BULETINUL INSTITUTULUI POLITEHNIC DIN IAŞI
Publicat de
Universitatea Tehnică „Gheorghe Asachi” din Iaşi
Volumul 63 (67), Numărul 4, 2017
Secţia
CHIMIE şi INGINERIE CHIMICĂ

POTENTIAL ANTIMICROBIAL ACTIVITY OF SOME NEW COMPOUNDS AGAINST PATHOGENIC STRAINS

BY

ANCA MIHAELA MOCANU*

"Gheorghe Asachi" Technical University of Iași,
"Cristofor Simionescu" Faculty of Chemical Engineering and Environmental Protection

Received: October 10, 2017
Accepted for publication: November 18, 2017

Abstract. The objective of this study is to evaluate antibacterial activity of new compounds obtained by the condensation of hydrazides with several substrata (aldehides, transition metals and coupling compounds) affording final compounds with potential biological activities such antibacterial, antifungal, antiviral, antitumor activity, fungicidal, tuberculostatic and plant growth regulative properties. The new compounds were studied for antibacterial activities, in vitro, by measuring zone diameters of bacterial growth inhibition on different types of strains microorganisms: *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The newly analyzed compounds exhibited a variable activity of inhibition on the growth of the bacteria.

Keywords: hydrazide, coupling compounds, microorganisms, difusimetric method, tested activity.

1. Introduction

In the recent decades, the synthesis of hydrazides, hydrazones and related compounds has attracted considerable attention because these

*Corresponding author; *e-mail*: ancamocanu@ch.tuiasi.ro

compounds show a wide range of applications pharmaceutical and industrial (Agarwal and Prasad, 2005; Alam *et al*., 2012; Eissa, 2013).

As biologically active compounds, hydrazides and derivatives of hydrazides has applications in biomedical research such as treatment for HIV, viral hepatitis, tuberculosis and as a potential therapeutic agents for a wide range of disorders, including cancer, infectious diseases and metabolic disorders Tuberculostatic activity is attributed to the formation of stable chelates with transition metals present in the cell, thus many vital enzymatic reactions as catalyzed by these transition metals (Amarzguioui and Lundberg, 2006; Boden *et al*., 2003; Kumar *et al*., 2007; Papadopoulou *et al*., 2005).

This also act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators (Hollay *et al*., 2006; Sherma *et al.*, 2003).

The new compounds were obtained by hydrazides condensation with a series of aldehides, transition metals and coupling compounds such as Schiffer acid (Mocanu *et al*., 2014; Mocanu *et al*., 2015; Mocanu *et al*., 2016).

The objective of the present *in vitro* study was to tested potential antimicrobial activities of new compounds against pathogenic strains of Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli by disc diffusion methods. The measured critical diameters afford the germs under study to be classified as "sensitive" and "resistant" (Mocanu *et al*., 2016; Amarzguioui *et al.*, 2006; Papadopoulou *et al*., 2005).

2. Experimental

The technical conditions referring to the culture medium (composition, pH), inoculum, type of the cylinders, test performing, inoculation require an exact standardization (Jorgensen and Turnidge, 2007; Filimon *et al*., 2009). The comparative inhibiting action was estimated by the diffusimetric method in the agar. The agar media were taken as culture media and placed in Petry plates as uniform layer of 4 mm thickness, pH = 7.2 being previously measured, to being poured into the plates. The nutrient value of the media promote the optimum development of a large variety of germs and apart from this they do not contain inhibitors of bacterial substances. From the young cultures of microorganisms (18 h) microbial suspensions of 1/100 for the micro-organisms to be tested, namely *Staphylococcus aureus*, and of 1/1000 for *Pseudomonas aeruginosa* and *Escherichia coli* have been prepared.

The inoculum from the germ under study must be representative. Every plate was inoculated with 3 mL of the obtained suspensions and let to stay for 3-5 min for the inoculum absorption. After removing the inoculum the plates were maintained for 30 min at the room temperature. Then stainless steel cylinders were applied on the medium surface by means of sterile nippers and 200 μL of every tested sample placed into them. The plates were incubated with the cover down, at 37°C for 24 h with bacteria.

