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Omega-3 Fatty Acids and Mental Health: Assessment of Pharmacists' Knowledge and Educational Needs

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Abstract

Introduction: There has been a growing interest in Omega-3 fatty acids (FAs) for mental/cognitive health. Cognitive impairment, a global problem affecting millions of people, is frequent among elderly, and it influences the individual's ability to function independently. Omega-3 FAs are natural health products (NHPs), and pharmacists are the front-line healthcare practitioners who provide counselling to patients. **Purpose**: To identify the current knowledge status of pharmacists on Omega-3 FA NHPs and their confidence levels in counselling patients on these products via a study done in pharmacies in Ontario, Canada. **Methods**: To identify areas for improvement we assessed knowledge and understanding of Omega-3 FA NHPs of community and hospital pharmacists via a survey. **Results**: Seventy-six percent of pharmacists were enquired about Omega-3 FA at least once per month. Pharmacists have good knowledge of Omega-3 chemistry, major components, and differences between Omega-3 and -6 FAs. Sixty-four percent of responders identified brain health as benefits; the other health benefits are less widely recognized. Sixty percent of pharmacists were concerned about the increased risk of bleeding; however, only 6% felt confident in counselling patients on Omega-3 FA NHPs. Previous training on Omega-3 was associated with better knowledge of Omega-3 and had positive impact on pharmacists' confidence in counselling. **Conclusion**: There are gaps in pharmacist's current knowledge on Omega-3 FA health benefits and there is unsatisfactory confidence in providing patient counselling. Thus, there is a need for comprehensive education on Omega-3 FA NHPs in addition to traditional medical, naturopathic, and pharmacy formal education.

Keywords: Omega-3, Fatty Acid, Pharmacist, Mental Health, Brain Health, Cognitive Health

Introduction

Cognitive impairment significantly influences an individual's ability to function independently (World Health Organization, 2022). Presently, there is no cure for cognitive

impairment such as dementia or late-onset Alzheimer's disease (AD), so prevention is the key management component. There has recently been an increasing interest in the benefits of polyunsaturated Omega-3 fatty acids (FAs) for mental/cognitive health. Omega-3 FAs have the first double bond between the third and fourth carbon atoms. The most common Omega-3 FAs are docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), alpha-linolenic acid (ALA), and docosapentaenoic acid (DPA). Omega-3 FAs, particularly EPA and DHA, play a key part in the regulation of neuronal structure and function, and have been shown to improve brain function (Bradbury, 2011). Since the brain cannot synthesize EPA and DHA, Omega-3 FAs need to be obtained via diet, be provided by the blood, and be transported across the blood brain barrier throughout life to support the building and maintenance of optimal brain structure and function. Foods containing Omega-3 FAs are mainly oily fish and algae; flax seeds and chia seeds are also examples of Omega-3 sources. Clinical evidence is available in supporting the use of Omega-3 in cognitively impaired patients, such as mild cognitive impairment (MCI), AD, and dementia. There is conflicting evidence as some studies show benefits, while others suggest that Omega-3 supplementation has limited effects on cognition. Overall, higher dose Omega-3 formulations with a total dose of >1,000mg are more efficient in supporting cognitive health. Efficacy response to Omega-3 FA natural health product (NHP) supplements was also more noticeable with formulations containing higher DHA amounts (Andriambelo et al., 2023; Wei et al., 2023; US National Institutes of Health, 2024).

Pharmacists are frequently asked by patients, caregivers, and/or general consumers for counselling on NHPs by using evidence-based information to ensure product selection for appropriate patient populations (Kwan et al., 2006). This includes the use of Omega-3 NHP over the counter (OTC) supplements and its benefits on cognitive health. Since pharmacists are the main healthcare practitioners who provide counselling on Omega-3 OTC products, we therefore assessed the current knowledge of community pharmacists on their knowledge in areas specifically relating to the safety and benefits of Omega-3 for cognitive and brain health.

