

Advancing Fucoxanthin Production from Microalgae: A Bibliometric Analysis of Research Trends and Innovations

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Abstract - Fucoxanthin is a bioactive carotenoid known for its extensive bioactive properties, including antioxidant, anti-inflammatory, and anti-obesity effects, with growing applications in pharmaceuticals, nutraceuticals, and functional foods. This study aims to explore global research trends and innovations in fucoxanthin production, particularly from microalgae, using bibliometric analysis. Publication data were retrieved from the Scopus database using specific keywords, and analyzed with VOSviewer to assess trends, key contributors, and keyword associations. Results show a significant rise in fucoxanthin research over the last two decades, led by countries such as Japan, China, and Germany. Microalgae are emerging as a preferred source due to higher fucoxanthin yields compared to brown seaweeds. Key institutions and authors have contributed to advancements in cultivation, extraction, and commercialization. This analysis offers a comprehensive overview of fucoxanthin research and highlights future directions for sustainable production while also addressing current challenges and opportunities in its utilization and the progress being made in its production. It supports informed decision-making for researchers, industries, and policymakers in the utilization of fucoxanthin for human health and sustainability.

Keywords - bibliometric analysis, bioactive compound, fucoxanthin, microalgae.

I. INTRODUCTION

Fucoxanthin, a naturally occurring carotenoid primarily derived from algae, has garnered significant attention due to its potent antioxidant, anti-inflammatory, and anti-cancer properties [1], [2], [3]. Despite being sources of fucoxanthin, brown algae like *Dictyota*, *Fucus*, *Sargassum*, *Laminaria japonica*, *Eisenia bicyclis*, and *Undaria pinnatifida* offer limited yields, producing only 0.001 to 0.356% of dry weight [4], [5], [6], [7]. Given the limitations of current fucoxanthin sources, finding new options is crucial, and microalgae are increasingly seen as a more viable choice than macroalgae due to their significantly higher fucoxanthin content, up to 100-fold [6],

[8].

As the global interest in sustainable and renewable resources intensifies, microalgae have emerged as a promising bio factory for fucoxanthin production [9]. Microalgae are considered an excellent candidate for fucoxanthin production due to their high growth rates, ability to thrive in diverse environments, and superior fucoxanthin content compared to macroalgae [10]. Microalgae, such as *Phaeodactylum tricornutum* (1.57%) [11], *Isochrysis galbana* (1.82%) [12], *Chaetoceros calcitrans* (1.75%) [13], *Cylindrotheca closterium* (0.52%) [14], have been extensively studied for their ability to accumulate high levels of fucoxanthin under optimized cultivation conditions. Moreover, microalgae can be cultivated in photobioreactors and open pond systems,

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allowing for large-scale and cost-effective production while minimizing environmental impact [10], [15].

Research on fucoxanthin production from microalgae has experienced exponential growth in recent years, driven by advancements in biotechnological processes and increasing awareness of the compound's health benefits [16]. Previous studies have focused on optimizing cultivation conditions, enhancing fucoxanthin yield, and developing cost-effective extraction methods. The application of fucoxanthin span functional foods, pharmaceuticals for managing obesity and metabolic disorders, and cosmetic products [17], [18], [19].

Although interest in fucoxanthin has grown rapidly, there is still a lack of in-depth and comprehensive understanding of the overall research landscape and scientific progress in this area. Bibliometric analysis offers a valuable approach to address this gap by systematically mapping the development of fucoxanthin research. This method allows for the structured evaluation of scientific publications, helping to uncover emerging trends, leading contributors, and key research areas. It also provides data-driven insights to anticipate future directions and build strong theoretical foundations for ongoing and future studies [20].

While several review articles have summarized the effectiveness, future research needs, and recent progress in microalgae fucoxanthin research [16], [21], [22], [23], a bibliometric analysis to reveal broader research patterns and trends has been lacking. Bibliometric analysis is essential for a deep understanding of a field's current status and future trajectory [24], employing mathematical, statistical, and visual techniques to examine scholarly works [25]. This approach allows for the evaluation of research trends and institutional contributions [26], [27]. Moreover, keyword co-occurrence analysis can uncover past trends, current themes, and potential future research directions [28]. This study addresses this gap by using bibliometric analysis on Scopus data to identify research patterns in microalgae fucoxanthin literature, pinpointing leading countries, and institutions. It also assesses the impact of international collaboration and uses keyword co-occurrence to map past, present, and future research, providing a comprehensive overview of microalgae fucoxanthin research. Additionally, this study will examine current challenges and potential opportunities in optimizing fucoxanthin production and highlight advanced strategies and cutting-edge technologies designed to improve production efficiency and scalability, ultimately facilitating the widespread commercialization of fucoxanthin as a valuable bioactive compound.

II. METHOD

A collection of research publications related to fucoxanthin was retrieved from the Elsevier Scopus database on January 13, 2024. The search was conducted using the query [TITLE-ABS-KEY (fucoxanthin*) AND (diatom*) OR (production*) OR (cultivation*) OR

(extraction*)], yielding a total of 2,967 publications. It is important to note that varying search parameters or databases may produce different results.

The publication data were manually extracted, including key metrics such as the total number of citations and the h-index, both obtained from the Scopus database (accessible at <https://www.scopus.com/search/form.uri?display=basic#basic>], collected on January 13, 2024). Additionally, bibliometric analyses were performed using VOSviewer software to visualize relationships among research subjects, such as countries and keywords. A visualization map was generated to illustrate the connections between different topics within the fucoxanthin research domain.

Furthermore, a research network and a keyword co-occurrence network were constructed using VOSviewer. The keyword co-occurrence analysis identified the most frequently used terms associated with fucoxanthin. To ensure relevance, only keywords appearing at least 15 times were included, and a manual review was conducted to remove any unrelated terms.

III. RESULT AND DISCUSSION

Fucoxanthin (C₄₂H₅₈O₆), a carotenoid sourced from microalgae, has attracted considerable research attention. The fucoxanthin market reached a valuation of \$209.45 million in 2023 and is expected to grow to \$280.68 million by 2030 [29]. This increase in production capacity, up by 15% in 2023, has also been accompanied by improved purity levels of 85-95% through modern extraction techniques [29]. Valued at approximately \$30,000 per gram, this compound can be utilized as nutraceutical and functional food [30]. Studies have demonstrated its antioxidant, anti-diabetic, anti-inflammatory, anti-obesity, and anti-cancer effects [16], [31]. It acts as a natural colour and nutritional booster in food, offering antioxidant and weight-management benefits [32]. In health supplements, its ability to address metabolic disorders, reduce inflammation, and protect against oxidative damage is highly valued [33]. For cosmetics, its skin-protective and brightening properties, stemming from its antioxidant and melanin-inhibiting effects, are key [34].

Diatoms, highly productive unicellular microalgae, along with brown seaweeds, have been extensively studied for fucoxanthin production through both in vitro and in vivo methods by modifying environmental factors and employing metabolic engineering [10]. The amount of fucoxanthin produced from microalgae is highly variable, influenced by factors such as the specific microalgae species, its growth stage, the inherent fucoxanthin concentration, and the effectiveness of the extraction process. Even without optimized cultivation, some microalgae naturally contain fucoxanthin levels ranging

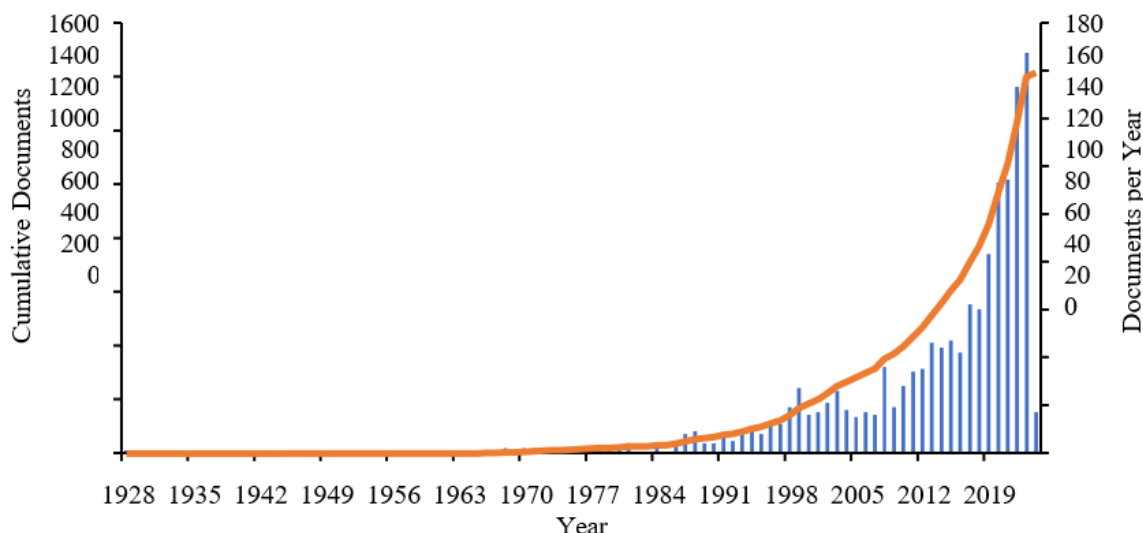


Figure 1. Numbers of publications from documents with TITLE-ABS-KEY search “fucoxanthin*”, and “diatom*”, or “production*” or “cultivation*” or “extraction*” from 1928 to January 2024. Line is cumulative document, bar is document per year

from 0.22% to 1.82% of their dry weight, though culture conditions significantly impact final yields [13], [35], [36],[37], [38].

Key parameters for optimizing fucoxanthin production from microalgae include environmental condition (light intensity, temperature, salinity) and nutrient supply. For instance, *T. lutea* and *Isochrysis zhangjiangensis* achieve peak biomass concentrations at 300 $\mu\text{mol}/\text{m}^2/\text{s}$, while *Isochrysis* sp. CCMP1324 prefers 60 $\mu\text{mol}/\text{m}^2/\text{s}$ [39]. High nitrogen levels (≥ 300 mg/L sodium nitrate) significantly enhance biomass, as observed in *P. tricornutum* (1.61 g/L) and *Cylindrotheca fusiformis* (1.52 g/L), with at least a 3.9-fold increase compared to nitrogen-deprived cultures [40]. Additionally, silica concentration (280 mg/L) boosts cell density and fucoxanthin content [41], while carbon sources like glucose and sodium bicarbonate further improve yield [6]. Salinity and temperature also play critical roles, with *Chaetoceros muelleri* reaching maximum fucoxanthin content at 45‰ salinity and *T. lutea* showing peak production at 25°C [39]. Likewise, the choice of culture medium affects fucoxanthin yield, as demonstrated in *Chaetoceros gracilis*, where Daigo IMK medium (200 mg/L nitrate) led to higher cell density (5.22×10^6 cells/mL) and fucoxanthin content (2.02 mg/L) compared to f/2 medium (75 mg/L nitrate) [18].

