

SYNTHESIS AND BIOEVALUATION OF NEW CARBOXYLIC ACIDS HYDRAZIDES WITH POTENTIAL BIOLOGIC ACTIVITY

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Starting from isoniazid and carboxylic acids as precursors, six hydrazides of 2-(4-substituted phenoxyethyl)-benzoic acids were synthesized and characterized by appropriate means (¹H-, ¹³C-NMR, IR, elemental analysis). Their biological properties were evaluated in terms of apoptosis (Annexin V-FITC Apoptosis Detection Kit I and qRT-PCR), antioxidant activity (DPPH method), cell cycle blocking (flowcytometry and qRT-PCR) and drug metabolism genes expression on HCT-8 and HT-29 cell lines. In vitro antimicrobial tests were carried out by the micro plate Alamar Blue assay (MABA) for the anti-mycobacterial activities and by an adapted agar-disk diffusion technique for other non-tubercular strains: *Escherichia coli*, *Enterobacter cloacae*, *Citrobacter koseri*, *Morganella morganii*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Salmonella typhimurium*, *Serratia marcescens*, *Shigella sonnei*, *Stenotrophomonas maltophilia*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Staphylococcus hominis*, *Enterococcus faecalis*, *Staphylococcus aureus* and coagulase-negative staphylococci. The best anti-oxidant and antibacterial activities (including anti-*Mycobacterium tuberculosis* effects) were proved by compound 6. Compounds 4, 5 and 6 determined blocking of G1 phase. Also, compound 4 proved to be the most toxic, inducing apoptosis in 54% of cells after 72 hours, an effect that can be predicted by the increased expression of mRNA caspase 3 and 7 after a 24 hours treatment. All compounds induced expression of NAT2, CYP1A1 and CYP2C19 genes in HCT-8 cells indicating that newly synthesized compounds could be metabolized on other pathways than NAT2, spanning adverse effects of isoniazid. In conclusion, compound 6 had the best antibacterial activity and, along with compounds 4 and 5, seemed to have anti-tumoral potential. Acknowledgements. We are grateful for the support of the grants: PNII-TE-13/2011 and PNII-PCCA-90/2012.