Sustainable Production and Multidisciplinary Applications of Phycocyanin: A Systematic Review

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Abstract. Phycocyanin holds significant promise across diverse scientific and industrial fields due to its bioactive properties. This systematic review employs PRISMA meta-analysis methodology to critically analyze recent advances in phycocyanin production, with the dual objectives of optimizing yield and purity, while examining its multidisciplinary applications in life sciences. A total of 252 peer-reviewed studies published between 2015 and 2025 were selected from leading databases. This study reveals that phycocyanin production efficiency heavily depends on optimized extraction and purification protocols to achieve maximal purity and functional quality. The multidisciplinary impacts of phycocyanin span key sectors such as food and nutrition, pharmaceuticals and medicine, cosmetics, environmental biotechnology, and analytical diagnostics. Despite these promising applications, several challenges persist, including low production yield and high cost, chemical and physical instability, purity requirement for applications as well as extraction and cultivation limitation. This review proposes strategic recommendations, including advancements in sustainable cultivation, innovative purification techniques, and promotes sustainability and cost-effectiveness. The study underscores the critical need for integrative, cross-disciplinary approaches to fully harness the potential of phycocyanin, promoting its role as a sustainable bio resource with broad life science and industrial relevance.

Keywords: Phycocyanin production, multidisciplinary applications, systematic review.

1 Introduction

Phycocyanin is a photosynthetic light-harvesting pigment protein complex that plays a central role in capturing and transferring light energy in cyanobacteria and certain algal species. It belongs to the phycobiliprotein family and is responsible for the distinctive blue coloration

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observed in these organisms. Structurally, phycocyanin is composed of protein subunits covalently linked to chromophores, which enable efficient absorption of visible light [1][2]. Specifically, C-phycocyanin is a water-soluble protein characterized by an intense blue color and red fluorescence. Its monomeric unit (approximately 35-40 kDa) consists of two subunits, α (162 amino acids) and β (172 amino acids). In vivo, C-phycocyanin predominantly exists in trimeric and hexameric forms, which constitute essential components of phycobilisomes responsible for light absorption and energy transfer in cyanobacteria and red algae [3]. Previous studies have demonstrated a clear association between phycocyanobilin (PCB), the chromophore of phycocyanin, and various health promoting effects. More recent findings suggest that the intact phycocyanin holoprotein may exhibit superior antioxidant and anticancer activities compared with isolated PCB alone [4]. Beyond its photosynthetic role, phycocyanin has gained recognition as a high-value bioactive compound, with the global market projected to reach approximately US$245.5 million by 2027 [5]. Market analyses encompassing the pre- and post-COVID 19 periods have highlighted increasing demand across multiple forms and applications, including biomedical research, diagnostics, food and beverages, nutraceuticals, and pharmaceuticals, with growing global distribution [5]. These trends underscore the broad industrial and biomedical relevance of phycocyanin.

Derived predominantly from *Spirulina* species, phycocyanin has experienced rapid expansion in industrial utilization, particularly within the food, pharmaceutical, cosmetic, and biotechnology sectors [6][7]. In the food industry, it is widely used as a natural blue colorant, driven by consumer preference and regulatory pressure to replace synthetic dyes due to associated health and environmental concerns [8]. Advances in processing technologies have significantly enhanced the stability and bioactivity of phycocyanin, enabling its incorporation into a broader range of food, cosmetic, and personal care products [9]. In addition to its coloring properties, phycocyanin exhibits notable antioxidant, anti-inflammatory, and potential anticancer activities, which have promoted its application in functional foods and dietary supplements. The pharmaceutical and nutraceutical industries are increasingly exploring phycocyanin as a bioactive ingredient for therapeutic development and drug delivery systems [10]. Its intrinsic fluorescence further supports its application in diagnostics, bioimaging, and analytical assays, while ongoing research seeks to expand its use in targeted drug delivery and advanced biotechnological platforms [11]. Numerous studies have reported its wide-ranging pharmacological activities, including antioxidant, anticancer, anticarcinogenic, anti-inflammatory, neuroprotective, hepatoprotective, immunomodulatory, renoprotective, and antidiabetic effects, with evidence supporting its safety and non-toxic nature in humans [12][13]. .

A wealth of bioactivity data (such as antioxidant, anti-inflammatory, anticancer, or antimicrobial) has been reported using a wide variety of models, dosages, and testing techniques. Reviews have summarized the main bioactive effects in various application contexts, but direct comparisons between production methods, formulations, or the effect of purity levels on the magnitude/durability of bioactive activity have not been systematically and comparatively conducted to date [7]. One major obstacle is the heterogeneity of methodologies and bioassay variables, which make it difficult to compare study results side-by-side. Thus, this knowledge gap makes it difficult to select the most effective and efficient method for industrial phycocyanin production while maximizing its bioactive effects. Systematic reviews with a meta-analysis-based approach (which assesses yield, purity, cost, and bioactive yield comparatively across techniques and strains) are urgently needed to provide a more targeted and measurable process innovation roadmap for the needs of the food, pharmaceutical, and cosmetics industries, particularly in realizing sustainable and high-value phycocyanin production [14]. The primary objective of conducting a systematic review on the topic of phycocyanin production and its multifunction is to provide a comprehensive, objective, and standardized evaluation of the current scientific evidence regarding various production methods, extraction efficiency, and the potential uses of phycocyanin. Through a systematic review, it is hoped that a comprehensive comparison between methods (such as culture, extraction, and purification techniques) can be obtained, including output yield, purity, stability, cost, and their impact on antioxidants, anti-inflammatory drugs, as well as pharmaceutical and food applications. The systematic review also aims to identify knowledge gaps, methodological biases, and determine strategic recommendations for further research or industrial needs.