Efficient extraction and purification techniques are also essential for obtaining high purity fucoxanthin. Ultrasonic-assisted extraction (UAE) is widely used to break the tough silica cell walls of diatoms. Ethanol is being the preferred solvent due to its environmental friendliness yielding 4.45 ± 0.73 mg/L from *H. toxoneides* (AQ9) after purified by silica gel chromatography with n-hexane and ethyl acetate (3:2) [42].

However, large-scale production remains challenging due to issues like biological contamination and high downstream processing costs. To tackle these obstacles, innovative approaches, including adaptive evolution, multi-stage cultivation, and advanced bioreactor systems, are being explored. Additionally, fucoxanthin’s poor bioavailability and instability in the gastrointestinal tract pose significant limitations [43]. Encapsulation methods, particularly lipid-based delivery systems, have shown promise in improving its stability and absorption, thereby expanding its potential applications in functional foods and nutraceuticals [40], [44]. Nevertheless, further research is needed to fully understand fucoxanthin’s molecular mechanisms and develop cost-effective strategies to meet the rising global demand.

Recent bibliometric analyses reveal an increasing global interest in fucoxanthin production, particularly in regions like Germany, France, China, and Japan. Most research outputs are in the form of articles, review papers, and book chapters, emphasizing the need for further exploration of system designs and scalability. Future research directions should focus on optimizing photobioreactor configurations, improving nutrient delivery systems, and exploring genetic engineering techniques to enhance fucoxanthin yield. Moreover, integrating advanced technologies, such as optimized cultivation condition, extraction and purification methods, and sustainable stability approach, will pave the way for efficient and eco- friendly production of fucoxanthin for commercial applications.

A. The Trend Of Publications Analysis From 1928 To 2024

Figure 1 illustrates the cumulative growth of

fucoxanthin-related research from 1928 to 2019. The blue bars represent the number of documents published per year, while the orange line reflects the cumulative number of publications. This figure reveals a slow and steady growth phase from the early 20th century until the late 1990s, followed by a rapid and exponential increase in research output from the early 2000s onward.

The initial slow progress can be attributed to limited technological advancements and a lack of awareness regarding the potential applications of fucoxanthin. However, the turning point occurred in the early 2000s when advancements in marine biotechnology and microalgae cultivation techniques spurred interest in fucoxanthin as a valuable carotenoid [45]. The exponential increase in publications aligns with the global shift toward sustainable and natural bioactive compounds [46].

Another factor contributing to this growth is the rising demand for functional foods and dietary supplements, especially in regions like Asia and Europe, where traditional medicine and natural products play a significant role in healthcare [18]. Moreover, international collaborations and government funding for marine biotechnology research have further accelerated the exploration of fucoxanthin's potential.

B. Most Impactful Affiliation

Figure 2 displays the top institutions contributing to fucoxanthin research. Goethe University Frankfurt am Main leads the global research efforts, followed by the CNRS Centre National de la Recherche Scientifique and the Chinese Academy of Sciences. Other significant contributors include Sorbonne University, the University of Tokyo, and Hokkaido University.

The dominance of European institutions such as CNRS and Goethe University reflects the strong emphasis on marine biotechnology and bioresource management in the

European Union. In Asia, the Chinese Academy of Sciences and Japanese institutions like the University of Tokyo and Hokkaido University have made significant strides in fucoxanthin production. These countries have leveraged their rich marine biodiversity to enhance fucoxanthin extraction and purification methods.

The ranking of institutions based on publication output provides insights into the leading research centers and their contributions to the field. This information can be valuable for identifying potential collaborators, understanding the major research trends, and assessing the overall research landscape in fucoxanthin research. The dominance of Japanese institutions in this list may reflect the country's strong focus on marine natural products and its advanced research infrastructure. The presence of institutions from other countries highlights the international interest in fucoxanthin and the collaborative nature of research in this field.

C. Type Of Document

Figure 3 presents a horizontal bar graph illustrating the distribution of document types in fucoxanthin research. The length of each bar corresponds to the number of documents in each category, providing a quantitative overview of the various forms of publications in this field. The "Article" category dominates, representing the largest proportion of publications with 836 documents. This is a typical pattern in scientific research, as original research articles form the core of scientific literature. The high number of articles signifies a substantial body of primary research on fucoxanthin, covering a wide range of topics, including its extraction, characterization, biological activities, and potential applications.

The "Review" category, with 32 documents, indicates a significant effort to synthesize and summarize the existing knowledge on fucoxanthin. Review articles play a crucial

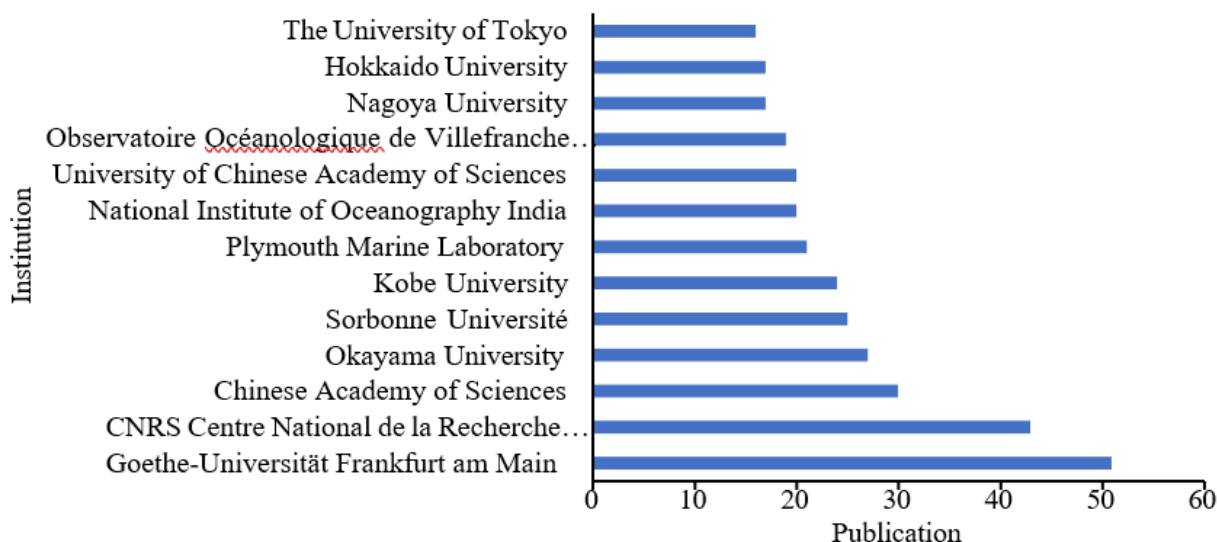


Figure 2. Top Institutions Contributing to Research on Fucoxanthin

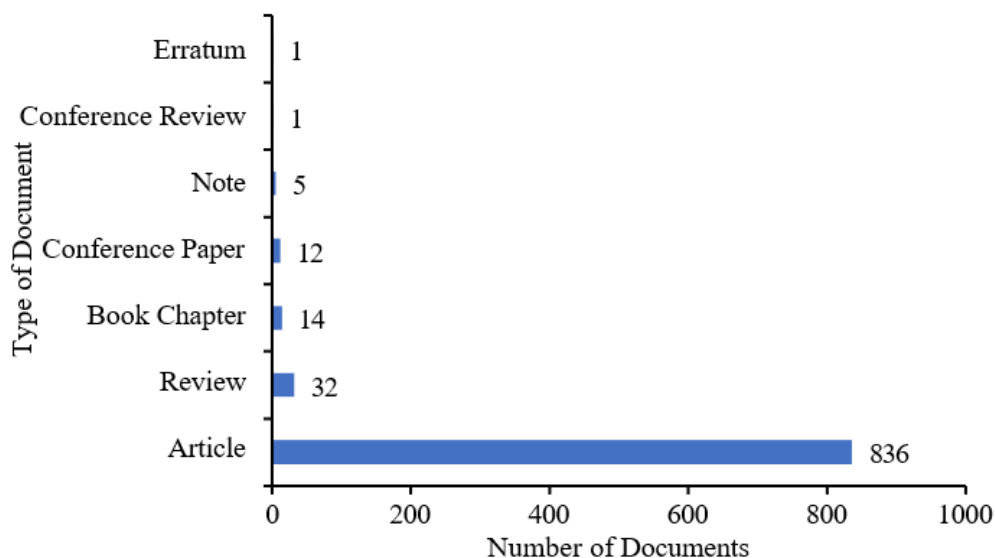


Figure 3. Distribution of the document type with TITLE-ABS-KEY search “fucoxanthin*”, and “diatom*”, or “production*” or “cultivation*” or “extraction*” extracted from Scopus database

role in consolidating research findings, identifying research gaps, and providing a comprehensive overview of the field. The presence of a substantial number of reviews suggests a growing body of literature that warrants synthesis and interpretation. The remaining categories, including "Book Chapter," "Conference Paper," "Note," "Conference Review," and "Erratum," represent a smaller fraction of the total publications. While these categories are less prominent, they still contribute to the overall knowledge base by providing supplementary information, preliminary findings, and corrections to published work.

The result highlights the importance of considering the diverse types of documents available in fucoxanthin research. It underscores the need to integrate findings from original research articles, review articles, and other sources to provide a comprehensive and balanced overview of the field.

By analyzing the distribution of document types, researchers can gain insight into the relative emphasis on different aspects of fucoxanthin research, identify areas where further synthesis is needed, and assess the overall maturity of the field.

D. Most Influential Country

Figure 5 presents a world map with color-coded regions, representing the geographical distribution of publications related to fucoxanthin research. The map highlights the concentration of research in specific regions, with North America, Europe, and Asia showing the highest activity. This reflects the presence of leading institutions and research centers in these areas, as well as the availability of resources and funding for marine natural product research. The bar graph at the bottom provides a quantitative measure of the number of documents from each region, further emphasizing the relative contributions of different geographical areas to fucoxanthin research.

