

## Photoautotrophic microorganisms with biotechnological potential unexplored

### Microorganismos fotoautótrofos poco explorados con potencial biotecnológico

#### Lina Rendón\*

CES University. ICIF CES Group, Colombia

#### Erika Obando

CES university professors. ICIF CES Group, Colombia

#### Tatiana Martínez

CES university professors. ICIF CES Group, Colombia

#### Paola Zapata

CES university professors. ICIF CES Group, Colombia

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\*Autor de Correspondencia: [rendon.linam@uces.edu.co](mailto:rendon.linam@uces.edu.co)

**Abstract**

The study of phototrophic organisms is becoming more common due to their high nutritional value and capacity to produce various bioactive compounds with potential use in food, pharmaceutical, nutraceutical, cosmeceutical, and chemical industries. These compounds have nutritional and therapeutic properties such as neuroprotective, antioxidant, anti-inflammatory, anticoagulant, hyperlipidemic, immunomodulatory, and immunoregulatory. For this reason, phototrophic organisms are an essential supply for different industries since they can satisfy their current commercial demand while reducing the environmental impact and promoting the bioeconomic development of the country. However, research on these microorganisms is still limited and focused on a limited group of species. This review examines the biotechnological applications of bioactive metabolites produced by several photoautotrophic microbial species from poorly explored environments and their industrial application. As a result, we could determine that there are many little-explored species with a wide variety of bioactive compounds. Moreover, they have potential uses in various industries such as nutraceuticals, cosmeceuticals, and energy. Furthermore, it was concluded that the bioindustry represents a business opportunity and can also be established as a platform for modernization and competitiveness for various country's economic sectors.

**Keywords:** bioactivity, bioeconomy, bioproducts, cosmetology, functional food, pharmacology

**Resumen**

El estudio de los organismos fototróficos es cada vez más frecuente debido a su alto valor nutricional y a su capacidad para producir diversos compuestos bioactivos con potencial uso en la industria alimentaria, farmacéutica, nutracéutica, cosmeceútica y química. Estos compuestos tienen propiedades nutricionales y terapéuticas como neuroprotectoras, antioxidantes, antiinflamatorias, anticoagulantes, hiperlipidémicas, inmunomoduladoras e inmunorreguladoras. Por esta razón, los organismos fototróficos son un suministro esencial para diferentes industrias, ya que pueden satisfacer su demanda comercial actual, al tiempo que reducen el impacto ambiental y promueven el desarrollo bioeconómico del país. Sin embargo, la investigación sobre estos microorganismos es todavía limitada y se centra en un grupo reducido de especies. Esta revisión examina las aplicaciones biotecnológicas de los metabolitos bioactivos producidos por varias especies microbianas fotoautótrofas procedentes de entornos poco explorados y su aplicación industrial. Como resultado, pudimos determinar que existen especies poco exploradas con una gran variedad de compuestos bioactivos. Estos tienen usos potenciales en diversas industrias como la nutracéutica, la cosmeceútica y la energética. Además, se concluyó que la bioindustria representa una oportunidad de negocio y también puede establecerse como una plataforma de modernización y competitividad para diversos sectores económicos del país.

**Palabras clave:** alimentos funcionales, bioactividad, bioeconomía, bioproductos, cosmetología farmacología

## **BACKGROUND**

Globalization and the vertiginous growth of the human population have led to the overexploitation of natural resources as a direct consequence of the demand, production, distribution, and consumption of food, goods, and services (Nayak & Waterson, 2019). The uncontrolled extraction of raw materials occurs dramatically affects the quality of natural resources. It causes irreversible effects such as the loss of native species, soil erosion and compaction, loss of organic matter, water retention, loss of biological activity, soil salinization, and decreased soil productivity. On top of that, there is an accumulation of recalcitrant pollutants produced from the use of agrochemicals and pesticides. These last ones have led to the emergence of resistant phytopathogens, have presented risks to human and animal health, and have caused the loss of non-target species such as pollinators, decreasing the genetic diversity of different habitats and polluting clean water resources (Villanueva-Mejía, 2018). All this has led to an ecological imbalance, which in turn hinders the production, distribution, and consumption chains of both food and raw materials, making it more complex to meet food demands, affecting the economic and socio-environmental sustainability and compromising the food security of the world's population (Mylona et al., 2018).

These effects in sustainability have led to a worldwide demand for products and raw materials obtained from alternative sources, using bioprocesses and non-traditional food sources like algae. Furthermore, the diversification of the existing value chains is possible by introducing low-cost nutritional ingredients, easily degradable, and lower gas emissions. Implementing these alternative ingredients in the supply chains would contribute to the valorization of primary and secondary metabolites and promote an economy based on the efficient use of biomass and its by-products (Brawley et al., 2017; Bernaerts et al., 2019; Andrade et al., 2020).

Consequently, it is necessary to develop and implement public policies that encourage food production with high nutritional content and high value-added bioproducts using technologies that allow high productivity while protecting natural resources (Brawley et al., 2017). Furthermore, the coordination and coherence between agricultural, nutritional, and environmental policies are essential to promote competitive services and products with high nutritional value, accessible to everyone, and sustainable.

Biotechnology is an essential tool for the research and innovation of microorganism production. It uses the microorganism's high growth rate, rapid adaptation, ecological, physiological, and biochemical diversity to obtain primary and secondary metabolites like vitamins, minerals, enzymes, dietary fiber, proteins, essential amino acids, polyunsaturated fatty acids, polysaccharides, toxins, and pigments, among others.

These metabolites have a multiplicity of biological activities (anti-inflammatory, antioxidant, antimicrobial, antiviral, antifungal, antifungal, binding, neuroprotective, hypolipidemic, antiallergic, antitumor, among others) not fully known by various industries that use microorganisms for the manufacture of their products (Lokko et al., 2018; Vargas-Hernández et al., 2018; Bernaerts et al., 2019; Andrade et al., 2020).

