Pharm Anal Acta 2019, Volume:10
DOI: 10.4172/2153-2435-C2-049

Effects of spiro-bis heterocycles on proliferation and apoptosis in human breast cancer cell lines

Lamia Hamdan Ramdani[1, 2, 3], **Oualid Talhi**[1, 5], **Nadia Taibi**[1], **Laetitia Delort**[2, 3], **Caroline Decombat**[2, 3], **Artur Silva**[5] and **Khaldoun Bachari**[1], **Marie-PauleVasson**[2, 3, 4] and **Florence Caldefie-Chezet**[2, 3]

[1]CRAPC, Algeria
[2]University Clermont Auvergne, France
[3]Research Center in Human Nutrition CRNH Auvergne, France
[4]Anticancer Center Jean-Perrin, France
[5]University of Aveiro, Portugal

Breast cancer is the first cause of cancer death in women worldwide and a major concern to public health. The main axes of this work consist in studying the antiproliferative and pro-apoptotic effects of spiro-bis heterocycles on human breast cancer cell lines MCF-7 and MDA-MB-231. On the structural point of view, the compounds feature a hydantoin moiety attached either to diazole, isoxazole, diazepine, oxazepine or benzodiazepine via the privileged tetrahedral spiro-linkage. The treatment with compounds three and six, corresponding to spiro [hydantoin-isoxazole] and spiro [hydantoin-oxazepine] respectively, resulted in a significant decrease of cell proliferation and the induction of the apoptosis in both breast cancer cell lines. However, the compound four (spiro [hydantoin-diazepine]) demonstrated an antiproliferative activity only against MDA-MB-231. The qRT-PCR revealed an up-regulation of MDM2, strictly p53-dependent, and an increase of the expression of pro-apoptotic genes such as caspase 3 and BAX in MCF-7 wild-type p53 and MDA-MB-231 mutant p53 breast cancer cells. In summary, the results suggested that our compounds promoted the apoptosis of breast cancer cell lines through p53-dependent and independent pathways.

lamia_pharm@yahoo.fr