The geographical distribution of publications provides insights into the global interest in fucoxanthin and the regional variations in research focus. The concentration of research in North America, Europe, and Asia may be attributed to the presence of advanced research infrastructure, established research networks, and a strong focus on marine biotechnology in these regions. The presence of research activity in other regions, albeit to a lesser extent, indicates a growing interest in fucoxanthin research worldwide.

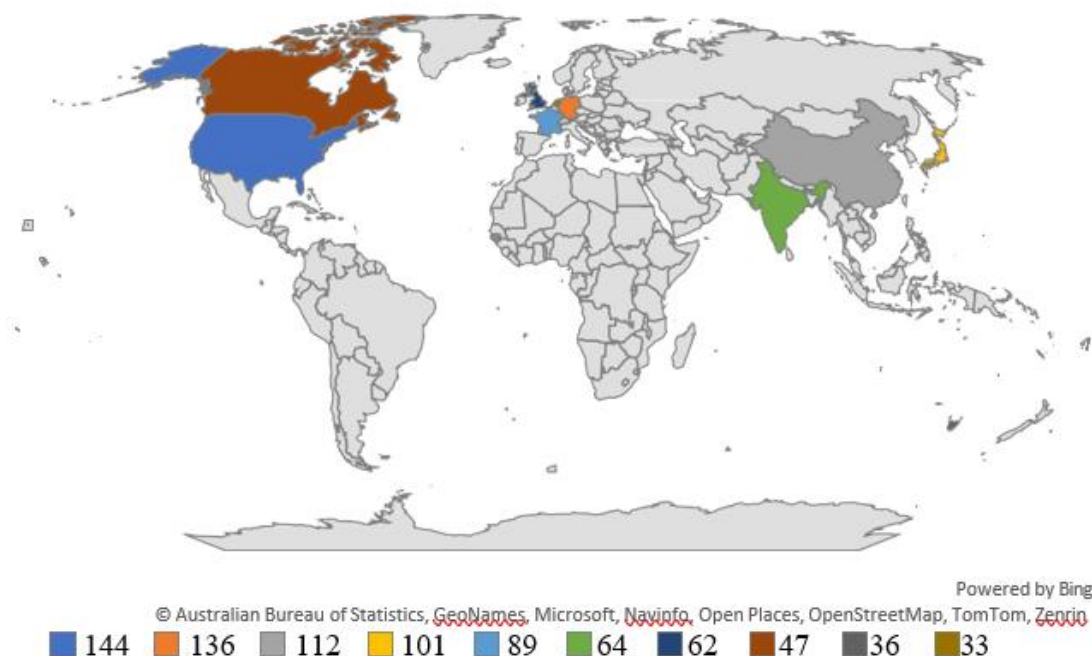


Figure 4. Top ten country with documents with TITLE-ABS-KEY search “fucoxanthin*”, and “diatom*”, or “production*” or “cultivation*” or “extraction*” extracted from Scopus database

This figure underscores the global nature of fucoxanthin research and highlights the regions that are at the forefront of this field. By analyzing the geographical distribution of publications, researchers can gain insights into the regional variations in research focus, identify potential collaborators, and assess the overall impact of fucoxanthin research on a global.

E. Keyword Analysis

This VOSviewer network visualization represents the "All keywords" map as depicted in Figure 5a, providing a comprehensive overview of the research landscape surrounding fucoxanthin within the context of diatoms. Each node in the network represents a keyword, and the size of the node reflects the frequency of its occurrence in the literature. The positioning and clustering of nodes indicate the relationships and co-occurrence patterns between keywords. The color gradient of the nodes, ranging from blue to yellow, represents the average publication year, with blue indicating earlier publications and yellow indicating more recent ones. The central and largest node, "fucoxanthin," underscores its pivotal role as the primary focus of research in this field. Surrounding it are key terms like "diatoms," "microalgae," "marine algae," and "phytoplankton," highlighting the ecological and biological contexts in which fucoxanthin is studied. The presence of terms like "antioxidant," "anti-inflammatory activity," "oxidative stress," and "inflammation" reveals the significant interest in fucoxanthin's bioactivities and

therapeutic potential. Keywords related to biochemical processes, such as "photosynthetic pigments," "xanthophylls," and "beta-carotene," illustrate the fundamental research aimed at understanding fucoxanthin's role in diatom physiology and metabolism. The inclusion of terms like "dietary supplements," "algal extract," and "plant extract" indicates the translational aspects of fucoxanthin research, focusing on its applications in nutraceutical and pharmaceutical industries.

The map also highlights recent advancements in extraction technologies, with keywords like "solvents," "ethanol," and "microalgae biomass." This indicates a shift towards eco-friendly and efficient extraction methods to enhance the commercial viability of fucoxanthin production. Additionally, the clustering of "oxidative stress," "obesity," and "cancer" underscores the potential therapeutic applications of fucoxanthin in combating chronic diseases.

The temporal analysis, represented by the color gradient, reveals the evolution of research trends. Earlier studies (blue nodes) focused on basic aspects such as "diatoms," "fucoxanthin," and "photosynthetic pigments," while more recent research (yellow nodes) has shifted towards exploring its bioactivities and applications, as evidenced by the prominence of terms like "antioxidant," "anti-inflammatory activity," and "dietary supplements." This temporal shift reflects the growing recognition of fucoxanthin's potential beyond its ecological role in diatoms. The clustering of nodes provides further insights

into the thematic organization of research, with distinct clusters focusing on bioactivity, biochemistry, and applications.

From Figure 5b, the central and largest node, "fucoxanthin," again highlights its central role in the research network. Surrounding it are clusters of interconnected keywords, revealing the major research themes. One prominent cluster includes terms like "diatoms," "Phaeodactylum tricornutum," "photosynthesis,"

and "pigments," representing the fundamental research on fucoxanthin's role in diatom physiology and ecology. Another cluster, comprising terms like "antioxidant," "antioxidant activity," "anti-inflammatory," and "oxidative stress," underscores the significant focus on fucoxanthin's bioactivities and therapeutic potential. The presence of terms like "bioactive compounds" and "carotenoids" further emphasizes the research on fucoxanthin as a valuable natural product.

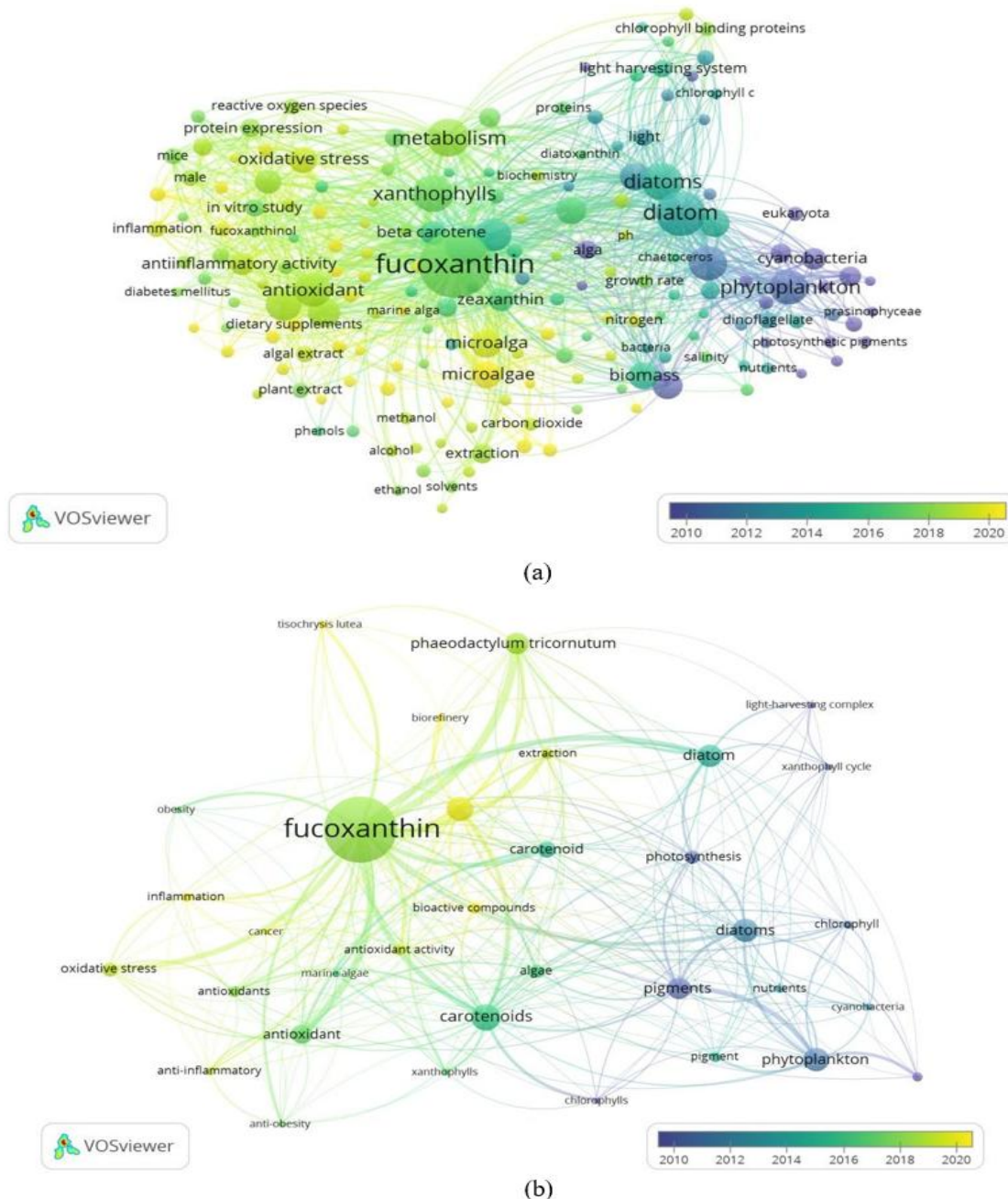


Figure 5. (a) All keywords and (b) term co-occurrence maps illustrating research trends on fucoxanthin from diatom in some application.

Both VOSviewer maps provide valuable insights into the evolving research landscape of fucoxanthin. The all-keywords map captures the broader trends and interdisciplinary nature of fucoxanthin studies, while the diatom-specific map offers a deeper understanding of the

biological and technological aspects of fucoxanthin production from diatoms. These findings align with recent literature and suggest promising avenues for future research in sustainable production and health applications.