The microorganism cultures were used for the impregnation of both samples and standard samples (represented by DMSO) since in every experimental model the three compounds were tested with the samples under study and also in comparison with impregnated standard samples under identical cultivation conditions (Mocanu *et al.*, 2014; Mocanu *et al.*, 2015).

Only the plates with cultures corresponding in purity and density were read. The reading was made to the naked eye by measuring 2-3 times the diameter of the inhibition area /mm in different directions by means of a rule.

2. Results and Discussions

The obtaining stages of the new compounds under study are presented in Fig.1 (Mocanu *et al*., 2014; Mocanu *et al*., 2015; Mocanu *et al*., 2016).

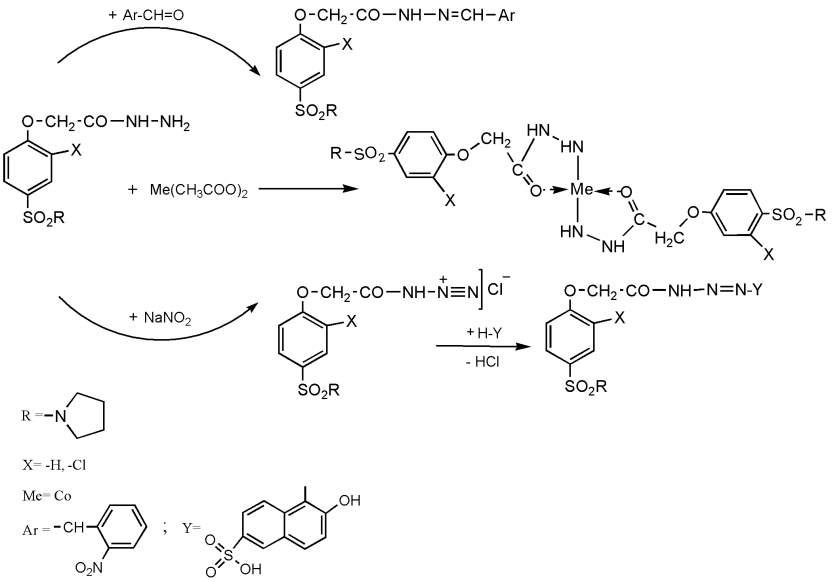


Fig. 1 − Preparation of new compounds.

The new compounds and their denominations data are given in Table 1.

As the research show there are different levels of sensitivity to the tested compounds against of the microorganisms (Table 2).

As the research show there are different levels of sensitivity to the tested compounds against of the three microorganisms (Fig. 2).

With *Staphylococcus aureus* the inhibition area diameters were different, especially for compound 3 (24 mm) and 1 (19 mm), while a slighter inhibition was noticed with compound 2 with an inhibition area diameter of only 17 mm compared to the standard sample.

Table 1
Structures of New Compounds

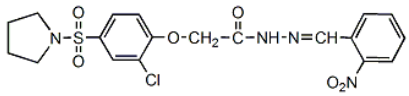
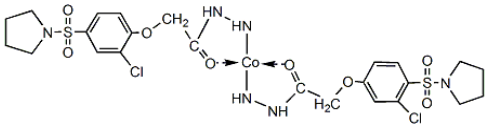
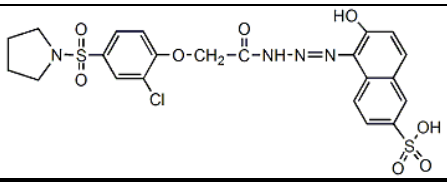
Chemical structure	Principal characteristics
	2-nitrobenzaldehyde{2-[4(pyrolidinosulfonil)-2-chlorphenoxy]ethyl}hydrazone) **(a)** Chemical formula: $C_{19}H_{19}N_4O_6SCl$ Molecular weight: 466.5 g/mol Melting point: 195-197°C
	Complexe with Co of di {2-[4 (pyrolidinosulfonil) -2chlorphenoxy]acetohydrazide} **(b)** Chemical Formula: $C_{24}H_{26}N_6O_8S_2Cl_2Co$ Molecular Weight: 713 g/mol Melting Point: 232-235°C
	1-(3-{2-[4-((pyrolidinosulfonil)2-chlorphenoxy] ethyl}triaz-1-enyl)-Schiffer **(c)** Chemical formula:$C_{22}H_{19}N_4O_8S_2Cl$ Molecular weight: 566.5 /mol Melting point: 209-211°C

