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Design, synthesis and structure-activity relationship studies of a novel focused library of 2,3,4-substituted oxazolidines with antiproliferative activity against cancer cell lines

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ABSTRACT

In the present work we describe the synthesis and antiproliferative evaluation of a focused library of 30 novel oxazolidines designed by modification of *N*-substituent, by ring variation, by alkyl variation or by extension of the structure. It was noted that carbamate and *N*,*O*-aminal groups were essential for activity. In general, replacement of the phenyl ring with pyridinyl was not tolerated. However, the introduction of a second phenyl ring with an appropriate spacer at the 3- or 4-position of the first phenyl ring generally enhanced the cytotoxic profile. Among all the prepared compounds, **24** was the most potent compound found in this class, being active on four of five cancer cell lines and it was 5-fold and 10-fold more potent than the lead compounds against HL60 and JURKAT cells, respectively. In addition, it showed relevant activity against MCF-7 and HCT-116 cells, which were resistant to lead. Moreover, **24** showed little antiproliferative activity against VERO, indicating low toxicity to normal cells. Thus, this compound has the potential to be developed as an anticancer agent.

Keywords: Oxazolidines, Chiral, Anti-cancer, Pro-apoptotic, Library