TABLE 1.
PREVIOUS STUDIES OF PRODUCTION FUCOXANTHIN FROM MICROALGAE

No.	Microalgae	Medium	Cultivation Condition	Extraction Method	Biomass	Fucoxanthin	References
1.	<i>Chaetoceros</i> sp.	Aquaculture wastewater mixed with NMB3# medium	Grown under 25 PSU, at 23 ± 2°C, pH 7.0 ± 0.2, and a light/dark cycle of 12 h:12 h	10 g freeze-dried algae extracted with 1 ml anhydrous methanol using ultrasound-assisted extraction with ice-water bath at 40 Hz	2.6 × 10 ⁵ cells/mL	40.13 mg/L	[47]
2.	<i>Phaeodactylum tricornutum</i>	f/2 medium supplemented with N and P	Maintained at 22°C, illuminated by 250 µmol/m ² /s white LED light, using a 16:8 light-dark cycle for 12 days of growth	Algae pellets were macerated with 5 ml clear methanol	30 million cells/mL	17 ppm	[48]
3.	<i>Phaeodactylum tricornutum</i>	Modified F/2 artificial seawater	Grown using photosynthetic autotrophic methods at 20°C, 60 µmol/m ² /s under a 12-hour light and 12-hour dark cycle using red, blue, green light.	Algal powder was repeatedly extracted with methanol in darkness, centrifuged, and the supernatant collected until the powder was colorless	1.02 g/L	11.07 ± 0.52 mg/g	[49]
4.	<i>Isochrysis galbana</i> LB 2307	Tomato waste hydrolysate	Growth occurred at 25°C under a 12:12 h light:dark regimen, with 4,000 lux of light	A 1:30 ratio of <i>I. galbana</i> powder (20 mg) to methanol was used for two extractions at 35°C	1.21 × 10 ⁷ cells/mL and 2.13 g/L biomass	21.02 mg/g	[50]
5.	<i>Odontella aurita</i> OAOSH22	Jeju lava seawater with f/2 medium	Cultivated at 17°C and 40 µmol photons/m ² /s under a 16:8 h light:dark cycle	Freeze-dried biomass extracted with 1 mL of 99% HPLC grade methanol	4.32±0.23 ×10 ⁴ cells/ml	0.59 µg/L	[51]
6.	<i>Phaeodactylum tricornutum</i>	F/2 seawater	Cultivated at 18°C and 12:12	1500 ± 20 mg freeze-died of biomass mixed	NA	8–9%	[52]

No.	Microalgae	Medium	Cultivation Condition	Extraction Method	Biomass	Fucoxanthin	References
			h light:dark cycle	with ethanol and extracted using supercritical CO ₂ at 13 MPa and 50°C)			
7.	<i>Phaeodactylum tricornutum</i>	Recycled-f/2-Si medium	Maintained at 20 ± 1°C, under continuous illumination of 100 µmol/m ² /s, with a 14-hour light and 10-hour dark cycle.	Algal powder was treated twice with DMSO, and then re-suspended three times in a 1:1 acetone/methanol solution in darkness, continuing until the algal pellet was devoid of color.	0.143 ± 0.009 g/L	14.316 ± 0.587 mg/g	[53]
8.	<i>Pavlova gyrams</i>	Daigo's IMK medium	Cultured at 30°C, pH 7-8, with 100 rpm shaking and continuous 100 µmol photons/m ² /s illumination.	Disrupted with glass beads and methanol/acetone (1:1), 30 cycles (670 ×g/0 rpm, 4°C). Supernatant was collected after centrifugation (10,000 ×g, 4°C) and vacuum-dried.	2.56 g/L	6.9 mg/g	[54]
9.	<i>Tisochrysis lutea</i>	f/2 medium	Grown at 21°C with continuous ~100 µmol photons/m ² /s white light.	Biomass was extracted with DES (1:25 w/v) at 25°C for 1 hour, then centrifuged and filtered (0.45µm).	NA	22.03 mg/g	[55]
10.	<i>Odontella aurita</i>	Modified L1 medium	Cultured in 1.2 L PBRs (25±1°C, 60-70 µmol/m ² /s light), aerated with 1% CO ₂ (0.2 vvm), and used after 5-6 days under red and blue light	Centrifuged cells were freeze-dried, then acetone-extracted (10 mg/5 mL, 4°C, 24 h) and filtered (0.2 µm) for HPLC	570 mg/L/d	9.41 mg/L/d	[56]
11.	<i>Phaeodactylum tricornutum</i>	f/2 medium with urea supplementation	Grown at 25 ± 0.5°C, 3000 lx light, 14/10 h light/dark	15 mg freeze-dried cells, extracted with ethanol (2x, 15 min), centrifuged, nitrogen dried, and redissolved in ethanol (1 mL), in dark conditions	NA	1.47 mg/g	[57]
12.	<i>Chaetoceros calcitrans</i>	NA	NA	Extracted with ratio of biomass:	NA	8.28 ± 0.49 mg/g	[58]

No.	Microalgae	Medium	Cultivation Condition	Extraction Method	Biomass	Fucoxanthin	References
13.	(UPMC-A0010) <i>Nitzschia laevis</i>	Modified Lewin's medium without yeast extract	Cultured at 23°C and pH 8.6 with 80 $\mu\text{mol photons/m}^2/\text{s}$ light in 700 mL photobioreactors	methanol is 1:250 w/v Powder (4g) was ground (liquid N ₂), extracted with methanol (120mL), centrifuged, re-extracted until colorless, then supernatants were concentrated (20°C) and lyophilized	3.04 g/L	1.68 mg/g	[38]
14.	<i>Phaeodactylum tricornutum</i>	f/2 medium (without the addition of vitamins)	Cultured in 50 mL medium (100 mL flasks) at 25 $\pm$ 3°C, 30 $\mu\text{mol photons/m}^2/\text{s}$, with air/CO ₂ bubbled from the base	Biomass washed (deionized water, 3x), freeze-dried, then extracted with ethanol (100:1, 2x), filtered (0.22 μm), and analyzed by HPLC, at room temperature and ambient light.	2.3 mg/L/day	59.2 $\pm$ 22.8 mg/g	[39]
15.	<i>Mallomonas</i> sp. (<i>Synurophyceae</i>)	f/2 medium	Grown under 24°C, 140 $\mu\text{mol/m}^2/\text{s}$ light intensity with a 16:8 light-dark regime and a consistent shaking at 150 rpm with 5% CO ₂ atmosphere.	Extracted using biomass: chloroform-methanol 3:1 with 96% ethanol and acetonitrile	26.6 mg/g	26.6 mg/g	[59]
16.	<i>Chaetoceros muelleri</i>	Seawater consisting F + Si media	150 $\mu\text{mol photons/m}^2/\text{s}$ light irradiance on a 12 h: 12 h light: dark cycle, 35‰ salinity, at 25 $\pm$ 3°C	Extracted using liquid nitrogen and 100% ice cold acetone under dim light	29 mg/L/d	2.92 mg/g	[60]

Table 1 reveals that some microalgae species, such as *Phaeodactylum tricornutum*, *Isochrysis galbana*, *Chaetoceros* sp., and *Odontella aurita* have been extensively studied for fucoxanthin production. The extraction methods range from traditional solvent-based approaches using methanol and ethanol to advanced techniques like ultrasound-assisted extraction and supercritical CO₂ extraction. For instance, *Phaeodactylum tricornutum* cultivated in f/2 medium with urea supplementation yielded 1.47 mg/g of fucoxanthin through ethanol extraction [57], while *Odontella aurita* produced 9.41 mg/L/day using

acetone extraction [56]. Additionally, *Tisochrysis lutea* demonstrated a high yield of 22.03 mg/g through deep eutectic solvent extraction [55]. These findings highlight the significance of optimizing cultivation conditions, such as light intensity, temperature, and nutrient supplementation, to enhance fucoxanthin yield.

This data is invaluable for researchers aiming to optimize fucoxanthin production from microalgae. By understanding the impact of different cultivation media, light regimes, and extraction techniques, future studies can focus on enhancing biomass productivity and improving extraction efficiency. For example, the use of ultrasound-

assisted extraction with an ice-water bath at 40 Hz for *Chaetoceros* sp. yielded 40.13 mg/L, demonstrating the potential of innovative technologies to improve yield [47]. Moreover, the supercritical CO₂ method used for *Phaeodactylum tricornutum* achieved an 8-9% yield, showcasing the benefits of advanced, eco- friendly techniques [52]. By leveraging these findings, researchers can develop sustainable and cost-effective strategies for large-scale fucoxanthin production, meeting the growing demand for natural bioactive compounds in various industries.

F. Utilization Of Fucoxanthin

Fucoxanthin is garnering significant attention for its diverse applications across various industries, particularly as feed, food, cosmetic, and pharmaceutical ingredients (Figure 5). Its potential in animal feed stems from its ability to enhance the nutritional profile and aesthetic appeal of

animal products. As evidenced by [61], supplementing quail feed with fucoxanthin significantly improves the docosahexaenoic acid (DHA) content in egg yolks. DHA, an omega-3 fatty acid, is crucial for brain development and cardiovascular health, making eggs enriched with it a valuable dietary source. Furthermore, Gumus et al. (2018) demonstrated fucoxanthin's antimicrobial properties against *Staphylococcus* spp. in broiler meat, suggesting its potential to improve meat safety and reduce reliance on antibiotics in poultry farming. This dual functionality, enhancing nutritional value and offering antimicrobial benefits, positions fucoxanthin as a promising additive in animal feed, contributing to both animal health and the production of high-quality animal products. Additionally, Sasaki et al., [62] showed that fucoxanthin can positively influence the appearance and shelf life of chicken meat, further underscoring its potential in improving animal-derived food products.

