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Marine fungal pigments; from Lab to potential applications

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ABSTRACT

The nation's request for the production of pigments from natural sources as a safe and eco-friendly option is considerably growing in recent times. Naturally produced pigments, particularly pigments from fungi, are getting more consideration and look worldwide due to their enormous benefits over synthetic sources, which in turn have released new opportunities for a varied series of applications in the market. Besides coloring characteristics and applications in industry, as well as other valuable properties of fungal pigments including cytotoxic activity, antioxidant, anticancer, and antimicrobial have extended their usage in divergent fields. The current review concerns production and optimization tools of different types of fungal pigments and focuses on different valuable applications in addition to challenges and future predictions in the area of fungal pigments.

INTRODUCTION

Color represents an imperative role for all organisms on Earth due to its usage in all features comprising furniture, food and clothes since early eras **(Lagashetti *et al*., 2019)**. The whole market has been occupied by synthetic pigments due to the extensive application range in divergent industries since the discovery of them in the ^{19}th century. However, there are adverse effects on environment and human. Several drawbacks of synthetic pigments, including longer persistence, humble degradation, possibility of causing allergies/cancers, etc., have augmented the request for eco-friendly, natural sources of pigments in the recent time **(Lagashetti *et al*., 2019)**.

In recent times, the request for pigments produced by fungi has amplified due to their numerous profits over synthetic dyes such as ease of extraction, safety in addition to exhibiting massive biotechnological applications **(Sajid and Akbar, 2018)**. Production of pigments by fungi is varied from species to species. Endophytic fungi, basidiomycetes, Zygomycetes, Yeast, filamentous fungi, halophiles and marine fungi are most significant clusters which yield valuable pigments. *Neurospora*, *Trichoderma*, *Monascus*,

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Drechslera, Penicillium, Aspergillus, and *Eurotium* have been established as the issue of several studies due to the prospective bio-pigments production **(Bezirhan Arikan *et al.*, 2020)**. The produced pigments comprise phenazines, melanin, carotenoids, indigo, prodigiosin, violacein, moascins, canthaxanthin, flavins and ankaflavins were extracted on industrial scale for different biotechnological applications **(Bezirhan Arikan *et al.*, 2020)**.

These natural pigments are rapidly developing in the pharmaceutical, textile, food, and cosmetic industries. In addition to wide-ranging applications, such as fabric and dyes of coatings, paints, leather and additives in cosmetics and food **(Kalra *et al.*, 2020)**.

1. HISTORICAL BACKGROUND

Spread of pigments as coloring agents has been developed from the beginning of human civilization. Dyeing with barks, plants, insects and leaves has been developed in Europe and China since more than 5000 years ago. Roman used the red colorants produced by marine molluscs, *Murex* sp. to dye tunics. Egyptians extracted natural indigo from the plant *Isatis tinctoria*. Also, Indigo, alizarin, and purpurin were used by Chinese Yanghai for dying of textiles in the Late Bronze Age (1700 BC) **(Bechtold and Mussak, 2009)**. Dyes produced by insects (kermes and cochineal) were mutual in the 15th century. England used wood to dye clothes in the 17th century. Later, in the 18th century, indigo started to progress in England. After that, another natural type of dye, cudbear, which was gained from different sources of lichen, was patented. The usage of natural colorants produced by animals and plants occurred until the intermediate of the 19th century **(Yusuf *et al.*, 2017)**. Thereafter, the industrial development quickly forced the manufacture of synthetic colorant, however, synthetic colorants face market resistance since 1960s due to their toxicity, allergencity, carcinogenicity problems, and teratogenicity **(Sen *et al.*, 2019)**. Moreover, the synthetic colorants depend on petroleum resources, which are non-renewable source **(Kumar *et al.*, 2015)**. These limitations, along with an increased marketing need to products mainly food as biological, natural, ecological and eco-friendly have flashed the research of biopigments. Natural pigments are regarded safe if they are biodegradable, non-allergenic, non-carcinogenic and non-toxic **(Sen *et al.*, 2019)**.