Biotechnological production is gaining strength due to its potential application in nutraceuticals, pharmaceuticals, cosmeceuticals, agriculture, and energy obtention. Also, thanks to biotechnology, it is possible to implement controlled cultivation systems of different organisms (i.e., medicinal mushrooms, plant cell cultures, algae (macroalgae and microalgae and bacteria). Implementing biotechnological or submerged cultures can present a challenge at the industrial level, but it can lead to higher productions under automated conditions, and it has short production cycles. Besides, since it uses products of biological origin and demands smaller production areas, it reduces the ecological impact of the industry and increases the efficiency, technical and economic feasibility of the productive process (Lokko et al., 2018; Rosemann & Molyneux-Hodgson, 2020; Yamakawa et al., 2020).

The use of biotechnological cultures will undoubtedly promote the technological transformation of various companies, improving their manufacturing process and product quality, thus generating an impact on the range of goods and services offered and their international commercialization (Rosemann & Molyneux-Hodgson, 2020). Therefore, economic development based on scientific knowledge allows the articulation of science, technology, and innovation by creating clusters between governmental, academic, and industrial entities. Thus, the cooperation between different actors has boosted the biotechnology sector since it makes possible the research, production, scale-up, transfer, and valuation of knowledge.

Biotechnology can be part of the solution to significant social, environmental, and economic challenges such as climate change, diseases, nutrition, alternative energy sources, and sustainable production forms (Yamakawa et al., 2020).

This review will show the variety of biologically active compounds from microorganisms and their application in the manufacture of traditional products and their benefits, as well as expose the importance of generating

public policies that promote biotechnology in Colombia, the research, and innovation in Colombian industries for the valorization and optimization of alternative sources for their production processes. Besides, we will show the enormous potential of our ecosystems for the exploration, production, and valorization of alternative photoautotrophic sources to satisfy the nutritional needs of the most vulnerable populations of our country.

## BIOECONOMY

Bioeconomy is a promising part of the economy that seeks to transform renewable biological resources into goods and services of greater commercial value, avoiding the abuse of natural resources. It includes formulating and implementing strategic options of bioproduction, biodistribution, and consumption that drive economic patterns and the current market structure through more sustainable development (Vargas-Hernández et al., 2018). The new policies required to spread bioeconomy in society must include agricultural, environmental, and food security issues and sustainable processes.

The biotechnological industry represents not only a business opportunity but also a platform for modernization and competitiveness. Therefore, different companies worldwide are pursuing biotechnology, looking forward to improving production processes and product quality. This technological transformation has increased the range of goods and services offered and the trade between countries and international cooperation to develop new technologies resulting in economic growth (Lokko et al., 2018). This economic growth based on scientific development strengthens science, technology, and innovation and promotes cooperation between government, academy, and industry, enabling the production, scaling, transfer, and validation of knowledge.

Investors and consumers are attracted to new production forms involving sustainable methods that can be useful in different fields. In 2019, the biotechnological market showed a profitability margin of 22.20% (MSCI World Pharmaceuticals, Biotechnology and Life Sciences Index, 2020), and its annual growth rate would reach 7.4% by 2025 approximately (Brasil et al., 2017). This metrics presents the biotechnological industry as an area suitable for conducting research focused on developing new processes and technologies. This research includes projects that aim to use different organisms to produce biomass and metabolites efficiently, projects studying the biological activities of novel metabolites, and those looking to develop new therapeutic tools and technologies. There is a diversity of photoautotrophic microorganisms with secondary metabolites that show biological functionalities and promise to manufacture new functional food ingredients, cosmeceuticals, drugs, chemical products, and devices to study chronic diseases, representing a bioeconomic source potential development of local economies.

## BIOTECHNOLOGICAL APPLICATIONS OF PHOTOAUTOTROPHIC MICROORGANISMS

Biotechnology has revolutionized and modified industrial practices while increasing the efficiency and quality of the produced goods. Biotechnological processes allow the production of several valuable compounds from biomass. These compounds include biofuels (i.e., biogas, synthesis gas, hydrogen, methane, bioethanol, biodiesel, bio-oil), detergents, dielectric fluids, dyes, hydraulic fluids, inks, lubricants, packaging materials, paints, coatings, paper, cardboard, plastic fillers, polymers, solvents, absorbents, cellulose fibers, wood fibers, pigments, acids, phenols, resins, among others (Rizwan et al., 2018; Sathasivam et al., 2019; Hingsamer & Jungmeier, 2019; Dragone et al., 2020). Likewise, these processes allow the diversification and improvement of products with nutritional value for humans and animals (Lokko et al., 2018). Biotechnology has even made significant contributions to other broader areas such as bioengineering, genetic engineering, diagnostic engineering, and crop engineering while increasing the processes involved in technical and economic viability (Bajpai, 2020).

Photoautotrophic organisms have been appreciated throughout history due to the variety of metabolites they produce of commercial and industrial interest (vitamins, minerals, proteins with essential amino acids, phycobiliproteins, enzymes, carbohydrates, polyunsaturated fatty acids, among others) (Rodriguez-Concepcion et al., 2018; Andrade et al., 2020). Also, they have phenotypic plasticity, the ability to grow with minimal nutritional requirements, and diverse metabolic pathways, which allow them to produce a wide variety of metabolites. Some of these metabolites have therapeutic uses and benefit human health (Brawley

et al., 2017; Serna-Loaiza et al., 2018). Additionally, these microorganisms are also crucial for the environment, producing half of the world's oxygen (Serna-Loaiza et al., 2018). These characteristics have attracted several industrial sectors' attention towards the microalgae, resulting in an emerging market that produces nearly 7,000 tons of biomass and revenues between 3,800 and 5,400 million dollars per year (Nayak & Waterson, 2019).

## PHOTOAUTOTROPHIC MICROORGANISMS

Photoautotrophic microorganisms have received several denominations. Microalgae is perhaps the most widely used name, referring to all those unicellular organisms capable of performing photosynthesis. The term phytoplankton is also widely spread, referring to autotrophic microorganisms commonly found floating on fresh or saltwater. Other terms used to refer to these microorganisms include Benthos, cyanobacterium, and zooplankton.

Most of this terminology is still used, even though some terms lack strict scientific meaning. In this review, the term 'photoautotrophic microorganisms' will be used to describe a heterogeneous group of microorganisms belonging to the supergroups Archaeplastida (*Rhodophyta*, *Chloroplastida*, and *Glaucophytes*) and SAR (Rhizaria) (Burki, 2014; Burki et al., 2020). This group includes around 200,000-800,000 species, which are ecologically, biochemically, and physiologically diverse (Dineshbabu et al., 2019).