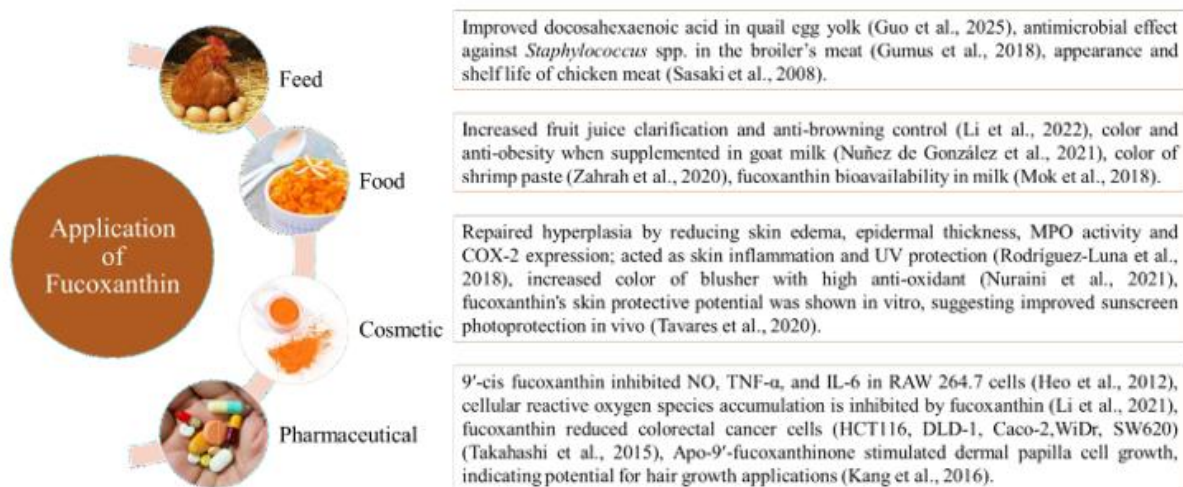


Figure 5. Application of Fucoxanthin

In the realm of food, fucoxanthin's applications are equally diverse, leveraging its antioxidant, anti-obesity, and color-enhancing properties. Li et al. [63] highlighted its role in enhancing fruit juice clarification and preventing browning, crucial for maintaining the visual appeal and nutritional integrity of fruit-based beverages. When supplemented in goat milk, as shown by Nuñez de González et al., [64], fucoxanthin not only imparts a desirable color but also contributes to anti-obesity effects, addressing the growing consumer demand for functional foods with health benefits. Its application in coloring shrimp paste, as documented by Zahrah et al., [65], illustrates its potential as a natural food colorant, offering an alternative to synthetic dyes. Moreover, Mok et al., [66] demonstrated the enhanced bioavailability of fucoxanthin when consumed with milk, suggesting that dairy products could serve as an effective delivery system for this beneficial compound.

Fucoxanthin also holds considerable promise in the cosmetic and pharmaceutical industries, primarily due to its

skin-protective, anti-inflammatory, and antioxidant properties. Rodriguez-Luna et al., [34] reported its efficacy in repairing hyperplasia by reducing skin edema and inflammation, hence, it has potential in treating skin disorders. In cosmetics, Nuraini et al., [67] explored its use in blushers, noting its ability to enhance color and provide antioxidant benefits, aligning with the trend towards natural and multifunctional cosmetic products. Tavares et al., [68] further demonstrated fucoxanthin's skin protective potential in vitro, suggesting its ability to enhance sunscreen photoprotection in vivo. In pharmaceuticals, Heo et al., [69] found that 9'-cis fucoxanthin inhibited the production of pro-inflammatory markers in RAW 264.7 cells, indicating its anti-inflammatory potential. Li et al., [70] highlighted its ability to inhibit cellular reactive oxygen species accumulation and combat oxidative stress-related diseases. Takahashi et al., [71] demonstrated its effectiveness in reducing colorectal cancer cells, indicating its potential in cancer therapy. Kang et al., [72] showed that Apo-9'-

fucoxanthinone stimulated dermal papilla cell growth improving hair growth.

As described, fucoxanthin's multifaceted benefits make it a valuable compound with broad applications across feed, food, cosmetic, and pharmaceutical industries. Its ability to enhance nutritional value, improve product quality, and offer therapeutic benefits underscores its potential as a functional ingredient and medicinal agent. As research continues to uncover its diverse properties, fucoxanthin is poised to play an increasingly significant role in various sectors, contributing to improved animal health, enhanced food products, and innovative cosmetic and pharmaceutical formulations.

G. Challenges And Opportunities

The production and development of fucoxanthin from microalgae present significant opportunities in various industries, including pharmaceuticals, cosmetics, food, and feed. One of the primary advantages is that microalgae are a

sustainable and renewable source of fucoxanthin, capable of producing high yields through controlled cultivation systems. Microalgae such as *Phaeodactylum tricornutum*, *Tisochrysis lutea*, and *Isochrysis galbana* have shown promising results in accumulating fucoxanthin under optimized light, nutrient, and temperature conditions. The use of advanced technologies like photobioreactors and genetic engineering can further enhance fucoxanthin production efficiency [18]. Additionally, the growing demand for natural antioxidants and functional ingredients in health and wellness products creates a lucrative market for fucoxanthin. Its potential applications in anti-obesity treatments, cancer prevention, and skincare products make it highly valuable in the pharmaceutical and cosmetic industries. Moreover, its role as a natural pigment in animal feed and functional food products opens new opportunities for sustainable and eco-friendly alternatives to synthetic additives.

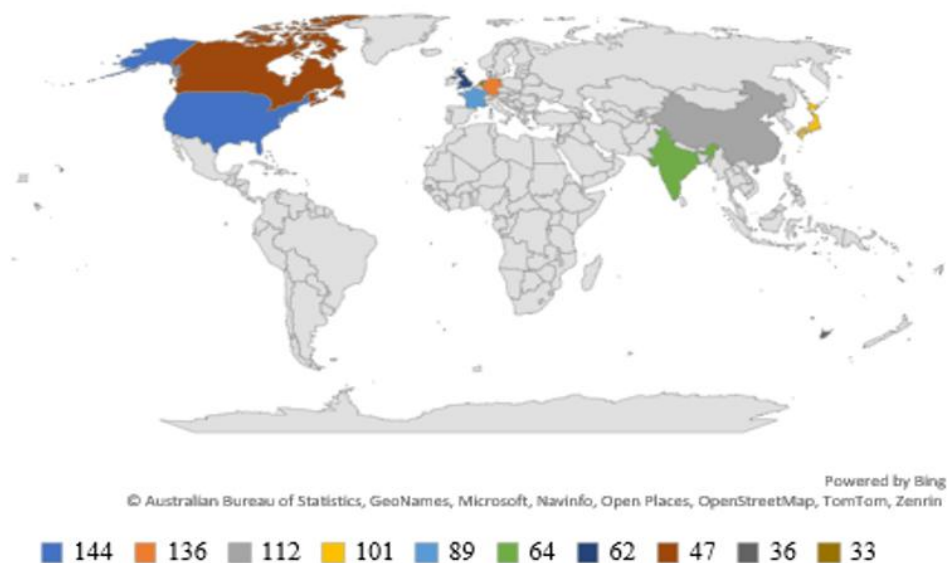


Figure 6. Current Advances in Microalgae-Based Fucoxanthin Production

Despite these opportunities, several challenges hinder the large-scale production and commercialization of fucoxanthin from microalgae. One major challenge is the high production cost associated with microalgae cultivation and downstream processing. The extraction and purification of fucoxanthin are complex and require environmentally friendly solvents and advanced techniques such as supercritical CO₂ extraction and ultrasound-assisted methods to improve yield and purity. Furthermore, microalgae cultivation is highly sensitive to environmental factors, such as light intensity, temperature fluctuations, and nutrient availability, which can affect fucoxanthin content and biomass productivity. Another challenge is the stability and bioavailability of fucoxanthin, as it is sensitive to light,

heat, and oxygen, limiting its shelf life and effectiveness in functional products. Addressing these challenges requires further research on strain selection, metabolic engineering, and innovative extraction technologies to enhance productivity and reduce costs. Collaboration between researchers, industries, and policymakers is essential to develop sustainable production systems and regulatory frameworks that support the commercialization of fucoxanthin from microalgae.

H. Current Advances In Microalgae-Based Fucoxanthin Production

Figure 6 outlines four primary strategies for optimizing fucoxanthin yields namely cultivation mode selection,

cultivation conditions, extraction methods, and genetic enhancement through molecular biology and mutagenesis. Cultivation mode significantly influences microalgal growth and fucoxanthin accumulation. Autotrophic cultivation uses light and CO₂ [73], while heterotrophic methods employ continuous organic carbon sources such as glucose, often yielding higher biomass [74]. Mixotrophic cultivation, combining both, has shown improved productivity and fucoxanthin content [75]. For instance, *Isochrysis galbana* grown under mixotrophic conditions (tomato waste hydrolysate) demonstrated enhanced fucoxanthin levels accounting for 21.02 mg/g [76]. Environmental factors such as light intensity and pH, along with key nutrients like nitrogen, iron, and silica, also play vital roles. Higher light boosts fucoxanthin in autotrophic cultures (300 µmol/m²/s), while it is less important in heterotrophic ones where carbon sources like glucose are key. Moderate light with organic carbon works best in mixotrophic systems (100-120 µmol/m²/s) [23]. Organic carbon enhances production in heterotrophic and mixotrophic cultures. Optimizing iron (e.g., 125 µM for *Pavlova* sp.) and using enriched media (e.g., F/2 for *Cyclotella* and *Isochrysis*) significantly increase fucoxanthin yields [76], [77]. The second half of the framework focuses on downstream and molecular strategies. Extraction methods have evolved from conventional solvent and maceration techniques to more advanced, green technologies such as enzyme-assisted, microwave-assisted, ultrasound-assisted, and supercritical fluid extraction. Various advanced extraction techniques have been employed to obtain fucoxanthin from different algal sources. For instance, methanol-based maceration extraction of *Isochrysis* sp. yielded around 14.8 mg/g [78], while enzyme-assisted extraction (EAE) using Viscozyme® L from *Fucus vesiculosus* achieved 657 µg/g under specific enzyme and seaweed ratios and incubation time [79]. Microwave-assisted extraction (MAE) with ethanol proved rapid for *Phaeodactylum tricornutum* [80], and optimized ultrasound-assisted extraction (UAE) using ethyl lactate from *Sargassum fusiforme* reached 696.85 µg/g [81]. Supercritical fluid extraction (SFE) with ethanol as a co-solvent also successfully extracted fucoxanthin from *Phaeodactylum tricornutum*, yielding 85.03 mg/g extract under specific pressure and temperature conditions [82].