2. FUNGAL PIGMENTS

Filamentous fungi have been given an extensive consideration due to their ability to yield colors of different shades including red, orange, green and yellow. The produced pigments may bepolyketides, carotenoids or melanin, where polyketides represent a greater portion of pigments generally created by fungi **(Venkatachalam *et al.*, 2018, Lagashetti *et al.*, 2019)**. These pigments exert different ecological and physiological

functions including protection of fungi against environmental pressure **(Lagashetti *et al.*, 2019)**, lethal radiation, and as cofactors in enzyme catalysis **(Spiteller, 2015)**. Marine derived fungi exhibit high diversity and distinctive types of secondary molecules which aid in the presence and survival in the extreme conditions including high salinity and pressure, absence of light and low temperature. These conditions cause the progress of extremophiles which have the ability to yield some exclusive metabolites **(Duarte *et al.*, 2019)**. Marine fungi represent a main basis of undiscovered pigment prospective and should be an object area of study for commercial applications. Fungi like *Fusarium*, *Laetiporus*, *Monascus*, *Aspergillus*, *Trichoderma* and *Penicillum* are stated to yield quinones, anthraquinones, ankaflavin, monascin, b-carotene, rubropuntamine and numerous other types responsible for several colors. These pigments exhibit a variability of medicinal characterestics, including antiproliferative, anticancer, antioxidant, etc. **(Mukherjee *et al.*, 2017)**. **Fig. 1** represents different types of pigments produced by marine fungi.

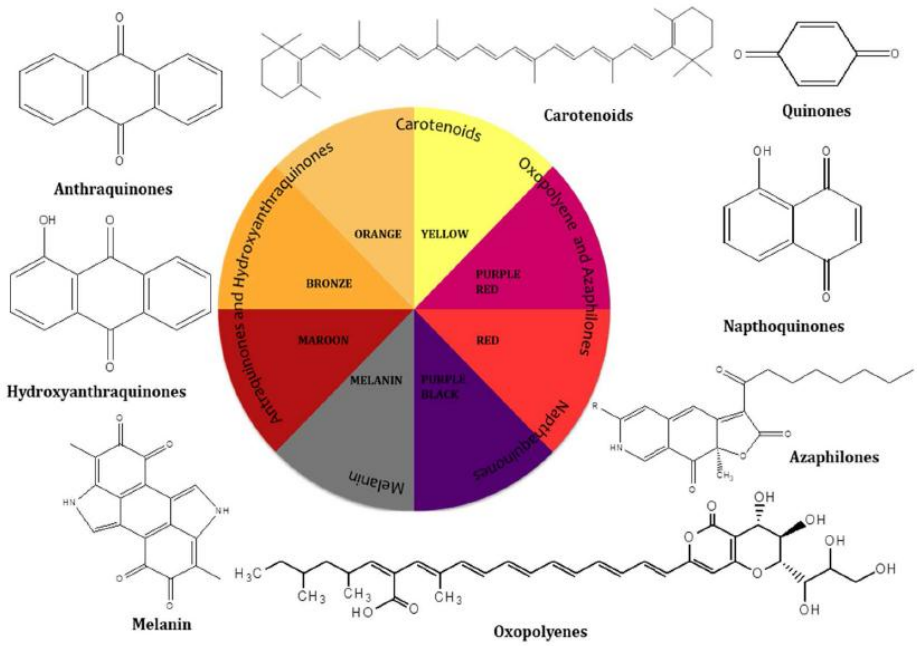

Fig. 1. Elucidation of diverse varieties of fungal compounds **(Kalra *et al.*, 2020)**

In some investigations, *Trichoderma atroviride* and *Talaromyces* spp. as a marine sediment-derived fungi were recognized as potential producers of red pigment **(Lebeau *et al.*, 2017)**. *Talaromyces albobiverticillius* 30548, was also isolated from Reunion Island silt (Indian Ocean) as a red pigment producer. The majority of the produced pigments were identified as azaphilones **(Venkatachalam *et al.*, 2019)**. Increasing interest for yellow and red varieties for coloring of food led to look for marine sediments as a virtuous habitation for promising pigment producer strains. **Table 1** displays several

types of pigments produced by different species. Several organizations have agreed the usage of pigments for humanity **(Mukherjee *et al.*, 2017)**.The Council of European Union (EU) has permitted forty three dyes to be used as food additives, including sixteen natural dyes **(Sezgin and Ayyıldız, 2017)**. Lycopene and β-carotene are the most mutual metabolites being produced by *Blakeslea trispora* and considered in industrial applications **(Xu *et al.*, 2007)**.