2 Material and methods

This study utilizes the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology to comprehensively analyze the existing literature on phycocyanin production and its various applications. The PRISMA technique is particularly appropriate for systematic reviews because of its clear, organized, and strict framework [15].

2.1 Formulating the research questions (RQ)

This systematic review established essential inquiries to investigate spesific aspects of phycocyanin synthesis and its diverse uses. The inquiries predominantly concentrated on:

(RQ1) : What methods can enhance phycocyanin production by concentrating on environmental factors to maximize yield?
(RQ2) : What are the multidisciplinary impacts of phycocyanin on human health, cosmetics, environmental sustainability, and industrial biotechnology?
(RQ3) : What are major challenges and recommendations exist for future research in phycocyanin?

2.2 Acquiring pertinent articles

This review work uniquely utilizes a specific body of literature, despite the extensive publication of studies on the manufacture and interdisciplinary applications of phycocyanin. The research primarily concentrates on papers or proceedings indexed in esteemed platforms, including MDPI, Wiley, Science Direct, Frontiers, Springer Nature, and Elsevier, IOP publishing through targeted categories and keyword searches. The authors imposed a publication timeframe from 2015 to 2025 ensuring a contemporary perspective. Articles sources are available in full text and written in English. Moreover, the sources should address keyword combinations.

2.3 Selecting based on the research Inquiry

The formulation of the research question established the fundamental criteria for determining the eligibility of publications included in this review. The literature search was conducted using specific keyword combinations, including *"optimizing phycocyanin production," "phycocyanin," "phycocyanin multidisciplinary,"* and *"phycocyanin challenges and recommendations,"* with restrictions applied to English-language publications and full-text availability. Studies that fulfilled these preliminary conditions were subsequently subjected to further evaluation. The inclusion and exclusion criteria, summarized in **Table 1**, were applied to systematically define the scope of eligible studies. To ensure temporal relevance, only publications released between January 2015 and April 2025 were considered, resulting in 140 English-language articles that satisfied this timeframe. During the screening process, 21 duplicate records were identified and removed, leaving 112 publications. After excluding non-journal articles and non–peer-reviewed conference proceedings, 72 studies remained for further assessment. **Figure 1** presents the PRISMA flow diagram illustrating the systematic process of article identification, screening, eligibility assessment, and final inclusion. This final phase resulted in the selection of 28 studies that most effectively address phycocyanin production optimization, multidisciplinary applications, associated challenges, and future recommendations.

Table 1. Inclusion and exclusion criteria.

Inclusion Criteria	Exclusion Criteria
Publications in Scopus-indexed journals (MDPI, Wiley, Science Direct, Frontiers, IOP Publishing, Springer Nature, and Elsevier	Books, reviews, short articles, magazine articles, and papers or proceedings not published in Scopus-indexed
Published from 1 January 2015 to 1 April 2025	Published outside the defined time range
Full-text accessibility	Articles without full-text availability
Papers written in English	Papers not written in English
Articles addressing predefined keyword combinations related to phycocyanin	Articles not included word combination

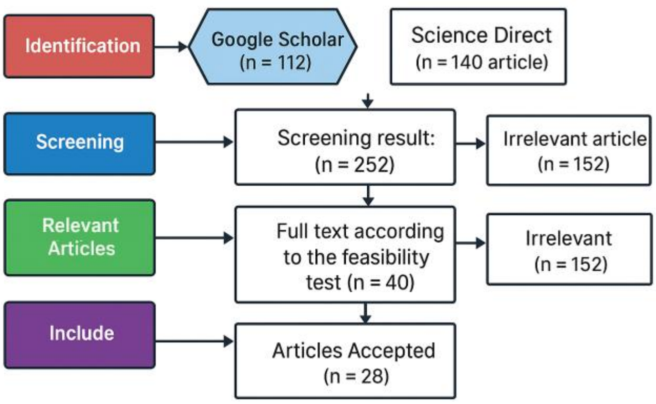

Fig. 1. PRISMA method.

2.4 Analyzing of selected articles

The selected studies highlight various limitations encountered in phycocyanin research, particularly in optimization strategies and multidisciplinary applications, along with the associated challenges and proposed recommendations. These investigations aim to improve the recovery and utilization of phycocyanin from biomass systems. The 28 Scopus-indexed articles demonstrate a wide range of optimization approaches and application perspectives, as summarized in **Table 2**.

Table 2. Selected paper.