Photoautotrophic microorganisms constitute nearly 70% of the world's biomass; they are distributed across aquatic, terrestrial, and extreme environments such as deserts, frozen lands, springs, wet rock surfaces, and soils (Dineshbabu et al., 2019). These microorganisms carry out half of the photosynthesis that occurs worldwide and regulate different biogeochemical cycles. In addition, they participate in processes necessary to establish microhabitats, like the formation and stabilization of sediments and retention of nutrients. These microhabitats are shelter areas for other aquatic organisms (fish and macroinvertebrates) to deposit their eggs and obtain food. Photoautotrophic microorganisms are the primary producers in lotic water systems as they are more abundant and permanent than aquatic vascular plants. In these systems, photoautotrophic microorganisms transform inorganic chemicals into organic substances used by organisms from other trophic levels (Gaignard, Gargouch, et al., 2018; Gaignard et al., 2019; Dineshbabu et al., 2019).

Photoautotrophic microorganisms fit the definition of renewable resources as they can be used as raw materials to produce renewable energy and active metabolites. Examples of these metabolites include phycocyanin, astaxanthin,  $\beta$ -carotene, unsaturated fatty acids such as Palmitic (16:1) and oleic (18:1), and polyunsaturated fatty acids (PUFAs) such as linolenic acid ( $\omega$ - 3) and linoleic acid ( $\omega$ - 6), precursors of eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA) (Li et al., 2019; Mobin et al., 2019; Torres-Tiji et al., 2020). In addition, photoautotrophic microorganisms are also helpful for producing fibers, polymeric elements, filler material, pigments, manures, cosmetics, and pharmaceutical formulations. Furthermore, they can restore soils contaminated with recalcitrant compounds and heavy metals, treat wastewater, and constitute animal and fish feed (Khanra et al., 2018; Bhattacharya & Goswami, 2020).

The cellular composition of photoautotrophic microorganisms varies between species, and it changes according to the habitat and the cultivation conditions. Proteins are the main cellular component of photoautotrophic microorganisms accounting for up to 70% of their total dry weight depending on the species (Bertsch et al., 2021). Lipids and carbohydrates account for nearly 40% of their total dry weight, and the remaining 10% corresponds to minerals, nucleic acids, pigments, and other components (Katiyar & Arora, 2020). Table 1 shows the general composition of some photoautotrophic species.

The photoautotrophic microorganism's protein content (nearly 50% of total dry weight) is high compared with that of other sources (i.e., soy (30%), milk (26%), meat (43%), and yeast (39%). This higher protein content makes these microorganisms an alternative protein source, with high nutritional value, low allergenicity, and therapeutic benefits (Fleurence & Levine, 2018; Roy & Rhim, 2019).

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**Table 1**  
General composition of different photoautotrophic microorganisms % of dry matter

ESPECIEES	PROTEINAS	CARBOHIDRATOS	LIPIDOS	REFERENCIA
<i>Phaeodactylum tricornutum</i> F&M-M40	63.9	12.8	10.7	Niccolai et al., 2019
<i>Nostoc sphaeroides</i>	50.8 ± 1.45	14.5 ± 0.53	15.1	Niccolai et al., 2019
<i>Chlamydomonas reinhardtii</i>	48	17	21	Rösch et al., 2019
<i>Ankistrodesmus falcatus</i>	20,2	49,6	41	Vijay et al., 2020
<i>Chlorella Vulgaris</i>	51–58	12–17	14–22	Katiyar & Arora, 2020
<i>Dunaliella salina</i>	57	32	6	Katiyar & Arora, 2020
<i>Spirulina platensis</i>	62	15	3	Rösch et al., 2019
<i>Porphyridium cruentum</i>	62,91	20,4	5	University CES

Carbohydrates are one of the main cellular constituents of photoautotrophic microorganisms, and they are found on cell walls or accumulated as reserve material of these microorganisms. The specific composition depends on the group of photoautotrophic microorganisms. For example, the major Archaeplastida group has lipopolysaccharides and peptidoglycan in their cell wall. Within this group, species in the kingdom Chlorophyta mainly have cellulose, starch, xylan, mannans, ionic polysaccharides hemicellulose. On the contrary, species in the kingdom Rhodophyta have mainly sulfated galactans (i.e., agar, fucanoids, alginates, and carrageenan) and xylan, mannans, calcium carbonate, and cellulose to a lesser extent. This cellular composition makes Rhodophyta species better suited than Chlorophyta species as sources of stabilizers, thickeners, gelling agents, biofuels, food supplements, and medicines (Manirafasha et al., 2016; Fleurence & Levine, 2018; Roy & Rhim, 2019).

Some photoautotrophic microorganisms contain phycobiliproteins. They are water-soluble pigments composed of a protein covalently linked to a phycobilin (i.e., phycocyanobilin, phycoerythrobilin, phycourobilin, and cryptoviolin) (Alghazwi et al., 2019). These pigments are natural colorants or preservatives for dairy products, caramels, chewing gum, beverages, sweets, pasta, cereals, cookies, and ice cream in the food industry (Alghazwi et al., 2019; Tang et al., 2020; Bertsch et al., 2021).

Phycobiliproteins have value in other industries as well. These compounds have antioxidant properties, and consequently, they have been used in the pharmaceutical industry to manufacture nutraceuticals, antioxidants, anti-inflammatories, anti-tumors, and anti-aging products. Furthermore, some evidence shows that phycobiliproteins also inhibit the formation of peroxy radicals induced by hemolysis of blood vessels. This inhibition hinders the progressive oxidation of the blood, preventing aging and various pathological diseases. In addition, phycobiliproteins also inhibit the developmental process of edema, histamine, and leukotriene inflammation (Tang et al., 2020). These two activities add value to phycobiliproteins as they give them different uses to be explored by the pharmaceutical industry.

All the above shows the potential that photoautotrophic microorganisms have as raw materials to produce high added value. It also shows the necessity for developing efficient methods to obtain biomass and metabolites from these microorganisms. It is crucial to continue exploring the diversity of photoautotrophic microorganisms and their metabolites to identify new sources of bioactive compounds beneficial for manufacturing high-value goods. Many microhabitats remain unexplored, and many species of photoautotrophic microorganisms are yet to be discovered, showing the potential of algal research to expand.