Table 1. Some examples of different fungal species producing pigments

Fungal/ lichen species	Pigment	Class of compound	Pigments color	Molecular formula and weight	References
Alternaria solani, Alternaria porri, Alternaria tomatophila	Altersolanol A	Hydroxyanthraqu-inone	Yellow	C16H16O8; 336.3	**(Andersn *et al.*, 2008)**
Alternaria sp. ZJ9-6B	Alterporriol K	Anthraquinone	Red	C32H26O10; 586.14	**(Huang *et al.*, 2011)**
Alternaria sp. (SK11)	Alterporriols C	Hydroxyanthraqu-inone	Orange	C32H26O13; 618.5	**(Xia *et al.*, 2014)**
Amygdalaria panaeola	Panaefluorolines A	Isoquinoline	Yellowish green	C19H24NO4; 330.4	**(Kinoshita *et al.*, 2003)**
Aspergillus sulphureus	Viopurpurin	Naphtoquinones	Purple	C29H20O11; 544.5	**(Durley *et al.*, 1975)**
Aspergillus ochraceus	Viomellein	Quinone	Reddish-brown	C30H24O11; 560.50	**(Stack and Mislivec, 1978)**
Aspergillus fumigatus	Melanin	1,8 dihydroxy-naphthalene	Dark-brown	C18H10N2O4;318.28	**(Gonçalves *et al.*, 2012)**
Blakeslea trispora	β-carotene	Carotenoids	Yellow-orange	C40H56; 536.87	**(Yan *et al.*, 2013)**
Curvularia lunata	Chrysophanol	Hydroxy-anthraquinone	Orange-red	C15H10O4; 254.2	**(Durán *et al.*, 2002)**
Curvularia lunata	Cynodontin	Hydroxyanthraqu-inone	Bronze	C15H10O6; 286.2	**(Durán *et al.*, 2002)**
Dreschlera teres, Dreschlera dictyoides, Dreschlera avenae.	Helminthosporin	Hydroxyanthraqu inone	Maroon	C15H10O5; 270.2	**(Durán *et al.*, 2002)**

Dreschlera teres, Dreschlera dictyoides, Dreschlera avenae.	Tritisporin	Hydroxyanthraqu-inon	Brownish-red	C15H10O4; 254.2	**(Durán *et al.*, 2002)**
Emericella purpurea	Epurpurins A	Dicyanide derivatives	Greenish-yellow	C28H28N2O2; 424	**(Takahashi *et al.*, 1996)**
Fusarium oxysporum	9-O-methylanhydrof-usarubin	Naphthoquinone	Purple	C16H14O6, 302.79	**(Tatum *et al.*, 1985)**
Monascus purpureus	Monapilol A	Azaphilone	Orange	C23H29O5; 385.20	**(Hsu *et al.*, 2011)**
Penicillium oxalicum	Arpink redTM	Anthraquinone	Red	C25H26O14	**(Caro *et al.*, 2017)**
Trypethelium eluteriae	5′-hydroxytrypethe-lone	Naphthoquinone	Violet red	C16H16O5; 289.10	**(Basnet *et al.*, 2019)**
Trichoderma harzianum	Emodin	Hydroxyanthraqu-inone	Yellow	C15H10O5;270.2	**(Lin *et al.*, 2012)**
Penicillium marneffei	Monascorubrin	Azaphilone	Orange	C23H26O5;382.45	**(Woo *et al.*, 2014)**
Graphis scripta	Graphenone	Furandione	Yellow-orange	C14H14O4;246.26	**(Miyagawa *et al.*, 1994)**

3. BIOTECHNOLOGICAL PROGRESS IN PRODUCTION OF PIGMENTS

3.1. Metabolomics

The modern beginning of biotechnological constructed methods has been recognized as a quick screening methods to select the most fitting strains and replacing the traditional methods of pigment production by several strains. Studying the molecular features of pigment generation can be gained by gene cluster elucidation and identification of the promoter's controller using numerous molecular biology methods including sequencing of fungal genomes. The usage of such an advanced approach will also help to understand the complication accompanying with the ways of pigment biosynthesis which can be exploited for applications in industry **(Kalra *et al.*, 2020)**.

Screening of potential fungal strains for pigment production with the aid of metabolomic methods assists to cluster strains depending on their distinguishing metabolites comprising functional groups related with color in addition to allowing for some regulation over the choice of the species with identified toxic components **(Kalra *et***

***al.*, 2020)**. This screening led to the unique creation of *Monascus* like pigments. Application of X-hitting algorithm to the UV-vis spectra of molecules was useful for this context **(Kalra *et al.*, 2020)**. Using this approach, a quick technique to screen ascomycetous filamentous fungi was carried out **(Mapari *et al.*, 2008)**.

