phenol-structured compounds are diverse groups of secondary metabolites of plants, which exhibit a variety of physiological characteristics, including antimicrobial activity

against a wide range of pathogenic bacteria. Phenol-structured compounds are ubiquitous in plants, aromatic plants such as herbs and spices are particularly rich in phenol content, and plant-structured food additives and industrial essential oils are good sources of phenol-structured compounds. Considering that the volume and economic load of processing by-products of agro-industrial production is significant, their commercial use as a source of compounds with phenol structures can provide an economical and environmentally friendly way to improve food safety. However, there are limited studies on their potential antibacterial activity. [5-13]. While plant-derived compounds have been used as the basis for several drugs for humans, a commercially successful antibiotic from plants has not yet been found, despite more than a thousand publications per year. This may be due to the wrong methods used or the wrong plants examined. When using methods such as agar diffusion, which do not work well with plant extracts, a lot of energy is wasted. Due to the use of incorrect methods, many manuscripts are rejected before being sent to reviewers. Research on the antimicrobial activity of plant extracts based on Agar diffusion has limited value [14]. There are some specific problems with the extracts of medicinal plants and their antimicrobial effectiveness, allowing for improved and selectable compounds to be obtained with appropriate and optimized extraction methodology depending on the type of plant. Antimicrobial sensitivity tests to determine the antimicrobial activity of plant extracts may show differences in results. In addition, a number of challenges and challenges have to be overcome to develop new antimicrobial agents from plant extracts, while efforts have been made to increase the antimicrobial activity of chemical compounds. Studies of the mechanisms of action, interactions with other substances and pharmacokinetic or pharmacodynamic profile of medicinal plant extracts should be prioritized to characterize them as potential antimicrobial agents. This review studies the antimicrobial activity of plant components, their possible mechanisms of action and chemical potential. The main focus is on current problems and future prospects associated with the antimicrobial activity of medicinal plants. [13].

The purpose of the studies carried out is to: analysis of literature data on antimicrobial activity of natural and synthetic structured substances in search of highly effective anti-microbial agents.

Object and materials of analysis. the analysis selected triazole, oxydiazole unums, vincanine derivatives, as well as medicinal plants with high toxicity as an objective a material and previously known antimicrobial activity [14-18, 23].

Epidemiology. Based on analytical studies using the long-term statistical models carried out, it can be seen that the proliferation of antibiotic-resistant pathogenic microbes around the world has increased paralelically with an increase in mortality. Worldwide, *Staphylococcus aureus* (SA) and *coagulazonegative staphylococci* (CNS) are the most important cause of gram-positive bacteremia, with increasing frequency. In particular, in 2019 alone, more than 1.5 million deaths were registered due to resistance of lower respiratory infections and about 1.3 million due to resistance caused by other pathologies. Antibiotic-resistant bacterial and microbial species and the severe cases caused by them have also been observed to be in different proportions in different regions and regions. In particular, at the regional level, the mortality rate due to stability at any age is the highest in the Kabir of Western Sahara in Africa, with 27.3 deaths per 100,000 inhabitants and the lowest in Australia at 6.5. There are also specific epidemiological spread and risk factors for each pathogenic stamp (fig. 1.)



Fige.1. Quantitative indicators of each pathogenic microbial species by AMR.

Escherichia coli (EC), followed by *Staphylococcus aureus*, *Pneumococcus klebsiella* (PK), *pneumococcus*, *Acinetobacter baumannii* (AB) and *Pseudomonas aeruginosa* (PA), are the six leading pathogens associated with antibiotic resistance, and are regarded as the leading cause of microbial-related death. The combination of a single pathogen and tricillin-resistant drug, SA, caused more than 100,000 antibiotic microbial resistent (AMR)-related deaths in a year, while another six resulted in between 50,000 and 100,000 deaths each: many drug-resistant tuberculosis, as well as cephalosporin-resistant broad drug-resistant non-tuberculosis generation E coli, carbapenem-resistant A baumannii, fluoroquinolone-resistant E coli, carbapenem-resistant K pneumoniae, and third generation cephalosporin-resistant these include resistant K pneumonia [19-22].

