In vitro assessment of the combined effect of eicosapentaenoic acid, green tea extract and curcumin C3 protein loss in C_2C_{12} myotubes

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Cachexia, a progressive wasting syndrome, which involves loss of both adipose tissue and skeletal muscle, which eventually leads to the death of the patient, has been witnessed in at least 50% of all cancer patients. Catabolic effect of cytokines (e.g. tumour necrosis factor-α, TNF-α) and tumour products (e.g. proteolysis-inducing factor, PIF) are considered to be majorly responsible weight loss, although anorexia is initially experienced by such patients. Hence, in addition to nutritional support, it is necessary to include an anti-catabolic agent, such as Eicosapentaenoic acid (EPA).

Eicosapentaenoic acid is a fish oil constituent known to attenuate the catabolic effect of TNF-α and PIF as well as increased protein degradation in cachexia, both *in vitro* and *in vivo*. Several clinical trials have also suggested the beneficial role of EPA in different types of cancer.

However, with higher cost, poor patient compliance and limited sources of fish oil, alternative methods of increasing the activity of EPA are viable. Hence, the current study was carried out to assess the effect of EPA, when combined with Curcumin and green tea extract (GTE), the other two known anti-catabolic agents *in vitro* experimental models.

Objective:

To investigate whether curcumin or GTE enhances the effect of low dose EPA in attenuating the depression of protein synthesis and protein degrad in C_2C_{12} murine myotubes.

Study Design:

Measurement of total protein degradation, protein synthesis and diameter was done in C_2C_{12} myotubes in the presence or absence of PIF and TNF-α

Results and Discussion:

Synergistic potential of combination of a low dose of EPA (having minimal anti-cachectic activity) with curcumin or GTE on TNF-α- and PIF-mediated protein synthesis and degradation was determined in C_2C_{12} myotubes

Individually, EPA (50 μM) or curcumin (10 μg/ml) did not show significant effect on PIF-induced protein degradation, however the combination produced complete inhibition ($p<0.05$)

Similarly, for TNF-α, combination of EPA with Curcumin showed better attenuation of protein degradation ($p<0.05$) than EPA alone

Although EPA completely attenuated TNF-α-induced depression of protein synthesis, but not that caused by PIF, whereas the combination of EPA with curcumin significantly enhanced protein synthesis to both agents ($p<0.05$)

A significant decrease in the diameter of myotube (23.5% for TNF-α and 11.8% for PIF) was observed. However, the triple combination of EPA, curcumin and GTE returned diameters to values as that of control (both $p<0.01$)

Researchers suggested that anti-catabolic effect of EPA (at low effective concentrations) was enhanced by curcumin and GTE by attenuating protein degradation as well as protein synthesis degradation induced by both PIF and TNF-α

Conclusion:

Overall, it was suggested that the combination of curcumin or GTE, or both with EPA enhanced its anti-catabolic effect, thus could be of utili attenuating muscle loss in cancer patients with cachexia.