Author	Publish Year	Publisher	Index
Yin, Z., Zou, J., Wang, M., Huang, R., Qian, Y., Zeng, M., & Li, F.	2024	Elsevier	Scopus
Amarante, M. C. A. de, Braga, A. R. C., Sala, L., Moraes, C. C., & Kalil, S. J.	2020	Elsevier	Scopus
Yu, Z., Zhao, W., Sun, H., Mou, H., Liu, J., Yu, H., Dai, L., Kong, Q., & Yang, S.	2024	Springer Nature	Scopus
García, A. B., Longo, E., & Bermejo, R.	2021	Elsevier	Scopus
Ferraro, G., Imbimbo, P., Marseglia, A., Illiano, A., Fontanarosa, C., Amoresano, A., Olivieri, G., Pollio, A., Monti, D. M., & Merlino, A.	2020	Elsevier	Scopus
Maria Kissoudi, Ioannis Sarakatsianos, V. S.	2017	John Wiley & Sons, Inc	Scopus
Narindri R. W, Birgitta, Lin, Y Ting. H, Hsin. T, & Chu, Hsin	2024	Elsevier	Scopus
Lin J. Y, Tan S. I.,Yi. Y. C, Hsiang, Chuan C. C, Chien H. C, Chun Y.C, & Jo S. N. I	2022	Elsevier	Scopus
Yu. Y.,Hou. X.,Yu. Q.,Huo. Y.,Wang. K.,Wen. X.,Ding. Y.,Li. Y &Wang. Z.	2023	Elsevier	Scopus
Ainoa Morillas-España, Ruperto Bermejo, Roberto Abdala-Díaz, Ángela Ruiz,Tomás Lafarga, Gabriel Acién, and J. M. F.-S.	2022	MDPI	Scopus
Mao, M., Han, G., Zhao, Y., Xu, X., & Zhao, Y.	2024	Elsevier	Scopus
García-Gómez, C., Aguirre-Cavazos, D. E., Chávez-Montes, A., Ballesteros-Torres, J. M., Orozco-Flores, A. A., Reyna-Martínez, R., Torres-Hernández, Á. D., González-Meza, G. M., Castillo-Hernández, S. L., Gloria-Garza, M. A., Kačániová, M., Ireneusz-Kluz, M., & Elizondo-Luevano, J. H	2025	MDPI	Scopus
Ziyaei, K., Abdi, F., Mokhtari, M., Daneshmehr, M. A., & Ataie, Z.	2023	Elsevier	Scopus
Liu, R., Qin, S., & Li, W	2022	Elsevier	
Jiang, L., Wang, Y., Yin, Q., Liu, G., Liu, H., Huang, Y., & Li, B.	2017	Ivyspring International Publisher	Scopus
Pakawan Setthamongkol, Wareeporn Kulert, Somkiaet Wanmanee, Ratchanekorn Swami, Maliwan Kutako, & Naphatson Chanthathamrongsiri, T. S.	2023	Springer Nature	Scopus
Zhou, Y., Bai, R., Huang, Y., Li, W., Chen, J., Cheng, Z., Wu, X., & Diao, Y	2023	IOP Publishing	Scopus
Ziyaei, K., Abdi, F., Mokhtari, M., Daneshmehr, M. A., & Ataie, Z.	2023	Frontiers	Scopus
Adli, S. A., Ali, F., Azmi, A. S., Anuar, H., Aimi, N., Nasir, M., Hasham, R., Khairul, M., & Idris, H.	2020	MDPI	Scopus

Author	Publish Year	Publisher	Index
Contreras-Ropero, J. E., García-Martínez, J. B., & Barajas-Solano, A. F.	2025	Frontiers	Scopus
Shafiei, M., Shafiei, M., Mohseni Sani, N., Guo, W., Guo, S., Vali, H., & Akbari Noghabi, K	2024	Frontiers	Scopus
Ashaolu, T. J., Samborska, K., Lee, C. C., Tomas, M., Capanoglu, E., Tarhan, Ö., Taze, B., & Jafari, S. M.	2021	Elsevier	Scopus
Jiang, L., Yu, S., Chen, H., & Pei, H.	2023	Springer	Scopus
Antecka, A., Szeląg, R., & Ledakowicz, S.	2025	Springer	Scopus
Martínez, J. M., Luengo, E., Saldaña, G., & , Ignacio Álvarez, J. R.	2017	Elsevier	Scopus
Pispas, K., Manthos, G., Sventzouri, E., Geroulia, M., Mastropetros, S. G., Ali, S. S., & Kornaros, M.	2024	MDPI	Scopus
Fernandes, R., Campos, J., Serra, M., Fidalgo, J., Almeida, H., Casas, A., Toubarro, D., & Barros, A. I	2023	MDPI	Scopus
Lucía Cortés Meneses, Juliana Da Luz Castro, Francinie Murillo Vega, Fabian Villalta-Romero, Adolfo Ulate Brenes, J. W. F. W.-W.	2025	John Wiley & Son, Inc	Scopus

3 Results and discussion

Phycocyanin is a blue pigment–protein complex that exhibits a wide range of bioactivities and has gained significant attention in the food, cosmetic, and pharmaceutical industries due to its antioxidant properties, bioactivity, and potential as a natural colorant. [7]. However, to produce phycocyanin on a large scale, it begins with microalgae cultivation, typically in open ponds or closed photobioreactors that provide the appropriate nutrients, adequate pH, light, agitation, and temperature, resulting in higher yields and consistency [16]. Several media are used, including BG-11 or modified Zarrouk media, enriched with nutrients [17]. These are suitable growth media solutions that significantly impact phycocyanin productivity. Environmental and operational factors such as temperature (optimal 30–35 °C), pH (8–10), and light intensity (lower intensity to increase pigment yield) are crucial for maximizing phycocyanin content [17]. Integrating advances in cultivation, gentle cell disruption, and stepwise purification allows for consistent, high-purity production of phycocyanin, enabling its rapid growth as a sustainable and high-value natural product for various industries are shown in **Table 3**.

Table 3. Phycocyanin optimization.

