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BOOK OF PROCEEDINGS

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ANTIMICROBIAL ACTIVITY OF 3- (1- (3- HYDROXYPHENYL) AMINO) ETHYLIDENE) CHROMAN-2,4-DIONE AND ITS CORRESPONDING PALLADIUM(II) COMPLEX

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Abstract

In this manuscript, the in vitro antimicrobial activity of the previously synthesized coumarin derivative 3- (1- (3-hydroxyphenyl) amino) ethylidene) chroman-2,4-dione (L) and its corresponding palladium (II) complex (C) were examined. Their antimicrobial activity was screened against four strains of bacteria *Bacillus cereus* (ATCC 11778) G^+; *Staphylococcus aureus* (ATCC 13709) G^+; *Klebsiella pneumoniae* (ATCC 27736) G^-; and *Escherichia coli* (ATCC 2592) G-) and three strains of fungi (*Aspergillus flavus* (ATCC15517); *Candida albicans* (ATCC 10231); *Fusarium oxysporum* (ATCC 695) using disc diffusion and microdilution method. The obtained minimum inhibitory concentration (MIC) values by microdilution method for ligand and complex are similar for all tested bacteria and fungi, which means that both compounds have a similar antimicrobial effect. On the other hand, analysis of zone of inhibition (ZI) values for the tested compounds shows that the complex is generally somewhat more active than the ligand.

Keywords: coumarine, palladium(II) complex, antimicrobial activity

1. Introduction

Coumarin and its derivatives are a widely present family of molecules in nature. They can be accumulated in fruits, vegetables, trees, seeds, and vines [1]. Coumarins have important biological activities, some of which include regulation of growth, control of respiration, defense against herbivores and microorganisms, and hormonal and signaling role [1].
Coumarins show significant activity against various types of microorganisms. Coumarin itself does not have a pronounced antibacterial activity, but derivatives with different substituents in their structure have a strong effect on a wide range of gram-positive and gram-negative bacteria [2]. The most active natural antibiotic from the coumarin group is novobiocin, amoresinol, and ostruhin. In addition, some synthetic coumarins, such as 3-acetyl-4-hydroxycoumarin and its derivatives, inhibit the growth of some bacteria and fungi [3,4]. Complexes of coumarins with

transition metals show significant biological activity [3,4]. A large number of palladium(II) complexes have been synthesized and their antimicrobial activity has been examined [3,4].
In accordance with the above, our research is based on further investigation of the biological activities of various coumarin derivatives and the corresponding palladium (II) complexes. This paper presents the results of the antibacterial and antifungal activity of the previously synthesized 4-hydroxycoumarin derivative and its palladium(II) complex.

2. Experimental

2.1. General procedure for the synthesis of ligands and palladium(II) complex

The synthesis and characterization of the test ligand and its corresponding Pd (II) complex have been previously reported [5]. Namely, ligand **L** was obtained by reacting 3-acetyl-4-hydroxycoumarin with meta-hydroxyaniline in methanol. The synthesis of corresponding palladium complex **C** was performed by reaction of K_2 [$PdCl_4$] and the bidentate ligands **L** in methanol (Fig. 1).