Materials and Methods

We designed a 13-item survey for pharmacists. Questions were designed in multiple choice format and aimed to assess the following domains: demographics, experience on Omega-3 and cognitive health, knowledge on Omega-3 components, sources and dosages, benefits, safety, previous training on Omega-3, and level of confidence to counsel patients about Omega-3 NHPs. We validated the questionnaire through confirmatory factor analysis described previously (Grew et al., 2019). We equally approached local retail community pharmacies in all areas of Barrie, Ontario, Canada, as well as local hospital to obtain equal representation from different geographic areas,

regardless of pharmacy size. After obtaining informed consent the questionnaire was given to random, unselected pharmacists at local hospital or retail community pharmacies in Barrie, Ontario, Canada. The responses were obtained between February and April 2024. Information was input into Microsoft Excel. Results were analyzed using GraphPad Prism computer software. Descriptive statistics were applied. Assuming that data was not normally distributed and due to relatively small sample size we used a non-parametric Mann-Whitney U test. Data yielding a $p<0.05$ was considered statistically significant. We calculated hazard ratios (HR) for pharmacists' previous training on Omega-3 and work experience on correct answers using Cox proportional Hazard Model. Prism 10.1 software was used for analysis.

Results

Demographics and Exposure to Omega-3 FAs

Fifty-two pharmacists were offered to participate in the study and 50 pharmacists (96%) completed the survey. Demographics demonstrated participant diversity is shown in Table 1.

Table 1: Demographics. Data presented as number of participants (N) and percentage (%)

Gender	N, (%)	Age (years)	N, (%)	Work experience (years)	N, (%)
Male	30, (60)	20-29	6, (12)	0-4	9, (18)
Female	20, (40)	30-39	23, (46)	5-9	16, (32)
-	-	40-49	16, (32)	10-14	12, (24)
-	-	50-59	4, (8)	15-19	5, (10)
-	-	60+	1, (2)	20-24	5, (10)
-	-	-	-	25-29	1, (2)
-	-	-	-	30+	2, (4)

In spite of the relatively overall younger age, 50% of respondents had 10 or more years of work experience, while 50% had less than 10 years of experience practicing as licensed pharmacists.

Of the 50 participants, 76% had experience with customers enquiring about Omega-3 NHPs. About a quarter (26%) of the participants were being enquired at least once per week or per day (Figure 1). Twenty-four percent of pharmacists, however, had never been approached by their customers about this topic.

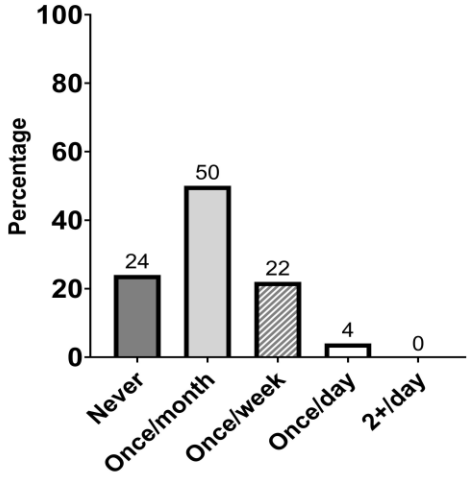

Figure 1: Omega-3 FA NHPs: How often pharmacists are asked about Omega-3 fatty acids

Omega-3 FA Chemistry and Components

We then assessed participants' knowledge of Omega-3 FA chemistry. In Omega-3, the double bond is located between the third and fourth carbon atoms (correct answer), while in Omega-6 it is between the sixth and seventh atoms. The question was correctly answered by 75% of responders (Figure 2).

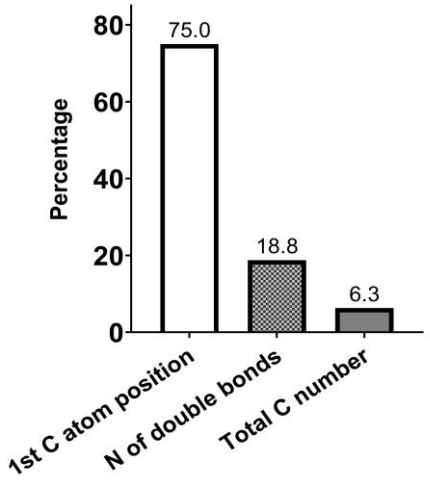

Figure 2: Knowledge of Omega-3 chemistry. C, carbon; N, number

Over 95% correctly recognized DHA and EPA as the main Omega-3 FA components; however, a significantly lower percentage of the participants identified alpha-linoleic acid (40%) and docosapentaenoic acid (18%) as other Omega-3 FA components (Figure 3). DHA, EPA, ALA and DPA are the main components of the Omega-3 FAs. There was no statistically significant correlation between correct identification of DHA or EPA and years of work experience as a pharmacist. However, the results of the Cox Proportional Hazard Model showed that previous training was associated with correct identification of DHA and EPA with a hazard ratio (HR) 0.29 (95% CI 1.07, 1.51; p=0.016).

