

Oxidative stability of omega-3 dietary supplements according to product characteristics

Hyeon Jeong Kwon[★], Ho Cheol Yun, Ji Yoon Lee, Eun Jung Jeong, Hyun Nho Cho, Da Young Kim, Sung Ah Park, Seung Ju Lee, and Jung Mi Kang

Food Analysis Division, Busan Metropolitan City Institute of Health & Environment, 120, Hambakbong-ro 140 beon-gil, Buk-gu, Busan 46616, Korea

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Abstract: The objectives of the present study were to assess the oxidative stability of South Korean n-3 (omega-3 fatty acid) supplements carried out from 2018 to 2019 and evaluate the influence of product characteristics on oxidative safety. A total of 76 n-3 supplements were analysed for oxidation safety by four markers, including acid value (AV), primary oxidation (peroxide value, PV), secondary oxidation (*p*-anisidine value, *p*AV) and total oxidation value (TOTOX). Among the supplements tested, 5.3 %, 55.3 %, 28.9 % and 46.1 % exceeded the international voluntary recommended levels for AV, PV, *p*AV and TOTOX, respectively. Purity (%) of products, remainder of expiration date (suggested shelf life), package in press through package (PTP) and products with additives had statistically significant differences oxidation assessment levels ($p < 0.05$). In addition, n-3 group found in Algae oil had significantly lower AV levels than the group that did not, and product with Alaska pollack oil, had significantly higher *p*AV levels than without group ($p < 0.05$). The high oxidation status of South Korean n-3 products in the present study could not be considered a public health problem right now. However, the levels of oxidation may affect a lot the efficacy and safety of using n-3 supplements. Thus, current oxidation safety limits should be reestablished by regulatory bodies to ensure the safety and efficacy of n-3 supplements, so that the standards could be applied to the products available to consumers.

Key words: omega-3 supplement, acid value, peroxide value, anisidine value, total oxidation value

1. Introduction

Naturally occurring fatty acids are typically classified into saturated and unsaturated fatty acids, which are solid and liquid or soft solid at room temperature, respectively. Saturated fatty acids are abundant in foods such as butter, shortening, lard, chicken skin,

and bacon, and present single C–C bonds. Conversely, unsaturated fatty acids, including omega-3 (n-3) fatty acids, are abundant in beans, nuts, and blue-backed fish and present double C=C bonds.^{1,2} N-3 fatty acids can reduce blood triglyceride (TG) levels by inhibiting the synthesis of TGs and very-low-density lipoproteins in the liver. The best-known n-3 fatty

[★] Corresponding author

Phone : +82-(0)51-309-2834 Fax : +82-(0)51-309-2839

E-mail : kakw11@korea.kr

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acids are α -linoleic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA).³ ALA is not synthesized in the body, whereas EPA can be synthesized in the body using ALA; however, the conversion rate is extremely low. Therefore, both ALA and EPA are essential fatty acids that require dietary intake.^{1,4}

EPA and DHA extracted from fish or poultry are frequently added to health functional food products to prevent n-3 deficiency and lower the risk of cardiovascular disease (CVD). However, because polyunsaturated fatty acids (PUFAs) contain numerous double bonds in the fatty acid chain, EPA and DHA are vulnerable to oxidation with atmospheric O₂.^{5,6} All n-3 PUFAs are chemically unstable and, upon exposure to oxidizing environments, might produce primary peroxides, which are rapidly oxidized into secondary products; this can lead to potential consumer safety concerns.⁶ Once primary oxidation is initiated, the peroxides generated via lipid oxidation accelerate the process, and increasing peroxide levels further accelerate oxidation.^{7,8} In addition, increasing oxidation levels lead to a decrease in the efficacy of n-3 products, which would, consequently, limit the benefits on TG and cholesterol levels in the body. In an *in vivo* experiment, prolonged exposure to oxidized n-3 PUFAs delayed growth, increased inflammation, and caused myocardial disease or cancer.⁹⁻¹¹ Therefore, the oxidation level of n-3 products could significantly affect the efficacy and safety of health functional food products containing n-3 fatty acids and could negatively affect consumer sensory evaluation.

