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Abstract

Bis-Pyridazine Derivatives with Anticancer Activity †

Amariucai-Mantu Dorina [1], Mangalagiu I. Ionel [1], Antoci Vasilichia [1] and Mangalagiu Violeta [2,*]

[1] Faculty of Chemistry, Alexandru Ioan Cuza University of Iasi, 11 Carol I, Iasi 700506, Romania
[2] CERNESIM Research Centre, Alexandru Ioan Cuza University of Iasi, 11 Carol I, Iasi 700506, Romania
* Correspondence: ionelm@uaic.ro
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Abstract: Over the last decades, pyridazine derivatives are considered "privileged structures" in medicinal chemistry, with special attention being given to pyridazinones derivatives, which were found to have a large range of biological activities, including anticancer. On the other hand, because of the huge difficulties in cancer treatment, there is an urgent need from the pharmaceutical industry for new anticancer drug candidates. As part of our ongoing efforts in searching for new biologically active entities with anticancer potential, we report here the design, synthesis, structure and in vitro anticancer activity of a new class of pyridazinones derivatives, namely bis-pyridazinones. The structures of the compounds were proven by elemental and spectral analysis: IR, LC-MS, 1H-NMR, 13C-NMR, two-dimensional experiments 2D-COSY, HMQC, and HMBC. A few of the compounds were accepted by the National Cancer Institute (USA) for anticancer screening and were evaluated for their in vitro cytotoxic activity against a panel of 60 human tumor cell lines, representing cancers of the brain, breast, colon, kidney, lung, ovary, prostate, as well as leukemia and melanoma. Three of the tested compounds have proven to be active against non-small cell lung cancer HOP 92 and NCI-H226, CNC cancer SNB-75, renal cancer A498 and UO-31, with a growth inhibition between 50–80 mM. Interestingly, one compound (unsubstituted bis-pyridazinones **I**) has a selective anticancer activity, being active only on non-small cell lung cancer HOP 92, with a growth inhibition of 51.45 mM. SAR correlation has been performed.

Keywords: non small cell lung cancer; CNC cancer; renal cancer; SAR; bis-pyridazinones

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