Ref	Source of Phycocyanin	Extraction and Purification Methods used	Environment	Yield/Purity
[18]	*Spirulina platensis* PCC 7345	Extraction buffer (sodium phosphate pH 7.0) and freeze-thawing for 12 h	Using Box Behnken Design for Extraction of Phycocyanin pH temperature Light Intensity	Ion-exchange chromatography and ammonium sulfate separation were used to get 4.03 results.
[19]	*Geitlerinema* sp. TRV57	Sodium sulfate precipitation, dialysis	Light intensity 150 nmol photons $m^{-2} s^{-2}$	Partial purity method : 60 mg

Ref	Source of Phycocyanin	Extraction and Purification Methods used	Environment	Yield/Purity
		and ion exchange chromatography	Temperature 25-30 °C pH 7.0 BG-11 medium	(with purity OD_{620}/OD_{280} ration of 2.64) High purity method : 20 mg (with purity OD_{620}/OD_{280} ratio of 4.05)
[20]	*Galdieria sulphuraria* and *Spirulina platensis*	Ammonium sulfate precipitate, ultrafiltration and hydroxyapatite chromatography	The cultures were cultivated in a sterile ASN III growth medium at 28 ± 2 °C under 12/12 h light/dark illumination cycle	It was 85.6% in a precipitation of 45% (NH4)2SO4, 82% in a DAE Sephadex purification, and 100% in a reduced crude extract (1:2).
[21]	*G. sulphuraria* and *S. Platensis*	50 mM potassium phosphate solution with a pH of 7.0. The suspension was frozen at 80 °C for a night.	In an environment with a pH of 7, the temperature should be between 50 and 65 °C. After 30 minutes of incubation at 60 °C and pH 7	C-phycocyanins from *G. sulphuraria* and *S. platensis* were 86.66% and 60.83%, respectively.
[22]	*Spirulina platensis* PCC 7345	1 M sodium phosphate buffer (pH 7.0) and freeze thawing.	The culture was cultivated in St. BG11 medium with constant agitation at 100 rpm	0.6948 in growth phase days 15 and concentration off buffer 1 M
[23]	*Geitlerinema* sp.	25 mM sodium phosphate buffer at pH 7.0.	BG-11 medium was maintained in an 8L Erlenmeyer flask at a light intensity of 150 µmol photons m-2 s-1 and a temperature of 45 °C, with a pH of 7.0.	C-phycocyanin extract of analytical grade (A_{620}/A_{280} = 4.12)l
[24]	*Thermosynechococcus* sp. Cl-1	Ion-exchange chromatography, freeze-dryer	DIC (CO_2) addition, high light intensity (2.00 µE/m²/s), livestock, flat panel photobioreactor	4.9% DCW; 6.46 ± 0.7 mg/L/h; purity 0.79–0.86; purity up to 3.34 after purification
[25]	*Synechococcus* sp. PCC7002	potassium phosphate buffer pH 7.00	2% CO_2, light 100 µmol/m²/s, 12:12 hours, 30 °C, nitrogen mix (nitrate+amonia)	0.439 g CPC DCW, high purity, with antioxidant activity 89%
[26]	*Arthrospira platensis*	Ammonium sulfate precipitation (one-step)	Two-stage: 4 days light 320 µmol/m²/s (growth), 2 days160 µmol/m²/s + $NaNO_3$ (C-PC accumulation)	18.86% content; 59.72 mg/L/h; purity 3.16 (reactive grade)

Table 4. Characterization of phycocyanin.

Ref	SDS-P	SA	HPLC	UV-S	FS	2DGE	FTIR	GCMS
[18]	✓	✓	✓	✓				
[19]			✓	✓				
[20]	✓			✓	✓	✓		
[21]				✓				
[22]				✓			✓	✓
[23]				✓				

Note : The check mark (✓) indicates that the characterization parameter was successfully analyzed and met the standard criteria for phycocynian.

The purity of phycocyanin (PC) was assessed via spectroscopic examination by determining the absorbance ratio at 616 nm to 280 nm, a recognized criterion for phycocyanin purity. Additional characterisation was conducted utilizing high-performance liquid chromatography (HPLC), with a mobile phase of 50 mM Tris-HCl buffer (pH 8.0) at a flow rate of 0.6 mL min^{-1}.

Spectroscopic analysis revealed that pure phycocyanin displayed a distinct maximum absorbance at 620 nm. Fluorescence spectroscopy demonstrated a peak emission at 637 nm upon excitation at 589 nm, thereby validating the chromophore's integrity. The SDS-PAGE study of isolated phycocyanin from *Geitlerinema sp*. revealed a singular protein band with an estimated molecular mass of 18 kDa. Two-dimensional gel electrophoresis further separated the protein into two areas with isoelectric points (pI) around 4 and 5, corresponding to the α and β subunits of phycocyanin [20]. Samples were incubated in buffer and subjected to heating in a water bath for 3 minutes before electrophoresis for subunit separation. A 4% stacking gel and a 12% resolving gel were utilized to differentiate the α and β subunits of C-phycocyanin obtained from Galdieria sulphuraria and Spirulina platensis. Molecular weight markers ranging from 10 to 150 kDa were utilized as protein standards. Lane studies verified the existence of separate α and β chains in purified samples in contrast to crude extracts [21]. Additional UV-Visible absorbance analysis conducted over the range of 250–700 nm consistently demonstrated a dominant absorption peak near 620 nm, which is characteristic of C-phycocyanin. These spectroscopic and chromatographic findings collectively confirm the successful extraction, purification, and structural integrity of C-phycocyanin [23].