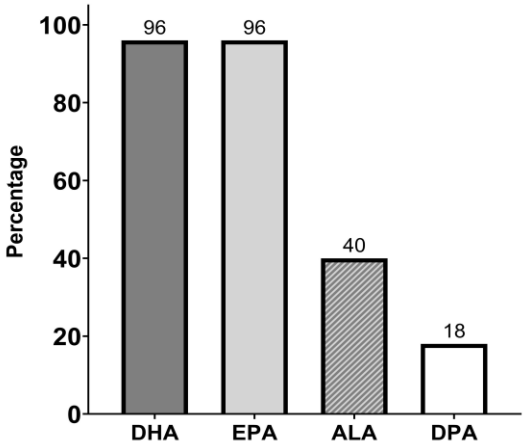

Figure 3: Familiarity with Omega-3 Components. DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; ALA, alpha-linoleic acid; DPA, docosapentaenoic acid

Omega-3 FA Source

Sixty-eight percent of respondents correctly identified diet as the main source of Omega-3 FA (Figure 4A). None of the responders mentioned the ability of human body to synthesize Omega-3 FA de novo as a solo source of Omega-3 FA. However, 32% mentioned both, which was incorrect. For primary sources of Omega-3 FA, 100% correctly identified fish, but only 18% mentioned algae as an additional source of Omega-3 FA (Figure 4B). Fatty fish and algae are the primary sources of Omega-3 FAs. Similar to the previous question, there was an association of the previous training with correct identification of algae, HR 1.42 (95% CI 1.23, 1.61; p=0.018).

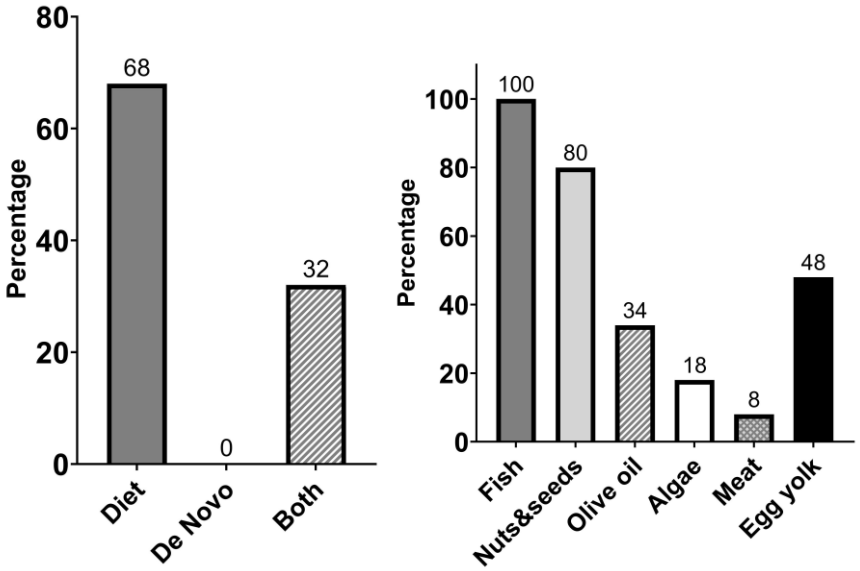

Figure 4: Familiarity with Omega-3 FA sources (A) Diet versus De Novo (B) Food sources

Omega-3 FA Benefits

One of the most recognized Omega-3 FA benefits is mental health (Phillips et al., 2015; Irving et al., 2009; Freund-Levi et al., 2008; Hooper et al., 2017; Boston et al., 2004; Yurko-Mauro et al., 2010; Quinn et al., 2010; Sinn et al. 2012.) Clinical benefits of Omega-3 FAs in patients with cognitive impairment, AD, and dementia (correct answer) were identified by 64-82% of the responders; the remaining health benefits are less well known (Figure 5). Interestingly, only 30% mentioned cardiovascular benefits of Omega-3 FAs.