## UNEXPLORED PHOTOAUTOTROPHIC MICROORGANISMS WITH BIOTECHNOLOGICAL POTENTIAL

The photoautotrophic microorganisms species currently known represent 1% of this group of microorganism's diversities. The real potential of these organisms is unknown. However, genomics research on these microorganisms shows a wide variety of uncharacterized genes and a great extent of functional genetic variability. For example, None et al. (2020) identified and characterized two Fatty Acid Genes from marine microalgae for eicosatetraenoic acid production. This genetic potential should be explored further to discover novel molecules of interest to biotechnology (Torres-Tiji et al., 2020).

The knowledge gap is even more significant for photoautotrophic microorganisms adapted to extreme environments, including freshwater and oceanic environments, extreme heat, and acidic environments (Patel et al., 2019; Garner et al., 2021). Hence, exploring extreme ecosystems is currently carried out to identify new species of phototrophic algal organisms with biotechnological potential (Table 2).

**Table 2**

*Species of photoautotrophic microorganisms and their secondary metabolites used for commercial purposes*

Super Group	Phylum	Group	Class/order	Species	Compound(s)	Activity biological	References	Collection
N.a	N.a	Cyanophyceae	Oscillatorales	<i>Oscillatoria nigroviridis</i>	Almiramides	Antibacterial activity, (gingival fibroblasts), Anti-cancer activity	(Patel et al., 2019)	Benthic zone Providence Island, Caribbean Sea, Colombia
				<i>Limnothrix</i> sp. strain 37-2-1	Phycobiliprotein	Antioxidant, anti-inflammatory, anticancer activity. Cosmetic production	(Quintana et al., 2014)	Isolated freshwater samples, Florida, EE.UU
				<i>Oscillatoria subbrevis</i> , <i>Oscillatoria tenuis</i> , <i>O. limnetica</i> , <i>O. angusta</i> , <i>O. articulate</i> , <i>Synechocystis aquatilis</i> , <i>S. cerdorum</i>	Fatty acids, phenols, alkaloids, flavonoids, and phenolic compounds	Antimicrobial activity against Gram-positive bacteria ( <i>B. subtilis</i> , <i>S. aureus</i> ); Gram-negatives ( <i>E. coli</i> , <i>S. epidemicus</i> , <i>E. fecalis</i> , and <i>B. pumilus</i> ). Antifungal activity ( <i>Candida albicans</i> ). Antibiotic production	(Gantar et al., 2012)	Geno Hot Springs, Bandar Abbas, Iran

				<i>Gracilaria birdiae</i>	Polysaccharides (glycans)	Antitrombolytic activity	(Rodrigues et al., 2017)	The coastline, Fortaleza, Brazil.
				<i>Flintella sanguinaria</i>	Exopolysaccharide	N.A	(Gaignard et al., 2019)	Culture Collection of Algae and Protozoa
				<i>Porphyridium cruentum</i>	Carotenoid (Zeaxanthin) Sulfated Polysaccharides	Protective activity against degenerative diseases. Activity antiviral, antimicrobial Skin protector	(Balti et al., 2018)	N. A
				<i>Porphyridium Purpureum</i>	Phycobiliproteins Sulfated Polysaccharides PUFAS	Immunomodulatory activity Anti-tumor activity Antimicrobial activity ( <i>S. aureus</i> , <i>S. pyogenes</i> )	(Fuentes-Grünwald et al., 2015; Kavitha et al., 2019)	Repository Center for Sustainable Development. University (SU), Wales, United Kingdom
						Blood sugar level controller Atheroprotective effect		Igen Kulturen, Universität Göttingen, Pflanzen Physiologisches Institut, Alemania
				<i>Rhodella reticulata</i>	Sulfated Exopolysaccharides Fatty Acids	Antibacterial activity ( <i>S. aureus</i> , <i>B.cereus</i> )	(Heidari et al., 2012)	Coastal Lakes, TX, USA, And USA
				<i>Purple Rhodella</i>	Lipids	Antibacterial activity	(Heidari et al., 2012)	Unknown collection of culture from THE INSTITUTE of Botany ASCR, Trebon, Czech Republic
				<i>Cosmarium sp</i>	Exopolysaccharides (EPS)	Antioxidant activity Bactericidal activity Antibiotic production	(Rafika et al., 2018)	Hot springs from Ain-Echeffa, Tunisia

**Tabla 2**  
Continuación



			Chroococcales	<i>Diclothrix utahensis</i>	Molasamide	Elastase inhibitor	(Rauf et al., 2021)	Medses reef samples in Long Key, and Brewer Bay, in St. Thomas, U.S. Virgin Islands. USA
				<i>Gloeocapsa sp.</i>	EPS Fatty acids	Antimicrobial activity	(Najdenski et al., 2013)	Hot Spring, Rupite, Bulgaria
Archeplastida	Rhodophyta	Cyanidiophytina	Cianidiophyceae	<i>Galdiera sulphuraria</i>	Phycocyanin	Antioxidant	(Wan et al., 2016)	Shanghai China University of Science and Technology Repository
					Floridosido	Antifouling and therapeutic activities		Collection of crops from the University of Gottingen, Gottingen, Germany
				N. A	Sulfated polysaccharides (agarenes)	Thickener, stabilizer, or gelling agent for the baking industry	(Torres et al., 2019)	N. A
					Phytol	Antidiarrheal Antioxidant activity Anticancer		
					Antimicrobial activity			
			Synechococcales	<i>Synechococcus sp.</i> PCC 6803	Poly-β- poly hydroxybutyrate	Biodegradable plastics	(Tanweer & Panda, 2020)	Culture Collection of Cyanobacteria, Pasteur Institute, Paris, France
				<i>Synechococcus sp.</i>	Squalene	Antiviral activity Drug production (hepatitis C), Hypolipidating Activities, Protector, Cardiovascular, Antioxidant and Moisturizing Activity (Making Cosmetics)	(Miyake et al., 1996)	Desert swamps, Mexico
				<i>Thermosynechococcus elongatus</i> E542	Thermostable phycocyanin	Conversion of CO2 into higher-value products such as biochemicals and biofuels	(Liang et al., 2019)	Lianhua Lake hot spring, china
				<i>Synechococcus sp.</i> PCC6715	Thermostable phycocyanin	Production of pigment thermostable	(Liang et al., 2018)	Yellowstone National Park (USA)
			Nostocales	<i>Fischerella sp. PRICE 298</i>	Unidentified	Antifungal activity	(Shishido et al., 2015)	Soil samples, Brazil
				<i>Lyngbya sp</i>	Jahanyne lipopeptido	Anticancer activity	(Iwasaki et al., 2015)	Costa Jahana, Okinawa Japan
				<i>Leptolyngbya crossbyana</i>	Crosbianoles (heptabromated polyphenolic ethers)	Transcriptional Activator Antimicrobial activity ( <i>Staphylococcus aureus</i> )	(Choi et al., 2010)	Coral Reefs, Hawaii

