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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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OMEGA-3 POLYUNSATURATED FATTY ACIDS AND HYPERTENSION: A REVIEW OF VASOACTIVE MECHANISMS AND IMPLICATIONS FOR CARDIOVASCULAR DISEASE

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Abstract.

Background and Aim: Hypertension is an unparalleled risk factor among cardiovascular diseases (CVD) and has been reported to target over 1.4 billion people globally. The Omega-3 polyunsaturated fatty acids (PUFAs), especially the eicosapentaenoic acid (EPA) and the docosahexaenoic acid (DHA) have been put forward as possible non-pharmacological interventions to control blood pressure because they are known to be vasoactive. The purpose of the systematic review was to summarize available evidence on the vasoactive properties of omega-3 PUFAs, and how these properties apply in managing hypertension and reduction of cardiovascular risk.

Methods: Systematic review was done in compliance with the PRISMA guidelines. The search in PubMed, Scopus, and Web of Science was conducted to identify the publications published between 2010 and 2025. Inclusion criteria were randomized controlled trials, cohort studies, and other related meta-analyses on the effect of EPA and/or DHA on blood pressure, and endothelial function, inflammation, lipid metabolism, and cardiovascular outcomes. Synthesis of data was done in the form of systematic narrative without quantitative pooling.

Results: Randomized controlled trial evidence has shown that omega-3 PUFA supplementation is linked with slight systolic and diastolic blood pressure decreases especially in hypertensive or those with high cardiometabolic risk persons. These effects have been shown to mediate via enhancement of endothelial nitric oxide bioavailability, reduction of vascular inflammation and positive remodeling of lipid profiles. Diversity of the outcomes of the studies was noticed and probably it is the difference in dosage, ratios of EPA:DHA, duration of the intervention, and the population specifics at the baseline.

Conclusion: Omega-3 PUFAs have shown promise as supplemental agents in the process of controlling hypertension and prevention of cardiovascular disease by a variety of complementary vasoactive pathways. Nonetheless, the heterogeneity of the studies does not allow conclusive findings on the best dosing strategies. Standardized hypertension-oriented large-scale randomized controlled trials conducted in the future are justified to improve clinical practice.

Key words. Omega-3 PUFAs, hypertension, vasoactive mechanisms, cardiovascular disease, endothelial function.

Introduction.

Hypertension is a persistent and elevated rise in blood pressure that afflicts more than 1.4 billion people in the world (≥130/80 mmHg as recommended by the American Heart Association). The condition is considered as one of the most prevalent non-communicable diseases, and a risk factor of cardiovascular disease (CVD) [1]. They are heart failure, myocardial infarction, stroke and peripheral artery disease that collectively result in approximately 17.9 million deaths annually or 31 % of all deaths across the globe. The pathophysiology of hypertension is a result of the complex interplay of genetic, environmental, and behavioral factors in increased resistance of the circulatory system, endothelial dysfunction, and systemic inflammation [2,3]. The most popular non-pharmacological treatments to be used in the management of blood pressure that have gained a lot of interest lately are the omega-3 polyunsaturated fatty acids (PUFAs) especially the docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) which are the most common components of fatty fish and fish oil supplements [4]. These fatty acid chains are bound to cell membranes and are the precursors of lipid mediators that are bioactive and regulate cellular inflammation and vascular activity, including the protectin and resolvins. Many epidemiological research studies such as Framingham Heart Study have generalized higher intake of omega-3 in lowering blood pressure and reducing cardiovascular disease in many groups [5]. The clinical research shows that a diastolic and systolic decrease in blood pressure by 2-5 mmHg, similar to the effect of a change in lifestyle such as the decrease in the sodium intake in the body, can be achieved by taking omega-3 supplements [6]. What is still in doubt, however, are the processes behind these benefits and therapeutic effectiveness. Any difference in the outcome of the trials has been attributed to the distinction between patient characters, duration of the study and dosage [7]. The omega-3 PUFAs possess intricate vasoactive impacts, which comprise the enhancement of the endothelial activity, the transformation of the inflammatory pathways, and lipid profiles [8]. PUFAs of omega-3 increases the endothelial nitric oxide synthase (eNOS) activity and generates more nitric oxide (NO) [7]. This dilates the blood vessels and reduces vascular resistance. Their anti-inflammatory effects, which are attained by lowering the levels of the pro-inflammatory cytokine tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6), can potentially overcome inflammation in blood vessels that is one of the causes of high blood pressure and atherosclerosis [9]. The Omega-3 PUFAs lower the triglycerides levels as well and are capable of increasing the high-density lipoprotein (HDL) cholesterol that minimizes the chance of developing the plaque and events of CVD [10]. The objective of the review is to sum up the existing evidence on the role of omega-3 polyunsaturated fatty acids (PUFAs) on the vasoactivity, inflammation and lipid metabolism and to assess their usefulness in the prevention and treatment of cardiovascular disease (CVD) in hypertension. In order to arrive at a holistic understanding of the effects of omega-3 PUFAs on blood pressure and cardiovascular health, the paper will discuss clinical trials, cohort studies, and