Based on references in table 4, UV-S was the most frequently used analytical method, appearing in almost all studies, indicating that it served as the primary technique for sample characterization. HPLC was also commonly applied in references [18] and [19], while SDS-P and SA were only utilized in a few specific studies. Other methods, such as FS, 2DGE, FTIR, and GCMS, were used less frequently, suggesting that these techniques functioned as complementary or specialized analytical tools. Overall, the data demonstrate variation in the selection of analytical methods depending on the objectives and focus of each study.

3.1 Phycocyanin usage in multidisciplinary of life aspect

Phycocyanin has gained significant attention in food science and technology due to its intense and rare blue hue. Phycocyanin is also increasingly utilized in novel food products, including plant-based foods, algae-based snacks, anti-aging and detox beverages, and low-calorie desserts. Its water solubility facilitates its incorporation into a variety of formulations; however, flavor adjustments are often necessary to mask the mild marine odor that can sometimes be present [27]. The technological challenges associated with phycocyanin primarily stem from its susceptibility to degradation caused by heat, low pH levels, light exposure, and oxidation. To overcome these limitations, innovative strategies such as microencapsulation with natural biopolymers like whey protein and gum Arabic, the addition of antioxidants, liposomal delivery systems, and bio-refinery models that co-extract phycocyanin with other bioactive compounds have been developed [28]. These advancements improve the stability and scalability of phycocyanin for industrial applications. From a sustainability perspective, spirulina the primary source of phycocyanin demonstrates rapid growth with minimal water and land requirements, effective carbon dioxide fixation, and high nutrient density. Utilizing phycocyanin within bio-refinery systems allows for the valorization of residual biomass for uses such as animal feed, biofertilizers, or the extraction of additional bioactive compounds [29]. This approach aligns with circular economy principles and contributes to achieving Sustainable Development Goals related to responsible production and climate action.

3.1.1 Food and nutrition

Phycocyanin, a water-soluble blue pigment-protein complex derived primarily from *Spirulina platensis*, has emerged as one of the most promising natural additives in the modern food and nutrition industry. Traditionally valued for its vivid blue coloration, phycocyanin is now recognized not only as a natural pigment but also as a bioactive compound with significant nutritional and therapeutic potential [30][31]. In food applications, phycocyanin serves as a natural colorant that provides an appealing blue shade to various products, including confectionery, dairy formulations, beverages, and bakery items. Its use is particularly aligned with the growing global demand for clean-label and plant-based ingredients, which emphasize natural origin, safety, and sustainability [32]. Compared to synthetic dyes such as Brilliant Blue FCF, phycocyanin offers the advantage of being non-toxic and environmentally friendly. However, its widespread application has been limited by its instability toward heat, light, and acidic conditions, leading to color degradation during processing and storage [33]. To overcome this, researchers have explored various stabilization and encapsulation strategies, including microencapsulation with biopolymers such as maltodextrin, gum arabic, chitosan, and alginate, which help to preserve pigment integrity and enhance shelf life [34]. Beyond its technological role, phycocyanin also exhibits remarkable nutritional and functional properties that support human health. **Table 5** shows researches regarding to food and nutrition aplication of phycocyanin.

Table 5. Phycocyanin aplication in foods and nutrition.

Ref	Product/Application	Findings	Solutions
[35]	Sour beverages, liquid foods	The combination of phycocyanin with whey protein isolate and chitosan forms stable particles, maintaining blue color and antioxidant activity after pasteurization/UHT processing.	Improves thermal and colloidal stability of phycocyanin.
[36]	Milk ice cream	The addition of C-phycocyanin maintains color stability for up to 182 days, increasing	Color stability and increased bioactivity after digestion.

Ref	Product/Application	Findings	Solutions
		antioxidant activity after in vitro digestion.	
[37]	Natural colorants, nanoparticles, hydrogels, emulsions.	Metabolic engineering and innovative delivery systems (nanoparticles, hydrogels, emulsions).	The need for advanced stabilization technology.
[38]	Natural blue colorants in beverages.	C-phycocyanin extract from Spirulina is stable at pH 9, color stable during cold storage for 11 days, an alternative to synthetic colorants.	Color stability in beverages.
[39]	Food, antioxidants, anticancer.	C-pycocyanin from thermophilic algae is stable up to >80 °C, remaining active as an antioxidant and cytotoxic agent against cancer cells.	High stability over a wide range of temperatures and pH.
[40]	Confectionery (candy)	Food-grade C-phycocyanin extraction and purification protocol, application in blue candy.	High-precision analytical method.
[41]	Natural colorant, functional food.	Pycocyanin complex for stability, bio refinery trends, major application as a natural colorant.	Complexion for stability.
[42]	Beverage colorant, bio stimulant.	C-pycocyanin from *Oscillatoria* sp. produces colors similar to commercial products.	Bio refinery process, economic efficiency.