3.2. Metabolic engineering

Overproduction of the target pigment can be achieved using engineered forms in precise tools **(Jiang *et al.*, 2010)**. Gene cloning and encoding for a designated biosynthesis of pigments into vectors such as *Pichia pastoris*, *Pseudomonas putida*, *Escherichia coli*, *Corynebacterium glutamicum* and *Bacillus subtilis* have been regarded as the most cost effective and reliable tool for pigment production in industry. Metabolic engineering and mutagenesis tools have been used for production of carotenoids in *Rhodotorula mucilaginosa* KC8 **(Wang *et al.*, 2017)**. Moreover, production of new derivative of betalain has been revealed to be prompted in *Saccharomyces cerevisiae* **(Grewal *et al.*, 2018)**. This approach is mainly significant because it leads to regulation of the biological method in industry and is the key to comprehending the prospective of this field. In a modern research carried out by **Chen *et al.* (2017)**, production of ankaflavin and monascin pigments have been considered by mrPigF gene knockout and biosynthesis explanation of the MonAzPs in *Monascus ruber* M7. The results of their study gave a roadmap for a controlled and selected biosynthesis of the target MonAzPs components **Fig. 2**.

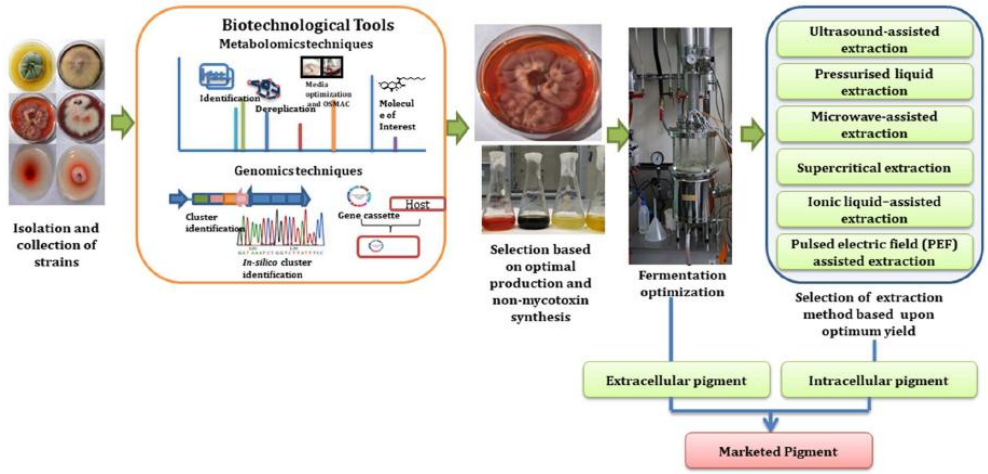

Fig. 2. Schematic roadmap for a pigment journey from lab scale to industrial

4. IMPROVEMENT OF PIGMENT PRODUCTION

Most of the studies have concentrated on the improvement of pigment production from diverse fungal species such as *Fusarium*, *Monascus*, *Penicillium*, *Talaromyces*, etc., by optimizing numerous fermentation parameters such as pH, light intensity, temperature,

orbital speed, medium composition, etc. **(Gmoser *et al*., 2017)**. Some researchers have studied the pigment production by diverse fungal species on natural substances (dehulled sorghum grain, whole sorghum grain, orbital speed, corn, rice, sorghum bran, cassava and wheat) and on dissimilar agro-industrial remains (rice husk, soybean meal, feather grape waste, cheese whey, meal, chicken feather, fish meal, orange processing waste and soybean protein) **(Srianta *et al*., 2016; Kantifedaki *et al*., 2018)**.

Some researchers have also assessed the consequence of dissimilar sugar sources such as lactose, fructose, maltose, sucrose and glucose on production of pigment from *Monascus*. These investigations have revealed that supreme production of pigment was realized upon using media containing fructose for *M. purpureus*, and lactose for *M. ruber* **(da Costa and Vendruscolo, 2017)**. Sodium chloride has been ascertained to be a worthy improver that encourages production of pigment and prevents production of citrinin in *M. purpureus* without disturbing the progress of the fungus **(Zhen *et al*., 2019)**. Also, High pigment production and small biomass by *Chlorociboria aeruginascens* was detected in case of low concentration of nitrogen **(Stange *et al*., 2019)**. In the case of different *Monascus* species, low medium pH has revealed the increase in pigment production **(Li *et al*., 2019)**. Similar researches have documented that the best pH for extreme production of pigments differs with the fungal strains in submerged fermentation **(Afshari *et al*., 2015; Stange *et al*., 2019)**. Another research has also showed the necessity of sufficient oxygen supply for production of xylindein by *C .aeruginascens* **(Stange *et al*., 2019)**.