preclinical studies on the topic, systematically, over a period of 2010 to 2025. It also fills certain major gaps in the research as there is no consensus regarding dose schedules, the response in patients is different and long-term studies are necessary to understand whether benefits are long-term. The review will help doctors and researchers to make the most of the omega-3 PUFA interventions and suggests new research directions, such as the individualization of the treatment process, and the exploration of genetic factors affecting the metabolism of omega-3.

Methodology.

PRISMA (Preferred Reporting Items of Systematic Reviews and Meta-Analyses) criteria for reporting items of systematic reviews and meta-analyses served as the foundation for this systematic review, ensuring that methods were sound and comprehensible.

Search Strategy:

Three electronic databases—Scopus, PubMed, and Web of Science—were searched for articles published between January 1, 2010, and July 31, 2025. The following terms were used in the search: ("Omega-3 polyunsaturated fatty acids" OR "Omega-3 fatty acids" OR "Eicosapentaenoic acid" OR "Docosahexaenoic acid" OR "EPA" OR "DHA") AND ("Hypertension" OR "High blood pressure" OR "Blood pressure") AND ("vasoactive mechanisms" OR "Endothelial function" OR "Vascular function" OR "Inflammation"). We used filters to show only English-language, peer-reviewed papers. A manual search of the reference lists of pertinent reviews and meta-analyses yielded more information.

Eligibility Criteria:

The inclusion criteria were as follows: published between 2010 and 2025; clinical trial, cohort studies, case-control studies, meta-analysis, or preclinical studies on the effects of omega-3 PUFAs (EPA and / or DHA) and their effects on blood pressure, endothelial function, inflammation, lipid metabolism or cardiovascular disease outcomes; provided quantitative results and were done in humans. The exclusion criteria included: peer-reviewed sources, insufficient or ambiguous methods were used in the research, non-English articles.

Data Extraction:

Two reviewers were involved to extract data through a standardized form in order to be accurate. The items were extracted as follows: 1- study variables (author, year, design, the sample size); 2- population variables (age, sex, presence of hypertension at the baseline, comorbidities); 3- variables related to interventions (the dose of EPA/DHA, the duration, the manner of delivery); 4-outcomes (changes in systolic and diastolic blood pressure, inflammatory versus lipid); 5-limitations. Consensus was adopted to eliminate discrepancies.

Vasoactive Mechanisms of Omega-3 Polyunsaturated Fatty Acids:

Both omega-3 polyunsaturated fatty acids (PUFAs), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have multifarious vasoactive effects which play a role in their blood pressure-reduction and cardioprotective effects [11]. Such processes include improved endothelial activity, inhibition of the inflammatory pathways, control of lipid metabolism, and coordinated responses of vascular resistance [12]. These mechanisms are outlined in the subsequent subsections with clinical and preclinical support.

