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Investigation of the selective cytotoxicity-induced by cannabidiol (CBD) in human ovarian carcinoma cells

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Introduction: CBD is one of the major non-psychotropic and several studies have shown an anti-tumour activity associated with CBD in different carcinoma cells[1]. Our early results indicated dose-dependent cytotoxic effects associated with CBD in human ovarian carcinoma cell line, A2780. The present study is focused to investigate the selectivity of CBD-induced cytotoxic effect and also to compare the effect of CBD when combined with carboplatin on human ovarian cancer cells.

Methods: A2780, A2780-CP70, human ovarian carcinoma cells sensitive and resistant to cisplatin, respectively, ARPE19 (human retinal epithelial) and PNT2 (human prostate) both non-carcinoma cell lines were maintained according to ECACC guidelines. 24 hours following seeding in 96 well plates cells were treated with CBD (1nM to 100µM) alone and/or plus carboplatin (1nM to 100µM), where CBD was added prior to the addition of carboplatin. MTT assay (2,5-diphenyltetrazolium bromide) was performed after 96 hours by addition of MTT which was replaced with DMSO after 4 h elapsed. Data were expressed as the mean± s.e.mean of N=4 and Normal 0 false false false EN-GB X-NONE X-NONE /* Style Definitions */ table.MsoNormalTable {mso-style-name:"Table Normal"; mso-tstyle-rowband-size:0; mso-tstyle-colband-size:0; mso-style-noshow:yes; mso-style-priority:99; mso-style-parent:""; mso-padding-alt:0cm 5.4pt 0cm 5.4pt; mso-para-margin-top:0cm; mso-para-margin-right:0cm; mso-para-margin-bottom:8.0pt; mso-para-margin-left:0cm; line-height:107%; mso-pagination:widow-orphan; font-size:11.0pt; font-family:"Calibri","sans-serif"; mso-ascii-font-family:Calibri; mso-ascii-theme-font:minor-latin; mso-hansi-font-family:Calibri; mso-hansi-theme-font:minor-latin; mso-fareast-language:EN-US;} analyzed using unpaired student's t-test. . Combination Index for CBD and carboplatin was calculated by the ratio of the applied concentration of CBD (C_{CBD} as part of the combination CBD+carboplatin) to its own IC50 and the ratio of the applied concentration of carboplatin. CI between 0.90 and 1.10 indicates an additive effect, whereas CI below this range indicates synergism and above this range indicates antagonism[2].

Results: CBD alone induced dose-dependent cytotoxicity on all the cell lines tested. IC_{50} values afforded by CBD on A2780 (3.1 ± 1.2 µM), A2780-CP70 (5.19 ± 2.28 µM) were much lower than those obtained in ARPE19 (13.01 ± 0.5 µM) and PNT2 (17.18 ± 0.5 µM) cells. SI values are shown in Table 1. IC50s of CBD in combination with carboplatin are given in Table 2. The combination index ($CI_{CBD+CARBOPLATIN}$) values of A2780 (0.33) and A2780-CP70 (0.81), respectively.

Table 1. SI values.

Selective Index (SI) at 96H	**Against ARPE19**	**Against PNT2**
A2780	5.82	6.78
A2780- CP70	3.08	3.59

Table 2. IC50 values.

IC_{50} at 96H	**Carboplatin alone**	**CBD(100nM) + Carboplatin**
A2780	2.5±0.3µM	0.23±0.13µM
A2780- CP70	44.9±3.2µM	23.6±0.5µM

Conclusion: The results suggested that CBD induces selective cytotoxicity on human ovarian cancer cells and a synergetic effect when it is combined with carboplatin.

References:

1.Javid et al., 2016. Eur J Pharmacology, Review. 775, 1-14.
2.Caffarel, *et al*., 2012. *Cancer Treatment Reviews*, 38**,** 911-918.