Supplementation with eicosapentaenoic acid and docosahexaenoic acid reduces high levels of circulating proinflammatory cytokines in aging adults: a randomized, controlled study

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BACKGROUND

- Inflammaging is a term used to describe the strong relationship between physiological aging and chronic systemic inflammation.
- Chronic systemic inflammation is involved in the aetiology of many age-related pathologies, including atherosclerosis, arthritis and non-healing wounds.
- Increasing n-3 EPA and DHA intake, has been found to reduce the amount of AA available for eicosanoid synthesis, as n-6 and n-3 PUFAs are competitively metabolised.
- Inflammaging is characterised by elevated levels of circulating pro-inflammatory cytokines, such as IL-6, IL-1β and TNF-α.
- Diets low in n-3 PUFAs relative to n-6 PUFAs could be problematic, as the n-6 PUFA arachidonic acid (AA) is metabolised to eicosanoids that induce proinflammatory cytokine production.

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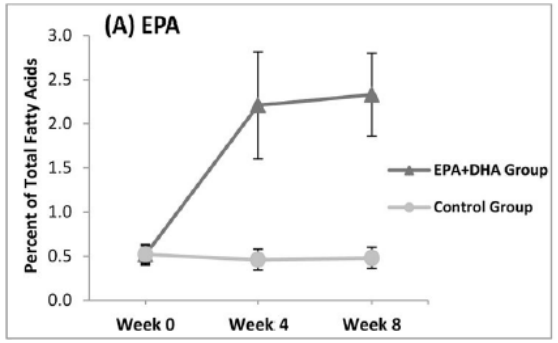
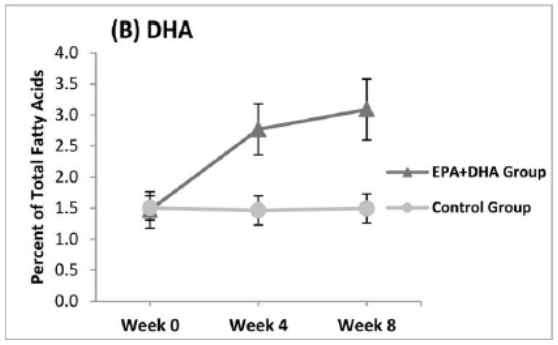
AIM

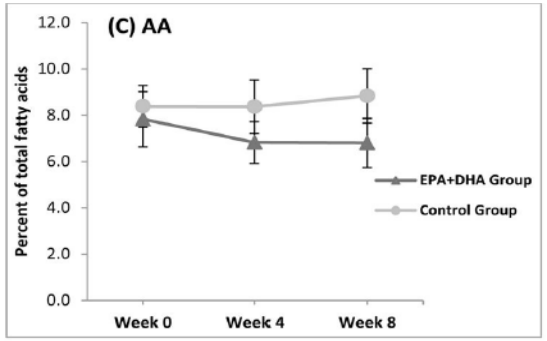
The aim of this study, was to assess the effects of EPA and DHA supplementation on circulating levels of proinflammatory cytokines, in middle to late adulthood adults with at least one known chronic inflammatory non-autoimmune condition (chronic venous leg ulcers).