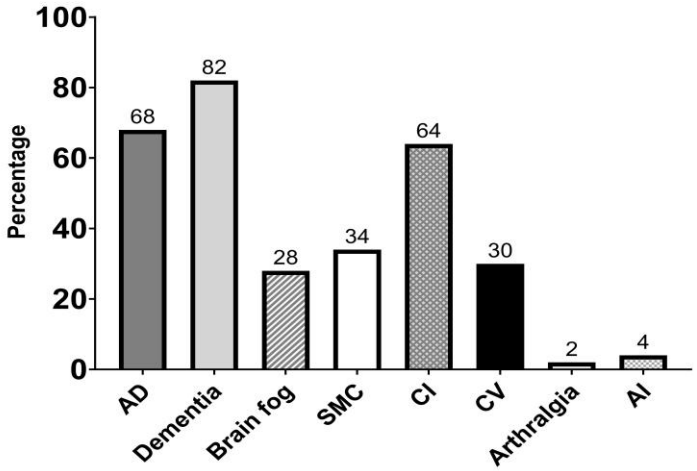

Figure 5: Benefits of Omega-3 NHPs. AD, Alzheimer's disease; SMC, subjective memory complains; CI, cognitive impairment; CV, cardiovascular; AI, autoimmune

Omega-3 FA Dosing

Thirty-eight percent of pharmacists recognized 5,000mg (correct answer) as the maximum recommended dose (MRD) listed in the product monograph. Only 2% considered MRD to be dependent on age and condition being treated (Figure 6A). Twenty percent identified the minimum and maximum doses listed in the Health Canada (HC) Fish Oil Monograph to support cognitive health (Figure 6B) and/or brain function. Six percent of those who answered the question correctly had previous training on Omega-3, HR 1.23 (95% CI 1.03, 1.52; p=0.012). Twelve percent of pharmacists had work experience over 10 years or more, and 2% had less than 10 years of experience. The correlation between work experience and correct answer was, however, not significant.

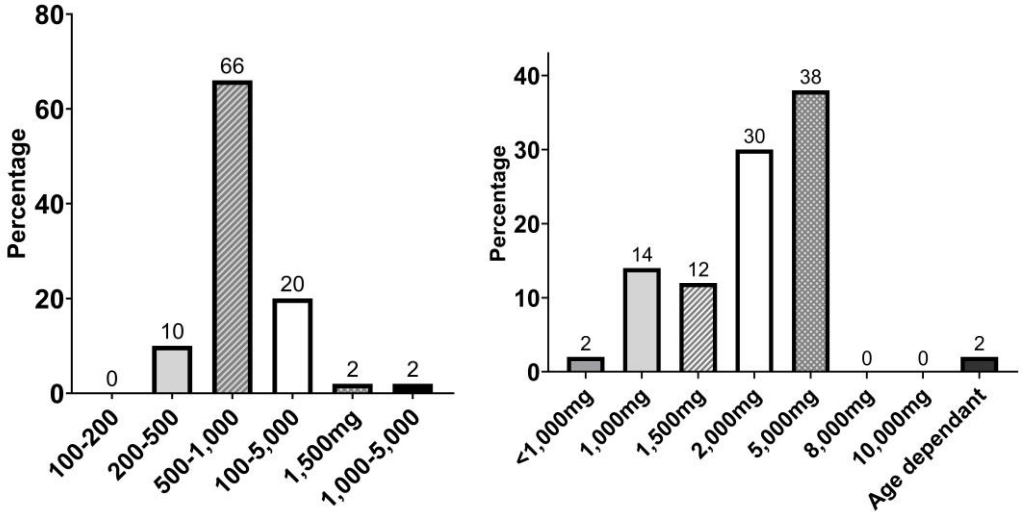

Figure 6: (A) Maximum recommended dose of Omega-3 NHPs (B) Health Canada minimum and maximum dose range of Omega-3 FAs for mental health support

Safety and Pharmacist's Confidence Level

Regarding adverse events that may be related to Omega-3 FA NHPs, 60% of pharmacists were concerned about increased risk of bleeding, 8% about atrial fibrillation, 16% about prostate cancer, 28% mentioned hypotension, and 26% were not aware of serious safety concerns (correct answer) associated with Omega-3 FAs (Health Canada, 2024b). (Figure 7).