The oxidation level of n-3 products can be measured using four indicators: acid value (AV), peroxide value (PV), *p*-anisidine value (*p*AV), and total oxidation (TOTOX) level, which indicate the free fatty acid content, primary oxidation level, secondary oxidation level, and overall oxidation level, respectively. During the initial oxidation stage, the numerous double bonds of n-3 PUFAs are broken to generate free radicals and promote the chemical formation of peroxides and dienes; moreover, further O₂ exposure would increase the amounts of secondary products, such as carbonyl compounds and aldehydes.¹² These oxidation

products reduce the quality of n-3 products as they create off flavor and undesirable colors. During oxidation, PV increases with time; however, upon continuous exposure to an oxidizing environment, PV decreases as the primary products are eventually decomposed into secondary products. Therefore, it is critical that *p*AV and TOTOX, which are indicators of secondary and overall oxidation levels, be analyzed.⁷

Currently, there are no legal restriction regarding the oxidation of n-3 products in the U.S. and Canada; however, voluntary management standards, which have been recommended by the Global Organization for EPA and DHA Omega-3s (GOED), Council for Responsible Nutrition (CRN), and International Fish Oil Standards (IFOS), are independently applied.⁶ In an effort to control n-3 product oxidation, in South Korea, the standards for AV and PV were set for the first time on Feb 28, 2018 in the *Standards and Specifications of Health Functional Foods*, as Notification 2018-12 of the Ministry of Food and Drug Safety. For a more integrated management of the oxidation stability of n-3 products, the criteria for *p*AV and TOTOX have been added in the revision of Notification 2019-82, which was implemented on Jul 1, 2020.¹³ In addition, as n-3 PUFA-containing health functional foods could present foreign taste or odor owing to the raw material characteristics and high probability of oxidation, food additives, including antioxidants and flavor enhancers, are often used to improve the oxidation stability and flavor of many products. Moreover, product characteristics vary depending on raw material types, purity, expiration date, capsule packaging, capsule type, product form, and place of origin. Nevertheless, there is a general lack of studies that monitored the oxidation levels of n-3 products in South Korea and abroad, and only a few reports comparing oxidation levels according to the individual characteristics of health functional foods containing n-3 fatty acids have been published.

Therefore, in this study we monitored the oxidation levels of commercially available health functional foods containing n-3 fatty acids using four indicators: AV, PV, *p*AV, and TOTOX, and compared the oxidation levels according to different product characteristics.

2. Experimental Design

2.1. Samples

We analyzed the oxidation levels of 76 commercially available health functional foods containing n-3 fatty acids. Samples were collected between Feb 6, 2018 and Sep 5, 2019, and the analyses were performed between May 13, 2019 and Oct 14, 2019. The expiration dates of the samples ranged between Jun 27, 2019 and Feb 15, 2022, and all analyses were performed within the expiration date. The time to expiration on the day of analysis ranged between 27 and 971 days. The EPA and DHA content (EPA + DHA) per capsule indicated on the product labels ranged between 200-1200 mg and the EPA + DHA content based on the daily intake (one capsule) ranged between 13.64-95.67 %.

2.2. Tests

To measure the oxidation levels of health functional foods containing n-3 fatty acids, we determined the AV, PV, pAV, and TOTOX levels of all samples. The standard for adequate oxidation level was determined using the standard for fish oils (CSX 329-2017) and the standard for edible fats and oils not covered by individual standards (CXS 19-1981), which are recommended by the Codex Alimentarius Commission created by the Food and Agriculture Organization of the United Nations.^{14,15}

2.3. Reagents

The reagents used for lipid extraction and oxidation level estimation were purchased from Merck KGaA (Germany), Sigma-Aldrich (USA), and Wako (Japan).