**Tabla 2**  
Continuación

SAR	Alveolata	Dinophyceae	<i>Heterocapsa triquetra</i>	Pigments (peridininol, peridininol, pyrooxanthin, diadinoxanthin, and diadinoxanthin)	Antiproliferative activity (human invasive melanoma cells (A2058))	(Haguet et al., 2017)	Penze Estuary (1999), northern Brittany, France
			<i>Gyrodinium impudicum</i> Strain KG03	Exopolysaccharides (EPS)	Antiviral activity (encephalomyocarditis virus)	(Yim et al., 2005)	Kang-Gu Korea Seawater Sample
	Stramenopiles	Synurophyceae	<i>Mallomonas</i> sp.	Fucooxanthin	The raw material for commercial production of natural dyes	(Petrushkina et al., 2017)	Freshwater Pond, Vietnam
			Bacillariophyceae	<i>Haslea ostrearia</i>	Marenina	Antimicrobial activity	(Falaise et al., 2019)
		<i>Chaetoceros</i> sp.		Fucooxanthin	Antioxidant activity	(Hamidi et al., 2019)	N. A
		<i>Stausirella pinnata</i>		PUFAS (Hexadecanoic acid, decanoic acid). Glutamate Aminoacids	Anticancer activity	(Savio et al., 2020)	Sediments Mediterranean lagoon, Sardinia, Italy
		Chlorophyta	Chlorophyceae	<i>Coelastrrella</i> sp. F169	Fatty acids	Biofuel production	(Suriya Narayanan et al., 2018)
	<i>Coelastrrella</i> FGS-001			Neoxanthin, pheophytina, astaxanthin, canthaxanthin, lutein, and violaxanthin PUFAS	Antioxidant activity	(Goecke et al., 2020)	Collected outside the Center for Climate Regulated Plant Research (SKP), Norwegian University of Life Sciences, South East Norway
	Trebouxiophyceae		<i>Lobosphaera incisa</i> Strain K-1	PUFAS (arachidonic acid, eicosapentaenoic acid)	Biofuel production Human Nutrition Production of drugs and cosmetics	(Lee et al., 2018)	The flat side in the yellow sea, Republic of Korea
			<i>Pantochloris grandis</i> sp. nov	PUFAS, linoleic acid, and oleic acid.	Biofuel food-additive	(Maltsev et al., 2018)	Pine soil of the artificial plantation, Samara forest, Ukraine
<i>Coccomyxa melkonianii</i>			Fatty acids	The raw material to produce food, cosmetics, and food supplements	(Soru et al., 2019)	Invi Sardinia River, Italy	

**Tabla 2**  
Continuación

			<p><i>Phaeodactylum tricomutum</i></p> <p>Essential and non-essential amino acids</p> <p>Fatty acid (fumarate, succinate, acetate)</p> <p>Polyunsaturated fatty acids (eicosapentaenoic acid, decanoic acid)</p>	<p>Cardiovascular Protector</p> <p>Anticancer activity</p> <p>Anti-inflammatory activity</p> <p>Hypoglycemic activity</p>	(Savio et al., 2020)	PhytoBloom commercial strain
			<p><i>Thalassiosira rotula</i></p> <p>Secologanin and prostaglandins</p> <p>Flavonoids</p> <p>Sphingolipids</p>	<p>Anticancer activity</p> <p>Immunosuppressive activity</p> <p>Antibacterial activity</p>	(Di Dato et al., 2019)	The Mediterranean Sea, Gulf of Naples, Italy
			<p><i>Haslea ostreana</i></p> <p>Marenina</p>	<p>Antiviral activity</p> <p>Antimicrobial activity</p> <p>Producing molecules for pharmacology, cosmetology, food, and biofuel</p>	(Gastineau et al., 2014)	N.A
Haptista	Pavlovophyceae		<p><i>Pavlova pinguis</i></p> <p>EPA-DHA</p> <p>Fatty alcohols</p> <p>Sterols (<math>\beta</math>-sitosterol, campesterol, stigmasterol)</p>	<p>Bactericidal activity,</p> <p>Lipid-lowering activity</p> <p>Production of phytochemicals of natural origin</p> <p>Production of nutraceuticals</p>	(Fernandes et al., 2020)	Roscoff Collection, Brittany, France

**Tabla 2**  
Continuación

The following are general characteristics of some of the organisms shown in table 2:

### **CYANOPROKARYOTES PHYLUM (CYANOPHYCEAE)**

The Cyanoprokaryotes phylum includes around 150 genera and 2000 species, and they are considered the most primitive life forms on earth. Their growth is favored by aerobic conditions in which they perform oxygenic photosynthesis. However, they can grow under anaerobic conditions and obtain their energy through anoxygenic photosynthesis using sulfide or atmospheric nitrogen as electron donors (Anand et al., 2019). Thallus organization varies widely in Cyanoprokaryotes species, it can be unicellular or colonial, and colonies might be filamentous or non-filamentous and might be cover by a sheat. Overall, Cyanoprokaryotes have an outer layer of muramic acid and glycopeptides in their cell wall, the water-soluble pigment called phycobilin, and a particular type of vacuoles know as gas vesicles (Vijayakumar, 2015; Carroll et al., 2019).

Cyanoprokaryotesa species inhabit most earth environments. Therefore, some can survive in extreme environments as they tolerate high temperatures and salinity, intense light, extreme pH, desiccation, and low nutrient availability (Vijayakumar, 2015; Anand et al., 2019). This adaptability provided these species with a versatile metabolism making them a good source of active metabolites to be exploited (Carroll et al., 2019). Consequently, different industries have been interested in several Cyanoprokaryotes orders, including Oscillatorales, Synechococcales, Nostocales, and Chroococcales (Vijayakumar, 2015).