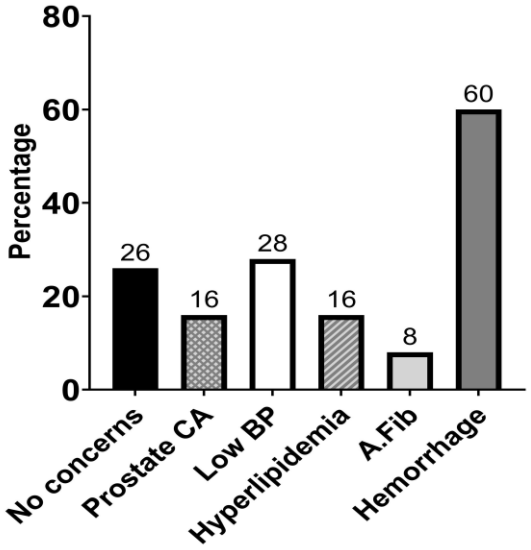

Figure 7: Adverse events: pharmacists concerned about Omega-3 FA. CA, cancer; BP, blood pressure; A.Fib, atrial fibrillation

Finally, when asked "how comfortable you are to counsel a patient about Omega-3 NHPs and cognitive health, only 6% ranked "9" and "10" on a scale of "1" to "10" (Figure 8), with "1" being not comfortable at all and "10" being very comfortable. All those pharmacists had previous self-training and were familiar with the literature on Omega-3. The Cox Proportional Hazard Model showed that previous training was associated with a higher level of confidence with a HR of 1.38 (95% CI 1.35, 1.42). The association was statistically significant, p=0.013. Fifty-four percent of the responders who identified themselves in the middle range of confidence, between "4" and "6", had no previous training on Omega-3. There was no correlation between previous work experience and level of confidence.

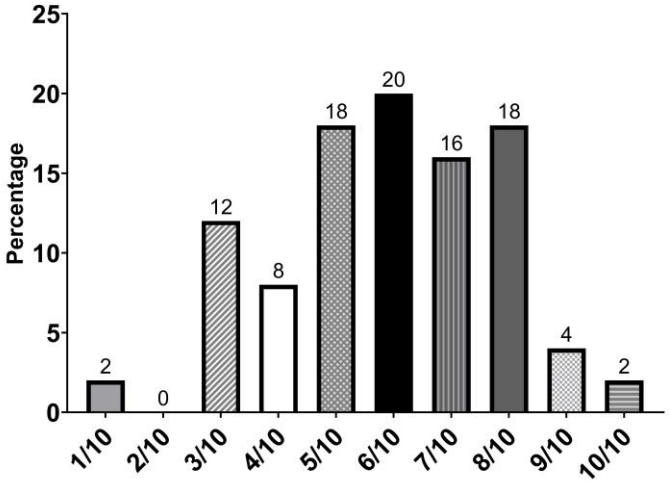

Figure 8: Level of comfort in counseling patients about Omega-3 FA

Discussion

Based on the results of our study we found in the "real-world" setting, there is an interest of customers on Omega-3 FAs, particularly for mental or cognitive health. The finding that 24% of pharmacists had never been enquired about this topic may be reflective of the geographical locations of each pharmacy and/or specific patient populations in the pharmacy catchment community. Overall, pharmacists are familiar with Omega-3 chemistry. The Omega-3 FA family is characterized by having their first carbon double bond at the third position counting from the terminal methyl group in the molecule; while the Omega-6 FAs have the first double bond located at the sixth carbon atom (Bradbury, 2011). Although most of the responders correctly mentioned the position of the first carbon atom from the methyl-end as a main difference in chemical structure between Omega-3 and Omega-6 FAs, about a quarter incorrectly mentioned the total number of carbon atoms and the number of double bonds in the FA molecule as the main differences.

