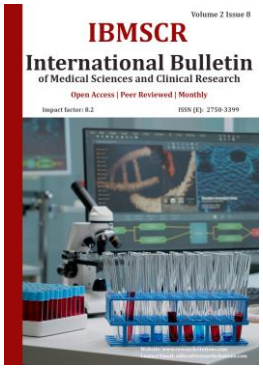

ANALYSIS OF ANTIMICROBIAL AND ANTIFUNGAL ACTIVITY OF SYNTHETIC STRUCTURAL COMPOUNDS

Aliev Shavkat Rozimatovich
Candidate of Medical Sciences, Associate Professor of the Department of Microbiology, Virology and Immunology of the Tashkent Medical Academy
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Abstract. This analysis examines data from authoritative sources, as well as some data without changes and citations. A review of 1,3,4-oxadiazole derivatives shows a high potential for their antimicrobial activity. The new structures have a very wide range of activity, from bacteria and fungi to protozoa and viruses. The possible mechanisms of action of some of the new compounds, which are based on the inhibition of various enzymes, for example, DNA gyrase, enoyl reductase and lanosterol-14α-demethylase, are described. Many of the new derivatives exceed the activity of already known antimicrobials. The variety of new structures and their high activity confirm their value as new drugs in the fight against antimicrobial resistance. Further studies are needed to confirm their efficacy and safety in vivo. The development of antimicrobial resistance around the world is forcing scientists to look for new compounds to which microbes would be sensitive. Many new structures contain a 1,3,4-oxadiazole ring, which exhibit various antimicrobial activity, for example, antibacterial, antituberculous, antifungal, antiprotozoal and antiviral. In many publications, the activity of new compounds exceeds the activity of already known antibiotics and other antimicrobials, so their potential as new drugs is very promising. The review of active antimicrobial derivatives of 1,3,4-oxadiazole is based on the literature for the period last 5 - 6 years.Thus, several conclusions can be drawn regarding the relationship between structure and activity. In the amino derivatives of 1,3,4-oxadiazole, it can be seen that the additional presence of another heterocyclic ring can expand the spectrum of antimicrobial activity.

Keywords. Heterocyclic compounds, derivatives of oxadiazoles and triazoles, antibacterial and antifungal activity.

Relevance. Currently, one of the urgent problems of pharmacology and pharmaceutical chemistry is the search for new antifungal substances. In this regard, one of the most promising in this regard are derivatives of oxadiazoles, triazoles and thiadiazoles, among which compounds with antibacterial and antifungal activity have been found. The broad-scale properties of these substances have been studied so far [1-5]. It is known that heterocyclic compounds occupy a special place in organic chemistry, which is associated with their important role in living organisms, as well as with wide practical application in various fields. So, in turn, among them, nitrogenous heterocycles participate in the storage and transmission of hereditary traits, ensure the work of the enzymatic apparatus, the central nervous system, and support the energy of the body [6]. Among the various biologically active derivatives of oxadiazoles, triazoles, including the acridone series, by now it is possible to distinguish a whole series of products with valuable pharmacological properties, for example, antitumor and antiviral activity, antifungal, antimicrobial and antiparasitic action. Derivatives of oxadiazoles, triazoles, including acridonacetic acid, are successfully used in medicine as

antiviral, immunomodulatory agents (preparations camedon, neovir, anandine, cycloferon) [7-10]. Poor treatment of infections, excessive prescribing of antibiotics and their improper use by patients have made some microorganisms insensitive to the currently used drugs. This causes great difficulties in treatment, as antibiotics or other antimicrobial drugs used so far are no longer effective, and infections are becoming more difficult to treat. Antimicrobial resistance is one of the main problems of modern medicine. Because antimicrobial resistance poses an increasingly serious threat to the life and health of the population. Without effective antibacterial therapy, the cost of caring for patients with drug-resistant infections increases, and there is a huge risk during surgery and other medical procedures. Antimicrobial resistance occurs when microorganisms develop the ability to resist drugs designed to destroy them. There is a wide variety of microbial protection strategies and therefore the search for new promising compounds in this series is a very important practical task [11,12].

Purpose of the work. Interpretation of literature data on antimicrobial and antifungal activity of compounds of various synthetic structures.

Antibacterial activity of 1,3,4-oxadiazole derivatives of different structures. So far, the 1,3,4-oxadiazole ring has aroused interest in medical chemistry and pharmacology as a bioisostere for carbonyl-containing molecules such as carboxylic acids, esters and amides. Because it is those containing the 1,3,4-oxadiazole core that showed a wide range of biological activity, which compound containing 1,3,4-oxadiazole showed stronger or comparable activity against Pseudomonas aeruginosa and Staphylococcus aureus than comparison drugs including ciprofloxacin and amoxicillin [13-17].