Results of analysis of antimicrobial activity of natural and synthetic substances. The results of the analysis carried out on the basis of the studies carried out are presented in the table below (Table.1.). In in vitro studies, it can be seen that synthetic waste birircles have high antimicrobial activity. It is definitely characterized by their toxicity, that is, the high activity of these substances that injure microbes. Because almost all of these compounds store phenols or similar halacas in themselves. Extracts or biologically active substances from the plant, on the other hand, do not exhibit stagnant activity-only work is being carried out on what exactly this instability is associated with [24-29].

Table.1. Analysis of the results of antimicrobial activity obtained on the basis of in vitro experiments

№	Natural and synthetic substances	Taps of Microbes				
		Escherichia coli	***Staphylococcus aureus***	***Pneumococcus klebsiella***	***Acinetobacter baumannii***	***Pseudomonas aeruginosa***
1.	**Triazole derivatives**	**+**	**+**	**+**	**+**	**+**
2.	**Oxadiazole derivativ**	**+**	**+**	**+**	**+**	**+**

	es					
3.	**Vinkanin derivatives**	**-/+**	**-/+**	**-/+**	**-/+**	**-/+**
4.	**Plant derivatives**	**-/+**	**-/+**	**-/+**	**-/+**	**-/+**

Note: "+"- high efficacy in vitro studies.
"-/+"- in vitro studies, efficacy is very low or absent.

Biologically active substances obtained on a plant basis, as shown in the table, are not as stable as synthetic-structured and heterohallous substances in itself. This necessitates large-scale work on the modification of substances obtained on the basis of tumor. Substances with high antimicrobial activity, on the other hand, impose the need to study pharmacotoxicological indicators under in vivo conditions [30].

Conclusions. Thus, the results of the research carried out can be concluded from the analysis as such.
In itself, hetero ring-preserving compounds have high activity under in vtiro conditions, requiring in vivo studies based on them.
The antimicrobial activity of biologically active substances obtained on the basis of plants is relatively unstable, which makes them the need for modifications.

References:

1.Parija, S.C., 2014. Textbook of Microbiology & Immunology, Elsevier Health Sciences.
2.W.R. Wikoff, A.T. Anfora, J. Liu, P.G. Schultz, S.A. Lesley, E.C. Peters, G. Siuzdak Metabolomics analysis reveals large effects of gut microflora on mammalian blood metabolites. Proc. Natl. Acad. Sci., 106 (2009), pp. 3698-3703
3.Todar, K., 2009. Todar's Online Textbook of Bacteriology. Kenneth Todar University of Wisconsin-Madison Dept. of Bacterology.
4.Mostafa M. Ghorab, Aiten M. Soliman, Mansour S. Alsaid, Ahmed A. Askar, Synthesis, antimicrobial activity and docking study of some novel 4-(4,4-dimethyl-2,6-dioxocyclohexylidene) methylamino derivatives carrying biologically active sulfonamide moiety, Arabian Journal of Chemistry, Volume 13, Issue 1, 2020, Pages 545-556, https://doi.org/10.1016/j.arabjc.2017.05.022
5.Eloff, J.N. Avoiding pitfalls in determining antimicrobial activity of plant extracts and publishing the results. BMC Complement Altern Med 19, 106 (2019). https://doi.org/10.1186/s12906-019-2519-3
6.Davidson, P. M., Critzer, F. J. & Taylor, T. M. Naturally occurring antimicrobials for minimally processed foods. Ann. Rev. Food Sci. Technol. 4, 163–190 (2013).
7.Nazir, F. et al. Natural antimicrobials for food preservation. J. Pharmacogn. Phytochem. 6, 2078–2082 (2017).