Meanwhile, fucoxanthin production can be enhanced through genetic engineering of algae, where modifying genes like DXS and PSY in *Phaeodactylum tricornutum* significantly increased yields up to 24.2 mg/g and 18.4 mg/g, respectively [83], [84]. Random mutagenesis, using methods like UV light, EMS, and X-rays, offers an alternative approach, with EMS treatment on *Phaeodactylum tricornutum* achieving a 35% increase in fucoxanthin content [85], [86]. However, the use of genetically modified organisms (GMOs) and random mutagenesis techniques, particularly chemical and physical methods, faces strict regulations in many countries due to

safety, efficacy, and environmental concerns [85], [87]. Notably, random mutagenesis is considered incompatible with organic agriculture standards due to the use of potentially hazardous chemicals and its non-natural alteration of an organism's genes [88].

IV. CONCLUSION

The bibliometric analysis reveals a robust and growing interest in fucoxanthin research, primarily due to its promising health benefits and commercial potential. Microalgae have become the focus of fucoxanthin production because of their high yield, adaptability, and sustainability. Research efforts are increasingly directed toward optimizing cultivation parameters, enhancing extraction techniques, and improving the bioavailability of fucoxanthin. Despite advancements, challenges remain in large-scale cultivation, and cost-effective extraction. Innovative solutions such as cultivation condition, environment modification, molecular biology and extraction methods are being explored. Ultimately, this analysis supports evidence-based strategies for advancing fucoxanthin utilization in food, pharmaceutical, and cosmetic industries, paving the way for its broader application in promoting human health and environmental sustainability. Furthermore, future research should focus on optimizing extraction methods, enhancing bioavailability, and conducting clinical trials to validate its efficacy. This analysis serves as a foundation for researchers and policymakers to make informed decisions and foster innovation in the utilization of fucoxanthin for human health and sustainability.

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REFERENCES

- [1] X. Liu, Y. Hong, and Y. Liu, "Cultivation of *Chlorella* sp. HQ in Inland Saline-Alkaline Water Under Different Light Qualities," *Front Environ Sci Eng*, vol. 16, no. 4, p. 45, Apr. 2022, doi: 10.1007/s11783-021-1479-2.
- [2] S. A. Ahmed, P. Mendonca, R. Elhag, and K. F. A. Soliman, "Anticancer Effects of Fucoxanthin through Cell Cycle Arrest, Apoptosis Induction, Angiogenesis Inhibition, and Autophagy Modulation," *Int J Mol Sci*, vol. 23, no. 24, p. 16091, Dec. 2022, doi: 10.3390/ijms232416091.
- [3] F. M. Abdoul-Latif et al., "Unlocking the Green Gold: Exploring the Cancer Treatment and the Other Therapeutic Potential of Fucoxanthin Derivatives from Microalgae," *Pharmaceuticals*, vol. 17, no. 7, p. 960, Jul. 2024, doi: 10.3390/ph17070960.
- [4] Y.-L. Dai, Y.-F. Jiang, Y.-A. Lu, J.-B. Yu, M.-C. Kang, and Y.-J. Jeon, "Fucoxanthin-rich Fraction from *Sargassum fusiforme* Alleviates Particulate Matter-Induced Inflammation In Vitro and In Vivo," *Toxicol Rep*, vol. 8, pp. 349–358, 2021, doi: 10.1016/j.toxrep.2021.02.005.
- [5] Y. K. Leong, C.-Y. Chen, S. Varjani, and J.-S. Chang, "Producing Fucoxanthin from Algae – Recent Advances in Cultivation Strategies and Downstream Processing," *Bioresour Technol*, vol. 344, p. 126170, Jan. 2022, doi: 10.1016/j.biortech.2021.126170.
- [6] A. Kanamoto, Y. Kato, E. Yoshida, T. Hasunuma, and A. Kondo, "Development of a Method for Fucoxanthin Production Using the Haptophyte Marine Microalga *Pavlova* sp. OPMS 30543," *Marine Biotechnology*, vol. 23, no. 2, pp. 331–341, Apr. 2021, doi: 10.1007/s10126-021-10028-5.
- [7] H. Won, E. Ro, S. Seo, B.-H. Kim, and E. Jin, "Isolation and Cultivation of Freshwater Diatom *Nitzschia palea* HY1 for Increasing Biomass and Fucoxanthin Production," *Algae*, vol. 38,

- no. 3, pp. 191–202, Sep. 2023, doi: 10.4490/algae.2023.38.9.3.
- [8] B. A. Guler, I. Deniz, Z. Demirel, O. Yesil-Celiktas, and E. Imamoglu, "A Novel Subcritical Fucoxanthin Extraction with a Biorefinery Approach," *Biochem Eng J*, vol. 153, p. 107403, Jan. 2020, doi: 10.1016/j.bej.2019.107403.
- [9] K. Seth, A. Kumar, R. P. Rastogi, M. Meena, V. Vinayak, and Harish, "Bioprospecting of Fucoxanthin from Diatoms — Challenges and Perspectives," *Algal Res*, vol. 60, p. 102475, Dec. 2021, doi: 10.1016/j.algal.2021.102475.
- [10] Y. S. Khaw et al., "Fucoxanthin Production of Microalgae under Different Culture Factors: A Systematic Review," *Mar Drugs*, vol. 20, no. 10, p. 592, Sep. 2022, doi: 10.3390/md20100592.
- [11] S. M. Kim et al., "A Potential Commercial Source of Fucoxanthin Extracted from the Microalga *Phaeodactylum tricornutum*," *Appl Biochem Biotechnol*, vol. 166, no. 7, pp. 1843–1855, Apr. 2012, doi: 10.1007/s12010-012-9602-2.
- [12] S. M. Kim, S.-W. Kang, O.-N. Kwon, D. Chung, and C.-H. Pan, "Fucoxanthin as a major carotenoid in *Isochrysis aff. galbana*: Characterization of extraction for commercial application," *J Korean Soc Appl Biol Chem*, vol. 55, no. 4, pp. 477–483, Aug. 2012, doi: 10.1007/s13765-012-2108-3.
- [13] K. S. Khoo, C. W. Ooi, K. W. Chew, S. C. Foo, and P. L. Show, "Bioprocessing of *Chaetoceros calcitrans* for the Recovery of Fucoxanthin Using CO₂-Based Alkyl Carbamate Ionic Liquids," *Bioresour Technol*, vol. 322, p. 124520, Feb. 2021, doi: 10.1016/j.biortech.2020.124520.
- [14] V. Pasquet et al., "Study on the Microalgal Pigments Extraction Process: Performance of Microwave Assisted Extraction," *Process Biochemistry*, vol. 46, no. 1, pp. 59–67, Jan. 2011, doi: 10.1016/j.procbio.2010.07.009.
- [15] R. N. Dewi et al., "Bioremediation of Seafood Processing Wastewater by Microalgae: Nutrient Removal, and Biomass, Lipid and Protein Enhancement," *Environmental Engineering Research*, vol. 29, no. 6, pp. 230673–0, Apr. 2024, doi: 10.4491/eer.2023.673.
- [16] S. Mohamadnia, O. Tavakoli, and M. A. Faramarzi, "Enhancing Production of Fucoxanthin by the Optimization of Culture Media of the Microalga *Tisochrysis lutea*," *Aquaculture*, vol. 533, p. 736074, Feb. 2021, doi: 10.1016/j.aquaculture.2020.736074.
- [17] A.-H. Lee et al., "Validation of Fucoxanthin from Microalgae *Phaeodactylum tricornutum* for the Detection of Amyloid Burden in Transgenic Mouse Models of Alzheimer's Disease," *Applied Sciences*, vol. 11, no. 13, p. 5878, Jun. 2021, doi: 10.3390/app11135878.
- [18] H. Sun et al., "Fucoxanthin from Marine Microalgae: A Promising Bioactive Compound for Industrial Production And Food Application," *Crit Rev Food Sci Nutr*, vol. 63, no. 26, pp. 7996–8012, Oct. 2023, doi: 10.1080/10408398.2022.2054932.
- [19] C. Lourenço-Lopes et al., "Biological Action Mechanisms of Fucoxanthin Extracted from Algae for Application in Food and Cosmetic Industries," *Trends Food Sci Technol*, vol. 117, pp. 163–181, Nov. 2021, doi: 10.1016/j.tifs.2021.03.012.
- [20] M. M. A. Nur et al., "Cultivating Microalgae with Biophotovoltaic to Produce Bioelectricity: A Bibliometric Analysis," *International Journal of Marine Engineering Innovation and Research*, vol. 9, no. 4, Dec. 2024, doi: 10.12962/j25481479.v9i4.21771.
- [21] Y. S. Khaw et al., "The Critical Studies of Fucoxanthin Research Trends from 1928 to June 2021: A Bibliometric Review," *Mar Drugs*, vol. 19, no. 11, p. 606, Oct. 2021, doi: 10.3390/md19110606.
- [22] Y. K. Leong, F.-C. Yang, and J.-S. Chang, "Extraction of Polysaccharides from Edible Mushrooms: Emerging Technologies and Recent Advances," *Carbohydr Polym*, vol. 251, p. 117006, Jan. 2021, doi: 10.1016/j.carbpol.2020.117006.
- [23] F. S. Budiarto et al., "Current Advances in Microalgae- Based Fucoxanthin Production and Downstream Processes," *Bioresour Technol*, vol. 428, p. 132455, Jul. 2025, doi: 10.1016/j.biortech.2025.132455.
- [24] E. Sahabudin et al., "Future Trends and Patterns in Diatom Fatty Acid Research from A Bibliometric Standpoint," *Biocatal Agric Biotechnol*, vol. 61, p. 103373, Oct. 2024, doi: 10.1016/j.bcab.2024.103373.
- [25] R. Han, B. Zhou, Y. Huang, X. Lu, S. Li, and N. Li, "Bibliometric Overview of Research Trends on Heavy Metal Health Risks and Impacts in 1989–2018," *J Clean Prod*, vol. 276, p. 123249, Dec. 2020, doi: 10.1016/j.jclepro.2020.123249.
- [26] N. Bezak et al., "Soil Erosion Modelling: A Bibliometric Analysis," *Environ Res*, vol. 197, p. 111087, Jun. 2021, doi: 10.1016/j.envres.2021.111087.
- [27] A. T. Ubando, A. D. M. Africa, M. C. Maniquiz-Redillas, A.B. Culaba, W.-H. Chen, and J.-S. Chang, "Microalgal Biosorption of Heavy Metals: A Comprehensive Bibliometric Review," *J Hazard Mater*, vol. 402, p. 123431, Jan. 2021, doi: 10.1016/j.jhazmat.2020.123431.
- [28] D. Ilmasari, E. Sahabudin, F. A. Riyadi, N. Abdullah, and A. Yuzir, "Future Trends and Patterns in Leachate Biological Treatment Research from A Bibliometric Perspective," *J Environ Manage*, vol. 318, p. 115594, Sep. 2022, doi: 10.1016/j.jenvman.2022.115594.
- [29] MMR, "Fucoxanthin Market: Global Industry Analysis and Forecast (2024-2030)," <https://www.maximizemarketresearch.com/market-report/global-fucoxanthin-market/98879/>.
- [30] J. Su et al., "Fucoxanthin, a Marine Xanthophyll Isolated from *Conticribra weissflogii* ND-8: Preventive Anti- Inflammatory Effect in a Mouse Model of Sepsis," *Front Pharmacol*, vol. 10, Aug. 2019, doi: 10.3389/fphar.2019.00906.
- [31] H. Pereira et al., "Fucoxanthin Production from *Tisochrysis lutea* and *Phaeodactylum tricornutum* at Industrial Scale," *Algal Res*, vol. 56, p. 102322, Jun. 2021, doi: 10.1016/j.algal.2021.102322.
- [32] X. Qiang et al., "The Complex of Phycobiliproteins, Fucoxanthin, and Krill Oil Ameliorates Obesity through Modulation of Lipid Metabolism and Antioxidants in Obese Rats," *Nutrients*, vol. 14, no. 22, p. 4815, Nov. 2022, doi: 10.3390/nu14224815.
- [33] M.-B. Kim, H. Kang, Y. Li, Y.-K. Park, and J.-Y. Lee, "Fucoxanthin Inhibits Lipopolysaccharide-Induced Inflammation and Oxidative Stress by Activating Nuclear Factor E2-Related Factor 2 Via the Phosphatidylinositol 3- Kinase/AKT Pathway in Macrophages," *Eur J Nutr*, vol. 60, no. 6, pp. 3315–3324, Sep. 2021, doi: 10.1007/s00394-021- 02509-z.
- [34] A. Rodríguez-Luna et al., "Fucoxanthin-Containing Cream Prevents Epidermal Hyperplasia and UVB-Induced Skin Erythema in Mice," *Mar Drugs*, vol. 16, no. 10, p. 378, Oct. 2018, doi: 10.3390/md16100378.
- [35] S. C. Foo et al., "Antioxidant Capacities of Fucoxanthin-Producing Algae as Influenced by Their Carotenoid and Phenolic Contents," *J Biotechnol*, vol. 241, pp. 175–183, Jan. 2017, doi: 10.1016/j.jbiotec.2016.11.026.
- [36] F. Derwenskus, S. Weickert, I. Lewandowski, U. Schmid- Staiger, and T. Hirth, "Economic Evaluation of Up- And Downstream Scenarios for the Co-Production of Fucoxanthin and Eicosapentaenoic Acid with *P. Tricornutum* Using Flat-Panel Airlift Photobioreactors with Artificial Light," *Algal Res*, vol. 51, p. 102078, Oct. 2020, doi: 10.1016/j.algal.2020.102078.
- [37] E. B. Medina Perez, M. C. Ruiz-Dominguez, J. E. Morales, and P. Cerezal Mezquita, "Fucoxanthin from Marine Microalga *Isochrysis galbana*: Optimization of Extraction Methods with Organic Solvents," *Dyna (Medellin)*, vol. 86, no. 210, pp. 174–178, Jul. 2019, doi: 10.15446/dyna.v86n210.72932.
- [38] P. Sun et al., "A Novel Strategy for Isolation and Purification of Fucoxanthinol and Fucoxanthin from the Diatom *Nitzschia laevis*," *Food Chem*, vol. 277, pp. 566– 572, Mar. 2019, doi: 10.1016/j.foodchem.2018.10.133.
- [39] D. D. McClure, A. Luiz, B. Gerber, G. W. Barton, and J. M. Kavanagh, "An Investigation into the Effect of Culture Conditions on Fucoxanthin Production Using the Marine Microalgae *Phaeodactylum tricornutum*," *Algal Res*, vol. 29, pp. 41–48, Jan. 2018, doi: 10.1016/j.algal.2017.11.015.
- [40] C. Wang, X. Chen, Y. Nakamura, C. Yu, and H. Qi, "Fucoxanthin Activities Motivate Its Nano/Micro- Encapsulation for Food or Nutraceutical Application: A Review," *Food Funct*, vol. 11, no. 11, pp. 9338–9358, 2020, doi: 10.1039/D0FO02176H.

