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The effect of cannabidiol (CBD) and cannabigerol (CBG) alone and combination on A2780, human ovarian carcinoma cell line

Introduction: Cannabinoids have been shown to alter the cell signalling receptors to induce apoptosis or/and the inhibition of angiogenesis of tumour cells, inhibition of the tumour metastasis, proliferation and growth arrest (Velasco et al., 2007). In this study, the effect of two non-psychoactive cannabinoids, CBD and CBG have been compared to the one of the major chemotherapeutic drugs, *cis-platin* on A2780 human ovarian carcinoma cell line.

Methods: A2780 cell line were maintained as monolayer culture in 75cm^3 flasks with 20 ml of complete media containing RPMI 1640, 10% FBS, 1% penicillin and streptomycin, 1% sodium Pyruvate and 1% 2Mm L-glutamine, incubated at 37C with 5% CO2. A2780 were seeded in round bottom 96-well plates at 10000 cells/ mL concentration. Plates were incubated at 37°C and 5% CO2 for 24 hours. After incubation the varying doses (1nm to 100µM) of pure CBD, CBG, a combination of CBD plus CBG (1:1, 1:5 and 5:1), *cis-platin*or vehicle were added to 96-well plate. Plates were further incubated for 24h, 48h and 72 hour contact points. MTT assay (2, 5-diphenyltetrazolium bromide) performed at different time points (24h, 48h and 72h) by addition of 200µL/ well MTT, after 4 hours incubation MTT was replaced with 150µL/well DMSO. The absorption values were read at 540nm. Statistical analyses of the data were performed to compare CBD, CBG and a combination of CBD plus CBG at different ratios with *cis-platin* using Excel 2010 and GraphPad Prism 5. Data were expressed as the mean ± s. e. mean of N=4, N represents the number of experiments.

Results: The administration of CBD alone, CBG alone, a combination of CBD plus CBG (1:1, 1:5 and 5:1) and *cis-platin* induced dose dependant cytotoxicity effect on A2780 cell line. At 24h contact time, the IC_{50} values of CBD (11.72±3.14µM) CBG (14.36± 2.25 µM) , CBD plus CBG 1:1 (14.275 ± 1.62 µM), 1:5 (14.57± 1.77 µM) and 5:1 (13.58± 1.88 µM) were lower than that in *cis-platin* (16.34± 2.39µM) however none of them achieved significance. In addition, there were no significant differences in the IC_{50} values between the different cannabinoid treatments after 24 hours of incubation. The cytotoxicity offered by CBD alone at 48 and 72 hour contact time (3.79± 1.4 µM, 3.12± 1.2 µM, respectively) were much closer to that afforded by *cis-platin*(1.34± 0.38µM, 0.35± 0.08 µM, respectively) which achieved significance ($p<0.05$) at 72 h contact time. After 48 hours of incubation with the cannabinoid treatments there were no significant differences between the ratios of CBD: CBG, however all the ratios had a significantly ($p<0.05$) higher IC_{50} than CBD alone or *cis-platin*. Additionally, the IC_{50}s of the 1:5 and 5:1 ratios of CBD: CBG were significantly ($p<0.05$) lower than that of CBG.

Conclusion: The results suggest that CBD alone induced a greater cytotoxicity compared to CBG alone or in combination with CBG. The combination of CBD and CBG was unable to show synergetic effect might be due to the pathway-pathway interaction so further experiments will be carried out to investigate if pre-treatment with CBG can increase the sensitivity of the tumour cells to CBD.

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References:

Velasco., G ,et al. (2007). Cannabinoids and Gliomas. Molneurobiol. 36, 60-67.