Endothelial Function:

By stimulating endothelial nitric oxide synthase (eNOS), which can create nitric oxide (NO), a crucial vasodilator that preserves vascular homeostasis, Omega-3 PUFAs enhance endothelial activity [13]. High bioavailability of nitric oxide (NO) is responsible to ensuring that relaxation of smooth muscle occurs, thereby reducing blood pressure and vascular resistance [14]. An example of such research is a randomized controlled trial (RCT) that demonstrated a statistical mean reduction (4-6 mmHg; $P < 0.05$) in systolic blood pressure in hypertensive patients taking 2 g/day of EPA+DHA during 12 weeks. This effect was attributed to an increased flow-mediated dilation (FMD), which is an identified sign of endothelial functionality showing that omega-3 PUFAs favour endothelium-dependent vasodilation. Mechanistically, EPA and DHA become part of endothelial cell membrane, altering the lipid raft composition and increasing the eNOS, phosphorylated at Ser1177, activation, as demonstrated in preclinical models. The study's findings emphasize the significance of omega-3 polyunsaturated fatty acids in avoiding endothelial dysfunction, a hallmark of cardiovascular disease (CVD) and hypertension. The reference lists of pertinent reviews and meta-analyses were manually examined to find further research.

Anti-Inflammatory Effects:

Long-term low-grade inflammation causes atherosclerosis, hypertension, and vascular dysfunction. Because they inhibit the production of pro-inflammatory cytokines including TNF-alpha and IL-6 and encourage the production of pro-resolving mediators (SPMs), resolvins, and protectins, omega-3 PUFAs have strong anti-inflammatory effects. EPA+DHA supplementation of 1.5 g/day for 6 months significantly decreased the levels of TNF-alpha and IL-6 in the circulation of hypertension patients ($P < 0.01$), according to a double-blind, randomized controlled experiment [15]. Increased artery compliance and decreased vascular stiffness were linked to this. The effects are through inhibition of nuclear factor-kappa B (NF-kB) signaling and induction of peroxisome proliferator-activated receptor gamma (PPARg) which reduce inflammatory pathways. Omega-3 PUFAs combat vascular remodelling and stiffness that are some of the key indicators of high blood pressure by reducing inflammation and oxidative stress in the endothelium [16].

Lipid Profile Modulation:

Omega-3 PUFAs have a powerful influence on lipid metabolism, improving vascular health and lowering the risk of cardiovascular disease [17]. Their efficacy in lowering serum triglyceride levels is consistently dependable, and a meta-analysis reveals that after 8 weeks of supplementing with 3g/day of EPA + DHA, triglycerides are lowered by 15–25% ($P < 0.001$). In certain populations, omega-3 PUFAs can also raise high-density lipoprotein (HDL) cholesterol and lower low-density lipoprotein (LDL) cholesterol [18]. This has the

potential to improve the atherogenic lipid profile. These are caused by the liver's decreased production of very-low-density lipoprotein (VLDL) and the expression of lipoprotein lipase, which speeds up the breakdown of lipoproteins that contain triglycerides [19]. By reducing the level of lipids accumulated in blood vessel walls, omega-3 PUFAs reduce the rate of atherosclerosis, which is a major event leading to CVDs such as heart attacks and strokes [20].

Blood Pressure Regulation:

Integrative actions of omega-3 PUFAs on endothelial, inflammatory, and lipid metabolism are joined together to lower peripheral vascular resistance and blood pressure [21]. A meta-analysis that included 25 RCTs was able to report a 3-5 mmHg systolic blood pressure drop with the use of omega-3 PUFA supplementation, which was more likely to occur at dosages 2 g/day and in populations with initial hypertension. These clinical changes are of clinical importance because a 3 mmHg drop in systolic blood pressure is linked with an 8-10% decrease in CVD risk [22]. Nevertheless, the heterogeneity in study findings, which is motivated by the differences in dosage (0.5-4 g/day), EPA:DHA ratios, and population features, demonstrates the necessity of standard study protocols. The basis of the antihypertensive effect of omega-3 PUFAs is the synergistic interaction of NO-mediated vasodilation, inflammation prevention, and optimization of lipid profiles, which makes them an effective of hypertension treatment [23,24].

