

Webinar on NATURAL PRODUCTS, CAM THERAPIES, AND TRADITIONAL CHINESE MEDICINE

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Piperlongumine based herbal approach for osteosarcoma treatment

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Statement of the Problem: The challenges in the cancer treatment increasing due to complexity and therapy resistance in the cancer. The current treatment modalities impose unbearable side effects like heart failure, dysfunction of vital organs and re-occurrence of secondary cancer. Researchers are working on the alternative therapies for the cancer but due to several subtypes of cancer it is very difficult to find a broad-spectrum therapy with low or nil side effects. Nowadays, researchers exploring the ancient or traditional medicines, for the treatment of several diseases including cancer. The herbal medicines like piperlongumine have proven their effects on the several cancers. In this study, we have explored their effects on osteosarcoma.

Methodology & Theoretical Orientation: A multi-parametric experiments were designed to evaluate the therapeutic efficacy of the piperlongumine on intestinal cancer. The cytotoxicity, apoptosis, ROS, nuclear toxicity were evaluated by standard experiments. Moreover, realtime PCR was performed to find the gene expression pattern. The effects of combination of piperlongumine and current chemotherapeutic drug doxorubicin were also evaluated in-vitro.

Findings: The cytotoxicity of PL was determined by MTT assay, which shows dose and time-dependent inhibition of MG-63, 143B and KHOS/NP cells. PL treatment elevates the ROS production, which possibly leads to lethal oxidative stress and this resulted in significant apoptosis and G2/M phase arrest. At the molecular level, PL treatment significantly upregulated the expression of genes BAX, P21, P53, and SMAD4; while the BCL-2, SURVIVIN, TNFA, and NFkB genes expression was down-regulated. Furthermore, PL treatment inhibited the migration of OS cells as the expression of migration marker genes CDH2, CTNNB1, FN1, and TWIST were found to be down-regulated. The drug combination studies show synergistic effect of PL with the conventional chemotherapeutic drug doxorubicin in OS cells.

Conclusion & Significance: The piperlongumine proved to be a strong anticancer drug with comparable doses with standard chemotherapy drug. The above results suggest that PL displays strong anticancer properties against osteosarcoma and can be used as a therapeutic drug or as a complementary medicine for OS treatment in clinical settings.



Figure 1: The Piperlongumine responsive mechanisms of apoptosis

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Recent Publications:

1. Rawat L, Nayak V. Piperlongumine induces ROS mediated apoptosis by transcriptional regulation of SMAD4/P21/P53 genes and synergizes with doxorubicin in osteosarcoma cells. *Chem Biol Interact.* 2022 Feb 25;354:109832. doi: 10.1016/j.cbi.2022.109832. Epub 2022 Jan 24. PMID: 35085581. (Accepted in chemico-biological interactions).
2. Rawat L, Nayak V. Ursolic acid disturbs ROS homeostasis and regulates survival-associated gene expression to induce apoptosis in intestinal cancer cells. *Toxicol Res (Camb).* 2021 Apr 12;10(3):369-375. doi: 10.1093/toxres/tfab025. PMID: 34141150; PMCID: PMC8201588.
3. Rawat L, Hegde H, Hoti SL, Nayak V. Piperlongumine induces ROS mediated cell death and synergizes paclitaxel in human intestinal cancer cells. *Biomed Pharmacother.* 2020 Aug;128:110243. doi: 10.1016/j.biopha.2020.110243. Epub 2020 May 27. PMID: 32470748.

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