3.1.2 Pharmaceutical and medical fields

Beyond its nutritional value, phycocyanin has attracted extensive attention in the pharmaceutical and medical fields due to its diverse biological and therapeutic properties. As a biliprotein complex composed of phycocyanobilin chromophores covalently bound to apoproteins, phycocyanin exhibits a molecular structure that contributes to its strong antioxidant, anti-inflammatory, neuroprotective, hepatoprotective, and anticancer activities [43]. These pharmacological potentials make phycocyanin an emerging bioactive molecule for the development of novel therapeutic agents and health-promoting formulations. Phycocyanin's antioxidant activity has been widely documented and is considered one of its most important biological functions. It acts as a scavenger of reactive oxygen species (ROS), including hydroxyl, superoxide, and peroxyl radicals, thereby preventing oxidative damage to lipids, proteins, and nucleic acids [44]. Phycocyanin also enhances the activity of antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, thereby strengthening the body's cellular defense mechanisms against oxidative stress [43]. These effects are particularly relevant in mitigating oxidative stress-related disorders such as diabetes mellitus, atherosclerosis, and neurodegenerative diseases [44][45]. **Table 6** depicts researches regarding to Pharmaceutical and Medical Fields.

Table 6. Phycocyanin aplication in pharmaceutical and medical fields.

Ref	Main Focus of Research	Research Findings
[46]	Applications, bioactivity, and extraction methods of phycobiliproteins (including phycocyanin).	Phycocyanin has antibacterial and antidiabetic activities and has broad therapeutic potential in the pharmaceutical and medical fields.
[47]	Anti-inflammatory effects and mechanisms of phycocyanin.	Phycocyanin is effective as an anti-inflammatory and antioxidant, suppressing various inflammatory diseases.
[48]	Antidiabetic effects of phycocyanin, molecular mechanisms.	Phycocyanin lowers blood glucose, increases insulin, and protects β-cells in animal and cell models.
[13]	Anticancer potential of phycocyanin.	Phycocyanin inhibits proliferation, cell cycle, and induces apoptosis in cancer cells, potentially as a drug.

3.1.3 Cosmetic applications

Phycocyanin has been shown to reduce UVB-induced skin damage by modulating MMP-1 and MMP-9 expression in keratinocytes, indicating its potential as a natural anti-photoaging agent in sunscreen or daily protection products [49]. For example, microencapsulation of phycocyanin using maltodextrin, sodium caseinate, and gum arabic has been shown to preserve pigment integrity under elevated temperatures and improve antioxidant performance in vitro [50]. Similarly, double emulsions (W1/O/W2) and nanoparticle-based delivery systems using chitosan or carrageenan have enhanced the topical bioavailability of phycocyanin while maintaining its physicochemical stability in cosmetic emulsions [51]. Topical application studies have also supported the bioefficacy of phycocyanin in improving skin hydration, barrier function, and cell regeneration. For instance, a skin cream containing phycocyanin extracted from Phormidium versicolor demonstrated favorable physicochemical stability and antimicrobial properties over 15 days under moderate storage conditions [52]. These results indicate that phycocyanin can serve not only as a functional pigment but also as a biologically active compound in formulations such as anti-aging creams, soothing gels, moisturizers, and serums [53]. **Table 7** shows researches regarding to cosmetics applications

Table 7. Phycocyanin application in cosmetics.

Ref	Research Main Focus	Findings	Challanges
[54]	Cosmetic cream with phycocyanin; Antioxidant, antimicrobial, 8-week stable.	Cream with phycocyanin has antioxidant activity, inhibits bacterial growth (*Staphylococcus, E. coli*) and is stable for up to 8 weeks at room temperature.	Chemical and physical stability, easily degraded, and limits its wide application.
[49]	Cream for hyperpigmentation, tyrosinase inhibitor, antioxidant.	Phycocyanin effectively inhibits tyrosinase, reduces melanin formation, and has potential as a skin lightening agent.	Low production yield.
[48]	Anti-photoaging, antioxidant, anti-inflammatory, nano-	Phycocyanin protects skin from UVB damage, reduces wrinkles	Complex extraction and purification process.

Ref	Research Main Focus	Findings	Challanges
	delivery system.	and inflammation, and increases effectiveness with a nano-delivery system.	
[55]	Biodegradable cosmetic patch, safe for skin and antioxidant.	Patch with phycocyanin is safe, non-toxic, and provides antioxidant effects on the skin.	Durability during storage
[56]	Hair dye Natural, safe, good color stability	Phycocyanin is safe for skin cells, non-toxic and 50% of hair color lasts after 5 shampoos: physically stable in hot/cold cycles.	Product formulation challenges

3.1.4 Environmental and biotechnological uses

Besides nutritional and pharmaceutical importance, phycocyanin has also gained considerable attention in the fields of environmental science and biotechnology. Its applications in these areas are largely driven by the sustainability, biocompatibility, and multifunctional nature of both phycocyanin and its microalgal sources. These organisms are recognized as renewable bioresources capable of converting solar energy and carbon dioxide into valuable biochemicals, thus offering environmentally friendly alternatives for various industrial processes [57]. Phycocyanin production itself represents a model for biotechnological valorization of microalgal biomass. While, the extraction and purification processes generate residual biomass rich which can be further utilized as biofertilizer, animal feed, or substrate for biofuel production [58]. In environmental biotechnology, phycocyanin-producing microalgae play a pivotal role in bioremediation and wastewater treatment [57].