The effect of color light and darkness on the amount of biomass and both intracellular and extracellular pigment has been determined by different researchers. Most of the studies reported the enhanced biomass and pigment production in condition of total darkness **(Stange *et al*., 2019)**. Effect of wood moisture content as a substrate on production of fungal pigments was studied showing that low content of moisture enhances the production in *T. versicolor* and *Xylaria polymorpha*. Contrarily, enhanced production of pigments by *Lentinus brumalis* and *Inonotus hispidus* was detected at a higher moisture content **(Tudor *et al*., 2012)**. Recently, co-culturing represents an efficient tool for the cryptic pathways activation by cell–cell interactions, which resulted in the gaining of novel secondary metabolites such as fungal pigments **(Serrano *et al*., 2017; Tan *et al*., 2019)**. For example, many reports stated that the enhancement or induction in production of pigments was possible using co-culturing of fungi with yeast or bacteria. It was efficient in case of *A. chevalieri* and *Monascus*, while was not effective in case of *F. oxysporum* **(Palacio-Barrera *et al*., 2019)**

5. EXTRACTION OF PIGMENTS

The selection of a suitable extraction technique according to nature of each pigment is a critical step for efficient recovery.

5.1. Extracellular pigments extraction

This type of pigments does not require solvent extraction methods and could be used directly in food applications because of its high safety **(Kalra *et al.*, 2020)**. On the other hand, extracellular pigment extraction could be performed via other advanced techniques such as Liquid biphasic system (LBS) or named, aqueous two-phase system (ATPS). That is designed specifically to overcome drawbacks of conventional extraction techniques. This method depends on formation of two layers of incompatible liquids separated by interfacial layer. There are several types of LBS such as;

- **Polymer-based LBS:**

It's typically composed of two different polymer layers of polyethylene glycol slat and dextran. This method is commonly compatible with low-ionic strength biomolecules.

- **Organic solvent-based LBS:**

It's usually formed from two layers of inorganic salts solution and water miscible alcohols. The use of alcohol facilitates recovery of biomolecules by simply alcohol evaporation.

- **Ionic liquid-based LBS**

This method uses ionic liquids composed from cationic and anionic ions with tunable biochemical properties. It has been used for recovery of the red pigment from fermentation broth of *Penicillium purpurogenum* DPUA 1275 **(Ventura *et al.*, 2013)**.

- **Surfactant/Detergent-Based LBS**

It's composed form cationic and anionic surfactants and separated into two liquid phases that are immiscible **(Khoo *et al.*, 2020)**. **Morales-Oyervides *et al*. (2017)** have used this method for enhanced recovery of the extracellular pigment produced by *Talaromyces* spp.

5.2. Intracellular pigments extraction

These techniques include; microwave-assisted extraction **(Qiaoling *et al.*, 2002)**, pulsed electric field assisted extraction **(Fincan *et al.*, 2004)**, supercritical CO_2 assisted extraction **(Chaudhari, 2013)**, ultrasound assisted extraction, ionic-liquid assisted extraction, and pressurized liquid extraction **(Kalra *et al*., 2020)**.

- **Microwave-supported extraction MAE**

The frequency of microwave radiations used in this method ranges from 300 MHz to 300 GHz. This energy heats up the sample and solvent mixture enhancing extraction process. This method reduces both the amount of the used solvent and time required for

extraction. Using water as a solvent for microwave assisted extraction improves safety of the method because water is not flammable, non-corrosive, and nontoxic alternative **(Seoane *et al.*, 2017)**.

- **Pulsed electric field assisted extraction PEFAE**

This method is preferable for thermolabile pigments because it relies on electro-permeabilization of cell contents using short pulses of electric field of high intensity. This increases cells permeability, causing rapid diffusion of the solvent into cell and releasing cell content to the outer environment **(Martínez Delso, *et al.*, 2020)**.

- **Supercritical CO_2 assisted extraction SFE**

It is an innovative technology uses the supercritical fluid of liquefied CO_2 for extraction of bioactive metabolites from solid substrates. The supercritical fluid combines liquid phase density and gaseous phase transport capabilities. The adjustable applied temperature and pressure control solvation power of the supercritical fluid and thus determine the targeted metabolites for extraction. Because of its hydrophobicity, supercritical CO_2 is only used for extraction of non-polar metabolites. Otherwise, its polarity could be slightly changed by addition of co-solvents **(Da Silva *et al.*, 2016)**.

