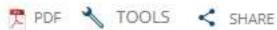
## Synthesis, in silico and in vitro Evaluation of Novel Oxazolopyrimidines as Promising Anticancer Agents

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Dedicated to Prof. Antonio Togni on the occasion of his 65th birthday and retirement

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## Abstract

New potential bioactive oxazolopyrimidines have been synthesized using two main approaches: the pyrimidine ring annulation on a functionalized oxazole and the benzoyl bromide trimerization followed by rearrangement and formation of the oxazolo[5,4-d]pyrimidine scaffold. The docking analyzes have shown that 7-piperazine substituted oxazolo[4,5-d]pyrimidines 8a-8c could be potential VEGFR2 inhibitors with high free energy of ligand-protein complex formation (ΔG: -10.1, -9.6, -9.8 kcal/mol, respectively). In vitro antitumor assays confirmed theoretical predictions that oxazolo[4,5-d]pyrimidines 8a-8c containing positively charged piperazine moiety should demonstrate significantly higher cytotoxic effects. 4-[5-(4-Chlorophenyl)-2phenyl[1,3]oxazolo[4,5-d]pyrimidin-7-yl]piperazin-1-ium trifluoroacetate (8c) exhibited a slightly higher antiproliferative effect (IC50=0.21 µm) than doxorubicin (IC50=0.36 µM) on MDA-MB-231 cell line and has relatively good results on OVCAR-3 (IC<sub>50</sub>=1.7 μм) and HCT-116 (IC<sub>50</sub>=0.24 μм) cells.