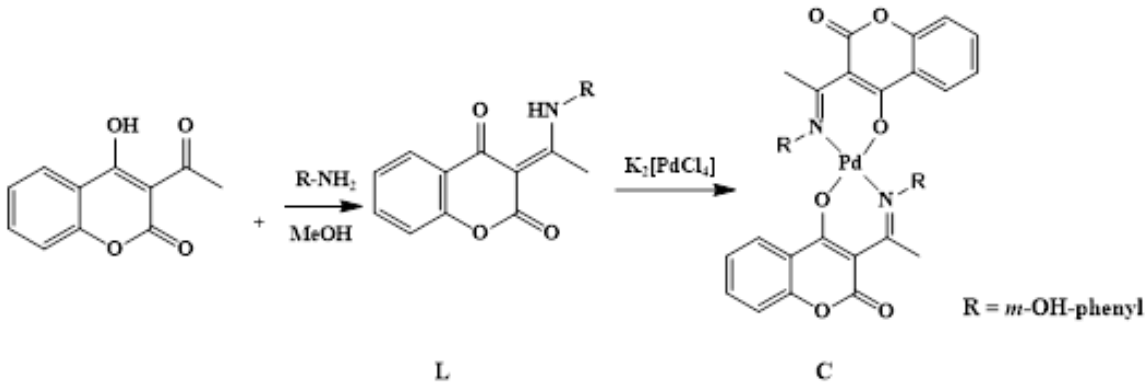

Fig 1. The general procedure for the synthesis of the ligand and complex

2.2. *Microbiological Assay*

The antimicrobial activity of the previously synthesized ligand and the complex was examined according to representative laboratory control microbial strains from the American Type Culture Collection (ATCC) (Rockville, Md., U.S.A.). The microbiological activity was done by disk diffusion and dilution method against 7 microorganisms, three strains of fungi, and four strains of bacteria.

2.3. *Microbial Strains*

The following microorganisms were used for the antimicrobial tests: *Aspergillus flavus* (ATCC15517); *Candida albicans* (ATCC 10231); *Fusarium oxysporum* (ATCC 695); *Bacillus cereus* (ATCC 11778)G^+; *Staphylococcus aureus* (ATCC 13709)G^+; *Klebsiella pneumoniae* (ATCC 27736) G^- and *Escherichia coli* (ATCC 2592)G^-.

2.4. *Antimicrobial Activity*

The disk diffusion method was used to determine the zone of inhibition [6,7]. 1 cm^3 of the suspension of microorganisms in physiological solution was homogenized with 9 cm^3 of dissolved Mueller-Hilton agar and poured into Petri dishes. After that Petri dishes were incubated under aerobic conditions at 27˚ C for 96h for fungi and at 37˚C for 48h for bacteria [8]. The determination of the minimum inhibitory concentration (MIC) is based on mixing a solution of a sample of known concentration with a nutrient medium. This test was performed in triplicate. The lowest concentration of the sample, which under these conditions completely

inhibited the growth of a certain microorganism, was presented as MIC and expressed in μg/mL. Control tests were performed with DMSO in which the substances were dissolved. DMSO was found not to inhibit the growth of the microorganisms tested [8].

3. Results

Comparative analysis of the antimicrobial activity of the ligand and the corresponding Pd(II) complex shows that the values of the minimum inhibitory concentration (MIC) are similar for all tested bacteria and fungi, which means that the compounds have a similar antimicrobial effect (Table 1). Comparing these values with a positive control indicates that the test compounds are less active than the standard, only the difference was observed in the case of *Candida albicans* for which the test compounds give almost the same MIC values as fluconazole. On the other hand, analysis of the zone of inhibition (ZI) values for the investigate compounds shows that the complex is generally somewhat more active than the ligand. By comparing the obtained values of the ZI complex with the ZI positive control, it can be clearly seen that these values are mutually comparable (Table 1). This suggests that the investigated palladium(II) complex shows promising antifungal activity.

Table 1. Antimicrobial activity of the ligand (**L**), corresponding complex (**C**) and positive control Flukonazole (fungi) and Chloramphenicol (bacteria)

Microorganism	**L**		**C**		**Flukonazole or Chloramphenicol**	
	ZI	**MIC**	**ZI**	**MIC**	**ZI**	**MIC**
Fungi						
Aspergillus flavus (ATCC15517)						
Candida albicans (ATCC 10231)	10.6±0.10	78	11.4±0.37	78	11.4±0.37	29
Fusarium oxysporum (ATCC 695)	12.1±0.10	52	13.8±0.27	52	11.0±0.10	50
	8.7±0.17	52	12.8±0.17	52	14.0±0.20	18
Bacteria						
Bacillus cereus (ATCC 11778)						
Staphylococcus aureus (ATCC 13709)	17.1±0.01	104	18.1±0.23	104	15.2±0.10	51
Klebsiella pneumoniae (ATCC 27736)	17.4±0.10	104	17.5±0.33	104	23.0±0.17	30
Escherichia coli (ATCC 2592)	11.0±0.20	78	13.8±0.27	78	15.1±0.2	62
	19.1±0.10	78	24.0±0.97	78	18.0±0.06	50