Omega-3 FAs include ALA, DHA, EPA and DPA (DeFilippis & Sperling, 2006). According to our results, DHA and EPA were the most recognized components of Omega-3 FAs. ALA, a precursor for their longer chain Omega-3 FA (EPA, DPA, and to a lesser degree, DHA), is not biologically active unless converted into longer-chain EPA or DHA (Venegas-Caleron et al., 2010). The Omega-3 ALA is an essential FA since it is not synthesized by the human body (Harris, 2010). While the majority of responders could correctly identify diet as the single source of Omega-3, some incorrectly identified that Omega-3 FAs could be synthesized by the human body.

The main source of Omega-3 is fatty fish. Fish higher in fat (salmon, herring, sardine, mackerel, herring) are excellent sources of EPA and DHA, whereas low-fat fish

(bass, perch, tilapia, and cod) are poor sources (US National Institutes of Health, 2024; Beutler, 2000; Gebauer et al., 2006; Spector, 1999). Routine dietary consumption of fatty fish is one of the primary ways of obtaining clinically important amounts of EPA and DHA. In addition to fish, there are other natural sources such as human milk, cultivated marine algae, marine mammals and krill. Microalgae, at the base of the marine food chain, are the primary producers of DHA (Lane et al. 2014**)**. In fact, Omega-3 FAs found in fish are originally synthesized by many types of ocean-borne algae. In our study we found a diversity of answers concerning the primary source of Omega-3 FAs, however fish was selected as a primary source of Omega-3 FA by only half of the responders.

In contrast to many other dietary supplements, clinical evidence is available in supporting the use of Omega-3 in cognitively impaired patients, such as MCI, AD, and dementia (Andriambelo et al., 2023; Wei et al., 2023; Vakhapova et al., 2010). However, we acknowledged the limitation of the scoping review, including the large number of studies with heterogeneous design, some studies with a low number of participants in each group that challenges an ability to determine a clear causality between Omega-3 and mental health benefits. In our study, the benefits of Omega-3 FAs for mental health were identified by all responders. A smaller proportion also mentioned aiding in post-chemotherapy brain fog as an additional benefit of Omega-3 FA, although to our knowledge no information is currently available on this topic. Since Omega-3 FAs and their metabolites, including specialized proresolving mediators, alleviate chronic inflammation and restoring tissue homeostasis, their use may counteract the negative effects of long COVID on the brain and improve brain fog (Yang et al., 2022). As reported in a recent meta-analysis assessed the Omega-3 specific effects on cognitive test performance in youths, there was no main effect of Omega-3 FA supplementation on domain-specific performance in youths; however, a subgroup analyses identified beneficial effects of EPA-enriched formulations on long-term memory, working memory, and problem solving (Emery et al., 2020).

Health Canada (HC) had previous issued a monograph for Omega-3, which includes the specific use in supporting cognitive health and/or brain function. According to the NHP Fish Oil Monograph in 2018, the daily dose for EPA and DHA in fish oil can range between 100 and 5,000mg for adults 19 years and older, including pregnant and breastfeeding women. Within this dose range, there is no special requirement for caution(s) and warning(s), no contraindication(s), and no known adverse reactions (Health Canada, 2018). The revised 2024 Fish Oil monograph had been updated to providing 150-5,000 mg EPA and DHA, including at least 100 mg DHA per day to help support/maintain cognitive health or brain function (Health Canada, 2024b). Under the NHP Multiple Ingredient Fixed Oil Products (Health Canada, 2024a), Schizochytrium (algae) oil with a dosage ranging from 200-2,000mg DHA also helps support cognitive health and/or brain function.

Depending on country-specific guidelines, the maximum dose considered safe for Omega-3 FAs ranges between 3,000 to 5,000mg/day (Andriambelo et al., 2023). The US

Food and Drug Administration (FDA) recommends that the general population does not exceed 3,000mg/day of EPA and DHA combined, with up to 2,000mg/day from dietary supplements, without the guidance of a clinician. Higher dosing, under the guidance of a clinician, is approved by the FDA (Mozaffarian, 2024). Given significant variations among NHP and country-specific regulations, it is not surprising that we found such diversity of answers regarding the Omega-3 dose recommended by HC for brain health and MRD. However, overall pharmacists were quite familiar with recommended therapeutic and MRD of Omega-3 FAs.