2.4. Lipid extraction

Lipid extraction for the n-3 fatty acid products that contained ingredients other than lipids, such as food additives, was performed in advance using the methods described in the Codex Alimentarius. In brief, the capsules were removed and approximately 50 g of homogenized sample was added to a 500 mL conical flask. Subsequently, the sample was mixed with 100 mL of diethyl ether and was allowed to

stand for approximately 2 h with occasional shaking. Next, the mixture was filtered using a No. 4 filter paper (Whatman, UK) and the filtrate was transferred to a separatory funnel. Thereafter, the sample in the conical flask was mixed with 50 mL of diethyl ether followed by shaking; the mixture was filtered using the same type of filter paper, and the second filtrate was added to the first filtrate. Subsequently, 100 mL of distilled water was added to the conical flask for washing with adequate shaking, and then the water layer was removed. This step was repeated twice. Next, the ether layer was collected and dehydrated with Na₂SO₄ followed by decompression in a 40 °C water bath to completely remove the residual ether. The resulting lipid was used for oxidation level measurements.

2.5. AV measurements

The AVs of the n-3 products were measured using the method described in the Codex Alimentarius. In brief, 5 g of sample was accurately weighed and placed in a 250 mL conical flask to be dissolved in 100 mL of a mixture of ethanol and diethyl ether (1:2, v/v). The solution was titrated with a 0.1 N KOH solution in ethanol in the presence of phenolphthalein as the indicator, until the solution remained light red for 30 s. The same method was used to titrate the blank for calibration. AV was calculated as follows:

$$\text{AV}(\text{mg KOH/g of sample}) = \frac{(A - B) \times N \times f \times 56.11}{M}$$

where A and B are the volumes of standard alkali solution (mL) used for titrating the sample and blank, respectively, N is the normality of the standard alkali solution (0.1 N), *f* is the factor of the standard alkali solution, and M is the mass of sample (g).

2.6. PV measurements

The PVs of the n-3 products were measured using the method described in the Codex Alimentarius. In brief, 5 g of sample was accurately weighed and added to a 100 mL conical flask with a lid to be dissolved in 25 mL of a mixture of acetic acid and chloroform (3:2, v/v) under shaking. After mixing

with 1 mL of a saturated KI solution via gentle shaking, the solution was allowed to rest for 10 min in a shaded area. Subsequently, 30 mL of water was added and mixed via strong shaking, and the resultant solution was titrated with 0.01 N sodium thiosulfate solution using 1 mL of starch reagent as the indicator. The same method was used to titrate the blank for calibration. PV was calculated as follows:

$$\text{PV(mEq peroxide/1000 g of sample)} = \frac{(S-B) \times N \times f \times 100}{M}$$

where S and B are the volumes of titrant (mL) used for titrating the sample and blank, respectively, N is the normality of the sodium thiosulfate solution (0.1 N), *f* is the factor of the sodium thiosulfate solution, and M is the mass of sample (g).

2.7. *pAV* measurement

The *pAV*s of the n-3 products were measured using the Official Method Cd 18-90 of the American Oil Chemists' Society.¹⁶ In brief, the test stock solution was prepared by adding 0.5 ± 0.001 g of sample, which was accurately weighed, to a 25 mL brown volumetric flask followed by adding isooctane to constant volume. The absorbance of the samples was measured at 350 nm using a UV-1900 (Shimadzu, Japan) UV-vis spectrophotometer with 10×10 mm quartz cells and utilizing isooctane as the blank. The *p*-anisidine standard stock solution was prepared by dissolving 0.25 g of *p*-anisidine, which was accurately weighed, in 100 mL of glacial acetic acid. Thereafter, the standard solution was prepared by mixing 1 mL of the standard stock solution with 5 mL of isooctane. Next, 1 mL of standard stock solution was mixed with 5 mL of test stock solution, and the mixture was allowed to stand for 10 min before it was used as the test solution. The absorbance of the test solution was measured using the aforementioned method and the standard solution as the blank. *pAV* was calculated as follows:

$$pAV = \frac{25 \times (1.2A_s - A_b)}{m}$$

where *A_s* is the absorbance of the test solution after

it reacted with *p*-anisidine (measured by filling the reference cuvette with sample solution), *A_b* is the absorbance of the test stock solution (measured by filling the reference cuvette with isooctane), and *m* is the mass of sample (g).

