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The Cancer Control Challenge:
Better Understanding It to Better Face It

IN SILICO PREDICTION OF ANTINEOPLASTIC POTENTIAL AND TOXICITY PROFILE OF DIHYDROCURCUBITACIN B

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Introduction: Cancer remains a major global health challenge, prompting the continuous search for new therapeutic candidates. Natural compounds and their derivatives, such as dihydrocurcubitacin B—a hydrogenated derivative of cucurbitacin B—have gained interest due to their potential anticancer properties. **Objectives:** This study aimed to evaluate the predicted antineoplastic activities and toxicity profile of dihydrocurcubitacin B using in silico methodologies, providing insight into its relevance as a candidate for oncology drug development. **Methods:** The compound was analyzed using PASS Online to predict its biological activities, and GUSAR for acute toxicity in rodents via multiple administration routes. Additionally, DIGEP-Pred was used to estimate gene expression modulation (mRNA and protein levels) and assess potential targets relevant to cancer biology. **Results:** Dihydrocurcubitacin B demonstrated a high probability of antineoplastic activity (Pa = 0.938), particularly against lung (Pa = 0.833), cervical (Pa = 0.773), and sarcoma (Pa = 0.727) cancers. The compound also showed potential as an apoptosis agonist (Pa = 0.918) and hepatic disorder treatment agent (Pa = 0.856). Despite moderate cytotoxicity predictions (Pa = 0.730), its predicted toxicity levels remained within acceptable ranges: IP LD_{50} = 214.8 mg/kg (Class 4), IV LD_{50} = 8.95 mg/kg (Class 3), SC LD_{50} = 9.27 mg/kg (Class 2), and Oral LD_{50} = 55.04 mg/kg (Class 3). Gene expression predictions (Pa > 0.7) indicated significant downregulation of cancer-related genes such as CHEK1 and SESN1, and upregulation of FOXO1 and VDR, both involved in tumor suppression. **Conclusion:** In silico analyses suggest that dihydrocurcubitacin B possesses promising antineoplastic properties and modulates gene expression pathways relevant to cancer, particularly apoptosis and tumor proliferation. These findings warrant further experimental validation and may contribute to the development of novel anticancer therapies.

Keywords: dihydrocurcubitacin B; in silico; PASS Online; GUSAR; DIGEP-Pred; antineoplastic activity; cancer; apoptosis; gene expression.