

Abstract ID: [438228](#)

ABSTRACT

Background: One potential way to protect the heart and reduce the risk for cardiovascular diseases is to consume sufficient long chain omega-3 fatty acids (n-3), especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from fish or supplemental fish oil. Several recent studies reported omega-3-index (O3I) as a potential marker for coronary heart disease (CHD), indicating O3I below 4% as a higher risk while $\geq 8\%$ as a lower risk.

Objective: The aim of the present study is to observe the correlation between red blood cell (RBC) O3I level and EPA+DHA intake from the supplemental fish oil in adults.

Methods: Seventy-six males (average age: 72 yr; BMI: 27.6) and 170 females (average age: 62 yr; BMI: 26.0) from USA and Canada voluntarily participated in the study after obtaining the informed consent form. Information on the supplemental n-3 intake from EPA+DHA in ethyl ester form was obtained by online questionnaires. RBC membrane fatty acid composition was analyzed by gas chromatography from overnight fasting blood samples, and O3I levels were expressed as EPA+DHA % of total fatty acids.

Results: The average supplemental EPA+DHA intake was 1.36 g/d in all subjects, 1.26 g/d in females, and 1.58 g/d in males. The average O3I was 8.63% in all subjects, 8.59% in females, and 8.70% in males. A significant and positive correlation ($p < 0.001$) was observed between EPA+DHA intake and O3I. There was no significant difference in O3I between females and males although females ingested significantly lower amount of supplemental EPA+DHA as compared to the males ($p = 0.01$).

Conclusion: The present study showed that the average O3I in adults supplementing with fish oil containing omega-3-fatty acids (average 1.36 g/d of EPA+DHA) was higher than 8.5% in average, suggesting that O3I is influenced by their daily EPA+DHA intake from the dietary supplements containing ethyl ester form of EPA+DHA.

INTRODUCTION

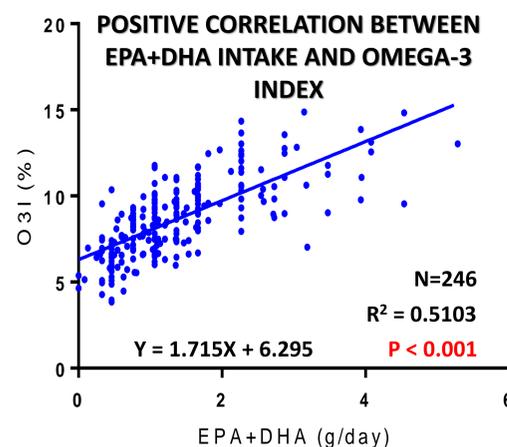
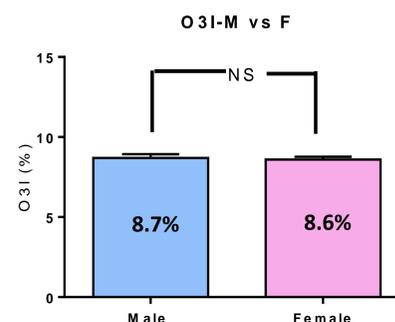
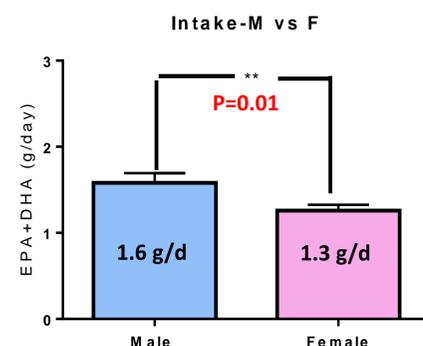
There have been numerous studies reporting the role of long-chain omega-3 polyunsaturated fatty acids (n3) intake, especially EPA and DHA, either from dietary fish intake or supplemental fish oil, in supporting heart health and lowering the risk for various cardiovascular diseases (CVD). Epidemiological evidence suggests 0.5 g – 1.8 g EPA+DHA significantly reduce the incidence of CVD, including coronary heart disease (CHD), and subsequent death as well as all-cause mortality. For adults, at least 2 servings of (fatty) fish a week is recommended, but for people who cannot achieve enough n3 intake from the diet, fish oil supplement can be an option. For patients with CHD, American Heart Association (AHA) recommends about 1 g of EPA+DHA intake a day from the diet or supplemental fish oil.