2.8. TOTOX measurements

The TOTOX levels of the n-3 products was calculated as follows:

$$\text{TOTOX} = 2\text{PV} + pAV$$

2.9. Statistical analysis

The R version 3.6.1 (The R Foundation for Statistical Computing, Austria) software was used to estimate the descriptive statistics parameters, such as the mean and standard deviation, for each variable. Statistical significance was tested using the t-test, one-way ANOVA, Pearson correlation analysis, and general linear regression analysis, and the level of statistical significance was set to $p < 0.05$.

3. Results and Discussion

3.1. Monitoring oxidation levels of n-3 dietary supplements

The oxidation levels of 76 health functional foods containing n-3 fatty acids purchased from department stores and hypermarkets in South Korea were monitored between Feb 2018 and Sep 2019. Among the 76 samples, 4 exceeded the standard level for AV by 5.3 %, 42 exceeded the standard level for PV by 55.3 %, 22 exceeded the standard level for *pAV* by 28.9 %, and 35 exceeded the standard level for TOTOX by 46.1 % (Table 1). The mean PV and TOTOX of the analyzed samples were 9.30 ± 16.46 meq/kg and 37.25 ± 40.13 , respectively, which indicated that the level of oxidation of the analyzed samples was higher than the average global recommended level.

3.2. Dependence of oxidation levels on EPA + DHA content and purity

The EPA and DHA content (the sum of the individual EPA and DHA contents; EPA + DHA) per capsule

Table 1. Oxidation levels for n-3 dietary supplements and number of products that failed safety standard

Oxidation assessment	Descriptive		Exceeded standard ¹⁾	
	N	Mean \pm SD	N	% of total
Acid value	76	0.82 \pm 1.14	4	5.3
Peroxide value	76	9.30 \pm 16.46	42	55.3
<i>p</i> -anisidine value	76	18.65 \pm 24.50	22	28.9
Total oxidation value	76	37.25 \pm 40.13	35	46.1

¹⁾Number of products that exceeded the CODEX/FAO standard for fish oils (CXS 329-2017) for AV (values > 3 mg KOH/g), PV (values > 5 mEq/kg), *p*AV (values > 20) and TOTOX (values > 26). but, that applied the CODEX/FAO standard for edible oils (CXS 19-1981) for AV (values > 0.6 mg KOH/g), PV (values > 10 mEq/kg) if the raw material of sample is Algae.¹⁴⁻¹⁵

indicated on product labels varied between 200 and 1200 mg. The products were divided into two groups: Group I with EPA + DHA \leq 600 mg and Group II with EPA + DHA > 600 mg, and the differences in mean oxidation level indicators between the groups were analyzed using the t-test. The mean oxidation level indicators were as follows: AV = 1.03 \pm 1.52, PV = 6.96 \pm 5.47, *p*AV = 26.66 \pm 29.43, and TOTOX = 40.57 \pm 30.51 for Group I and AV = 0.69 \pm 0.85, PV = 10.67 \pm 20.25, *p*AV = 13.98 \pm 20.00, and TOTOX = 35.32 \pm 45.00 for Group II. The differences between the mean values for Groups I and II were not statistically significant ($p > 0.05$). To analyze the effect of product purity on the oxidation level, the EPA + DHA content based on the daily intake indicated on the product label was expressed as purity (%) and correlation analysis was performed. The purity ranged between 13.64-95.67 %, with a mean of 65.4 \pm 22.11 %, and was not significantly correlated with PV, *p*AV, or TOTOX

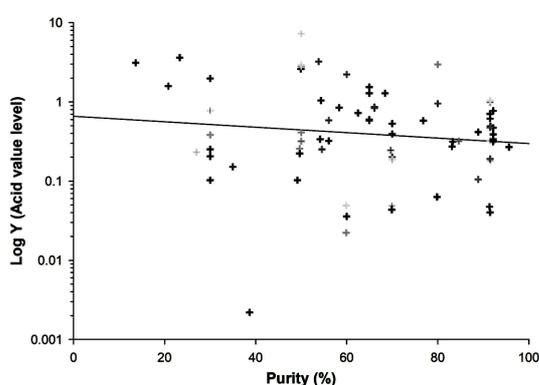


Fig. 1. Correlation between purity and AV in n-3 dietary supplements (Correlation is significant at the 0.05 level in Pearson's 2-tailed test, $r = -0.292$).

