Eleostearic Acid inhibits breast cancer proliferation by means of an oxidation-dependent mechanism.

Abstract:
Eleostearic acid (alpha-ESA) is a conjugated linolenic acid that makes up approximately 60% of Momordica charantia (bitter melon) seed oil. Prior work found that water extract from bitter melon was able to inhibit breast cancer. Here, we investigated effects of alpha-ESA on both estrogen receptor (ER)-negative MDA-MB-231 (MDA-wt) and ER-positive MDA-ERalpha7 human breast cancer cells. We found that alpha-ESA inhibited proliferation of both MDA-wt and MDA-ERalpha7 cells, whereas conjugated linoleic acid had comparatively weak antiproliferative activity at 20 to 80 micromol/L concentrations. We also found that alpha-ESA (40 micromol/L) treatment led to apoptosis in the range of 70% to 90% for both cell lines, whereas conjugated linoleic acid (40 micromol/L) resulted in only 5% to 10% apoptosis, similar to results for control untreated cells. Addition of alpha-ESA also caused loss of mitochondrial membrane potential and translocation of apoptosis-inducing factor as well as endonuclease G from the mitochondria to the nucleus. Additionally, alpha-ESA caused a G(2)-M block in the cell cycle. We also investigated the potential for lipid peroxidation to play a role in the inhibitory action of alpha-ESA. We found that when the breast cancer cells were treated with alpha-ESA in the presence of the antioxidant alpha-tocotrienol (20 micromol/L), the growth inhibition and apoptosis effects
of alpha-ESA were lost. An AMP-activated protein kinase inhibitor (Dorsomorphin) was also able to partially abrogate the effects of alpha-ESA, whereas a caspase inhibitor (BOC-D-FMK) did not. These results illustrate that alpha-ESA can block breast cancer cell proliferation and induce apoptosis through a mechanism that may be oxidation dependent.