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The susceptibility of certain bacterial strains to fused 1,2,4-triazole derivatives

1,2,4-Triazole system is the structural element of many drugs that have different pharmacological activity. The following 1,2,4-triazole derivatives are applicable in medicine: alprazolam (tranquilizer), estazolam (hypnotic, sedative, tranquilizer), rilmazafon (hypnotic, anxiolytic, used in the case of neurotic insomnia), benatradin (diuretic), trapidil (hypotensive), trazodon (antidepressant, anxiolytic), etoperidone (antidepressant), nefazodone (antidepressant, 5-HT_2 A-antagonist), anastazole (antineoplastic, non-steroidal aromatase inhibitor), letrozole (antineoplastic, aromatase inhibitor), ribavirin (antiviral), fluconazole, itraconazole, terconazole (antifungal) (5).

Besides, from the literature data it follows that depending on the type of substituent derivatives of 1,2,4-triazole show antibacterial (1,3,9,10), antifungal (10,11) and anti- inflammatory (8) properties.

The following compounds obtained due to the reaction of 1-arylimidazolidin-2-one hydrazones with carbon disulfide were tested *in vitro* in relation to bacterial strains:

I. 7-(2-methylphenyl)-2,5,6,7-tetrahydroimidazo[2,1-c][1,2,4]triazol-3(H)-thione;
II. 7-(4-methylphenyl)-2,5,6,7-tetrahydroimidazo[2,1-c][1,2,4]triazol-3(H)-thione;
III. 7-(4-ethoxyphenyl)-2,5,6,7-tetrahydroimidazo[2,1-c][1,2,4]triazol-3(H)-thione;
IV. 7-(2,3-dimethylphenyl)-2,5,6,7-tetrahydroimidazo[2,1-c][1,2,4]triazol-3(H)-thione.

Their chemical structures were confirmed on the basis of elemental analysis and spectral data (nuclear magnetic resonance, infrared and mass spectra). All the compounds were characterized by solubility in propan-2-ol, dimethylformamide and dimethylsulfoxide (12).

MATERIAL AND METHODS

Assay of antimicrobial activity *in vitro*. The synthesized compounds were tested for their antibacterial activity by disc-diffusion method by Kirby-Bauer, using Mueller - -Hinton medium for bacteria. The tested microorganisms were isolated from clinical specimens of the Laboratory of Medical Microbiology Department, Medical University of Lublin. The assayed collection included 54 strains of Gram-positive bacteria (*Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Streptococcus agalactiae*) and 52 strains of Gram-negative bacteria (*Escherichia coli, Pseudomonas aeruginosa, Proteus spp., Klebsiella pneumoniae, Enterobacter aerogenes* (Table 1).

Table 1. Microorganism cultures used microbiological screening

Group	Strain	Number of strains
Gram-positive bacteria	*Staphylococcus aureus*	21
	Staphylococcus epidermidis	15
	Streptococcus pyogenes	12
	Streptococcus agalactiae	6
Gram-negative bacteria	*Escherichia coli*	16
	Pseudomonas aeruginosa	12
	Proteus spp.	10
	Klebsiella pneumoniae	8
	Enterobacter aerogenes	6

In the disc-diffusion method, sterile paper disc (ϕ 5mm) impregnated with dissolved in dimethylsulfoxide (DMSO) compound at concentrations of 100 μgml^{-1} and 200 μgml^{-1} were used. Discs containing DMSO were used as control. The microorganisms cultures were spread over the following appropriate medium: Mueller-Hinton agar for *Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pyogenes, Streptococcus agalactiae, Escherichia coli, Pseudomonas aeruginosa, Proteus spp., Klebsiella pneumoniae, Enterobacter aerogenes*. Then, the paper discs impregnated with the solutions of the compound tested were placed on the surface of the media inoculated with the microorganism. The plates were incubated at 35°/24 h for the microorganisms cultures. After incubation, the zones of growth inhibition around the discs were observed indicating that the examined compound inhibits the growth of microorganism (2, 4, 6).

RESULTS AND DISCUSSION

Based on microbiological tests conducted on four compounds it has been shown that all the tested compounds I-IV in the examined concentrations of 100 $\mu g\ ml^{-1}$ and 200$\mu g\ ml^{-1}$ had no influence on the growth of 54 Gram-positive and 52 Gram-negative bacterial strains. The conducted tests afforded to limit the possible spectrum of biological activity of the examined compounds and exclude their potential antibacterial activity. The negative results do not exclude antifungal activity of synthesized compounds, especially against the following fungal species: *Aspergillus, Fusarium, Trichophyton, Penicillum, Microsporum*. The investigations into that field will be conducted, taking into account that their chemical structures are similar to novel antifungal agents described in the literature (11).

CONCLUSION

1. All the tested compounds were inactive against 54 Gram-positive and 52 Gram-negative bacterial strains.
2. The microbiological screening tests afforded to limit the possible biological spectrum of activity of the tested compounds.

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SUMMARY

1,2,4-Triazole is the structural element of many drugs that have different biological spectrum of activity. Besides, from the literature data it follows that 1,2,4-triazoles and its fused systems show antibacterial, antifungal and antinflammatory activities. The obtained compounds were tested for their potential antibacterial activity. Microbiological tests conducted on 106 strains of bacteria have shown that all the tested compounds in the examined concentrations (100 μgml^{-1} and 200 μgml^{-1}) had no influence on the growth of the tested bacteria.

Wrażliwość pewnych szczepów bakteryjnych na skondensowane pochodne 1,2,4-triazolu

Układ 1,2,4-triazolu występuje w strukturze leków wykazujących szerokie spektrum aktywności biologicznej. Ponadto z danych literatury wynika, że 1,2,4-triazole, a także układy skondensowane zawierające w swojej strukturze ten układ wykazują aktywność przeciwbakteryjną, przeciwgrzybiczą i przeciwzapalną. Określono aktywność przeciwbakteryjną otrzymanych związków. Przeprowadzone na 106 szczepach bakteryjnych testy aktywności przeciwdrobnoustrojowej wykazały, że otrzymane związki w badanych stężeniach nie hamowały wzrostu bakterii.