($p > 0.05$). However, AV was significantly correlated with purity ($p < 0.05$), with a correlation coefficient (r) of -0.292, which indicated a negative correlation at $p = 0.05$. Therefore, it could be hypothesized that the lower the purity, the higher the AV. For a more accurate statistical analysis, the values were further tested using the multiple regression equation. The correlation between AV and purity was significant ($b = -1.863$, $t = -2.403$, $p = 0.020$), which indicated that a decrease in purity would lead to an increase in AV (Fig. 1).

3.3. Dependence of oxidation levels on expiration date

All samples were analyzed within the expiration date on the product label. Based on the test date, the products were divided into Group I, with a time to

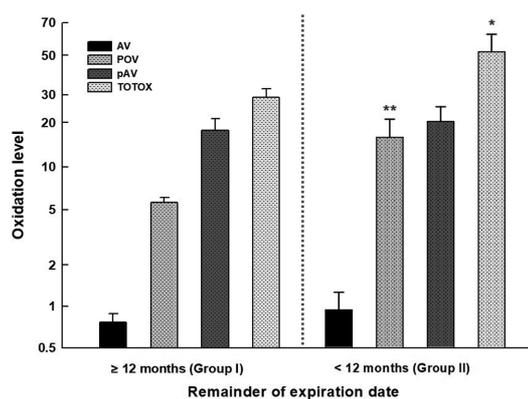


Fig. 2. Oxidation mean levels of total products tested that were divided into two groups by remainder of expiration date. Error bars represent \pm standard error (Values were significantly different by t-test, *: $p < 0.05$, **: $p < 0.01$).

expiration longer than 1 year, and Group II, with a time to expiration shorter than 1 year. The differences in mean oxidation level indicators were analyzed using the t-test (Fig. 2).

The mean oxidation level indicators of the 49 products in Group I were as follows: AV = 0.76 ± 0.89 , PV = 5.66 ± 3.26 , pAV = 17.75 ± 24.03 , and TOTOX = 29.08 ± 25.47 , and those of the 27 products in Group II were as follows: AV = 0.94 ± 1.58 , PV = 15.91 ± 26.30 , pAV = 20.27 ± 25.72 , and TOTOX = 52.10 ± 55.62 . The differences between the mean oxidation level indicators for Groups I and II indicated that AV and pAV were not significantly correlated with the expiration date ($p > 0.05$). However, the mean PV of Group II was 10.25 higher than that of Group I ($t = 2.706$, $p = 0.008$) and the mean TOTOX of Group II was 23.02 higher than that of Group I ($t = 2.036$, $p = 0.050$), which were statistically significant. Therefore, the result indicated that PV and TOTOX increased as the expiration date approached.

3.4. Dependence of oxidation levels on capsule packaging

The capsule packaging of n-3 products could be divided into two types: packages obtained using a pressure-based method known as *press through package*

(PTP) (Group I) and bottles made of polyethylene, polypropylene, or polyethylene terephthalate (Group II). The differences in the mean oxidation level indicators of n-3 products stores in these two types of packages were analyzed using the t-test. The oxidation levels of the 22 products in Group I were AV = 1.44 ± 1.70 , PV = 9.44 ± 5.89 , pAV = 21.28 ± 19.17 , and TOTOX = 40.17 ± 23.92 . and those of the 54 products in Group II were AV = 0.56 ± 0.68 , PV = 9.25 ± 19.23 , pAV = 17.58 ± 26.46 , and TOTOX = 36.07 ± 45.25 . The mean PV, pAV, and TOTOX of Groups I and II were not significantly different ($p > 0.05$); however, the mean AV of Group I was 0.88 higher than that of Group II ($t = 2.341$, $p = 0.028$), which was significantly different. This was attributed to common PTP materials (i.e., polyvinyl chloride and polyvinylidene dichloride) being unable to completely prevent oxidation caused by temperature, humidity, or air exposure.¹⁷