Table 2
The Levels of Sensitivity to the Tested Compounds

Microorganism tested	1	2	3	Standard (DMSO)
Staphylococcus aureus	19	17	24	0
Escherichia coli	36	40	43	0
Pseudomonas aeruginosa	8	20	6	0

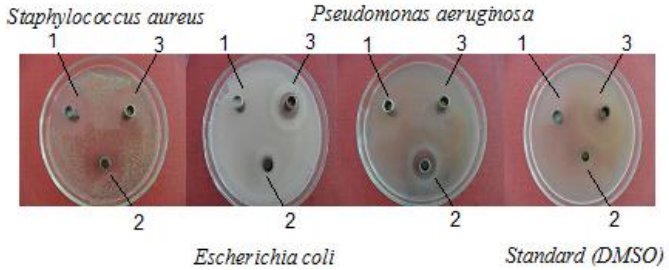


Fig. 2 − Testing of the antimicrobial action against pathogenic strains.

As made evident by the data of the anti-microbial tests the sensitivity/resistance of the microorganisms is different toward the tested compounds due to both the different chemical structures of the compounds and the different types of the microorganisms under study differing in their cell ultra-structures and response manner to the chemical compounds.

By testing the antibacterial action with *Escherichia coli* a clear antibacterial effect shown by every sample under study was made evident. This effect is significant with the **3** compound (diameter of the inhibition area of 43 mm) decreasing then from **2** and **1** with the diameters of the inhibition areas of 40 and 36 mm, respectively, while no inhibition area was noticed with the standard. As revealed by the data obtained with the *Escherichia coli* species all the tested compounds showed antibacterial action decreasing in the following order: $3 < 2 < 1$. The results are close to those of the standard sample.

The obtained results are indicative of an increased sensitivity of the *Escherichia coli* bacterium as well as the resistance of the *Staphylococcus aureus* and *Pseudomonas aeruginosa* and species to the tested compounds.

Compound 1 influence, also, differentially the development of the microorganisms, antibacterial activity being obvious in case of *Escherichia coli* bacteria which presents a higher level of sensitivity to nitro group ($-NO_2$) from aldehyde. In the case of testing the antibacterial action of compounds 2 and 3 there was highlighted a greater sensitivity of *Escherichia coli* bacteria compared with *Staphylococcus aureus* and *Pseudomonas aeruginosa* bacteria, phenomenon given by the presence of substitutes of chlorine and hydroxyl type (-OH) of compounds, which can obviously influence the growth and spreading of this microorganism (Mocanu*et al*., 2015; Mocanu*et al*., 2016).

The results are indicative of an increased sensitivity of the *Escherichia coli* bacterium as well as the resistance of the *Staphylococcus aureus* and *Pseudomonas aeruginosa* species to the tested compounds. The new compounds indicates the presence of potent antibacterial activity. The assessment of antimicrobial activity was based on measurement of inhibition zones formed around the discs.

3. Conclusions

The results obtained in this study have pointed out the antimicrobial activity of new compounds against some pathogenic bacteria.

According to the results of the study the compounds present antimicrobial effects against Gram-positive and Gram-negative bacteria.

The antimicrobial activity towards some microorganisms presented by this compounds, provides useful information for potential therapeutic use.

Considering the results obtained in this work, we may suggest that new compounds presents different effects, depending on the involved micro-organisms and respective strains.

REFERENCES

Agarwal R.K., Prasad S., *Synthesis, Spectroscopic and Physicochemical Characterization and Biological Activity of Co(II) and Ni(II) Coordination Compounds with 4-Aminoantipyrine Thiosemicarbazone*, Bioinorg. Chem. Appli., **3**, 271-288 (2005).

Alam M.S., Choi J.H., Lee D.U., *Synthesis of Novel Schiff Base Analogues of 4-Amino-1,5-Dimethyl-2-Phenylpyrazol-3-one and their Evaluation for Antioxidant and Anti-Inflammatory Activity*, Bioorg. Med. Chem., **20**, *13*, 4103-4108 (2012).

