

## Enhancing the therapeutic chemosensitivity of hepatocellular carcinoma cells using alpha-solanine

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**Background:** Anti-cancer chemotherapy although effective it induces serious adverse effects. In addition, cancer cells can develop resistance to chemotherapy. **Aim:** The clinical application of cisplatin is limited by severe side effects associated with high applied doses. The synergistic effect of a combination treatment of a low dose of cisplatin with the natural alkaloid  $\alpha$ -solanine on human hepatocellular carcinoma cells was evaluated. **Materials and Methods:** HepG2 cells were exposed to low doses of  $\alpha$ -solanine and cisplatin, either independently or in combination. The efficiency of this treatment modality was evaluated by investigating cell growth inhibition, cell cycle arrest, and apoptosis enhancement. **Results:**  $\alpha$ -solanine synergistically potentiated the effect of cisplatin on cell growth inhibition and significantly induced apoptosis. This synergistic effect was mediated by inducing cell cycle arrest at the G2/M phase, enhancing DNA fragmentation and increasing apoptosis through the activation of caspase 3/7 and/or elevating the expression of the death receptors DR4 and DR5. The induced apoptosis from this combination treatment was also mediated by reducing the expression of anti-apoptotic mediators Bcl-2 and survivin, as well as by modulating miR-21 expression. **Conclusion:** Our study provides strong evidence that a combination treatment of low doses of  $\alpha$ -solanine and cisplatin exerts a synergistic anticancer effect and provides an effective treatment strategy against hepatocellular carcinoma.

**Keywords:** Cisplatin; Bcl-2; HepG2 cells; miR-21;  $\alpha$ -solanine

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