**PO-33 / Farmaceutske znanosti**

**NEW GENERATION OF PRIMAQUINE UREA AND BIS-UREA DERIVATIVES – CYTOTOXICITY STUDY**

**NOVA GENERACIJA UREA I BIS-UREA DERIVATA PRIMAKINA – ISPITIVANJE CITOTOKSIČNOSTI**

**K. Pavić1, Z. Rajić1, L. Uzelac2, M. Kralj2, I. Perković, B. Zorc1**

1 University of Zagreb Faculty of Pharmacy and Biochemistry, Zagreb, Croatia

2 Rudjer Bošković Institute, Division of Molecular Medicine, Zagreb, Croatia

e-mail: kpavic@pharma.hr

In our previous work we have prepared several generations of primaquine derivatives bearing one or double urea moieties (1). We have also shown that some of them possess a strong antimalarial, cytostatic or antimycobacterial activities. In our novel urea **1a-f** and bis-urea compounds **2a-f**, primaquine core and spacer type were preserved, but amino alcohol part of the molecule contained (*i*) more rigid amino alcohols bearing small cycloalkane moieties, (*ii*) amino phenol or (*iii*) fluoro-substituted amino alcohols (2). The first modification was chosen based on the literature finding that conformation restrictions enhance anti-TB activity. The second one was made in order to enhance lipophilicity that could facilitate the passage of the target compounds through the bacterial membrane. Introduction of fluorine atom(s) was suggested following a common strategy in drug design and development: incorporation of fluorine in a drug candidate might increase bioavailability and selectivity.



To get insight into cytotoxicity of compounds **1a-f** and **2a-f**, we have evaluated their cytostatic activity *in vitro* against four human cancer cell lines: HCT 116 (colorectal carcinoma cell line), MCF-7 (breast adenocarcinoma cell line), H 460 (lung carcinoma cell line) and SW620 (colon carcinoma cell line). The results confirmed general low cytotoxicity of the tested compounds. Most of the compounds showed no activity against HCT 116, H 460 and SW620 cell lines. MCF-7 cells were susceptible to practically all compounds (except **2d**), but IC50 were in high micromolar range, comparable with the results for the parent compound primaquine.

Keywords: primaquine, urea, bis-urea, cytostatic activity

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