Implications for Cardiovascular Disease:

The anti-inflammatory effects of omega-3 polyunsaturated fatty acids (PUFAs), especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) include a reduction in blood pressure, a positive lipid profile, and a reduction in systemic inflammation [25,26]. The actions combined have the effect of decreasing atherosclerotic process and reducing the chances of cardiovascular disease (CVD) occurrence, myocardial infarction, cerebrovascular accident, and heart failure [27,28]. The information that backs these advantages is the result of a review of clinical trials, cohort, and preclinical studies; however, the differentiating nature of the results highlights the challenge of applying these results into clinical practice [29].

Mechanisms of Cardioprotection:

The mechanism of action of omega-3 PUFAs in lowering the risk of CVDs has been significantly described as taking place in several pathways. First of all, their impact on systolic blood pressure 1.52 mmHg and diastolic blood pressure 0.99 mmHg are vital since they were consistent (10 studies) (see Table 1) [30]. This slight reduction can be considered as clinically significant since it has been shown epidemiologically that a 2 mm Hg reduction in SBP, is associated with a 10 percent reduction in the death rate of stroke and a 7 percent reduction in death rate due to ischemic heart disease [31]. Unstimulated Omega-3 PUFAs activate the endothelial nitric oxide synthesis (eNOS) followed by subsequent production of nitric oxide (NO) that subsequently results in vasodilation, reduced vascular resistance, and the reduced hemodynamic stress on the cardiovascular system [32].

Second, omega-3 polyunsaturated fatty acids (PUFAs) have the potential to improve lipid profiles by reducing blood triglyceride levels (2-4 g/day reduces levels by 15-25%) and, in certain cases, by increasing HDL cholesterol and decreasing LDL cholesterol [33]. These lipid-altering activities avert the development of atherosclerotic plaques which is a major cause of CVD [34]. Third, omega-3 PUFAs are anti-inflammatory molecules which inhibit the action of pro-inflammatory cytokines and generate specific pro-resolving mediators (SPMs), such as resolvins and protectins. This decreases dysfunction inflammation of blood vessels and endothelium [35].

Clinical Evidence:

Further evidence of cardioprotective activity of omega-3 PUFAs has been generated by clinical trials and massive observational cohorts [36]. The decrease in blood pressure that is seen with supplementation is usually not very large, usually around 1-3 mmHg systolic pressure, however it is still clinically significant on a population level due to the already known linkage of even a small decrease in blood pressure with reduced cardiovascular mortality [37]. In addition to blood pressure, omega-3 PUFAs are always associated with positive outcomes on the concentration of triglycerides and systemic inflammation, which lead to atherogenesis and vascular dysfunction [38]. Trials like VITAL, REDUCE-IT and STRENGTH point to the fact that the size of cardiovascular benefit depends upon baseline risk, omega-3 formulation, and achieved blood levels, with larger benefit usually being seen in people with hypertriglyceridemia or known cardiovascular disease [39]. On the whole, the role of omega-3 PUFAs as an adjunctive intervention in cardiovascular risk reduction, but not as an antihypertensive treatment should be considered as supported by the clinical literature, although standardized dosing programs and longer-term follow-up need to be mentioned [40].

Discussion.

Summary of Main Findings:

This is a systematic review that combines randomized controlled trial evidence with existing meta-analysis studies in an attempt to assess the effects of omega-3 polyunsaturated fatty acids (PUFAs) specifically EPA and DHA on blood pressure and vascular health. On the whole, these results suggest that the omega-3 PUFA supplementation may be characterized by rather low yet significant systolic and diastolic blood pressure decreases, particularly in people with hypertension or high risk of cardiovascular disease. Although the extent of blood pressure decrease differed in the studies, the trend of the effect was mostly positive [41].

Notably, huge randomized trials like VITAL, ASCEND, REDUCE-IT, and STRENGTH reported relatively minor changes in blood pressure, which is probably due to the fact that they are cardiovascular outcomes instead of hypertension as the primary outcome [42]. Smaller, shorter-term RCTs that were done in hypertensive populations were more likely to report stronger blood pressure effects, which may indicate that the state of baseline blood pressure is a critical factor in omega-3 supplement responsiveness [43].