- **Ultrasound assisted extraction UAE**

This method relies on creating cavitation causing rupture of cell membrane and releasing of cellular content. Unfortunately, this method is reported to cause undesirable changes to chemical composition of targeted molecules or cause free radicals formation **(Chemat *et al*., 2017)**.

- **Pressurized liquid extraction PLE**

This is considered an efficient technique for intracellular pigment extraction from natural sources. It depends on using solvents under high temperature and high pressure (4-20 MPa) that keep solvents in liquid state even with high temperature. **Lebeau *et al*. (2017)** used this method for efficient recovery of red polyketide pigments from ascomycetous fungi *Talaromyces* spp. and *Penicillium purpurogenum rubisclerotium.* They used water as first solvent followed by methanol, ethanol and mixture of both and then ethanol again. This sequence aimed to decrease polarity profile.

6. CHARACTERIZATION OF PIGMENTS

Understanding the structural properties of microbial pigments, as well as their chemical and physical properties, key functional groups, and bonds stability are crucial **(Valenzuela-Gloria *et al*., 2021)**. Raman spectroscopy, Ultraviolet-Visible (UV-VIS), Infrared (IR), and High-Performance Liquid Chromatography (HPLC) are examples of spectrophotometric approaches **(Valenzuela-Gloria *et al*., 2021)**.

6.1. Ultraviolet-Visible (UV-VIS)

At the preliminary stage, ultraviolet and visible spectrometry can be used to characterize pigments **(Roy and Rhim, 2021)**. In a range of solvents, it compares the spectra of unknown structures to those of recognized compounds **(Sudha and Aggarwal, 2014)**. The spectral range of this radiation is roughly around 185-800 **(Renjini and Dileep, 2017)**. The characterization of an orange pigment 'extracted in ethanol' generated by *Bacillus clausii* using the UV-Visible spectrum revealed absorption maxima at 447 and 472 nm and a spectral pattern that was very similar to that of β-carotene **(Korumilli and Mishra, 2014)**. Furthermore, it was revealed prominent peaks (λmax) at 223, 259, 322, 398, and 502 nm, as well as a high absorption peak beyond 300 nm for *Penicillium purpurogenum* Li-3 **(Jin *et al.*, 2018)**.

6.2. Infrared (IR)

IR spectrometry can detect the significant cluster of groups of a pigment by creating wavelengths with a spectrum range of 500 to 4000 nm, based on the principle that molecules absorb specific frequencies that are distinctive to their architecture **(Moussa *et al.*, 2018)**. FTIR spectroscopy was achieved for the detection of functional groups present in pigments extracted from halophilic bacteria *Halomonas aquamarina* MB598, *Salinicoccus sesuvii* MB59 and *Aquisalibacillus elongatus* MB592 7 obtained from Khewra Salt (Pakistan). In addition, IR spectrum showed the presence of alkenes, carbonyl groups, carboxylic acid, esters, and ether functional groups **(Fariq *et al.*, 2019)**. Furtheremore, pigment extracted from the Antarctic black fungus *Cryomyces antarcticus* was analyzed by IR spectrum **(Claudia *et al.*, 2020)**.

6.3. Raman spectroscopy

Raman is a non-destructive light scattering technique that evaluates the light dispersed by a material after its exposure to a monochromatic ray of light **(Martínez Schottroff, *et al.*, 2020; Valenzuela-Gloria *et al.*, 2021)**. In vivo, Raman spectrum of pigment produced by *Sarcoscypha coccinea* linked most of its major bands to carotenoids. In this fungus, β-carotene, plectaniaxanthin, γ-carotene, astaxanthin, and toruleneas have all been characterized as potential carotenoid species. Also, the ratio of plectaniaxanthin and astaxanthin to lycopene and β-carotene can be measured using two distinguishing ring vibrations, at 1131 and1283 cm^{-1} **(Dzhagan *et al.*, 2021)**.

6.4. High-Performance Liquid Chromatography (HPLC)

For characterizing pigments, chromatographic techniques as High-Performance Liquid Chromatography (HPLC) and Thin Layer Chromatography (TLC) can be applied. In the first approach, stationary phase is a column packed with exceedingly small particles while the stationary phase in the latter one is usually a thin coating of adsorbent

material, such as silica gel, aluminum oxide, or cellulose which is commonly coated on a sheet of aluminum, glass, or even plastic. A liquid (solvent/s) mobile phase is present in both approaches **(Sahu *et al*., 2018)**. Similarliy, a pigment extract generated by a mutant strain of *Monascus purpureus* CFR410-11 was analyzed by TLC and HPLC methods,. These approaches validated the compound's purity and allowed the material inspection by other spectrometric techniques **(Mondal *et al*., 2019)**.