- [41] T. K. Marella and A. Tiwari, "Marine diatom *Thalassiosira weissflogii* Based Biorefinery for Co-Production of Eicosapentaenoic Acid and Fucoxanthin," *Bioresour Technol*, vol. 307, p. 123245, Jul. 2020, doi: 10.1016/j.biortech.2020.123245.
- [42] C.-H. Lin, Y.-F. Chang, S. J. Prasetya, F.-Y. Yu, S.-Y. Lai, and M.-Y. Wang, "An Integrated Process for Enhanced Production and Purification of Fucoxanthin and Sulfated Polysaccharides in Diatom *Hyalosynedra toxoneides* cultures," *J Taiwan Inst Chem Eng*, vol. 155, p. 105308, Feb. 2024, doi: 10.1016/j.jtice.2023.105308.
- [43] V. Fernandes and B. S. Mamatha, "Fucoxanthin, a Functional Food Ingredient: Challenges in Bioavailability," *Curr Nutr Rep*, vol. 12, no. 4, pp. 567–580, Aug. 2023, doi: 10.1007/s13668-023-00492-x.
- [44] R. Li et al., "Encapsulation and Delivery Systems Based on Natural Biological Macromolecules: Focusing on Nutrients in Infant Formula," *Trends Food Sci Technol*, p. 104974, Mar. 2025, doi: 10.1016/j.tifs.2025.104974.
- [45] Y. Nishida et al., "Astaxanthin: Past, Present, and Future," *Mar Drugs*, vol. 21, no. 10, p. 514, Sep. 2023, doi: 10.3390/md21100514.
- [46] R. R. Narala et al., "Comparison of Microalgae Cultivation in Photobioreactor, Open Raceway Pond, and a Two-Stage Hybrid System," *Front Energy Res*, vol. 4, Aug. 2016, doi: 10.3389/fenrg.2016.00029.
- [47] F. Ma et al., "Optimizing Fucoxanthin Production in *Chaetoceros* sp. Using Conditioned Wastewater and Tailored Culture Conditions," *Journal of Water Process Engineering*, vol. 72, p. 107450, Apr. 2025, doi: 10.1016/j.jwpe.2025.107450.
- [48] P. Reynolds-Brandão et al., "Integration of Spectroscopic Techniques and Machine Learning for Optimizing *Phaeodactylum tricornutum* Cell and Fucoxanthin Productivity," *Bioresour Technol*, vol. 418, p. 131988, Feb. 2025, doi: 10.1016/j.biortech.2024.131988.
- [49] Q. Song, C. Liu, R. Xu, and L. Cai, "Enhancement of Fucoxanthin Accumulation in *Phaeodactylum tricornutum* by Light Quality and Intensity Shift Strategy," *Chemical Engineering Journal*, vol. 505, p. 159388, Feb. 2025, doi: 10.1016/j.cej.2025.159388.
- [50] X.-W. Fan et al., "Optimizing Tomato Waste Hydrolysate for Enhanced Fucoxanthin Biosynthesis in Mixotrophic Cultivation of *Isochrysis galbana*," *Bioresour Technol*, vol. 413, p. 131453, Dec. 2024, doi: 10.1016/j.biortech.2024.131453.
- [51] S. M. An et al., "Development of a Cost-Effective Medium Suitable for the Growth and Fucoxanthin Production of the Microalgae *Odontella aurita* Using Jeju Lava Seawater and Agricultural Fertilizers," *Biomass Bioenergy*, vol. 188, p. 107310, Sep. 2024, doi: 10.1016/j.biombioe.2024.107310.
- [52] M. K. M. Lane, E. B. Gilcher, M. M. Ahrens-Viquez, R. S. Pontious, N. E. Wyrzten, and J. B. Zimmerman, "Elucidating Supercritical Fluid Extraction of Fucoxanthin from Algae to Enable the Integrated Biorefinery," *Bioresour Technol*, vol. 406, p. 131036, Aug. 2024, doi: 10.1016/j.biortech.2024.131036.
- [53] S. Wu, W. Gu, S. Jia, X. Xie, L. Wang, and G. Wang, "Optimizing Fucoxanthin Production from *Phaeodactylum tricornutum*: Impact of Harvesting Methods on Culture Medium Reusability," *Algal Res*, vol. 74, p. 103150, Jul. 2023, doi: 10.1016/j.algal.2023.103150.
- [54] E. Yoshida, Y. Kato, A. Kanamoto, A. Kondo, and T. Hasunuma, "Metabolomic Analysis of the Effect of Nitrogen on Fucoxanthin Synthesis by the Haptophyte *Pavlova Gyraus*," *Algal Res*, vol. 72, p. 103144, May 2023, doi: 10.1016/j.algal.2023.103144.
- [55] D. Xu, J. Chow, C. C. Weber, M. A. Packer, S. Baroutian, and K. Shahbaz, "Evaluation of Deep Eutectic Solvents For the Extraction of Fucoxanthin from the Alga *Tisochrysis lutea* – COSMO-RS Screening and Experimental Validation," *J Environ Chem Eng*, vol. 10, no. 5, p. 108370, Oct. 2022, doi: 10.1016/j.jece.2022.108370.
- [56] H. Zhang, P. Gong, Q. Cai, C. Zhang, and B. Gao, "Maximizing Fucoxanthin Production in *Odontella aurita* by Optimizing the Ratio of Red and Blue Light-Emitting Diodes in An Auto-Controlled Internally Illuminated Photobioreactor," *Bioresour Technol*, vol. 344, p. 126260, Jan. 2022, doi: 10.1016/j.biortech.2021.126260.
- [57] Z. Wu et al., "Evaluation of Nitrogen Source, Concentration and Feeding Mode for Co-Production of Fucoxanthin and Fatty Acids in *Phaeodactylum tricornutum*," *Algal Res*, vol. 63, p. 102655, Apr. 2022, doi: 10.1016/j.algal.2022.102655.
- [58] S. C. Foo, N. M. H. Khong, and F. Md. Yusoff, "Physicochemical, Microstructure and Antioxidant Properties of Microalgae-Derived Fucoxanthin Rich Microcapsules," *Algal Res*, vol. 51, p. 102061, Oct. 2020, doi: 10.1016/j.algal.2020.102061.
- [59] M. Petrushkina et al., "Fucoxanthin Production by Heterokont Microalgae," *Algal Res*, vol. 24, pp. 387–393, Jun. 2017, doi: 10.1016/j.algal.2017.03.016.
- [60] T. Ishika, N. R. Moheimani, P. A. Bahri, D. W. Laird, S. Blair, and D. Parlevliet, "Halo-adapted Microalgae for Fucoxanthin Production: Effect of Incremental Increase in Salinity," *Algal Res*, vol. 28, pp. 66–73, Dec. 2017, doi: 10.1016/j.algal.2017.10.002.
- [61] W.-L. Guo et al., "Fucoxanthin Promotes the Conversion Efficiency of Alpha-Linolenic Acid in Feeding to Docosahexaenoic Acid in Quail Egg Yolk," *Food Chem*, vol. 472, p. 142915, Apr. 2025, doi: 10.1016/j.foodchem.2025.142915.
- [62] K. Sasaki et al., "Effects of Fucoxanthin Addition to Ground Chicken Breast Meat on Lipid and Colour Stability during Chilled Storage, before and after Cooking," *Asian-Australas J Anim Sci*, vol. 21, no. 7, pp. 1067–1072, Jul. 2008, doi: 10.5713/ajas.2008.70670.
- [63] D. Li et al., "Fabricating Hydrophilic Fatty Acid-Protein Particles to Encapsulate Fucoxanthin: Fatty Acid Screening, Structural Characterization, and Thermal Stability Analysis," *Food Chem*, vol. 382, p. 132311, Jul. 2022, doi: 10.1016/j.foodchem.2022.132311.
- [64] M. T. Nuñez de González, R. Attaie, A. Mora-Gutierrez, S. Woldeesenbet, and Y. Jung, "Stability of Fucoxanthin in Pasteurized Skim and Whole Goat Milk," *Foods*, vol. 10, no. 7, p. 1647, Jul. 2021, doi: 10.3390/foods10071647.
- [65] Z. Zahrah, M. N. G. Amin, and M. A. Alamsjah, "The Effect of Fucoxanthin as Coloring Agent on the Quality of Shrimp Paste," *IOP Conf Ser Earth Environ Sci*, vol. 441, no. 1, p. 012079, Feb. 2020, doi: 10.1088/1755-1315/441/1/012079.
- [66] I.-K. Mok, J. K. Lee, J. H. Kim, C.-H. Pan, and S. M. Kim, "Fucoxanthin Bioavailability from Fucoxanthin-Fortified Milk: In Vivo and In Vitro Study," *Food Chem*, vol. 258, pp. 79–86, Aug. 2018, doi: 10.1016/j.foodchem.2018.03.047.
- [67] D. Nuraini, Moch. A. Alamsjah, and E. Saputra, "Application of Fucoxanthin Pigment Extract from *Sargassum* sp. on the Physical Quality of Blusher Preparation," *Journal of Marine and Coastal Science*, vol. 10, no. 2, p. 74, Jun. 2021, doi: 10.20473/jmcs.v10i2.27659.
- [68] R. S. N. Tavares et al., "Fucoxanthin for Topical Administration, a Phototoxic vs. Photoprotective Potential in a Tiered Strategy Assessed by In Vitro Methods," *Antioxidants*, vol. 9, no. 4, p. 328, Apr. 2020, doi: 10.3390/antiox9040328.
- [69] S.-J. Heo et al., "Anti-inflammatory Effect of Fucoxanthin Derivatives Isolated from *Sargassum siliquastrum* in Lipopolysaccharide-Stimulated RAW 264.7 Macrophage," *Food and Chemical Toxicology*, vol. 50, no. 9, pp. 3336–3342, Sep. 2012, doi: 10.1016/j.fct.2012.06.025.
- [70] Y. Li, M.-B. Kim, Y.-K. Park, and J.-Y. Lee, "Fucoxanthin Metabolites Exert Anti-Fibrogenic and Antioxidant Effects in Hepatic Stellate Cells," *J Agric Food Res*, vol. 6, p. 100245, Dec. 2021, doi: 10.1016/j.jafr.2021.100245.
- [71] K. Takahashi et al., "Anticancer Effects of Fucoxanthin and Fucoxanthinol on Colorectal Cancer Cell Lines and Colorectal Cancer Tissues," *Oncol Lett*, vol. 10, no. 3, pp. 1463–1467, Sep. 2015, doi: 10.3892/ol.2015.3380.
- [72] J.-I. Kang et al., "Promotion Effect of Apo-9'- fucoxanthinone from *Sargassum muticum* on Hair Growth; the Activation of Wnt/ β -Catenin and VEGF-R2," *Biol Pharm Bull*, vol. 39, no. 8, pp. 1273–1283, 2016, doi: 10.1248/bpb.b16-00024.
- [73] M. Thompson, D. Gamage, N. Hirotsu, A. Martin, and S. Seneweera, "Effects of Elevated Carbon Dioxide on

