Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol111ssue3abst118P.pdf

The effect of a combination of GWCBD, cannabidiol, plus GWTHCV, tetrahydrocannabivarin, on A2780, human ovarian carcinoma cells

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Introduction

Recent studies have shown that cannabidol can potentiate the effectiveness of tetrahydrocannabinol and there is evidence for the alterations to the metabolism of tetrahydrocannabinol by cannabinoids (Marcu et al., 2010; Jones et al., 1972). Therefore, the aim of the present study was to investigate the potential anti-tumour activity of cannabinoid extracts rich in cannabidiol and tetrahydrocannabinol together on ovarian tumour cells.

Method

A2780 cells were grown and maintained in RPMI 1640 medium supplemented with 10% fetal bovine serum at 37°C, 5% CO₂ .The cells were plated in 96-well culture plates at a density of 1×10^4 cells/well and allowed to adhere at 37°C for 24 hours. The following day, various doses (1 nM-100 µM) of GWCBD, GWTHCV, a combination of both GWCBG plus GWTHCV (1nM-100 µM) or vehicle were added to the cells and further incubated for 24, 48, 72 and 96 hours. Then the supernatant was removed and MTT (3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) was added for 4 hours. The ability of cells to form formazan crystals by active mitochondrial respiration was determined by using a Microplate reader after dissolving the crystals in DMSO. Cytotoxicity was expressed as a relative percentage of the absorbance measured at 540 nm in the control and extract-treated cells. Data were presented as the mean±s.e.mean and analysed using ANOVA followed by Dunnet's t-test; n=4.

Results

The extracts induced dose-dependent cytotoxic effects on A2780 cells with an IC50 of $12.5\pm2.5\mu$ M for GWCBD, $16.25\pm1.25\mu$ M for GWTHCV in 24 hours, IC50 of $8.125\pm0.43\mu$ M for GWCBD, $35\pm2.4\mu$ M for GWTHCV in 48 hours, IC50 of $5.87\pm1.01\mu$ M for GWCBD, $14.75\pm2.25\mu$ M for GWTHCV in 72 hours and IC50 of $5.62\pm0.375\mu$ M for GWCBD, $10.5\pm0.5\mu$ M for GWTHCV in 96 hours. Interestingly, the cytotoxicity was potentiated by the combination of both the extracts (GWCBD+GWTHCV) added simultaneously with an IC50 of $8.25\pm0.25\mu$ M in 24 hours, $0.0225\pm0.0063\mu$ M in 48 hours, $0.008\pm0.0014\mu$ M in 72 hours and $0.00588\pm0.00153\mu$ M in 96 hours. The application of the vehicle alone did not affect the cells at any time. Results showed that GWCBD significantly (p<0.001) induced a greater cytotoxicity as compared to the toxicity induced by GWTHCV when used alone. In addition, a combination of GWCBD plus GWTHCV significantly (p<0.001) increased the cytotoxicity as compared with the single addition of compounds.

Conclusion

The data confirms that a combination of cannabidol plus tetrahydrocannabinol induces a greater cytotoxicity effect in A2780 tumour cells than CBD and THCV when used alone. Further experiments are required to investigate the receptor type/subtypes involvement and the mechanism of cell death.

Acknowledgement: We thank GW Pharmaceuticals for providing the extract and fund for consumables.

References

Marcu et al., (2010) Mol Cancer Ther January; 9(1): 180–189

Jones et al., (1972) Br J Pharmacol June; 45(2): 375–377