More than 800 metabolites have been isolated from Cyanoprokaryotes species so far. However, these metabolites are only a fraction of the Cyanoprokaryotes' metabolites (Hadi et al., 2016). These metabolites include some cytotoxins with antitumor, antibiotic, antiviral, bactericidal, and antiparasitic effects, such as apratoxins A, F, and G, borophycin, Antillatoxin, cryptophycin, Microviridin Toxin BE-4, siatoxin, among others; as well as some fatty acids, alkaloids, flavonoids, phenolic compounds and peptides with antifungal and antimicrobial activities of biomedical interest for the treatment of some health conditions (Vijayakumar, 2015). Heidari et al. (2012) evaluated the biological activity of various secondary metabolites (Fatty acids,

phenols, alkaloids, flavonoids, and phenolic compounds) of some Cyanoprokaryotes species. They reported antimicrobial activity against the Gram-positive bacteria *B. subtilis*, *S. aureus*, the Gram-negative bacteria *E. coli*, *S. epidermidis*, *E. fecalis*, *B. pumilus*, and antifungal activity over *Candida albicans*. This antibiotic production indicates a potentially broad field of application for these organisms (Heidari et al., 2012).

Interestingly, five out of the 20 most used therapeutic agents are produced by Cyanoprokaryotes (Singh et al., 2020). However, despite the value of these metabolites, their scale-up production continues to be weak because of the lack of state-of-the-art production technology. Consequently, the implementation of new production methods and processes and the use of genetic tools will make the biomass production of these species on a large scale and obtain their bioactive compounds. Finally, these advances would represent an opportunity to consolidate alliances between national private, governmental, and academic entities to improve and modernize technology that encourages the production, distribution, and exportation of products from Cyanoprokaryotes microorganisms.

### **RHODOPHYTA LINAGE**

The Rhodophyta lineage, or red algae, has unique characteristics that provide them potential high commercial value. These microorganisms have essential ecological adaptations that allow them to thrive in many habitats, including highly specialized and extreme environments. They also produce a wide variety of secondary metabolites, some of which are sources of economically relevant products such as agar and carrageenan. These valuable metabolites make Rhodophyta the group most exploited at the industrial level, especially those belonging to the genera *Rhodella* and *Phormidium* (Yoon et al., 2017; Gaignard et al., 2019).

Rhodophyta species possess phycobilisomes containing water-soluble pigments, including allophycocyanin, phycocyanin, phycoerythrin, and carotenoids canthaxanthin and astaxanthin (Yoon et al., 2017; Balti et al., 2018). This group of microorganisms has different carbohydrates as storage polymers and extracellular polymeric substances, most highly sulfated. These sulfated carbohydrates provide the cell with protection from environmental changes in pH, temperature, salinity, and light irradiation and facilitate the assimilation of proteins. The Rhodophyta also contains non-essential amino acids, lipids, and polyunsaturated fatty acids, such as eicosatetraenoic acid, docosahexaenoic acid, and arachidonic acid, which can be used as a pigment used in cosmetics and as a fluorescent reagent (Balti et al., 2018; Lupette & Benning, 2020). Even though red algae constitute a large group, they are still overlooked, and their use is restricted to a few species.

For this reason, several studies have been developed on the biotechnological use and the productive improvement of bioactive metabolites in some species of Rhodophyta. For example, Wan et al. (2016) evaluated the production of phycocyanin from *Galdieria sulphuraria* under photoinduction, photoautotrophic and heterotrophic conditions and determined that photoinduction is the best process for phycocyanin production since it is 147 times higher than photoautotrophic and 12 times higher than heterotrophic production processes; it was also found a phycocyanin accumulation of 13, 88, which exceeds those reported in the literature. Hence, this strategy provides a promising approach for the large-scale production of high-efficiency phycocyanin from *Galdieria sulphuraria* for commercial purposes (Wan et al., 2016). In an additional study, Gaignard et al. (2018) evaluated the production of exopolysaccharides from *Flintiella sanguinaria* in an engineered culture medium called FS. The authors obtained a methylated and acetylated galactoxylan exopolysaccharide (EPS) that includes a significant amount of rhamnose and glucuronic acid, as well as low levels of sulfated groups (0.6%) highly methylated and acetylated (5.1 and 3.2% (w/w), respectively). The authors concluded that the EPS had an original structure from other red microalgae EPS, with biological potential for treating various diseases. Finally, they suggested that other studies should be conducted to study the biological activity of these compounds and their possible use in food products (Gaignard et al., 2018a).

Nayak & Waterson (2019) y Balti et al. (2018) studied batch and semi-continuous cultures for biomass and metabolite formation in *Porphyridium purpureum*. The biomass macromolecular composition and quality of the metabolites produced were characterized and determined that the semi-continuous culture was the best strategy for biomass production, with productivity of 47.04 mg L<sup>-1</sup> day<sup>-1</sup>, the EPS production was 2.1 g/L and, the carotenoids were 0.17 g/L per mg of biomass (Fuentes-Grünwald et al., 2015).

Moreover, new studies on the valorization of new food sources could significantly impact the demand, production, and distribution of biotechnological food products. Thus, they would strengthen the economic and socio-environmental sustainability that would ultimately improve food security in the country.

### **VIRIDIPLANTAE GROUP**

Viridiplantae, also known as green algae, is a well-known group of photosynthetic eukaryotes. This group represents approximately 40% of the total number of autotrophic picoplankton cells on the planet and includes the embryonic terrestrial plants from the Viridiplantae phylum (Leliaert, 2019). Nearly 7000 species belong to this group of eukaryotes, and they distribute across diverse habitats, including poles, marine environments, and some terrestrial ecosystems (Sherwood, 2016). The Viridiplantae divide into two clades, i.e., Chlorophyta and Streptophyta. These clades include species that vary widely in their morphology, including single-celled to large multicellular complex thallus (Liu et al., 2020).