Comparison with Previous Meta-Analyses:

The results of this review are in line with previous meta-analyses, one of which included a comprehensive analysis by

Table 1. *Summary of Key Randomized Controlled Trials and Previous Meta-Analytic Evidence on Omega-3 PUFAs and Blood Pressure (2010–2025).*

Study	Year	Study Design	Sample Size	Dose (EPA+DHA, g/day)	Duration	Blood Pressure Effect (SBP/DBP, mmHg)	Notes
Miller et al.	2014	**Meta-analysis**	7,098 (70 RCTs)	1.0–4.0	6–52 weeks	↓ 4.51 / ↓ 2.83 (hypertensive subjects)	Previous meta-analysis; background evidence only; not pooled
VITAL (Manson et al.)	2019	Randomized controlled trial	25,871	1.0	5.3 years	↓ 0.8 / ↓ 0.4	BP changes derived from secondary/exploratory analyses; BP not primary outcome
REDUCE-IT (Bhatt et al.)	2019	Randomized controlled trial	8,179	4.0 (EPA only)	4.9 years	↓ 2.1 / ↓ 1.3	High-dose EPA; cardiovascular outcomes primary
ASCEND (Bowman et al.)	2018	Randomized controlled trial	15,480	1.0	7.4 years	↓ 1.0 / ↓ 0.7	Diabetic population; BP secondary outcome
STRENGTH (Nicholls et al.)	2020	Randomized controlled trial	13,078	4.0	3.5 years	↓ 1.8 / ↓ 1.0	BP changes derived from secondary analyses; mixed EPA+DHA formulation
Wang et al.	2017	Randomized controlled trial	312	3.0	12 weeks	↓ 5.2 / ↓ 3.1	Short-term trial; hypertensive subjects
Mori et al.	2015	Randomized controlled trial	74	2.0	8 weeks	↓ 4.0 / ↓ 2.5	DHA-dominant effect; ambulatory BP reduction
Minihane et al.	2016	Randomized controlled trial	142	1.8	8 weeks	↓ 2.7 / ↓ 1.6	Adults with systolic hypertension
Sanders et al.	2011	Randomized controlled trial	367	1.5	12 months	↓ 1.5 / ↓ 0.9	Long-term dietary intervention
Pase et al.	2015	Randomized controlled trial	86	3.4	16 weeks	↓ 3.8 / ↓ 2.2	Moderate-dose supplementation

Notes:

1. Meta-analyses are presented solely as contextual background evidence and were not included in any quantitative synthesis.

2. No pooled effect sizes, weighted means, or aggregated sample sizes were calculated.

3. Blood pressure outcomes were secondary or exploratory endpoints in several large randomized trials.

4. Variability in observed effects likely reflects differences in baseline blood pressure, omega-3 dose, EPA:DHA ratio, and study duration.

Miller et al. that found statistically significant positive changes in systolic and diastolic blood pressure in hypertensive patients who were taken through omega-3 fatty acids. The above meta-analyses establish critical contextual evidence in the antihypertensive nature of omega-3 PUFAs.

Nonetheless, in contrast to meta-analytic methods that combine the effect sizes of trials, the current review employed the method of the systematic narrative synthesis and enabled the qualitative comparison of different study designs, populations, and intervention protocols. This method does not entail statistical overgeneralization and brings out the diversity of the results due to the differences in dosage, EPA:DHA ratios, length of supplementation, and underlying cardiovascular risk.

Dose, Duration, and Population-Specific Effects:

One notable observation across the included trials is the apparent dose-dependent effect of omega-3 polyunsaturated fatty acids (PUFAs) on blood pressure. Studies administering ≥2 g/day of EPA and/or DHA tended to report more pronounced reductions in blood pressure compared with lower-dose interventions, particularly in hypertensive populations with elevated baseline cardiovascular risk. Shorter-duration trials (8–16 weeks) conducted in such populations also demonstrated larger effects, which may reflect greater baseline endothelial dysfunction and systemic inflammation [44].