Amarzguioui M., Lundberg P., *Rational Design and in vitro and in vivo Delivery of Dicer Substrate siRNA*, Nat. Protoc., **1**, 508-517 (2006).

Boden D., Pusch O., Lee F., Tucker L., Ramratnam B., *Human Immunodeficiency Virus Type 1 Escape from RNA Interference*, J. Virol., **77**, *21*, 11531-11535 (2003).

Eissa H.H., *Synthesis, Characterization and Antibacterial Activity of Macrocyclic Schiff Bases Based on 1,3-Docarbonyl Phenyl Dihydrazide, 1,4-Docarbonyl Phenyl Dihydrazide*, Organic Chem. Curr. Res., **2:3**, doi:10.4172/2161-0401.1000122 (2013).

Filimon A., Avram E., Dunca S.I., Stoica I., Ioan S., *Surface Properties and Antibacterial Activity of Quaternized Polysulfones*, J. Appl. Polym. Sci., **112**, *3*, 1808-1816 (2009).

Hollay K.L., Kookana R.S., Noy D.M., Smith J.G., Wilhelm N., *Persistence and Leaching of Imazethapyr and Flumetsulam Herbicides over a 4-Year Period in the Highly Alkaline Soils of South-Eastern Australia*, Aust. J. Exp. Agric., **46**, *8*, 669-674 (2006).

Jorgensen J.H., Turnidge J.D., *Susceptibility Test Methods: Dilution and Disk Diffusion Methods*, In: Manual of Clinical Microbiology, Washington: ASM Press (2007).

Kumar P., Wu H., McBride J.L., Jung K.E., Kim M.H., Davidson B.L., Lee S.K., Shankar P., Manjunath N., *Transvascular Delivery of Small Interfering RNA to the Central Nervous System*, Nature, **448**, 39-43 (2007).

Mocanu A.M., Luca C., Ciobanu G., Dunca S.I., *Antibacterial Activity of Some New Hydrazide Derivatives with Potential Biological Action*, Rev. Chim. (Bucharest), **65**, *11*, 1363-1368 (2014).

Mocanu A.M., Luca C., Ciobanu G., Dunca S.I., Sandu I.G., Luca A.C., *Synthesis, Characterization and Antimicrobial Activity of Some New Hydrazine Metallic Complexes*, Rev. Chim. (Bucharest), **66**, *8*, 1137-1142 (2015).

Mocanu A.M., Luca C., Sandu I., Dunca S.I., *Synthesis, Characterization and Evaluation Antimicrobial Activity of Some New Derivatives Theophylline Sulfonyl Phenoxyacetic Acids*, Rev. Chim. (Bucharest), **67**, *3*, 584-588 (2016).

Papadopoulou C., Soulti K., Roussis I. G., *Antimicrobial Activity of Wine Phenolic Extracts*, Food Technol. Biotechnol., **43**, *1*, 41-46 (2005).

Sherma J., *Recent Advances in the Thin-Layer Chromatography of Pesticides:A Review*, J. of AOAC Internat., **86**, *3*, 602-611 (2003).

POTENȚIALA ACTIVITATE ANTIMICROBIANĂ A UNOR NOI COMPUȘI OBȚINUȚI FAȚĂ DE UNII AGENȚI PATOGENI

(Rezumat)

Obiectivul acestui studiu este de a evalua activitatea antibacteriană a unor noi compuși obținuți prin condensarea unor hidrazide cu diverse substraturi (aldehide, metale tranziționale și componente de cuplare) care formează compuși finali cu potențiale activități biologice cum ar fi proprietăți antibacteriene, antifungice, antivirale, antitumorale, fungicide, tuberculostatice și regulatoare de creștere a plantelor. Noii compuși au fost studiați pentru activități antibacteriene, *in vitro*, prin măsurarea diametrelor zonei de inhibare a creșterii bacteriene pe diferite tipuri de microorganisme: *Escherichia coli, Staphylococcus aureus* și *Pseudomonas aeruginosa*. Compușii au prezentat o activitate variabilă de inhibare a creșterii bacteriilor.