Blood n3 level can be used as a marker for fish or supplemental fish oil intake. Another biomarker for n3 intake is Omega-3-Index (O3I), which reflects a longer term n3 intake reducing day-to-day variability. O3I is expressed as % EPA+DHA of total fatty acids in the Red Blood Cell (RBC) membrane, which also corresponds to the other cell membrane EPA+DHA level, such as cardiac cells. The O3I level $\geq 8\%$ indicates a lower risk for CHD and $\leq 4\%$ a higher risk. The average O3I for US adults was 4.3%. O3I, a great biomarker for EPA and DHA intake, may also play a role as a risk factor for CVD including CHD and the death caused by various CVD.

DEMOGRAPHIC INFORMATION, SUPPLEMENTAL EPA+DHA INTAKE, and O3I (%)

| | Subject Number | Average Age (year) | Average BMI | Average EPA+DHA intake (g/d) | Average O3I (%) |
|--------------|------------------|--------------------|-------------|------------------------------|-----------------|
| All Subjects | 246 | 65 | 26.5 | 1.4 | 8.6 |
| Females | 170 [†] | 62 | 26.0 | 1.3 | 8.6 |
| Males | 76 ^{††} | 72 | 27.6 | 1.6* | 8.7 |

* Significantly higher in men than in female ($p = 0.01$); 7 women from Canada; 1 man from Canada



OMEGA-3 INDEX BY EPA+DHA INTAKE*

| EPA+DHA (g/day) | Omega-3 Index (%) |
|-----------------|-------------------|
| 0.5 | 7.2 |
| 1.0 | 8.0 |
| 1.5 | 8.9 |
| 2.0 | 9.7 |
| 2.5 | 10.6 |
| 3.0 | 11.4 |
| 3.5 | 12.3 |
| 4.0 | 13.2 |

* Calculated based on $Y = 1.715X + 6.295$

METHODS

SUBJECT - Two hundred forty six subjects, who have been using supplemental fish oil manufactured by Shaklee Corporation at least 1 year, were recruited. After signing the informed consent form approved by Hummingbird IRB, information on the fish oil intake and 30 mL blood were collected during Shaklee Annual Convention in August 2015 (See the Table for Subject Demographic Info).

FISH OIL SUPPLEMENT PRODUCTS – Two ethyl ester form of fish oil products contained either 460 mg (280 mg EPA + 180 mg DHA) per serving, or 603 mg (363 mg EPA + 240 mg DHA) per serving.

EPA+DHA INTAKE – Intake questions/answers on (1) which fish oil product, (2) how many servings per day, and (3) the number of days taking fish oil product(s) per week were used to calculate the average daily EPA+DHA intake level.

OMEGA-3 INDEX – RBC membrane fatty acid composition was analyzed by gas chromatography using overnight fasting blood samples, and O3I level was expressed as % EPA+DHA of total fatty acids.

STATISTICAL ANALYSIS – Unpaired Student-t test was used to compare the male vs. female; Linear Regression was used to analyze the correlation between n3 intake and O3I level; $P < 0.05$ was considered significant.

SUMMARY OF THE RESULTS

- The average supplemental EPA+DHA intake was 1.4 g/d in all subjects, 1.6 g/d in males, and 1.3 g/d in females.
- EPA+DHA intake was significantly higher in men than in women ($p < 0.01$).
- The average O3I was 8.6% in all subjects, 8.7% in males, and 8.6% in females.
- There was no significant difference in O3I between females and males.
- A significant and positive correlation ($p < 0.001$) was observed between EPA+DHA intake and O3I.

DISCUSSION

- The average intake of 1.4 g/d of ethyl ester form of EPA+DHA gave an average omega-3 index of 8.6% which supports bioavailability of this form of fish oil supplements.
- As compared to the 9% of US population, 57% of this population showed O3I $> 8\%$.
- Most of the subjects (99%) showed O3I $> 4.3\%$, the average for US population.
- Higher O3I level in this cohort than the general US adults (8.6% vs. 4.3%) may be due to their higher EPA+DHA intake than general US adults (1.4 g vs. 0.1 g/d per NHANES 2003-2008).
- Subjects who achieved O3I of $\geq 8\%$ had 1g/d or more of supplemental EPA+DHA intake, which is comparable to AHA recommendation.

CONCLUSIONS

Present study shows a positive correlation between supplemental EPA+DHA intake and omega-3 index and provides a validation for use of omega-3 index to assess adequate EPA+DHA intake. The levels of EPA+DHA observed in the majority of this cohort might be associated with a lower CVD risk.

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