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Gamma-linolenic and pinolenic acids exert anti-inflammatory effects in cultured human endothelial cells through their elongation products

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Abstract

It is recommended that humans consume fatty fish twice a week to increase dietary intake of eicosapentaenoic acid (EPA) and docosapentaenoic acid (DHA) to achieve long-term health benefits. However current stocks of fish are likely insufficient to meet the needs of humans. Plant-derived polyunsaturated fatty acids (PUFAs) gamma-linolenic acid (GLA) and pinolenic acid (PIN) may provide sustainable land-based sources of bioactive fatty acids.

Anti-inflammatory effects of GLA and PIN were compared to EPA and DHA in cultured EA.hy926 cells. Cells were treated with PUFAs (10, 25 and 50 μM) for 48 hours prior to stimulation with tumour necrosis factor for 24 hours. Incorporation of PUFA was measured by gas chromatography; inflammatory responses were measured by ELISA and flow cytometry.

All fatty acids were incorporated into EA.hy926 cells, after 48 hours, in a dose dependent manner (10 and 50 μM). Pre-treatment with GLA and PIN (50 μM) resulted in significant increases in their elongation products, dihomo-γ-linolenic acid (DGLA) ($p < 0.0001$) from GLA and eicosatrienoic (ETrA) ($p < 0.0001$) from PIN.

Pre-treatment with GLA, PIN, EPA or DHA (50 μM) had differential effects depending on fatty acid and cytokine examined. Pre-treatment of EA.hy926 cells with both GLA and PIN resulted in a lower concentration of soluble ICAM-1 ($p < 0.01$); however EPA and DHA showed greater reduction ($p < 0.0001$). MCP-1 production was significantly lower after treatment with PIN ($p < 0.05$), again to a lesser extent than EPA and DHA ($p < 0.0001$). Pre-treatment with EPA and DHA (50 μM) resulted in lower cell surface expression of ICAM-1 ($p < 0.001$, $p < 0.0001$), an effect not observed with GLA or PIN.

Anti-inflammatory effects of GLA and PIN were possibly due to their elongation products, and therefore silencing of elongase 5 (ELOVL5) was explored. ELOVL5 siRNA significantly inhibited the production of DGLA and ETrA in EA.hy926 cells pre-treated with GLA and PIN (50 μM). Furthermore significant decreases in sICAM-1 and MCP-1 were not seen after pre-treatment with GLA or PIN in ELOVL5 siRNA silenced EA.hy926 cells.

Plant PUFAs (GLA and PIN) demonstrate anti-inflammatory effects in this model using endothelial cells, but are less potent than EPA or DHA. Anti-inflammatory effects of GLA and PIN may be due to their elongation metabolites; DGLA and ETrA.

Conflict of Interest

There is no conflict of interest