In the broader context of environmental sustainability, the use of phycocyanin and its producing microalgae offers a green solution for addressing global challenges related to food, energy, and environmental pollution. The scalability of microalgal cultivation, coupled with advances in bioreactor design, genetic engineering, and downstream processing, is expected to further enhance phycocyanin yield and reduce production costs [59][60]. Future research is likely to focus on integrating phycocyanin production with other bio-based processes, such as biohydrogen generation, carbon capture, and bioplastic synthesis, to create multi-output biorefineries that support both industrial and ecological sustainability. Overall, phycocyanin exemplifies a natural biomolecule whose relevance extends far beyond the boundaries of food and medicine.

3.1.5 Analytical and diagnostic applications

Phycocyanin has also become a valuable biomolecule in the fields of analytical chemistry and diagnostic biotechnology due to its distinct spectroscopic and fluorescent properties. As a light-harvesting biliprotein belonging to the phycobiliprotein family, phycocyanin exhibits intense absorption in the orange-red region (around 620–625 nm) and strong fluorescence emission in the red region (around 640–650 nm) [61][62]. These characteristics, combined with its high quantum yield and excellent photostability under physiological conditions, have made phycocyanin an ideal fluorescent marker in bioanalytical assays and imaging applications. One of the earliest and most established uses of phycocyanin is as a fluorescent probe in immunoassays, such as fluorescence-linked immunosorbent assays (FLISA) and flow cytometry [63]. Its covalent linkage to immunoglobulins allows quantitative detection of antigens and cellular targets in very low concentrations, outperforming many synthetic fluorophores in sensitivity and biocompatibility. On the other hand, microbial pigments offering natural coloration with additional pharmacological benefits (anticancer, antimicrobial, antioxidant), broad industrial applicability, and promising potential for improvement through genetic and fermentation-based innovations [64]. Its integration into diagnostic platforms supports the ongoing trend toward eco-friendly biotechnological innovation and green analytical chemistry. In conclusion, phycocyanin has evolved from a biological pigment to a multifunctional analytical tool, offering high fluorescence efficiency, low toxicity, and strong conjugation capability.

3.2 Major challenges and recommendation in phycocyanin research and application

Phycocyanin research and application face several major interrelated challenges, from the production stage to industrial utilization. Biological and production challenges arise from the variability of cyanobacteria strains such as *Spirulina platensis, Synechocystis* sp.*, and Anabaena* sp., resulting in significant differences in phycocyanin yield and stability [14][65][66]. Growth optimization is complex due to the influence of numerous factors such as light intensity, temperature, pH, and nutrient composition, making it difficult to reproduce on a large scale. In the extraction and purification stages, cell lysis efficiency is a constraint, as each method (mechanical, chemical, or enzymatic) has advantages and disadvantages related to cost, efficiency, and potential pigment degradation (**Table 8**).

Table 8. Major challenges in phycocyanin research and application.

Categories	Challenges	Ref
Biological and Production Barriers	Strain Variability : Significant in yield and stability exist among cyanobacteria strains; no universal high-yield drain is standardized Growth Optimization: yield is highly sensitive to multifactorial conditions (light, pH, nutrients), complicating reproducibility and scale-up Scale Up and Cost: Industrial photo bioreactors face light attenuation, contamination, and mass-transfer issues, with downstream, processing accounting for up to 80% of total cost	[67]
Extraction, Purification and Stability	Cell Disruption : Methods like freeze-thaw, ultrasound, and pulsed electric field each have trade-offs in efficiency Purity and Yield : Achieving high purity (A_{615}/A_{280} > 4.0) often reduce yield and increase solvent/energy uses Instability : Phycocyanin I is sensitive to light, heat and pH, limiting shelf life and application	[68]
Analytical and Standardization Issues	Inconsistent Metrics: Lack of standardized units and protocols for yield and purity hinders cross-study comparison and benchmarking. Limit Mechanistic Understanding : Biochemical regulation of biosynthesis and stress responses remains poorly understood	[69]
Application and Regulatory Hurdles	Translational Gaps : Few studies bridge lab-scale production with real-word applications Regulatory Uncertainly : Approval processes and safety data are incomplete and vary by region Sustainability Concerns : Solvent use and biomass disposal raise environmental issues	[69]

To obtain high-purity phycocyanin, multiple purification steps are often required, which reduces the final yield and increases solvent and energy consumption. Pigment stability is also a critical issue because phycocyanin is highly sensitive to light, heat, and pH, making it easily degraded during processing and storage. From an analytical and standardization perspective, the lack of standard protocols leads to differences in yield units and purity indices between studies, limiting reliable comparisons and benchmarking [70]. Challenges in multidisciplinary application and integration also arise because there are still few studies bridging laboratory production with real-world applications in the food, pharmaceutical, or diagnostic sectors. Regulatory uncertainty, limited safety data and sustainability and waste issues are also major obstacles. Finally, significant gaps in scientific knowledge remain, particularly regarding the mechanisms of phycocyanin biosynthesis, and interdisciplinary collaboration remains limited [28][71]. Therefore, to address these challenges, the integrated approaches are needed to accelerate the translation of research findings into industrial applications (**Table 9**).

Table 9. Recommendation in Phycocyanin Research and application.