- Photosynthesis and Carbon Partitioning: A Perspective on Root Sugar Sensing and Hormonal Crosstalk,” *Front Physiol*, vol. 8, Aug. 2017, doi: 10.3389/fphys.2017.00578.
- [74] A. Barros, H. Pereira, J. Campos, A. Marques, J. Varela, and J. Silva, “Heterotrophy as A Tool to Overcome the Long and Costly Autotrophic Scale-Up Process for Large Scale Production of Microalgae,” *Sci Rep*, vol. 9, no. 1, p. 13935, Sep. 2019, doi: 10.1038/s41598-019-50206-z.
- [75] L. Gao et al., “New Insights into the Production of Fucoxanthin by Mixotrophic Cultivation of *Ochromonas* and *Microcystis aeruginosa*,” *Bioresour Technol*, vol. 363, p. 127922, Nov. 2022, doi: 10.1016/j.biortech.2022.127922.
- [76] X.-W. Fan et al., “Optimizing Tomato Waste Hydrolysate for Enhanced Fucoxanthin Biosynthesis in Mixotrophic Cultivation of *Isochrysis galbana*,” *Bioresour Technol*, vol. 413, p. 131453, Dec. 2024, doi: 10.1016/j.biortech.2024.131453.
- [77] B. Guo et al., “Screening of Diatom Strains and Characterization of *Cyclotella cryptica* as A Potential Fucoxanthin Producer,” *Mar Drugs*, vol. 14, no. 7, p. 125, Jul. 2016, doi: 10.3390/md14070125.
- [78] D. Li et al., “*Isochrysis* sp. Cultivation in Pilot-Scale to Concurrently Produce Sustainable Triacylglycerols for Human Milk Fat Substitutes and Fucoxanthin,” *Algal Res*, vol. 69, p. 102937, Jan. 2023, doi: 10.1016/j.algal.2022.102937.
- [79] E. Shannon and N. Abu-Ghannam, “Enzymatic Extraction of Fucoxanthin from Brown Seaweeds,” *Int J Food Sci Technol*, vol. 53, no. 9, pp. 2195–2204, Sep. 2018, doi: 10.1111/ijfs.13808.
- [80] A. del Pilar Sánchez-Camargo, N. Pleite, M. Herrero, A. Cifuentes, E. Ibáñez, and B. Gilbert-López, “New Approaches for the Selective Extraction of Bioactive Compounds Employing Bio-Based Solvents and Pressurized Green Processes,” *J Supercrit Fluids*, vol. 128, pp. 112–120, Oct. 2017, doi: 10.1016/j.supflu.2017.05.016.
- [81] J. Nie, D. Chen, J. Ye, Y. Lu, and Z. Dai, “Optimization and Kinetic Modeling of Ultrasonic-Assisted Extraction of Fucoxanthin from Edible Brown Algae *Sargassum Fusiforme* Using Green Solvents,” *Ultrason Sonochem*, vol. 77, p. 105671, Sep. 2021, doi: 10.1016/j.ultsonch.2021.105671.
- [82] M. C. Ruiz-Domínguez et al., “Supercritical Fluid Extraction of Fucoxanthin from the Diatom *Phaeodactylum tricornutum* and Biogas Production through Anaerobic Digestion,” *Mar Drugs*, vol. 20, no. 2, p. 127, Feb. 2022, doi: 10.3390/md20020127.
- [83] U. Eilers, A. Bikoulis, J. Breitenbach, C. Büchel, and G. Sandmann, “Limitations in the Biosynthesis of Fucoxanthin as Targets for Genetic Engineering in *Phaeodactylum tricornutum*,” *J Appl Phycol*, vol. 28, no. 1, pp. 123–129, Feb. 2016, doi: 10.1007/s10811-015-0583-8.
- [84] A. Kamal et al., “Genetically Engineered Microalgae for Enhanced Bioactive Compounds,” *Discover Applied Sciences*, vol. 6, no. 9, p. 482, Sep. 2024, doi: 10.1007/s42452-024-06116-5.
- [85] S. M. Miller, R. M. Abbriano, A. Herdean, R. Banati, P. J. Ralph, and M. Pernice, “Random Mutagenesis of *Phaeodactylum tricornutum* Using Ultraviolet, Chemical, And X-Ray Irradiation Demonstrates the Need for Temporal Analysis of Phenotype Stability,” *Sci Rep*, vol. 13, no. 1, p. 22385, Dec. 2023, doi: 10.1038/s41598-023-45899-2.
- [86] S.-K. Bai, Y. Hong, and Y.-R. Wu, “Emerging Technologies for Genetic Modification of Solventogenic *Clostridia*: From Tool to Strategy Development,” *Bioresour Technol*, vol. 334, p. 125222, Aug. 2021, doi: 10.1016/j.biortech.2021.125222.
- [87] T. E. Nickson, “Planning Environmental Risk Assessment for Genetically Modified Crops: Problem Formulation for Stress-Tolerant Crops,” *Plant Physiol*, vol. 147, no. 2, pp. 494–502, Jun. 2008, doi: 10.1104/pp.108.118422.
- [88] NOSB, “Materials Subcommittee Discussion Document Induced Mutagenesis,” 2024.