7. APPLICATIONS OF MARINE FUNGAL PIGMENTS

7.1. Medical applications

7.1.1. Antimicrobial activity

Several pigments produced by microorganisms have been described to have many health profits over pigments from synthetic sources. Numerous researches have proved that the pigments produced by fungal genera *Aspergillus, Fusarium, Monascus, Penicillium, Talaromyces* and *Trichoderma* in addition to yeast, *Rhodotorula glutinis* exhibits antagonistic activity against pathogenic yeast, fungi and bacteria, which suggests the prospective use of these pigments as antibacterial ingredients or food preservatives in both pharmaceutical and food industries. Also, the antimicrobial activity against certain bacterial pathogens of diverse types of silk, cotton and other types of fabrics stained with fungal pigments of *Thermomyces* spp. and *Alternaria alternata* has also been assessed showing positive antimicrobial results, which suggests their potential use in manufacturing specific products for therapeutic uses, including suture threads, face masks, bandage, etc. **(Devi and Karuppan, 2015; Parthiban *et al*., 2016)**.

7.1.2. Antioxidant activity

Some indications in human and experimental trials designate that oxidative stress represents a vital role in the pathogenesis of some degenerative and chronic processes, such as aging, autoimmune disorders, rheumatoid, cancer, inflammation, cataract, arthritis, neurodegenerative diseases, and cardiovascular **(Sakaki *et al*., 2002)**. Several groups of molecules produced by microbes revealed scavenging and antioxidant activities; such as xanthones, anthraquinones, phenolic compounds, carotenoids, indole derivatives and alkaloids, in addition to polymers like carbohydrates. In parallel, the creation of antioxidant compounds was detected in the fungus *Aspergillus versicolor* isolated from the deep-see **(Zheng *et al*., 2017)**, upon growth on rice. Also, the antioxidant activity showed that all the phenolic compounds exhibited a scavenging activity close or more than the positive control and a twenty eight extra phenolic compounds were obtained from the same fungus **(Zheng *et al*., 2017)**. Numerous Benzaldehyde products from marine-derived fungi have also gained awareness due to their scavenging characteristics. **Wang *et al*. (2017)** reported scavenging properties of the metabolite chaetopyramin, from the a marine fungi.

7.1.3. Anticancer

Pigments produced by *Monascus* and *M. pilosus* species including monaphilone A–B , monapilol A–D, monasphilone A–B, monascin, monapurone and A–ankaflavin have been shown to have antitumor /anticancer prospective toward diverse kinds of cancers, for instance , human laryngeal carcinoma, human colon adenocarcinoma, human hepatocellular carcinoma mouse, pulmonary adenocarcinoma, and skin carcinoma **(Su *et al*., 2005)**. Also, norsolorinic acid produced by *A. nidulans*, shiraiarin produced by *Shiraia bambusicola*, alterporriol K, alterporriol L, and alterporriol M produced by *Alternaria* spp., in addition to benzoquinone produced by *Fusarium* spp., have also been described to have antitumor, antiproliferative or anticancer activity mostly against human breast cancer cell lines (MCF-7 b , MCF-7 and MDA-MB-435). Moreover, hypocrellin D produced by *S. bambusicola* exhibited anticancer action toward extra cancer cell lines (Anip-973, A-549 and Bel-7721) **(Soumya *et al*., 2018)**.

7.1.4. Fungal pigments as cytotoxic agents

The pigments of different fungal species including *Trichophyton verrucosum, Chaetomium,* and *Fusarium oxysporum*, spp. Have been tested for cytotoxic activity in different studies using different procedures such as yeast toxicity test (YTT), sour orange or using brine shrimp and *Saccharomyces cerevisiae,* lethality bioassay. These researches confirm the probable industrial applications of pigments, especially in pharmaceutical and health ones. A modern research on the estimation of pigment cytotoxicity of *P. purpurogenum* and *Thermomyces* spp. has showed the nontoxic property of the tested pigments and recommended their potential applications in dyeing and cosmetics **(Poorniammal *et al*., 2019)**.

