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Cannabidiol (CBD) Priming Enhances Cisplatin Killing Of Cancer Cells

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Introduction

Cisplatin is a commonly used treatment for cancer [1]. Cannabidiol (CBD) is a phytocannabinoid that has been shown to have beneficial properties in inflammation, pain relief and neuroprotection [2-4] and can induce cell death in tumour cell lines including breast and prostate cancer [5-7]. Recent data suggests that pre-treating tumour cells with a "priming agent" prior to the chemotherapeutic agent can enhance the efficacy of standard therapies [8]. Bioactive plant compounds, such as curcumin and quercetin, have been shown to have this property [9]. The aim of the study was to determine if CBD has a role as a priming agent.

Methods

A human breast cancer cell line, MDA-MB231 and an immortalised cell line derived from normal human breast epithelial cells, MCF10-A, were grown under standard conditions. Cell viability was measured using the MTT assay (Sigma). Cells were exposed to: cisplatin alone (0-150 μM); CBD alone (0-5 μM, GW pharma); primed with CBD (0-5 μM) for 24 hours, then treated with cisplatin (50 & 100 μM) for a further 24 hours; a combination of CBD and cisplatin for 48 hours – in 5 well plate replicates across 3 separate culture plates. Analysis was calculated using one-way ANOVA with Tukey correction. Significance was taken when $p<0.05$.

Results

Treatment of both cell lines with cisplatin alone for 24 hours showed a dose-dependent reduction in cell growth ($p<0.001$), with the MDA-MB231 cells showing a greater sensitivity at 50 μM compared to the MCF10-A cells. Treatment of the MDA-MB231 cells with CBD alone for 24 hours showed a dose-dependent decrease in cell growth, which reached significance at 5 μM CBD ($p<0.01$), while MCF10-A cells showed a dose-dependent trend ($p = 0.09$). When both treatments were given in combination at the same time (e.g. 1 μM CBD and 100 μM cisplatin), cell viability actually improved for both cell lines ($p<0.01$). However priming MDA-MB231 cells for 24 hours with CBD, prior to 24 hour treatment with 100 μM cisplatin, lead to a significantly higher reduction in cell viability than either treatment alone or in combination ($p<0.01$). In an identical experiment with MCF10-A cells, the results were only significant at higher CBD concentration compared to the cisplatin treatment alone (2.5 μM CBD; $p<0.001$). Repeating these same experiments with 50 μM cisplatin indicated that the priming effect only became significantly apparent at concentrations of CBD above 2.5 μM, with the MDA-MB231 cells being more sensitive than the MCF10-A cells.

Conclusion

Priming with CBD can significantly improve the ability of cisplatin to induce loss of cell viability in cancer cells. In combination, or at low concentrations during priming, there appears to be some protective effect by CBD. Although similar trends were observed with a non-cancer cell line, these cells appeared much more resistant. This data suggests that CBD could, through 'priming', be an important adjunct to standard chemotherapy. Furthermore, there appears to be biphasic concentration effects with the "normal" cell line being far more robust. Potential underlying mechanism for these effects will be presented.

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