8.Giannenas, I., Sidiropoulou, E., Bonos, E., Christaki, E. & Florou-Paneri, P. The history of herbs, medicinal and aromatic plants, and their extracts: past, current situation and future perspectives. In Feed Additives: Aromatic plants and herbs in animal nutrition and health (eds Florou-Paneri, P. et al.) 1–18 (Academic Press, 2020) https://doi.org/10.1017/CBO9781107415324.004.
9.Balasundram, N., Sundram, K. & Samman, S. Phenolic compounds in plants and agri-industrial by-products: Antioxidant activity, occurrence, and potential uses. Food Chem. 99, 191–203 (2006).
10.Chun, S.-S., Vattem, D. A., Lin, Y.-T. & Shetty, K. Phenolic antioxidants from clonal oregano (Origanum vulgare) with antimicrobial activity against Helicobacter pylori. Process Biochem. 40, 809–816 (2005).
11.Gyawali, R. & Ibrahim, S. A. Natural products as antimicrobial agents. Food Control 46, 412–429 (2014).
12.Poimenidou, S. V. et al. Effect of single or combined chemical and natural antimicrobial interventions on Escherichia coli O157:H7, total microbiota and color of packaged spinach and lettuce. Int. J. Food Microbiol. 220, 6–18 (2016).
13.Vaou N, Stavropoulou E, Voidarou C, Tsigalou C, Bezirtzoglou E. Towards Advances in Medicinal Plant Antimicrobial Activity: A Review Study on Challenges and Future Perspectives. Microorganisms. 2021 Sep 27;9(10):2041. doi: 10.3390/microorganisms9102041
14.Mirzaev Yu.R., Khamraev T.T., Ruzimov E.M., Khamdamov B.N., Abduazimov B.B., Adizov Sh.M., Elmurodov B.J., Yuldashev P.H.. (2022). Study of the effect of alkaloids isolated from the vinca erecta plant on cardiac activity under experimental conditions. Eurasian journal of medical and natural sciences, 2(11), 250–255. https://doi.org/10.5281/zenodo.7220861
15.Mirzaev Yu.R., Khamroev T.T., Ruzimov E.M., Khamdamov B.N., Abduazimov B.B., Adizov Sh.M., Yuldashev P.Kh., & Elmuradov B.J. (2022). Comparative assessment of acute toxicity of vincanin hydrochloride derivatives in research conditions. International Journal of Medical Sciences And Clinical Research, 2(10), 9–15. https://doi.org/10.37547/ijmscr/Volume02Issue10-03
16.Yu.R. Mirzaev, T.T. Khamraev, E.M. Ruzimov, Sh.M. Adizov, B.B. Abduazimov, B.N. Khandamov, B.J. Elmurodov, P.H. Yuldashev. (2022). Toxicological characteristics of vincanin hydrochloride and its derivatives in an experimental condition. Eurasian journal of academic research, 2(11), 1027–1033. https://doi.org/10.5281/zenodo.7244593
17.Yu.R. Mirzaev, T.T. Khamroev, E.M. Ruzimov, B.N. Khamdamov, B.B. Abduazimov, Sh.M. Adizov, P.Kh. Yuldashev, & B.J. Elmuradov. (2022). Evaluation of the effect of vincanin hydrochloride and its derivatives on blood pressure and respiration under experimental conditions. Oriental Journal of Medicine and Pharmacology, 2(04), 1–11. https://doi.org/10.37547/supsci-ojmp-02-04-01
18.Yu. R. Mirzaev, T. T. Khamroev, E. M. Ruzimov, B. N. Khandamov, & Sh. M. Adizov. (2022). Evaluation of the Effect on the Nervous System of Substances with an Alkaloid Structure Having Antitumor Activity. Journal Healthcare Treatment Development(JHTD) ISSN : 2799-1148, 2(06), 6–10. Retrieved from http://journal.hmjournals.com/index.php/JHTD/article/view/1577
19.Ashraf A. Mostafa , Abdulaziz A. Al-Askar , Khalid S. Almaary , Turki M. Dawoud , Essam N. Sholkamy , Marwah M. Bakri. Antimicrobial activity of some plant extracts against bacterial