3.5. Dependence of oxidation levels on raw material type

The 76 samples of n-3 products were divided into 13 groups (Groups A–M) depending on the raw material type, as follows: anchovy (A), sardine (B), mackerel (C), salmon (D), tuna (E), Alaska pollack

Table 2. Oxidation levels of n-3 dietary supplements by material groups

Group	Materials	N	AV	PV	pAV	TOTOX
A	Anchovy	14	1.04 ± 1.91	7.30 ± 4.88	12.22 ± 7.06	26.82 ± 14.11
B	Sardine	1	0.38	6.77	17.92	31.45
C	Mackerel	4	1.85 ± 0.94	7.79 ± 2.72	17.08 ± 14.22	32.65 ± 18.99
D	Salmon	8	0.55 ± 0.29	7.07 ± 3.98	14.88 ± 4.47	29.02 ± 12.12
E	Tunas	1	0.53	21.27	31.77	74.31
F	Alaska pollack	10	0.95 ± 1.12	5.15 ± 2.30	37.73 ± 47.07	48.03 ± 46.70
G	Algae ¹⁾	8	0.57 ± 1.03	6.67 ± 8.28	34.71 ± 44.51	48.06 ± 43.57
H	Pacific cod	1	0.06	20.74	32.27	73.75
I	Anchovy and Sardine	9	0.72 ± 0.91	5.82 ± 2.38	11.11 ± 6.40	22.75 ± 10.86
J	Anchovy, Sardine and Mackerel	15	0.83 ± 0.99	18.68 ± 35.03	9.97 ± 7.84	47.33 ± 71.13
K	Anchovy, Mackerel and Salmon	1	0.61	4.04	7.47	15.56
L	Anchovy, Sardine, Mackerel and Salmon	2	0.36 ± 0.04	4.57 ± 2.32	15.31 ± 4.58	24.44 ± 9.22
M	Refined fish oil	2	0.28 ± 0.07	8.89 ± 1.52	17.08 ± 7.69	34.85 ± 10.73
Total		76	0.82 ± 1.14	9.30 ± 16.46	18.65 ± 24.50	37.25 ± 40.13

Values are Mean \pm SD

¹⁾Include commodity of *Schizochytrium sp.*

(F), algae (G), Pacific cod (H), anchovy + sardine (I), anchovy + sardine + mackerel (J), anchovy + mackerel + salmon (K), anchovy + sardine + mackerel + salmon (L), and refined fish oil (unknown raw material) (M), and the oxidation levels were analyzed (Table 2). In addition, correlation and multiple regression analyses were performed to examine whether the oxidation levels of the products obtained from certain raw materials were significantly different from those of the products that were not derived from those raw materials (Fig. 3).

Group C presented the highest mean AV of 1.85 ± 0.94 . Correlation and multiple regression analyses indicated that AV did not depend significantly on the raw material for most groups ($p > 0.05$), except for Group G ($p < 0.05$), for which r was -0.171 . Moreover, while correlation analysis indicated that AV did not depend significantly on the raw material of Group G

at $p = 0.05$ ($p = 0.077$), multiple regression analysis of product characteristics revealed a significant correlation between the raw material of Group G and AV ($b = -1.525$, $t = -2.669$, $p = 0.010$), which could indicate that the AV of algae-derived n-3 products might be low.

Group J presented the highest mean PV of 18.68 ± 35.03 , and PV did not depend significantly on the raw material for any group ($p > 0.05$).

