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Impact of cannabidiol on viability of normal and tumorigenic human kidney cells: are the effects serum-dependent?

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Abstract

Background: Cannabidiol (CBD), the main non-psychotropic cannabinoid of *Cannabis sativa*, has several pharmacological actions with therapeutic potential, including antitumor effects [1]; however, its effect on renal cell carcinoma (RCC) is unknown. Considering that recent research suggests that cell culture conditions, particularly the presence of serum in culture medium, may modulate the cannabinoids' antitumor effects [2], the potential influence of this growth supplement on the response to CBD should be explored. **Objective:** To fill this gap, we investigated the sensitivity of human kidney cells to CBD in different growth conditions. **Methods:** CBD's cytotoxic profile was assessed in non-tumoral (HK-2) and tumoral (Caki-1 and 769-P) human renal cell lines, using 0% or 5% FBS. The MTT assay was performed at different time-points (24 and 48h) after cells were exposed to a wide range of CBD concentrations (1-100 µM). **Results:** CBD induced a concentration-dependent decrease in cell viability across all cell lines and conditions. After 24h at 5% FBS, it was found that HK-2 and Caki-1 cells were the most sensitive to CBD toxicity, followed by 769-P cells (IC_{50} values were respectively 14.5, 14.8, and 20.0 µM). In a serum-free medium, after 24h, IC_{50} values markedly decreased (5.2, 7.6, and 6.8 µM for HK-2, Caki-1 and 769-P cells, respectively; $p<0.004$ *vs*. 5% FBS), demonstrating that FBS has a large impact on cellular sensitivity to CBD. IC_{50} values obtained for 48h were similar since no time-dependent effect was observed ($p>0.05$). **Conclusions:** Our findings support that CBD has *in vitro* anticancer potential against RCC cells, with greater cytotoxic efficacy in the absence of serum. However, CBD cytotoxicity was not selective for tumoral cells, which may be a significant limitation to its safe use in clinical practice. More research is being conducted to investigate the cell death signaling pathways activated by CBD in each cell line.

Keywords: cannabidiol; renal cell carcinoma; antitumoral activity; serum

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