Herb-Drug Synergy: Targeting the PI3K/AKT Pathway for Enhanced Apoptosis in Cancer Cells

P-27-092

G. Petrosyan[I], T. Harutyunyan[I], N. Avtandilyan[II]

[I]Junior researcher, Research Institute of Biology, Yerevan State University, Yerevan, Armenia, [II]Research Institute of Biology, Head of Laboratory of Fundamental and Pathological Biochemistry, Yerevan State University, Yerevan, Armenia

Cancer remains a prominent cause of mortality globally, underscoring the urgency for innovative treatment modalities. Emerging strategies integrate natural compounds and targeted therapies to disrupt specific signaling pathways crucial for tumor progression. The PI3K/AKT pathway plays a central role in cell proliferation and survival and presents an attractive therapeutic target in oncology.

This study investigates the efficacy of combining herbal extracts (Inula helenium L. and Alchemilla smirnovii Juz) with the L-arginine pathway enzymes inhibitors Nω-hydroxy-nor-arginine (nor-NOHA) and NG-Nitro-L-arginine Methyl Ester (L-NAME) to target the PI3K/AKT pathway and induce apoptosis in cancer cells.

By combining Inula helenium and Alchemilla smirnovi with nor-NOHA and L-NAME, which indirectly inhibit the PI3K/AKT pathway, enhanced apoptotic effects are expected. This research investigated the anticancer effect of herb-drug combinations on MCF7 and A549 cancer cell lines in vitro, and 7,12-dimethylbenz[a]anthracene-induced breast cancer rat model in vivo, with a view to the efficacy of our treatment model in suppressing PI3K/AKT signaling, stimulating caspase-3 (CAS-3) activation, and inducing apoptosis.

Results indicate reduced levels of phosphorylated and total PI3K and Akt following herb-drug combined treatment, indicating pathway inhibition in cancer cell lines and breast tumors. ELISA assays measure CAS-3 levels and measure chromatin segmentation and degradation by Hoechst 33342, demonstrating increased CAS-3 levels and apoptosis post-combined treatment. Herb-drug combinations induce cell death by stimulating Caspase-3 through negative regulation of the PI3K/Akt pathway.

These results emphasize the therapeutic potential of this combined approach as a novel cancer treatment model, offering insights into targeted therapies that exploit the molecular vulnerabilities of cancer cells.