Indian Journal of Experimental Biology
Vol. 62, April 2024, pp. 254-265
DOI: 10.56042/ijeb.v62i04.982

# Downregulation of HSP27 by isoindole-derived pyrrolidines suppressing multidrug resistance (MDR) and inducing apoptosis in MCF-7 and DLD-1 cell lines

Seda Mesci[1]*, Burak Yazgan[2], Melek Gül[3] & Tuba Yıldırım[4]

*[1]Machine and Manufacturing Technologies Application and Research Center, Hitit University, Çorum, Turkiye
[2]Department of Medical Services and Techniques, Sabuncuoğlu Serefeddin Health Services Vocational School, Amasya University, Amasya, Turkey
[3]Department of Chemistry; [4]Department of Biology, Faculty of Arts and Sciences, Amasya University, Amasya, Turkiye

*Received 28 April 2023; revised 23 October 2023*

In most cancer treatments, major problem arises from the prevention of cell death (apoptosis suppression) with the development of drug resistance. Anticancer agents that ensure elimination of drug resistance and drug-resistant cells to apoptosis, are among the main targets. Here, we evaluated a series of synthesized N-phenyl maleimide substituents in tetracyclic compounds as anticancer drug candidate. We selected compounds may lead to death and eliminate drug resistance in breast and colon cells. In MCF-7 and DLD-1 cell lines; multidrug resistance genes (*ABCB1*, *ABCC3*, *ABCC10*, *ABCC11* and *ABCG2*), apoptosis mechanism genes (*BAX*, *BCL-2*, *p53*, *PARP* and *CASP3*), heat shock genes (*HSP27*, *HSP40*, *HSP60*, *HSP70* and *HSP90α*) and endoplasmic reticulum (ER) chaperone genes (*GRP78* and *GRP94*) mRNA levels were determined by qPCR method. Amounts of proteins of apoptosis and signalling pathways were measured by human apoptosis antibody array. The compounds have been shown to have downregulation on multidrug resistance genes other than ABCC3. It was found that all compounds in MCF-7 and DLD-1 cells showed significant increase in p53, BAX and CASP3 gene expressions. Also, the compounds have the potential to reduce gene expression of heat shock genes (HSPs). While the compounds have been determined to increase protein expression in BAD, BAX, BID, BIM, Caspase-3, Caspase-7, Caspase-8, Cytochrome-C, Fas, TNF, TRAIL, p27, p38 and p53; decrease protein expression in AKT, BCL-2, ERK1/2, HSP27, HSP60, IGFs, JNK, $NF_KB$, PARP, TAK1, Survivin in MCF-7 and DLD-1 cells. The compounds stand out with their inhibition of HSP27 in DLD-1 cells and their inhibition with HSP27 and NFκB in MCF-7 cells. Overall, it has been shown that these compounds increase intrinsic and extrinsic proapoptotic proteins, decrease antiapoptotic proteins, decrease HSPs and some growth factors, and they may serve as potential anticarcinogenic molecules.

**Keywords:** Breast cancer, Colorn cancer, Heat shock proteins (HSPs), Isoindole