Group F presented the highest mean pAV of 37.73 ± 47.07 . Moreover, statistical analysis revealed that pAV was significantly correlated with the raw material of Group F ($p < 0.05$), and r was 0.420 , which indicated a positive correlation at $p = 0.01$ ($p = 0.001$). This could indicate that the pAV of Alaska pollack-derived n-3 products might be high. Therefore, for more accurate statistical analysis, the pAV levels were tested using the multiple regression equation,

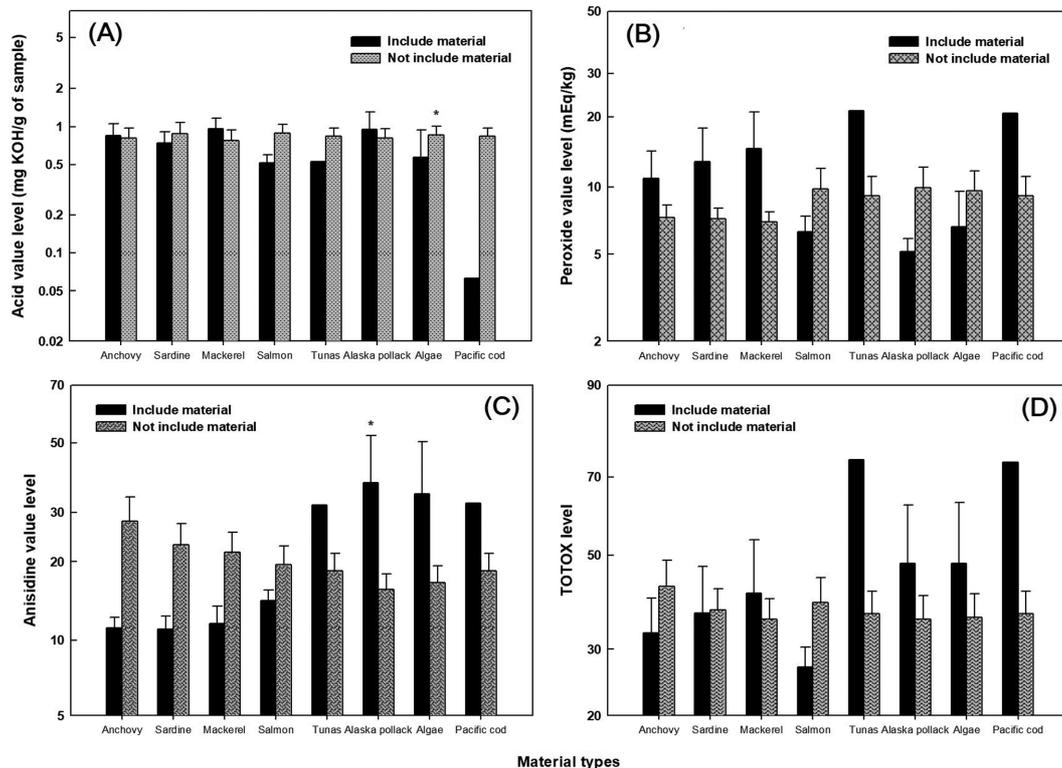


Fig. 3. AV (A), PV (B), pAV (C), TOTOX (D) levels (mean \pm SD) of n-3 dietary supplements available in South Korea grouped by the material types. Error bars represent \pm standard error (Values were significantly different by regression analysis, *: $p < 0.01$).

which is typically used to perform factor analysis of product characteristics. The correlation between *pAV* and raw material of Group F was significant ($b = 29.193$, $t = 2.642$, $p = 0.011$), which indicated that Alaska pollack-derived n-3 products presented high *pAV*s.

Group G presented, the highest mean TOTOX of 48.06 ± 43.57 , and statistical analysis revealed that TOTOX was not significantly correlated with the raw material of any group ($p > 0.05$).

Recently, plant-derived lipids such as flax and evening primrose seed oils have received significant attention.¹⁸ This has been attributed to health functional foods containing plant-derived materials, unlike those containing animal-derived materials, being good sources of saturated and unsaturated fatty acids and also rich sources of vitamins and antioxidants. Bialek *et al.* (2017) studied¹⁹ the oxidation levels of plant-derived lipids and reported the following data: $AV = 2.07 \pm 0.01$ and $PV = 12.0 \pm 3.43$ for borage oil, $AV = 1.28 \pm 0.04$ and $PV = 11.0 \pm 1.56$ for evening primrose seed oil, $AV = 1.20 \pm 0.05$ and $PV = 12.5 \pm 1.12$ for flax seed oil, and $AV = 0.90 \pm 0.03$ and $PV = 13.3 \pm 2.33$ for safflower seed oil. Therefore the *AV*s and *PV*s of the analyzed plant-derived lipids were similar and slightly higher, respectively, than those of the n-3 dietary supplements in this study.

