Synthesis of Some Novel Chromandione Derivatives with Biological Activity

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The intense investigation in medicinal chemistry showed that many of the coumarin derivatives with expressed anticoagulant activity, are showing anticancer effects in the same time. Thus, very known and commercially available medicaments like Warfarin, Phenprocoumon (marcumar), Sintrom (acenocoumarol) and Bromadiolone are intensively studied for their cytostatic, apoptotic and antiproliferative activities. This triggered interest of design and synthesis of novel coumarin derivatives with high cytotoxic and antiproliferative potential. 2-Aminothiazoles were used in order to couple them with 4-hydroxycouamrin, and a series of novel chromandione derivatives were synthesized. The thiazolohydrazilidene-chromane-2,4-diones had shown to exhibit cytotoxicity on human breast cancer cell line MDA-MB-231. MDA-MB-231 cells are very sensitive to treatment with B-Raf kinase inhibitors blocking the RAF/MEK/ERK signaling pathway and affecting in this way the tumour growth. Among the three RAF isoforms in humans (A-Raf, B-Raf, and C-Raf), B-Raf is the most critical to mediate Ras activity. A significant fraction of melanoma, colorectal, thyroid and breast cancers have activating B-Raf mutations, particularly at valine 599. The compounds that were synthesized had shown significant B-Raf kinase inhibition.

References

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