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MEETING ABSTRACTS

INTERACTION OF NEW POTENTIAL ANTIMICROBIAL COMPOUNDS WITH PORCINE MICROSOMAL CYP2D

Alena Špičáková [1], Zuzana Horáčková [2], Pavel Kopel [3], Eva Anzenbacherová [4], Pavel Anzenbacher [1]
Presenting author: Alena Špičáková (alena.spicakova@upol.cz)

[1] Department of Pharmacology, Faculty of Medicine and Dentistry, Palacký University Olomouc, Hněvotínská 3, 779 00, Olomouc, The Czech Republic
[2] Department of Experimental Biology, Faculty of Science, Palacký University Olomouc, Šlechtitelů 27, 783 71 Olomouc,The Czech Republic
[3] Department of Inorganic Chemistry, Faculty of Science, Palacký University Olomouc, Křížkovského 511/8, 779 00, Olomouc, The Czech Republic
[4] Department of Medical Chemistry and Biochemistry, Faculty of Medicine and Dentistry, Palacký University Olomouc, Hněvotínská 3, 779 00, Olomouc, The Czech Republic

Antimicrobial drugs are chemical substances (of natural or synthetic origin) that suppress the growth of (or destroy) microorganisms (e. g. antibiotics act primarily against bacteria). Copper complexes ($[Cu_2(pmdien)_2(H_2O)_2(\mu\text{-fu})](ClO_4)_2$ – complex No. 5; $[Cu_2(pmdien)_2(H_2O)_2(\mu\text{-dtdp})](ClO_4)_2$ – complex No. 6), on which this study is focused, show antibacterial activity (1). As with every promising compound, these copper complexes were tested for their potential to inhibit activities of liver microsomal cytochromes P450 (CYP) *in vitro*. Porcine liver microsomes served as a model system. In the first step, possible effect of these copper complexes on enzyme activity of CYP2D (bufuralol 1´ hydroxylation) was determined. Copper complexes decreased enzyme activity of CYP2D to 1 % ($IC_{50\ complex\ No.\ 5}$ = 3.4 μmol.l^{-1}), 4 % ($IC_{50\ complex\ No.\ 6}$ = 24.9 μmol.l^{-1}), respectively, at 50 μmol.l^{-1} concentration of individual complexes in the reaction mixture. The Dixon plots and Lineweaver–Burk plots indicate most probably a partially noncompetitive inhibition in both cases. Verification of this interaction was confirmed with human liver microsomal CYP2D6. Enzyme activity of human CYP2D6 was affected too (decrease to 0 % of activity in both cases at 50 μmol.l^{-1} concentration of individual complexes in the reaction mixture). $IC_{50\ complex\ No.\ 5}$ = 12.4 μmol.l^{-1} and $IC_{50\ complex\ No.\ 6}$ = 6.3 μmol.l^{-1} for human CYP2D6 were determined. Potential adverse drug interactions could occur in patients taking e. g. antidepressants (amitriptyline, paroxetine) or analgesics (codeine, tramadol) which are known to be metabolized by the CYP2D6 enzyme (2). However, determination of interaction of this copper complexes with another important liver microsomal drug metabolizing CYP should be studied in further experiments *in vitro*.

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Keywords: antimicrobial; compounds; pig; microsomal; CYP2D

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