3.6. Statistical analysis to determine the dependence of oxidation levels on other factors

Vitamin E, the most popular antioxidant, was present mostly as *D- α -tocopherol*, and the oxidation levels of the antioxidant-containing samples did not significantly change with the antioxidant content (t-test, $p > 0.05$).

All samples were capsulated; most capsules were soft and were made of pork skin gelatin, and some capsules were made of bovine skin gelatin or modified starch. One-way ANOVA was used to compare the differences in the mean oxidation level indicators of samples with different capsule materials, and the results revealed no statistically significant differences ($p > 0.05$).

Correlation and regression analyses were performed

to investigate the effect of re-esterified triglycerides, a representative n-3 product, on mean oxidation levels, and no significant differences were observed ($p > 0.05$).

The place of origin of the raw materials of the 76 commercially available health functional foods containing n-3 fatty acids were divided into 11 groups as follows: the largest number of raw materials originated from the U.S. (28), followed by Canada (19), Norway (14), Peru (4), New Zealand (2), Germany (2), Chile (2), China (1), France (1), South Korea (1), and unknown (2). The oxidation levels were not correlated with the place of origin of the raw materials, and regression analysis revealed no significant differences ($p > 0.05$).

4. Conclusions

Omega-3 fatty acids are essential fatty acids that are not synthesized in the body, and therefore, require dietary intake. Omega-3 fatty acids, and in particular the well-known EPA and DHA are abundant in blue-backed fish and poultry and can reduce the risk of CVD by improving blood circulation. Owing to their benefits, n-3 fatty acids have been recently used in health functional food products; however, the large number of double bonds in their structure renders them prone to oxidation. Therefore, in this study we comparatively analyzed four oxidation level indicators (i.e., *AV*, *PV*, *pAV*, and TOTOX) of commercially available n-3 products and examined the dependence of oxidation levels on product characteristics based on the fatty acid content of the samples. Our results revealed that the *PV* during the initial oxidation stage and TOTOX for the overall oxidation process exceeded the standard levels by approximately 50%, which indicated that the analyzed products presented low oxidation stability regardless of the time to expiration. This indicated that product efficacy could be reduced and consumer sensory evaluation could be negatively affected. An increase in oxidation level can limit the blood TG and cholesterol level lowering effects of n-3 products; moreover, prolonged exposure to oxidated lipids was hypothesized to increase

inflammation or cause cancer. However, there is a general lack of clinical and hazard assessment studies regarding the intake of oxidized lipids. Currently, the international criteria for n-3 products include recommendations for raw materials but not for final products; moreover, the international recommendations are based on highly conservative standards and the findings regarding oxidation levels cannot be used to predict possible negative effects on human health. The South Korean standards for n-3 products, as revised and implemented since Jul 1, 2020, are only recommended for raw materials and antioxidant-containing products. Therefore, because the standards cannot be used for products that contain additives other than antioxidants, products with low oxidation stability may be commercially distributed. If such n-3 products with low efficacy and safety are used to maintain healthy blood circulation, the probability that they could cause significant consumer health problems is high. Therefore, policy-related efforts should be made, including an extensive revision of the standards, which should adequately consider potential hazards and should take into account the safety of the products used by consumers and the manufacturing reality in South Korea.

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Authors' Position:

Hyeon Jeong Kwon : Researcher
 Ho Cheol Yun : Researcher
 Ji Yoon Lee : Researcher
 Eun Jung Jeong : Researcher
 Hyun Nho Cho : Researcher

Da Young Kim : Researcher
 Sung Ah Park : Research team leader
 Seung Ju Lee : Research team leader
 Jung Mi Kang : Research manager