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Antimicrobial properties of thiazolo[4,5-*d*]pyrimidine and 1,2,4-triazole derivatives

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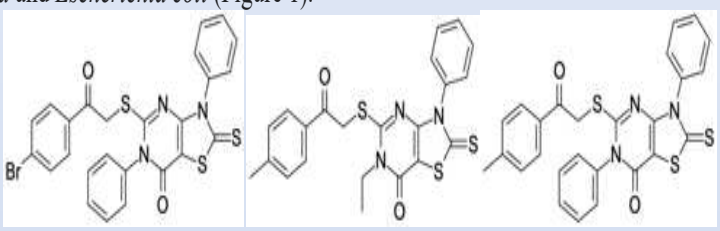
INTRODUCTION

The development of bacterial resistance to currently used antibiotics and their ability to constantly mutate is a huge problem in modern therapy of infectious diseases and forces research teams to search for new compounds with antibacterial potential. The key direction of research are chemotherapeutic agents to which bacteria are unable to develop resistance. Examples of such structures are 1,2,4-triazole and thiazolo[4,5-*d*]pyrimidine derivatives.

These compounds are characterized by a broad spectrum of activity, including high antibacterial activity, as well as antifungal, antiviral, antituberculosis, hypoglycaemic, antiepileptic, analgesic and even antitumor activity.

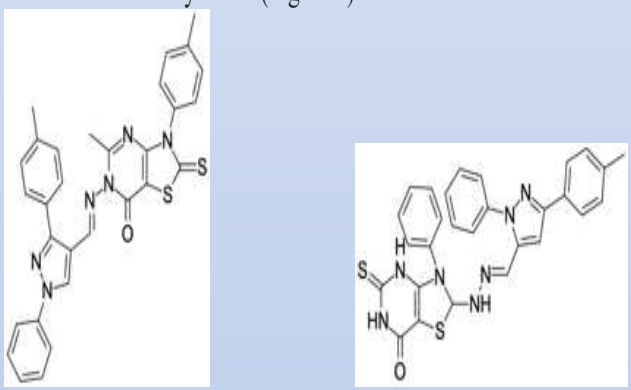
ACTIVITY OF HETEROCYCLIC COMPOUNDS

A number of thiazolo[4,5-d]pyrimidines exhibit a broad antimicrobial spectrum against Gram (-) bacteria. Particularly high activity is characterized by 6-alkyl / aryl-2,3-dihydro-3-phenyl-2-thioxothiazolo[4,5-*d*]pyrimidin-7(6*H*)-one derivatives, they are bactericidal against *Pseudomonas aeruginosa* and *Escherichia coli* (Figure 1).[1,2]



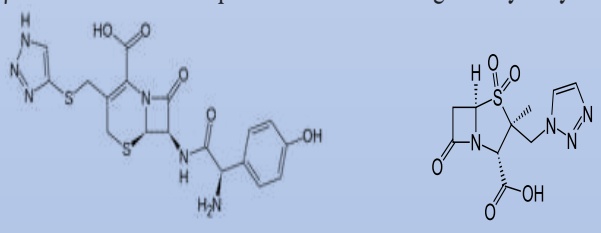
1 **2** **3**

An interesting group of derivatives are compounds that combine antimicrobial activity with anti-inflammatory activity. Examples of such compounds are 5-methyl-3-(4-methylphenyl)-6-[3-(-4-methylphenyl)-1*H*-pyrazole-4-methylideneamino]-2-thioxo-2,3-dihydrothiazolo[4,5-*d*]pyrimidin-7(6H)-one (4) and 5-methyl-2-(1*H*-pyrazole-4-methylidenehydrazono)-3-phenyl-2,6-dithioxo-2,3-dihydrothiazolo[4,5-*d*]pyrimidin-7(6*H*)-one (5). These compounds have an antibacterial activity and at the same time selectively block cyclooxygenase 2 (COX 2), causing an anti-inflammatory effect (Figure 2).[3]



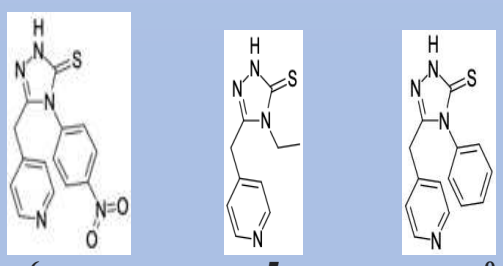
4 **5**

The 1,2,4-riazole system is present in the structure of the β-lactam antibiotic cefatrizine, as well as the inhibitor of β-lactamase -tazobactam enzymes. (6*R*,7*R*)-7-{[(2*R*)-2-Amino-2-(4-hydroxyphenyl)acetyl]amino}-8-oxo-3-[(1*H*-1,2,3-triazol-4-ylsulfanyl)methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (Cefatrizine) is a broad-spectrum cephalosporin antibiotic. Cefatrizine inhibits eukaryotic elongation factor-2 kinase (eEF2K), which is known to regulate apoptosis, autophagy and human cancers formation. (2*S*,3*S*,5*R*)-3-methyl-4,4,7-trioxo-3-(triazol-1-ylmethyl)-4λ6-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (Tazobactam) belongs to the β-lactamase inhibitors that can be administered together with β-lactam antibiotics to protect them from being destroyed by bacterial β-lactamases (Figure 3).



Cefatrizine **Tazobactam**

Many 1,2,4-triazole derivatives show strong anti-tuberculosis activity against *Mycobacterium smegmatis*, *Mycobacterium phlei* and *Myobacterium H* $_{37}$*Ra*. Particularly active in this direction are 4-(4-nitrophenyl)-3-(pyridine-4-ylmethyl)-1,2,4-triazoline-5-thione (6), 4-ethyl-1-hydroxymethyl-3-(pyridine-3-yl)-1,2,4-triazo-line-5-thione (7) and 4-phenyl-3-(pyridine-4-ylmethyl)-1,2,4-triazoline-5-thione (8) (Figure 4).[4]



6 **7** **8**

CONCLUSION

Derivatives of heterocyclic systems may be an alternative to the currently used antibiotics. Especially those that can be classified as chemotherapeutic agents. Due to the different mechanisms of their action and the inability to acquire resistance to them by bacteria, these compounds are the key to future therapies for ubiquitous bacterial infections.

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