Table.1. Antimicrobial activity of compounds containing 1,3,4-oxadiazole nuclei

№	Structure modifications		Activity in relation to microorganisms
1.	Hybrids of 1,3,4-oxadiazole quinolone antibacterial drugs	Compounds containing a thiosemicarbazide/acidocarbazide chain instead of a carboxyl group	They affect *Pseudomonas aeruginosa* and *Staphylococcus aureus,* also have *antituberculous* activity
		Containing an isosteric 1,3,4-oxadiazole ring	Affect gram-positive strains of *S. aureus, Bacillus cereus* and gram-negative strains of *Escherichia coli, Klebsiella pneumoniae, P. aeruginosa*
		Norfloxacin derivatives containing 1,3,4-oxadiazole ring	S. aureus, устойчивых к метициллину штаммов S. aureus
		Containing hybrid compounds fluoroquinolone-piperazine-azole	Affect gram-positive and gram-negative bacteria

When analyzing the data presented above, it can be seen that modifications of quinolone antibacterial drugs are carried out in two main directions. Firstly, in the case of nalidixic acid, the 1,3,4-oxadiazole ring replaces the carboxylic part in the form of a bioisosteric structure. Secondly, in the case of fluoroquinolones (norflaxacin/ciprofloxacin), a 1,3,4-oxadiazole molecule is introduced into a piperazine substituent preceded by a methylene linker. Thus, methoxy or halogen substituents in the aromatic ring often enhance the activity of derivatives.

Compounds with antibacterial activity are also sought among aromatic or heteroaromatic derivatives of 1,3,4-oxadiazole, and it is antimicrobial activity that is most manifested by structures with a 1,3,4-oxadiazole ring containing an aryl substituent directly associated with the heterocycle. By separating new compounds due to the direct environment of the 1,3,4-oxadiazole ring, we can distinguish aryl derivatives, aryl and/or heteroaryl structures, and derivatives with an aryl and/or heteroaryl bi-/tricyclic ring [12,18-23].

Table.2. Antimicrobial activity of compounds containing 1,3,4-oxadiazole nuclei.

№	Structure modifications		Activity in relation to microorganisms
1.	Antibacterial activity containing aryl/heteroaryl derivatives of 1,3,4-oxadiazole	Compound of benzodiazepine and benzodiazepine derivatives	They have activity against *P. aeruginosa* and *S. aureus* strains. In addition, the *antituberculous* and *antiprotozoal* activity of the obtained compounds was demonstrated
		derivatives of aryl-1,3,4-oxadiazole-benzotriazole	They affect especially Gram-positive bacteria, including *Epidermal Staphylococcus, Staphylococcus aureus, Enterococcus faecalis*
		combinations of three heterocyclic rings: 1,3,4-oxadiazole, thiazole and pyridine	*Mycobacterium bovis*
		derivatives of 1,3,4-oxadiazole framework based on pyridine	*Mycobacterium bovis* *M. tuberculosis*
		hybrid derivatives by combining 1,3,4-oxadiazole and isoxazole rings	Affect gram-positive bacteria: *S. aureus, S. pyogenes* and gram-negative: *P. aeruginosa and E. coli.* M. tuberculosis
		containing 1,3,4-oxadiazoles with substituted azetidine-2-one.	*B. subtilis, S. aureus, E. coli,* and *P. aeruginosa*

From the derivatives discussed, several conclusions can be drawn regarding the relationship between structure and activity. The type and position of the substituent in the aryl ring strongly influence the activity of compounds; often the para-position is preferable to other substitution sites. An additional heterocyclic ring associated with 1,3,4-oxadiazole enhances the antimicrobial effect. Antituberculous derivatives often have an additional pyridine ring in their structure, which is one of the key elements of the molecule.

In addition, antimicrobial activity was also characterized among many 1,3,4-oxadiazole derivatives as well as amino derivatives and 1,3,4-oxadiazole derivatives containing a free thion or thiol group or S-substituted structures. Among them we distinguish simple or more complex molecules.

Table.3. Antifungal activity of compounds containing 1,3,4-oxadiazole nuclei.

№	Structure modifications		Activity in relation to microorganisms
1.	1,3,4-oxadiazole derivatives	1,3,4-oxadiazole-1,3,4-thiadiazole derivatives	four *Candida* strains
		1,3,4-oxadiazole-benzimidazole hybrids and containing 6-chloro-9*H*-carbazole	were as strongly active against the *C. albicans*
		1,3,4-oxadiazole derivatives containing a thiazole ring in their structure	*Aspergillus fumigatus*
		containing 1,3,4-oxadiazole-2-thione in the structure	*A. fumigatus* and *C. glabrata*
		2,5-disubstituted 1,3,4-oxadiazoles	*A. niger* and *C. albicans*

Derivatives of 1,3,4-oxadiazole, in addition to their antibacterial activity, also had an effect on various types of fungi. When analyzing the data presented above, in antifungal structures, it can be seen that one substituent is preferable to another, and also the substitution site is crucial. Electron acceptor groups, for example, NO_2, play an important role, which additionally affects the physicochemical properties of the compound (lipophilicity, hydrophobic interactions and pKa). Some derivatives are synthesized on the basis of already known drugs (fluconazole), and other structures, in addition to their own activity, can increase the effectiveness of standard antifungal drugs [24-33].

Conclusions. Thus, several conclusions can be drawn regarding the relationship between structure and activity. In the amino derivatives of 1,3,4-oxadiazole, it can be seen that the additional presence of another heterocyclic ring can expand the spectrum of antimicrobial activity.

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