Several Viridiplantae species have biotechnological applications, they can produce high-value compounds such as lipids, triacylglycerols, polyunsaturated fatty acids, and other molecules considered potential alternative sources to produce energy (Minhas et al., 2020). In addition, the cells of some Viridiplantae species produce functional groups, such as carboxyl (COO<sup>-</sup>), amino (NH<sub>2</sub>-), sulfate (SO<sub>4</sub><sup>2-</sup>), and hydroxyl (OH<sup>-</sup>), which serve as binding sites for metals and makes them valuable to eliminate some metals. Then, these Viridiplantae could be used in bioremediation processes (Zaidi et al., 2019). Some Viridiplantae species also produce different pigments and active metabolites. The pigments include astaxanthin, lutein, canthaxanthin, and β-carotene and are used as food supplements, natural antioxidants, or dyes. Their active compounds vary widely and include antimicrobial, antioxidant, neuroprotective, hypolipidemic, hypoglycemic, and immunizing metabolites (Sherwood, 2016; Zhang et al., 2016; Al-Homaidan et al., 2018). Rafika et al. (2018) compared the antibacterial, antioxidant, and cytotoxic activities of EPS and different extracts (methanol, hexane, acetone, acetone: methanol, and water) from *Cosmarium* sp. The results showed minimum inhibitory concentrations in the range of 28 - 85 µg/ml for biomass extracts and 50 - 150 µg/ml for EPS. Additionally, the extracts showed LC<sub>50</sub> values greater than 100 µg/m, indicating no toxicity. Finally, the aqueous extract of EPS showed a moderate antioxidant activity of 24.97% (Rafika et al., 2018). Suriya et al. (2018) compared the effect of CO<sub>2</sub> concentration (0.04%, 1.5% and 5% v/v) on *Coelastrella* sp. and obtained that 1.5% CO<sub>2</sub> aeration is the most suitable for biomass growth. In addition, the biomass registered 18% (w/w) of total lipids, and the fatty acid profile of the lipids showed a higher presence of C18:1, concluding that *Coelastrella* sp. can be a valuable species to produce biofuels to mitigate the current energy demand (Rafika et al., 2018). In a different study, Lee et al. (2018) found that *Lobosphaera incisa* (Strain K-1) produces polyunsaturated fatty acids (PUFAs) like the arachidonic acid. Additionally, it showed proportions of the ω<sub>3</sub> series of fatty acids (FAs), including α-linolenic acid (C18:3ω<sub>3</sub>) and eicosapentaenoic acid (C20:5ω<sub>3</sub>), concluding that the strain is a potential source for producing biofuel, drugs, cosmetics, and human nutrition (Lee et al., 2018).

The studies above show a vast field of applications that indicate that these microorganisms can be sources to manufacture medical substances, chemical reagents, dyes, and functional foods to produce alternative energy sources. Besides, the diversity of microclimates and geographical diversity in Colombia can be a source of those microorganisms. Its use can strengthen national and international research units and the possible internationalization of the national industry.

### **DINOPHYCEAE CLASS**

The Dinophyceae class comprises most marine plankton and includes nearly 2000 species of photosynthetic and mixotrophic single-cell organisms. However, some species of obligate heterotrophs also belong to this class. Dinophyceae species have vesicles composed of cellulose, which gives them a rigid appearance. Dinophyceae are associated with harmful blooms because they produce cytolytic, hepatotoxic, or neurotoxic compounds (Efimova et al., 2019).

Several Dinophyceae species play vital roles as primary biomass producers in different environments. Other species are essential for coral reef formation, and they form symbiotic associations with protists and invertebrates. In addition, Dinophyceae are a source of bioactive compounds for biomedical, toxicological, and pharmacological research. Their main toxins include okadaic acid, dinophysistoxin, saxitoxin, brevetoxin, palytoxin, and yessotoxin. These toxins are helpful in medical and seafood safety research as they have shown enzymatic-inhibitory activity (PKC and PP2A) (Kellmann et al., 2010; Efimova et al., 2019; Prabhudessai & Rivonker, 2020). Also, some Dinophyceae species produce carotenoids (i.e., peridininol, pyroxanthin, diadinochrome, and diadinoxanthin) with antiproliferative activity on human invasive melanoma cells (A2058). This activity makes these carotenoids candidates for treating various pathologies (Haguet et al., 2017; Prabhudessai & Rivonker, 2020). However, studies assessing the therapeutic properties and biotechnological potential of these metabolites are scarce. For instance, Haguet et al. (2017)

obtained a pigment from *Heterocapsa triquetra* (a non-toxic dinophyte) by developing a new assisted extraction technique called MAE. They analyzed it by chromatography and evaluated its inhibitory activity on melanoma cell growth. The MAE (microwave-assisted extraction) allowed a faster and more efficient extraction than conventional processes (soaking, sonication); some of the carotenoids obtained were P457, peridininol, peridinin, pyroxanthin, diadinoxanthin, and diadinoxanthin. In addition, the authors found that peridinin, dinoxanthin, and diatoxanthin possess antiproliferative activity against melanoma cell lines. Finally, they concluded that *Heterocapsa triquetra* and other dinophytes are attractive sources of bioactive pigments with antiproliferative activity in chemoresistant melanoma cells. These results reinforce previous findings on the anticancer activity of phytoplankton pigments and the interest in these molecules as natural cytostatic drugs (Haguët et al., 2017). Therefore, focusing efforts on detecting and isolating new dinoflagellate specimens may represent an opportunity to identify an essential source of chemically interesting and biologically active secondary metabolites.

### **STRAMENOPILES**

The Stramenopiles line comprises many photosynthetic single-celled organisms and diatoms found in a wide variety of habitats (Thakur et al., 2019). Stramenopiles typically have two flagella, one covered by tripartite hairs and the other smooth. Among the Stramenopiles, the Synurophyceae and Bacillariophyceae (diatoms) classes are the most important at the biotechnological level (Torres-Tiji et al., 2020). Members of the symphyte class are characterized by having cells covered with silicon scales. They also have metabolic diversity, which allows them to develop in different habitats, including extreme acidic environments with low nutrient content and conductivity (Prabhudessai & Rivonker, 2020). Both characteristics make these organisms worth to be studied. There are nearly 220 subspecies or taxa in the Synurophyte class, the vast majority belonging to the genus *Mallomonas*. Species in this genus produce several pigments, including fucoxanthin used to manufacture artificial dyes and antioxidants (Derelle et al., 2016; Thakur et al., 2019). Contrary, diatoms are the center of many studies because of their mineral shell, which has potential value for nanotechnological, industrial, and technological processes. These organisms also have high growth rates, modulated by the addition of silicate to the growth media.