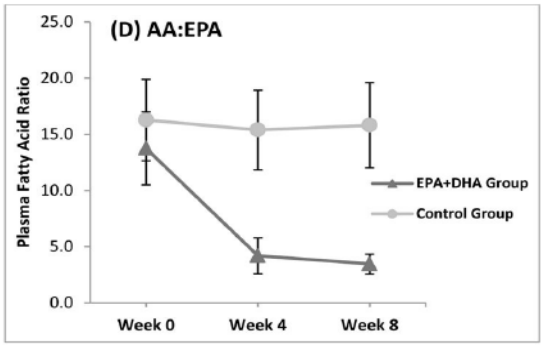
RESULTS: PUFA CONCENTRATIONS

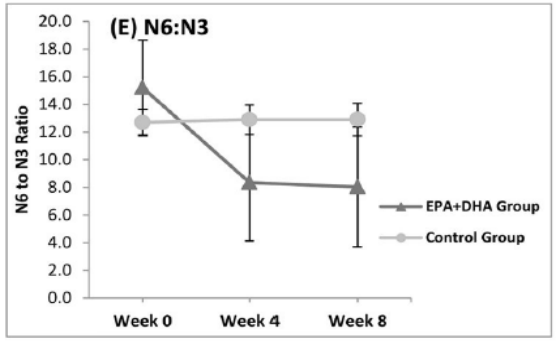
- **Within group comparisons**
  - Supplementation with EPA and DHA resulted in:
    - Significantly higher EPA and DHA levels at week 4 and 8
    - Significantly lower AA levels at week 4 and 8
    - Significantly lower levels of AA:EPA ratio and n-6:n-3 ratio at week 4 and 8
  - No significant changes on EPA, DHA, AA, AA:EPA or n-6:n-3 ratio were observed in the control group, over time.
- **Between group comparisons**
  - Week 4: Supplementation with EPA and DHA resulted in significantly higher EPA and DHA plasma levels, lower levels of AA and significantly lower ratios of AA:EPA and n-6:n-3, compared to the control group.
  - Week 8: Supplementation with EPA and DHA resulted in significantly higher EPA and DHA plasma levels, significantly lower levels of AA and significantly lower ratios of AA:EPA and n-6:n-3, compared to the control group.











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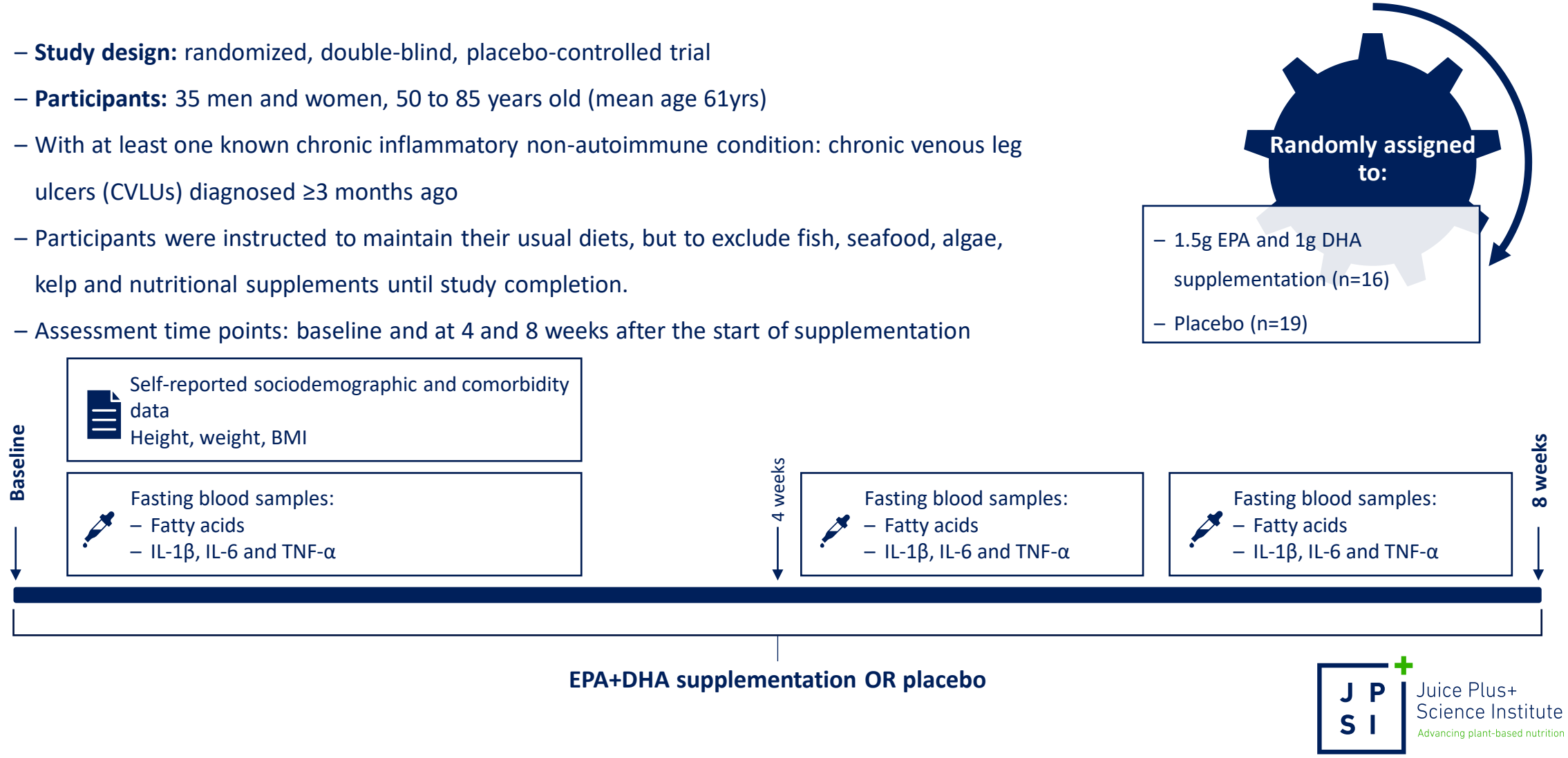
METHODS