7.2. Industrial applications

7.2.1. Fungal pigments in dyeing woods or as color modifiers

Fungal Pigments produced by *Arthrographis cuboidea*, *Bjerkandera adusta*, *X. polymorpha*, *I. hispidus*, *C. aeruginascens* and *S. cuboideum* have been utilize for staining of diverse kinds of wood samples to rise their marketable uses **(Robinson, 2014)**. Scientists have effectively used the green, yellow and red pigments obtained from *S. ganodermophthorum, C. aeruginosa* and *S. cuboideum,* respectively, to reduce the existence of blue stain on some wood samples of *Pinus* spp. **(Hernandez *et al*., 2016)**. In additon, the gained pigment xylindein from *C. aeruginosa* has showed high photostability and electron mobility in amorphous films, thus recommends its possible usage for the improvement of sustainable semiconductor and organic materials **(Giesbers *et al*., 2018; Giesbers *et al*., 2019)**.

7.2.2. The textile industry

Industry of textile is the biggest sector next to agriculture in relations to service generation and economic impact. It chiefly rests on dyes from synthetic sources for staining diverse forms of fabrics (wool, silk and cotton). Presently, natural fungal pigments have been recognized to be a respectable alternative to dyes from synthetic sources due to their advantages as being non-toxic, eco-friendly, easily degradable, and their high colorfastness and staining proficiency. However, only few studies have surveyed the applications of pigments in the textile manufacturing. Diverse fungal species including *Curvularia, Chlorociboria, Alternaria, Trichoderma, Aspergillus, Scytalidium, Thermomyces, Penicillium, Monascus, Fusarium, Talaromyces, Bisporomyces, Cordyceps, Phymatotrichum, Acrostalagmus,* and *Cunninghamella* were applied to diverse kinds of fabrics such as silk, wool, cotton, nylon, and polyester **(Lagashetti *et al.*, 2019)**. In another work, it has shown that it is not preferable to combine the fungal pigments with natural oils, due to the instability of the fungal pigments in natural oils **(Palomino Agurto *et al.*, 2017)**. Results of all investigations have revealed that the tested fungal pigments have worthy stability of color, dye uptake potentiality and colorfastness characteristics. Additionally, no presence of hostile effects on the fabric and also, a non-toxic effect on the skin of human. Consequently, the possibility of applications of fungal pigments can be expanded into the clothing and textile industry.

7.2.3. Cosmetic industries

The increase request for natural products in the market, led to search for new kinds of natural pigments in cosmetic industries to substitute synthetic ones. Among them, the usage of pigments produced by fungi is rapidly increased in cosmetics due to their benefits. Fungal pigments, particularly lycopene, carotenoids, melanin, etc., have been recommended for the application in sun lotions, anti-aging facials, sunblocks, cosmetics, face creams, and sunscreens. Wonderfully, definite kinds of pigments (*Monascus* - like pigments and *Monascus* pigments) have previously used in the marketplace in the form of lipsticks, skin care and skin conditioning products. **(Caro *et al.*, 2017)**.

7.2.4. Food industry

Fugal pigments represent efficient and safe sorts for food handling. For example, lycopene from *Erwinia uredovora*, pink-red pigment extracted from *Penicillium oxalicum*, β-carotene extracted from *Blakeslea trispora*, red pigment produced by *Monascus* sp, astaxanthin produced by *Xanthophyllomyces dendrorhous*, riboflavin from *Ashbya gossypii* are broadly used in industries of food **(Dharmaraj *et al.*, 2009)**. Fungal pigments can be used in particular purposes for protection of food like Canthaxanthin which is used in; meat , candy, cheese, snacks, boflavin, beverages, fish and wine **(Chattopadhyay *et al.*, 2008)**.

7.2.5. (Opto) Electronics

A modern study regarding (opto) electronic characteristics of mixtures of xylindein pigments gained from *Chlorociboria aeruginascens* has showed high electron mobility and photostability in amorphous films, which encourages the use of it for the manufacture of semiconductor, and organic materials **(Giesbers *et al.*, 2018; Giesbers *et al.*, 2019)**.

CONCLUSION

In recent years, the crucial necessity for natural pigments over synthetic alternatives has been developed due to their eco-safety, cleanliness, and their decreased ecological negative impact. Moreover, the increased public awareness, along with the request of strict environmental and ecological instructions, have directed researchers to undertake both quantitative and qualitative sudies on pigments originating from clean, eco-friendly bio-resources, such as fungi. Although various fungal species are recognized as producers of pigments, a big number of fungal species exhibiting potential production of pigments have not been systematically revealed. Large numbers of studies have focused on different applications of fungal pigments in different fields; however, the produced pigments require passing tests of quality and toxicity and needing several regulatory approvals before entry into the market.

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