ABSTRACT

Within the framework of this Thesis, several series of 3,4-diphenylfuranones related to both combretastatin A-4 and antifungal 5-(acyloxymethyl)-3-(halophenyl)-2,5-dihydrofuran-2-ones was prepared. Cytotoxic effects on a panel of cancer and normal cell lines as well as antiinfective activity were evaluated, and the data were complemented with tests for the activation of caspase 3 and 7. High cytotoxicity was observed in some of the halogenated analogues, eg. 3-(3,4-dichlorophenyl)-4-(4-methylphenyl)-2,5-dihydrofuran-2-one with IC_{50} 0.12–0.23 μM, but the compounds were also highly toxic against non-malignant control cells. Interestingly, notable antibacterial activity indicating G(+) selectivity has been found in the 3,4-diarylfuranone class of compounds for the first time. Hydroxymethylation of furanone C5 knocked out cytotoxic effects (up to 40 μM) while maintaining significant activity against Staphylococcus strains in some derivatives. MIC_{95} of the most promising compound, 3-(4-bromophenyl)-5,5-bis(hydroxymethyl)-4-(4-methylphenyl)-2,5-dihydrofuran-2-one against S. aureus strain ATCC 6538 was 0.98 μM a 3.9 μM after 24 h and 48 h, respectively.

Following synthesis of closely related pyrrolidinones, enantioselectivity of the key step (Seyferth–Gilbert homologation) was tested. A new conditions towards enantiopure (racemization < 5 %) 3,5-disubstituted pyrrol-2-ones has been developed. This conditions were also tested with using ALA, PHE, VAL and LEU as a starting material with similar results of enantioselectivity (< 10 %).