- **Study design:** randomized, double-blind, placebo-controlled trial
- **Participants:** 35 men and women, 50 to 85 years old (mean age 61yrs)
- With at least one known chronic inflammatory non-autoimmune condition: chronic venous leg ulcers (CVLUs) diagnosed ≥3 months ago
- Participants were instructed to maintain their usual diets, but to exclude fish, seafood, algae, kelp and nutritional supplements until study completion.
- Assessment time points: baseline and at 4 and 8 weeks after the start of supplementation



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RESULTS: CYTOKINES

- EPA and DHA supplementation resulted in significantly lower levels of IL-6, IL-1β and TNF-α at 4 weeks at even lower levels at 8 weeks.
- IL-6 decreased by 12% at week 4 and 22% at week 8 in the EPA and DHA group, compared to a 3% and 4% increase, respectively, in the control group.
- IL-β decreased by 29% and a 44% at 4 and 8 weeks respectively in the EPA and DHA group, compared to 8% and 2% increases in the control group.
- TNF-α decreased by 12% and 23% at 4 and 8 weeks respectively in the EPA + DHA group, compared to a modest 1% decrease at both time points in the control group.

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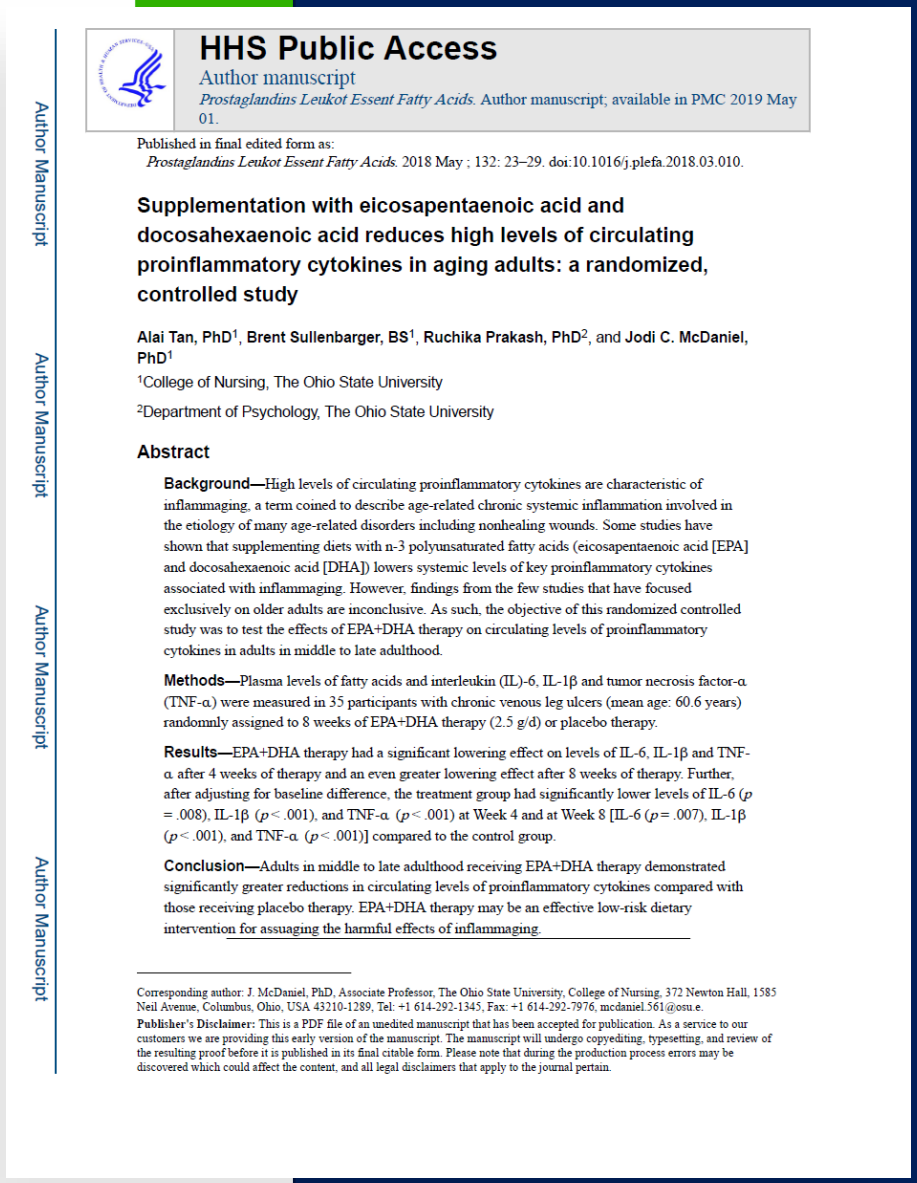
CONCLUSION

"Adults in middle to late adulthood receiving EPA+DHA therapy demonstrated significantly greater reductions in circulating levels of proinflammatory cytokines compared with those receiving placebo therapy. EPA+DHA therapy may be an effective low-risk dietary intervention for assuaging the harmful effects of inflammaging".



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Supplementation with eicosapentaenoic acid and docosahexaenoic acid reduces high levels of circulating proinflammatory cytokines in aging adults: a randomized, controlled study

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Abstract

