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The effect of omega 3fatty acid derivatives onPC3, humanprostate carcinomac line

Introduction: Fatty acids derived from algal oils such as docosahexaenoic acid(DHA)have been shown to act as anticancer modulators in certain cancers such as prostate cancers[1].The aim of the present study is to investigate the effect of docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and their derivatives on the human prostate carcinoma cell line, PC3.

Methods: PC3 cells (purchased from ATCC) were grown and maintained in RPMI 1640 medium supplemented with 10% fetal bovine serum, 5% penicillin streptomycin at 37^{o}C, 5% CO_2/95 % Air. The cells were plated in 96-well culture plates at a density of 1x10^{4} cells mL^{-1} and allowed to adhere at 37^{o}C for 24 hours. The following day, different doses of DHA ethyl ester (DHA EE), EPA ethyl ester (EPA EE),1-eicosapentaenoyl glycerol (1-EPA), 1-docosahexaenoyl glycerol (1-DHA), doxorubicin andcis-platin or vehicle were added to the cells in concentrations of 1nM-100 µM and were further incubated for 24, 48, 72 and 96 hours. Following the aforementioned incubation times 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 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 was presented as the mean±s.e.mean (n=4) and statistical analysis was performed using one way ANOVA via IBM SPSS statistics 22.

***Table 1:IC50 concentrations of DHA EE, EPA EE, 1-DHA,1-EPA and trieicosapentaenoin compared to cis-platin and doxorubicin over selected incubation time with PC3 cell line.* * = *p=>0.05*, **= p=>0.01, *** = p=>0.001 *compared to cis*-platin,‡ = p=>0.05, ‡‡ = p=>0.01, ‡‡‡= p=>0.001 compared to doxorubicin**

	IC50 (µM) on exposure to PC3 cells over selected time periods			
Compound	**24h**	**48h**	**72h**	**96h**
cis-platin	>100	18.07 ± 1.93‡	4.88 ± 1.77	2.75 ± 0.85
Doxorubicin	62.93 ± 26.78	2.12 ± 0.18 *	0.59 ± 0.19	0.11 ± 0.03
EPA EE	>100	>100	>100	46.67 ± 6.84*‡
1-eicosapentaenoyl glycerol (1-EPA)	>100	>100	>100	>100
Trieicosapentaenoin	44.17 ± 1.40	39.94 ± 5.34	29.30 ± 5.85	15.07 ± 0.60***‡‡
DHA EE	78.33 ± 24.07	63.88 ± 12.48‡	46.18 ± 5.74 * ‡	46.43 ± 17.86
1-docosahexaenoyl glycerol (1-DHA)	90.16 ± 15.38	46.48 ± 4.02 ** ‡‡	50.82 ± 5.31 **‡‡	59.05 ± 6.87*‡

Results: As seen in table 1, all compounds except 1-EPA induced dose-dependent cytotoxic effects on PC3 cells. Further experiments are required to investigate the ability of other EPA and DHA derivatives in inducing cytotoxicity. The application of the vehicle alone did not affect the cells at any time.DHA EE showed to be more effective in inducing cytotoxicity than EPA EE and their 1-monoglyceride derivative, however, trieicosapentaenoin, an EPA triglyceride showed more cytotoxicity after 96 hours than both of the ethyl ester compounds. Further experiments are required to investigate if a combination of trieicosapentaenoin and doxorubicin or *cis*-platin would induce a greater cytotoxicity compared to doxorubicin or *cis*-platin alone. Furthermore other derivatives will be investigated.

Reference

1. Brown, I., et al., *Cannabinoids and omega-3/6 endocannabinoids as cell death and anticancer modulators.* Progress in Lipid Research, 2013. **52**(1): p. 80-109.