strains causing food poisoning diseases. Saudi Journal of Biological Sciences. Volume 25, Issue 2, February 2018, Pages 361-366 https://doi.org/10.1016/j.sjbs.2017.02.004
20.Sahu JK, Ganguly S, Kaushik A. Synthesis and antimicrobial activity of some novel fused heterocyclic 1,2,4-triazolo [3,4-b][1,3,4] thiadiazine derivatives. J Adv Pharm Technol Res. 2014 Apr;5(2):90-5. doi: 10.4103/2231-4040.133434
21.Akova M. Epidemiology of antimicrobial resistance in bloodstream infections. Virulence. 2016 Apr 2;7(3):252-66. doi: 10.1080/21505594.2016.1159366
22. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. VOLUME 399, ISSUE 10325, P629-655, February 12, 2022. DOI:https://doi.org/10.1016/S0140-6736(21)02724-0
23.Aliev Shavkat Rozimatovich. (2023). Analysis of antimicrobial and antifungal activity of synthetic structural compounds. International bulletin of medical sciences and clinical research, 3(3), 84–90. https://doi.org/10.5281/zenodo.7781219
24.Aripov A.N, Akhunjanova L.L, Khamroev T.T, Aripov Abdumalik Nigmatovich, Akhunjanova Lola Lazizovna, & Khamroev Tolmas Tolibovich. (2022). Differential Analysis of Chronic Toxic Hepatitis Caused by The Introduction of Heliotrin Solution in Various Ways. Texas Journal of Medical Science, 4, 58–62. Retrieved from https://zienjournals.com/index.php/tjms/article/view/670
25.Арипов А.Н., Арипов О.А., Ахунджанова Л.Л., Набиев А.Ў., Нишанбаев С.З., Набиева Д.А., Намроев Т.Т. Тажриба шароитида сафорофлавонолозиднинг гепатотроп фаоллигини ўрганиш. Oriental Journal of Medicine and Pharmacology, 2(02), 55–64. https://doi.org/10.37547/supsci-ojmp-02-02-07
26.Aripov A.N., Aripov O.A., Akhunjanova L.L., Nabiev A.O., Nabieva D.A., & Khamroev T.T. (2022). Study the antifibrous efficacy of plant proanthocyanidin in rats with chronic heliotrine liver damage. Frontline Medical Sciences and Pharmaceutical Journal, 2(05), 16–25. https://doi.org/10.37547/medical-fmspj-02-05-03.
27.Aripov A.N., Aripov O.A., Akhunjanova L.L., Nabiev A.O., Nabieva D.A., & Khamroev T.T. (2022). Study the antifibrous efficacy of plant proanthocyanidin in rats with chronic heliotrine liver damage. Frontline Medical Sciences and Pharmaceutical Journal, 2(05), 16–25. https://doi.org/10.37547/medical-fmspj-02-05-03.
28.Aripov A.N., Aripov O.A., Akhundjanova L.L., Nabiev A.U., Nabieva D.A., & Khamroev T.T. (2022). Study the effect of yantacin on some indicators of cellular renewal and on the level of protein expression on rat hepatocytes in chronic heliotrine liver damage. International Journal of Medical Sciences And Clinical Research, 2(05), 06–13. https://doi.org/10.37547/ijmscr/Volume02Issue05-02.
29.Т.Т.Ҳамроев, Н.М.Маматқулова, П.А.Нурмахмадова, С.З.Рашидов, И.Т.Абдиназаров, С.Д.Раҳимбоев, Н.Қ.Хидирова, У.М.Якубов. (2022). Adonis turkestanica ўсимлигининг экстракция жараёнида ҳосил бўлган қолдиқ моддаларнинг ўткир заҳарлилиги ва биологик фаоллигини скрининг тадқиқотларда ўрганиш. Eurasian journal of academic research, 2(12), 447–454. https://doi.org/10.5281/zenodo.7332870
30.Muhammadjonov Bakhriddin Bakhromjon ogli, Ganiev Rustam Ravshan ogli, Nurmetova Yulduz Baltaevna, Madvaliev Baxodirjon Tolibjon ogli, Ilmiyaminov Otabek Alisher ogli, & Khamroev Tolmas Tolibovich. (2022). Evaluation of the Effect of Collecting Plants with Medicinal Properties on the Course of Hemolytic Anemia in the Study Conditions.

International journal of health systems and medical sciences, 1(5), 45-51. Retrieved from http://inter-publishing.com/index.php/IJHSMS/article/view/338