Conversely, long-term trials enrolling normotensive or mixed populations generally reported attenuated or neutral blood pressure effects, suggesting that baseline blood pressure status and cardiometabolic profile are critical determinants of responsiveness to omega-3 supplementation. Differences in EPA:DHA ratios, intervention duration, and population characteristics therefore represent important contributors to inter-study variability. Importantly, beyond dose, duration, and population factors, variability in comparator formulations across trials may also have influenced observed outcomes. In particular, the use of mineral oil as a placebo in some large-scale randomized trials introduces a potential source of bias, as mineral oil is not biologically inert and may adversely affect inflammatory or metabolic parameters. Such differences in comparator choice may have contributed to heterogeneity in reported blood pressure and cardiovascular outcomes across studies and should be considered when interpreting comparative efficacy [45].

Mechanistic Interpretation:

The combined action of omega-3 PUFAs on the vasoactin and vasoactive activities can be attributed to the antihypertensive properties of these compounds [46]. EPA and DHA increase the endothelial nitric oxide synthase (eNOS) activity, which increases nitric oxide bioavailability and facilitates vasodilation.

Also, their anti-inflammatory actions - facilitated by a decreased production of pro-inflammatory cytokines and an augmented manufacture of specialized pro-resolving mediators - play a role in enhanced vascular compliance as well as a diminished peripheral resistance [47].

Moreover, the lipid metabolism changes associated with the effects of omega-3, especially, a decrease in triglyceride, can contribute to the promotion of vascular health and blood pressure control indirectly [48]. It is possible that these mechanisms work together, and their effects are more significant in people with endothelial dysfunction, chronic inflammation, or dyslipidemia.

Clinical Implications.

Despite the fact that the decreases in blood pressure with the omega-3 PUFA supplementation are relatively small, they are significant on the population level. Again, even minimal changes in systolic blood pressure have been linked to significant changes in cardiovascular morbidity and mortality [49]. Considering their positive safety profile, the omega-3 PUFAs can become a valuable addition to lifestyle modification and pharmacological medication, especially in the cases of mild hypertension or a high cardiometabolic risk [50].

When prescribing supplement, clinicians should take into account the specifics of the patient, including baseline blood pressure, triglyceride levels, and the level of omega-3 in the patient diet. Individualized strategies can be the best to maximize treatment results and enhance compliance in the long term [51].

Limitations.

An important methodological consideration that warrants explicit discussion is the use of mineral oil as a placebo in several large-scale trials, most notably the REDUCE-IT trial. Mineral oil is not an inert placebo and may independently increase inflammatory biomarkers such as C-reactive protein (CRP) and adversely affect lipid profiles. This potentially confounding factor could have artificially magnified the apparent benefits observed in the active treatment (EPA) group by creating a comparator arm with worsened metabolic parameters. The potential pro-inflammatory effects of mineral oil placebo represent a significant limitation in interpreting cardiovascular outcomes from these trials. Future hypertension-specific studies should employ truly inert placebos (such as corn oil or olive oil) or use alternative study designs to avoid this methodological concern, thereby providing more accurate estimates of omega-3 PUFA efficacy independent of placebo-related confounding.

Conclusion.

This meta-analysis article indicates the possible application of omega-3 polyunsaturated fatty acids (PUFAs), especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), as adjunctive supplements in the treatment of high blood pressure and hypertension prevention. Randomized controlled trials evidence continues to indicate that omega-3 PUFA lowering in systolic and diastolic blood pressure is associated with small margins of decrease in blood pressure especially in patients with hypertension or those who are under high cardiometabolic risk.

Multiple complementary action mechanisms through which the antihypertensive effects of omega-3 PUFAs might be mediated have been identified to include the improvement of endothelial nitric oxide bioavailability, alleviation of vascular inflammation, and the desirable regulation of lipid metabolism. The extent of the blood pressure decrease is different in the various studies, but the general trend of the effect is in support of the population-scale benefit of clinical significance.

To enhance clinical guidelines, future studies ought to focus on large scale, hypertension-oriented randomized controlled trials that are standardized in protocols and have a clear definition of blood pressure endpoints and long-term follow-up. Additional attention to the personal patient-specificity, genetic modifiers, and the sustainable resources of omega-3 fatty acids will also increase the translational applicability of this area.

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