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Lipid nanoparticle-encapsulated cannabidiol enhances selective cytotoxicity in melanoma cells

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Abstract

Background: Melanoma is the most lethal form of skin cancer, accounting for approximately 325,000 new cases and 57,000 deaths worldwide in 2020 [1], with incidence projected to exceed 500,000 cases annually by 2040 [2]. Despite therapeutic advances, treatment remains limited by drug resistance and off-target toxicity. Cannabidiol (CBD) has shown promising anticancer potential [3,4]; however, its clinical use is hindered by poor physicochemical properties. Lipid nanoparticle-based delivery systems may overcome these limitations by enhancing CBD stability, cellular uptake, and tumor selectivity [5]. **Objective:** This study aims to evaluate the effect of CBD-loaded lipid nanoparticles (NP-CBD) on cell viability in metastatic melanoma (MeWo) and normal keratinocyte (HaCaT) cell lines, focusing on their ability to enhance cytotoxic efficacy and selectivity compared to free CBD. **Methods:** MeWo and HaCaT cells were exposed to increasing concentrations (0.05–100 µM) of free CBD or NP-CBD (mean diameter of 205.6 ± 3.4 nm) for 48 h. Cell viability was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) reduction assay. **Results:** Free CBD induced a concentration-dependent reduction in cell viability in both MeWo and HaCaT cells, with comparable IC_{50} values (4.6 µM and 3.9 µM, respectively), indicating limited selectivity toward tumor cells. In contrast, NP-CBD enhanced cytotoxic effects in MeWo cells (IC_{50} 3.2 *vs* 4.6 µM, $p = 0.0001$), while significantly reducing toxicity in HaCaT keratinocytes (IC_{50} 8.6 *vs* 3.9 µM, $p < 0.0001$). This resulted in a clear shift toward increased tumor cell sensitivity and a more favorable safety profile. **Conclusions:** Lipid nanoparticle encapsulation significantly improves the biological performance of CBD by enhancing its antitumor activity and selectivity. NP-CBD represents a promising nanotechnology-based strategy to optimize CBD delivery, supporting the development of more effective and less toxic therapeutic approaches for melanoma.

Keywords: melanoma; cannabidiol; lipid nanoparticles; cytotoxicity; anticancer therapy; nanotechnology

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