University *of Ljubljana*
Faculty *of Pharmacy*

2nd Meeting of the Paul Ehrlich MedChem Euro-PhD Network

BOOK OF ABSTRACTS

9th-11th September 2012

Ljubljana, Slovenia

http://www.medchemeurophd2012.eu/

FUSED PYRROLO[2,3-*b*]PYRIDINE DERIVATIVES AS TOPOISOMERASE I INHIBITORS

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Cancer always constitutes one of the principal causes of death; so it is necessary to find out new drugs to introduce in therapy. Polycyclic nitrogen heterocycles can be good pharmacophores for classes of antineoplastic drugs because of their potential ability to bind to DNA by intercalating between the base pairs of the DNA duplex. Many 1,2,3-triazine and cinnoline derivatives are well known compounds endowed with a wide range of biological properties such as antineoplastic activity (1-4).
In our attempts of looking for novel antitumor agents, we extended our interest to the 7-azaindole[1,2-c][1,2,3]benzotriazines and 7-azaindole[3,2-*c*]cinnolines with the aim of evaluating their antitumor activity.
Five derivatives tested by the National Cancer Institute exhibited antitumor activity against the total number of the 60 cell lines panel from micromolar to nanomolar concentrations. Flow cytometry experiments were also performed in order to evaluate the mode of cellular death.
Results showed that these compounds are able to induce cell death by apoptosis involving some cellular organelles, such as mitochondria.
Further studies were also performed in order to clarify their mechanism of action. In particular, DNA cleavage reactions with human topoisomerase I were carried out in presence of various concentrations of compounds to verify a possible inhibition of the enzyme activity. Results suggested that these molecules act as poisons of topoisomerase I.

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