Synthesis and EPIs activity of phenylpiperazine derivatives of 5-arylidenehydantoin tested in *Enterobacter aerogenes*

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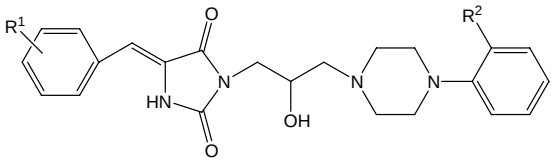
Multidrug resistance (MDR) has become a factor seriously limiting treatment of various diseases. One of strategies to combat MDR is blocking the efflux capacity of bacterial cell: alteration of efflux pump function. In our previous studies, a number of hydantoin derivatives, including 5-arylidenethiohydantoins, were obtained and evaluated on their efflux pumps inhibition (EPIs) properties in *Enterobacter aerogenes*. Most of the tested arylidenethiohydantoins showed significant decrease of minimal inhibition concentration (MIC) of chloramphenicol and sparfloxacine. Thus, further chemical modifications were performed to obtain new potential EPIs by introduction of phenylpiperazine-alkyl moieties at N3-position of 5-arylidenehydantoins (Fig.1)



R^1 – H, Cl, $N(CH_3)_2$, OCH_3, diOCH_3

R^2 – H, OCH_3, OC_2H_5

Fig.1

New compounds were obtained within 4-steps synthesis consisting of following steps: Knoevenagel condensation, Mitsunobu reaction, microwave irradiation and transfer of the obtained basic derivatives into the hydrochloric form. The compounds were tested on their EPIs-activity in microbiological assays (*E. aerogenes* strains: ATCC13048 and CM64). Results of microbiological tests indicated weak EPIs-activity for the new compounds, lower than that of N-unsubstituted thiohydantoins.