There is no documented toxicity in doses of Omega-3 FA exceeding MRD. In small trials, fish oil up to 12,000mg/day (containing 6,000mg/day Omega-3 FA) have been administered for over two years without serious adverse events (Mozaffarian, 2024). While 26% of participants of our study answered that there are no serious safety issues, more than half of pharmacists expressed concerns about increased risk of hemorrhage. However, Omega-3 FAs do not increase the risk of clinically significant bleeding. The FDA concluded that consumption of ≤5,000 mg/day of EPA and DHA does not increase the risk of excessive bleeding based on clinical trials that measured clinical outcomes such as bleeding episodes and blood loss (Food and Drug Administration). A systematic review of 52 publications, including 32 on healthy subjects and 20 on patients undergoing surgery, showed that fish oil (mainly Omega-3 FA) supplements reduced platelet aggregation in healthy subjects. However, this biochemical effect did not translate into increased bleeding risk in randomized controlled trials. Fish oil exposure in surgical patients did not increase bleeding or blood transfusions either during or after surgery. Consequently, this systematic review did not support the need for discontinuation of fish oil (Omega-3 FA) supplements prior to surgery or invasive procedures (Begtrup et al., 2017). Therefore, the concerns about hemorrhage are unnecessary and are not justified by scientific evidence. Patients asking about the risk of bleeding with the use of Omega-3 FAs should be counselled accordingly. In a more recent 2020 systematic review of Omega-3 FAs for the primary and secondary prevention of cardiovascular disease, increased intake of Omega-3 FAs did not increase the risk of bleeding (Mozaffarian, 2024). High-dose of highly purified marine Omega-3 FAs, specifically Icosapent Ethyl, reduces cardiovascular risk. Use of marine Omega-3 FAs in patients with moderate hypertriglyceridemia who have high risk atherosclerotic cardiovascular disease is widely recognized (Khan et al., 2021). Omega-3 polyunsaturated fatty acids (Omega-3 PUFAs) have been used to treat joint pain associated with several inflammatory conditions (Xie & Zhang, 2023). There was a slightly increased risk of atrial fibrillation reported in people with cardiovascular disease when consuming ≥4,000mg/day of Omega-3 FA supplements for several years (US National Institutes of Health, 2024); nevertheless, only 8% of the participants from our study had identified atrial fibrillation as an adverse event. There is also no proven association between high levels of Omega-3 FA and increased risk of cancer (Mozaffarian, 2024). Overall, the available evidence does not

support any major effects of fish or fish oil consumption on cancer risk. Systematic reviews and meta-analyses of numerous large prospective observational studies have generally found no significant effects of fish consumption on risk of any type of cancer, nor have randomized trials of fish oil. Some studies, though not all, have suggested an association between higher levels of Omega-3 FAs and increased risk of prostate cancer; however, meta-analyses of all studies found no consistent associations between dietary or blood biomarker levels of Omega-3 FAs and prostate cancer (Alexander et al., 2015; Fu et al., 2015). While Omega-3 FAs are known for their cardiac benefits, including lowering elevated blood pressure, they do not directly cause hypotension (Clark et al., 2018).