Background—High levels of circulating proinflammatory cytokines are characteristic of inflammaging, a term coined to describe age-related chronic systemic inflammation involved in the etiology of many age-related disorders including nonhealing wounds. Some studies have shown that supplementing diets with n-3 polyunsaturated fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) lowers systemic levels of key proinflammatory cytokines associated with inflammaging. However, findings from the few studies that have focused exclusively on older adults are inconclusive. As such, the objective of this randomized controlled study was to test the effects of EPA+DHA therapy on circulating levels of proinflammatory cytokines in adults in middle to late adulthood.

Methods—Plasma levels of fatty acids and interleukin (IL)-6, IL-1β and tumor necrosis factor-α (TNF-α) were measured in 35 participants with chronic venous leg ulcers (mean age: 60.6 years) randomnly assigned to 8 weeks of EPA+DHA therapy (2.5 g/d) or placebo therapy.

Results—EPA+DHA therapy had a significant lowering effect on levels of IL-6, IL-1β and TNF-α after 4 weeks of therapy and an even greater lowering effect after 8 weeks of therapy. Further, after adjusting for baseline difference, the treatment group had significantly lower levels of IL-6 ($p = .008$), IL-1β ($p < .001$), and TNF-α ($p < .001$) at Week 4 and at Week 8 [IL-6 ($p = .007$), IL-1β ($p < .001$), and TNF-α ($p < .001$)] compared to the control group.

Conclusion—Adults in middle to late adulthood receiving EPA+DHA therapy demonstrated significantly greater reductions in circulating levels of proinflammatory cytokines compared with those receiving placebo therapy. EPA+DHA therapy may be an effective low-risk dietary intervention for assuaging the harmful effects of inflammaging.

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