Categories	Recommendation	Ref
Low Production Yield	Screen and genetically engineer robust, high-yield strains, use mathematical modelling and fed-batch strategies for scalable, reproducible growth	[72]
Extraction and Purification	Develop integrated, low-energy and green extraction methods	[73]
Stability	Formulate with stabilizers (saccharides, polymers), optimize pH and temperature	[74]
Standardization	Establish global protocols for cultivation, extraction	[14]
Application and Regulation	Foster interdisciplinary research, conduct translational and safety studies, and harmonize regulatory frameworks	[7]
Sustainability	Implement bio refinery concept and green solvents, valorize	[75]

3.3 Research findings

Based on the research findings **Figure 2**, the production phycocyanin can be significantly enhanced through systematic environmental optimization and robust characterization methods. Environmental factors play a crucial role in determining the yield and quality of phycocyanin. Optimal production occurs under low to moderate light intensity. The temperature range of 25–30 °C supports efficient pigment synthesis and protein stability, while maintaining the pH between 7.0 and 8.5 promotes healthy cyanobacterial growth and pigment accumulation. Adjusting salinity according to the specific cyanobacterial strain minimizes stress that can inhibit pigment production. Enhancing CO_2 availability through aeration or bubbling stimulates photosynthetic activity and overall pigment yield, and modifying growth medium composition with trace elements and vitamins further supports optimal biosynthesis.

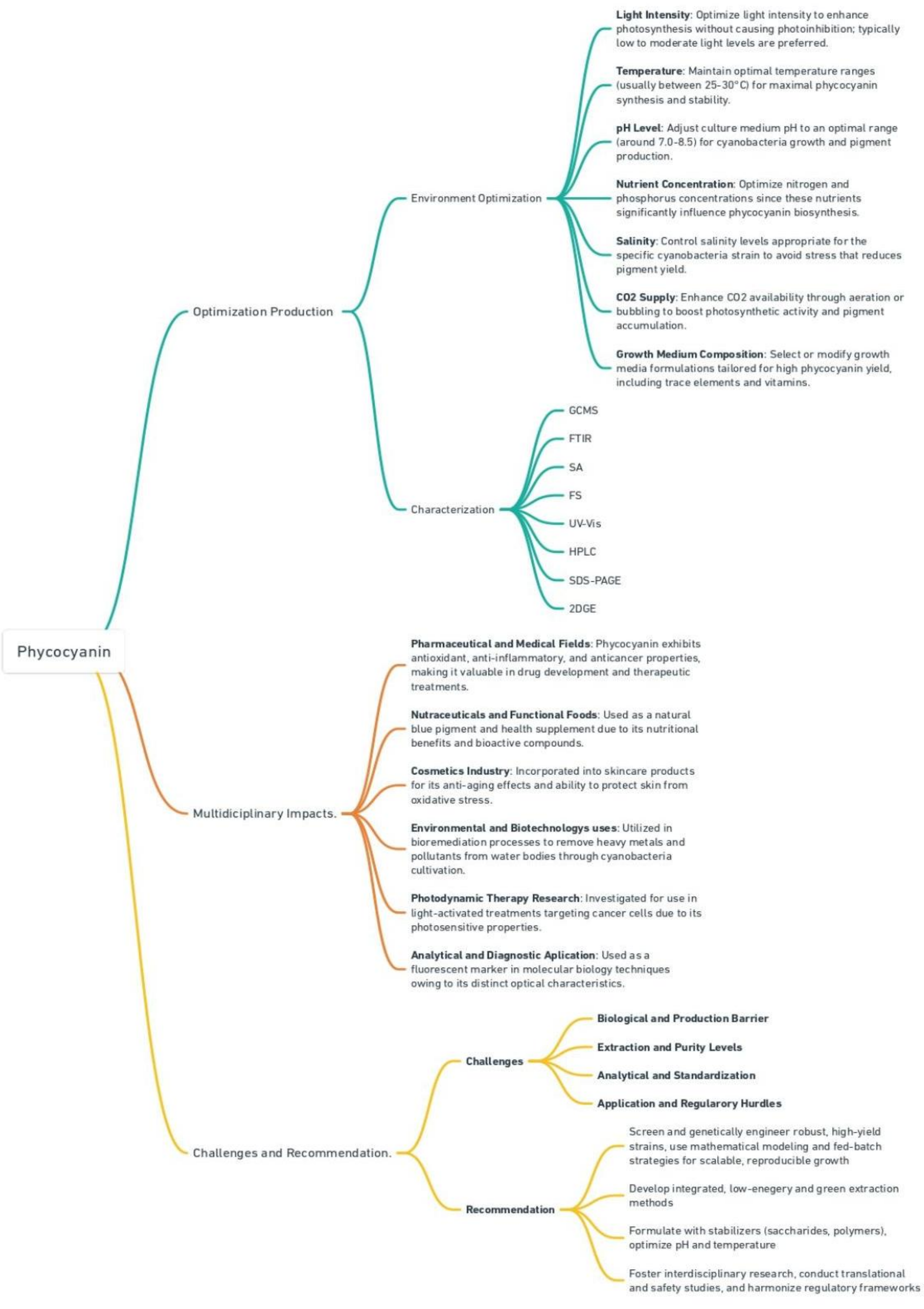

Fig. 2. Research findings.

4 Conclusion

Research shows that phycocyanin production can be significantly increased through optimization of environmental factors. Phycocyanin has broad potential in various fields, including pharmaceuticals, functional foods, cosmetics, environmental biotechnology, and medical diagnostics due to its antioxidant, anti-inflammatory, and bioactive properties. However, large-scale production still faces challenges related to strain efficiency, purity, quality standards, and regulations. Solutions include genetic engineering, development of environmentally friendly extraction methods, improvement of stable formulations, and cross-disciplinary collaboration to realize sustainable and industrially applicable phycocyanin production.

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