Overall, we found that pharmacists have good general knowledge of Omega-3 chemistry, however not on specific details about Omega-3 safety in specific populations. More importantly, the survey found unsatisfactory confidence of pharmacists in patient counselling on this topic. It correlated with the lack of education and previous training on this topic. Our results also concur with a previous study where pharmacists considered their knowledge and vigilance of dietary supplements inadequate to provide proper patient counselling (Kwan et al., 2006). It is interesting that the results of our study showed better knowledge of Omega-3 NHPs as compared to a previous study, where the majority of participants had average to poor knowledge about NHPs and only around 7% had good knowledge (Kheir et al., 2014). The difference may be due to the specificity of Omega-3, the frequent need to counsel patients, or attributed at least partially to the difference in regulatory requirements. Since January 1, 2004 NHPs and other supplements have been regulated in Canada as a subset of drugs under the Food and Drugs Act. Pharmacists have a professional obligation to have knowledge to address patients' questions about NHPs, especially about potential interactions with other drugs (Farrell et al., 2008). We acknowledge that our study included only 50 participants from one geographical area, thus, the results have limited generalizability. Although the number of participants in our study is relatively low, the demographics of respondents were balanced and likely correctly represent the current knowledge of community and hospital pharmacists on Omega-3 FAs. If we were to repeat our study, we would enroll a higher number of pharmacists with wider geographical distribution and obtain information about practice details to explore and better understand more specifics on patients' needs. We would also include more questions specific to clinical evidence of Omega-3 FAs, in particular the effects of different doses of Omega-3 FAs and specific components (e.g., DHA), and differences among Omega-3 FA formulations for cognitive health that are available in Canada. Different variables, such as workplace setting (hospital vs. community pharmacy) or additional training in nutritional supplementation, could play a role and might influence pharmacist knowledge and confidence level.

Unlike pharmaceutical or biological products that are provided in specific formulations with clear indication(s), and specific dosage(s); the formulations,

compositions and dosages of Omega-3 FA NHPs may vary significantly from product to product. Most Canadian Omega-3 FA NHPs are intended for more than one use (e.g., cardiovascular, cognitive health, and others). Recognizing that Omega-3 FA NHPs in Canada can have a different number of uses with various doses with different components (i.e., DHA:EPA ratio), it is particularly important for healthcare practitioners (including pharmacists) to have good knowledge on the benefits and risks of Omega-3 in different patient groups which allow them to select the appropriate Omega-3 NHPs based on the customer's need and identify the Omega-3 FA OTC NHPs for non-cognitive versus cognitively-impaired patients. Closing the knowledge gaps on Omega-3 FAs and cognitive health benefits will help pharmacists to counsel patients about Omega-3 FAs and their benefits with great confidence. This in turn can benefit the increasing and aging population who suffer from cognitive health issues, and that is what this project aims to accomplish. We suggest that interested pharmacists may benefit from a formal education on Omega-3 NHPs. It could be done via continuing education programs, pharmacy curriculum, or professional guidelines. To our knowledge there is no formal educational material about Omega-3 FAs targeting pharmacists. Proposed educational material should include review of the major members within the Omega-3 family, as well as their connection to the Omega-6 family in their respective metabolic pathways, the major sources of Omega-3 FAs which will help in selecting the appropriate Omega-3 products for consumers with different dietary needs, such as fish and non-fish eaters, vegan or vegetarians, review of Omega-3 FA formulations in supporting cognitive health and / or brain function based on available human clinical data, and the safety precautions or interactions with other medications associated with the consumption of Omega-3 FA.

Conclusions

There are gaps in pharmacist's current knowledge on Omega-3 FA health benefits and there is unsatisfactory confidence in providing patient counselling. A history of previous training on Omega-3 have shown a positive impact on the confidence in such counselling. As Omega-3 FA NHP is a popular topic; there is a need in comprehensive education on Omega-3 FA NHP supplements. By equipping healthcare practitioners with the necessary knowledge about Omega-3 FA NHP supplements, these healthcare professionals can better assist patients in making informed decisions about optimal Omega-3 FA supplementation, which in turn play a vital role in helping consumers achieve optimal health benefits while ensuring consumers' safety and well-being.

Ethical Statement

This project was a low-risk project involving human participation. Ethics

approval was in full compliance with Policy 4.1.1 Participation of Humans in Research – Low Risk, Youth Science Canada. Informed consent was obtained from each participant before participation. Informed verbal consent was obtained from all participants involved in the study before completing the questionnaire. Our study does not contain any data from an individual person, including individual details, images or videos.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

Conceptualization, A.K. and M.K.; methodology, M.K.; formal analysis, A.K.; resources, M.K.; data curation, M.K.; writing original draft preparation, A.K.; writing, review and editing, M.K.; visualization, A.K.; supervision, M.K.; project administration. All authors have read and agreed to the published version of the manuscript.

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Supplementary Data

The raw data supporting the conclusions of this article will be made available by the authors on request.

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