

Investigation of anticancer activity of pure CBD and pure CBG both individually and in combination on chemo resistant ovarian carcinoma cells

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Introduction: The unwanted effects of chemotherapeutic drugs are one of the major problems in cancer chemotherapy meaning there is a demand for alternative strategies to cure cancer (Mangal *et al.*, 2013). In this study, the anti- proliferative of two non-psychoactive cannabinoids CBD and CBG have been compared individually and in combinations on cisplatin resistant A2780 CP70 human ovarian carcinoma cell line.

Methods: A2780 CP70 cell line were maintained in media comprising RPMI 1640, 10% FBS, 1% penicillin and streptomycin, 1% sodium Pyruvate and 1% 2mM L-glutamine, incubated at 37C with 5% CO₂. Cells were seeded in 96-well plates at 2000 per well and incubated at 37°C and 5% CO₂ for 24 hours. After incubation the varying doses (1nm to 100µM) of CBD, CBG, a combination of CBD plus CBG (1:1, 1:5 and 5:1) or cisplatin were added to 96-well plates and cells were further incubated for 24h, 48h and 72 hour contact time. MTT assay (2,5-diphenyltetrazolium bromide) performed at different time points by addition of 20µL MTT (5mg/mL) per well with final concentration 5µg/mL, 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 all cannabinoid treated cells with cisplatin using Microsoft 2010 and GraphPad Prism 5. Data were expressed as the mean ± standard error of mean of N=4, N represents the number of experiments.

Results: CBD, CBG, CBD+ CBG (1:1, 1:5 and 5:1) and cisplatin induced dose dependant cytotoxicity. At 24h contact time, the pIC50 values of CBD (4.83±0.04) CBG (4.7± 0.02) , CBD+CBG 1:1 (4.74± 0.12), 1:5 (4.77± 0.11) and 5:1 (4.87± 0.04) were significantly (p<0.05) lower than cisplatin (4.58 ± 0.07). The cytotoxicity offered by CBD alone at 48h (5.16± 0.23) was not significantly lower than (p>0.05) cisplatin (4.98 ± 0.01) CBG (4.80± 0.04), CBD+CBG 1:1 (4.89± 0.07), 1:5 (4.99± 0.14) and 5:1 (5.22± 0.20). At 72 hour contact point CBD (5.31±0.20) cytotoxicity was comparable to cisplatin (5.54± 0.14).

Conclusion: CBD alone induced greater cytotoxicity as compared to CBG alone or in combination with CBG. The lower toxicity induced by CBD compared to cisplatin indicates a potential value for CBD as an alternative drug in cisplatin resistant ovarian carcinoma, however further investigations are required to understand its mechanism of action. References: Mangal M *et al.* (2013). *Nucleic Acids Research*.41.1124-1129.