Furthermore, diatoms cells have a lipid content of up to 25% lipids and a cover of specialized structures called frustules, which have crystals behavior. Diatoms biotechnological value lies in their potential use to manufacture biomedical devices, and they are sources of several proteins, pigments (i.e., xanthophyll and fucoxanthin), lipids, polyunsaturated fatty acids, and health-promoting phytochemicals (Siver, 2015; Petrushkina et al., 2017). However, it is essential to point out that Academics underestimate diatoms' diversity, and other applications are yet to be discovered by the community. For example, Fernandes et al. (2020) characterized the metabolic composition of *Pavolona pinguis* and determined 29 fatty acids, 14 sterols, 13 fatty alcohols, and 16 other lipophilic compounds; the primary fatty acids found were myristic, palmitic, palmitoleic, and eicosapentaenoic acids. Minor amounts of sugars and other compounds were also detected, leading the authors to conclude that the high content of unsaturated fatty acids, long-chain aliphatic alcohols, and stigmaterol shows that aquaculture, nutraceutical, and pharmaceutical industries could use this alga. Therefore, studying its biology, geographic distribution, species diversity, and bioactive compounds could represent the development and valorization of an alternative source for pharmaceutical inputs and molecular markers. Moreover, in a country like Colombia, with an incalculable natural wealth like ours, these studies would represent these products' economic and industrial development and a drop in import costs of these kinds of raw materials.

### **CHALLENGES, OPPORTUNITIES, AND STRATEGIES**

This research work shows us the variety of photoautotrophic microorganisms and their wide spectrum of application at the biotechnological level; and allows us to identify opportunities for improvement for the biotechnological sector in Colombia, thus taking advantage of its great potential, generated by the geographical location that represents a source of photoautotrophic microorganisms rich in bioactive compounds with potential for the manufacture of high value-added goods. Furthermore, the exploration and exploitation of photoautotrophic microorganisms are still scarce, therefore, the appropriation of the national diversity is required and the population needs to be made aware of the importance of these natural resources, as well as their proper management.

In addition, commercialization as nutritional products is limited, largely because Colombian regulations are ambiguous and lack adaptation to the current model of promoting public health through the use of non-conventional sources of nutrients. The government must generate regulations to promote this developing field. There is also evidence of difficulty in scaling up biomass production processes, so that there is greater

integration of knowledge from various biological and engineering areas. This is needed to promote technological development for biological production, which will facilitate increased productivity while reducing the cost of production, to diversify the portfolio of sources and alternatives of materials, to supply the demand of the population and contribute to the energy, food, cosmetic, pharmaceutical and chemical industries of the Colombian industries, at the same time that strengthens the research capabilities to strengthen the knowledge society at a national and regional level and contribute to the social welfare of its population.

In this sense, it is necessary that the state, NGOs, as well as economic and academic associations, promote and support sustainable multidisciplinary (social, biological, and technological) projects and contribute to the implementation of a biomass production plant of photoautotrophic microorganisms. This should be a complementary strategy for the use of the nation's biological resources, for the sake of promotion, transformation and bioeconomic growth at the regional and national level. In addition there should be the promotion of biotechnological research dynamics that allows for: the transfer to the industrial and governmental sector of traditional knowledge and the results of research aimed at technological improvement; development of alternative products; the creation of policies or the improvement of existing ones that promote the bio-economy of the region; and finally, the country will be a center for the growth of biotechnological and energy industries in the region.

It is proposed that with this mutual support, systems will be created for the implementation of complementary aquaculture systems based on integrated photoautotrophic microorganisms in coastal areas of Colombia, which are isolated or with populations in a state of vulnerability as a source of food; which becomes an alternative to face the social and environmental problems of these communities. It also requires an interdisciplinary body to monitor, compile, disseminate and measure the economic, social, and environmental impact that these proposals can generate.

The aforementioned represents a small group of alternatives that can be very useful to face the economic, social, and environmental challenges exposed in this research.

## CONCLUSION AND PROSPECTS

The biological functionality and high content of active metabolites from photoautotrophic organisms attract the attention of different industries and governmental entities to promote national industrial development. This intention has encouraged the bioprospection of extremophilic species in little-explored environments, the scale-up production of various microorganisms, and the genetic engineering of different strains to produce high purity active metabolites. Thus, their use has spread through different industries and has promoted collaborative work between industry, academia, and government.

The number of photoautotrophic species studied and exploited is increasing since their use had been restricted to a few species in the past years, leaving aside a great variety of species that currently exist.

Currently, *P. cruentum* is a microorganism of commercial interest due to its high growth rate and rich nutritional content. Its contents include the following compounds: Carbohydrates, proteins, lipids, proteins with pigments (phycobiliproteins), cell wall lipopolysaccharides, exopolysaccharides (EPS), polyunsaturated fatty acids (PUFAS  $\omega$ -6 and  $\omega$ -3), precursors of EPA (arachidonic acid) and ARA (eicosapentaenoic acid). Moreover, several studies have shown their biological potential for antimicrobial, neuroprotective, and immunological properties. Additionally, international reports of its use to manufacture food and cosmetic product are marketed mainly in the USA and France.

For this reason, CES University, in alliance with governmental and industrial entities of the country, is currently conducting studies for the generation of a prototype, characterization, optimization, valorization, and incorporation of *P. cruentum* biomass as a functional ingredient in food matrices. However, more studies and efforts are necessary, and working cooperatively among scientific and technological development actors is compelled.

The generation of public policies that favor the production and commercialization of bio-based products is urgent, and the internationalization of companies would allow the transference of knowledge and the strengthening of the biotechnology industry in Colombia.

The bio-based industry of photoautotrophic microorganisms represents a business opportunity due to the multiple benefits of bioactive compounds in human health and the high number of materials generated from them. Nonetheless, it is also established as a platform for modernization and competitiveness for various economic sectors. It promotes innovation and transformation from existing processes, methods, and

production systems. Moreover, it has implemented biotechnological techniques (molecular biology, genetic engineering, cellular biology, biochemistry, microbiology, process engineering) that have helped to create high-quality, bio-based inputs commercially competitive.

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