4. Conclusions

Derivative 4-hydroxycoumarin and corresponding Pd(II) complex were tested as antibacterial and antifungal agents. In general, the results of antimicrobial activity showed that the investigated compounds were less active than the standard, only a difference was observed in the case of *Candida albicans* (ATCC 10231) for which the test compounds give almost the same minimum inhibitory concentration (MIC) values as fluconazole. In conclusion, preliminary studies, ligand, and complex could be a useful starting point for the development of future antifungal agents.

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References

[1] D.S. Dimić, Z.S. Marković, L. Saso, .H. Avdović, J.R. Đorović, I.P. Petrović, D.D. Stanisavljević, M.J. Stevanović, I.Potočňák, E.Samoľová, S.R. Trifunović, J.M. Dimitrić Marković, *Synthesis and characterization of 3-(1-((3,4-dihydroxyphenethyl) amino)*

ethylidene)-chroman-2,4-dione as potentional anti-tumor agent, Oxidative Medicine and Cellular Longevity, 2019 (2019) 12-24.

[2] K. Hodák, V. Jakesová, V. Dadák, *On the antibiotic effects of natural coumarins. VI. The relation of structure to the antibacterial effects of some natural coumarins and the neutralization of such effects,* Ceskoslovenska Farmacie, 16 (1967) 86.

[3] E. H. Avdović, D. Lj. Stojković, V.V. Jevtić, D. Milenković, Z.S. Marković, N. Vuković, I. Potočňák, I.D. Radojević, Lj.R. Čomić, S.R. Trifunovića, *Preparation and antimicrobial activity of a new palladium(II) complexes with a coumarin-derived ligands. Crystal structures of the 3-(1-(o-toluidino) ethylidene)-chroman-2,4-dione and 3-(1-(m-toluidino)ethylidene)-chroman-2,4-dione,* Inorganica Chimica Acta, 206 (2019) 421–429.

[4] E.H. Avdović, Ž.B. Milanović, M.N. Živanovića, D.S. Šeklić, I.D. Radojević, Lj.R. Čomić, S.R. Trifunović, A.Amić, Z.S. Marković, *Synthesis, spectroscopic characterization, biological activity, DFT and molecular docking study of novel 4-hydroxycoumarine derivatives and coresponding palladium(II) complexes*, Inorganica Chimica Acta, 504 (2020) 119465.

[5] E.H. Avdović, I.P. Petrović, M.J. Stevanović, L. Saso, J.M. Dimitrić Marković, N.D. Filipović, M.Ž. Živić, T.N. Cvetić Antić, M.V. Žižić, N.V. Todorović, M.Vukić, S.R. Trifunović , Z.S. Marković, *Synthesis and Biological Screening of New 4-Hydroxycoumarin Derivatives and Their Palladium (II) Complexes,* Oxidative Medicine and Cellular Longevity, 2021 (2021) 18.

[6] A. Turkoglu, M.E. Duru, N. Mercan, I. Kivrak, K. Gezer, *Antioxidant and antimicrobialactivities of Laetiporus sulphureus (Bull.) Murrill*, Food Chemistry, 101 (2007) 267–273.

[7] C. Papadopoulou, K. Soulti, I.G. Roussis, *Potential antimicrobial activity of red and white wine phenolic extracts against strains of Staphylococcus aureus, Escherichia coli and Candida albicans*, Food Technology and Biotechnology, 43 (2005) 41–46.

[8] E.H. Avdović, D.S. Dimić, J.M. Dimitrić Marković, N. Vuković, M.Đ. Radulović, M.N. Živanović, N.D. Filipović, J.R. Đorović, S.R. Trifunović, Z.S. Marković, *Spectroscopic and theoretical investigation of the potential anti-tumor and anti-microbial agent, 3-(1-((2-hydroxyphenyl)amino)ethylidene) chroman-2,4-dione,* Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 206 (2019) 421–429