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REVIEW ARTICLE OPEN ACCESS

Microbial Pigments: A Healthy Alternative of Synthetic Dyes in Food Industry

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Abstract

Colours are being used in the food industry not only to increase the intensity of the physical appearance of food but also to protect it from oxidative and light-induced damage. In present food market, the acceptability of chemically synthesized food colour is gradually decreasing due to several health issues. So, the need for natural organic colours has flourished to the food industry. The advantage of using microbial colours in the food industry over other natural sources lies on their user-friendly and cost-effective handling conditions. This review assembles the details of different types of microbially originated colours used in the food industry and how to improve their industrial production. Pigments like riboflavin, melanin, chlorophyll, and phycobilins are widely used in the food industry for colouring purposes. The production of these pigments depends on various physiological and environmental factors. All categories of microorganisms like bacteria, algae, and fungi are industrially used for the production of microbial pigments. Impact of this article on research for societal benefits: Natural colours produced from different types of bacteria, algae, and fungi are now being commercialized for use in the bakery, confectionery, and beverage industries. In this review, we have discussed the varieties of microbial pigments currently being used in the food industry and their industrial production parameters with their related advantages and disadvantages. The projected modifications at the production level have also been discussed here. This detailed knowledge may help food industrialists as well as household cooks to select organic food colour with lesser health impact. This review gives the idea about the present position of microbial pigment in the food industry at a glance.

Keywords: Food Colour, Organic Colour, Pigmentation, Microbe

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INTRODUCTION

Food coloration is an age-old process to make a food more lucrative to consumers without altering its palatability and nutritional value. The colour, odor of food stimulate our salivary gland through the resulting impulse from the optic and oculomotor nerve. Most bakery, beverages, and confectionery industries use food colour to make their product presentable to consumers. The coloration of food and drinks was initially done using various phytochemicals until the invention of Perkin's Mauve Pigment, the first ever synthetic colour in 1856.[1] As per Food Safety and Standard Act, 2006, only eight synthetic dyes can be used for food coloration within their prescribed limit - Brilliant Blue FCF (Blue 1), Indigo Carmine (Blue 2), Fast Green FCF (Green 3), Tartrazine (Yellow 5), Sunset Yellow FCF (Yellow 6), Erythrosine (Red 3), Carmoisine (Red 10) and Ponceau 4R (Red 18).[2] World Health Organization (WHO), U.S. Food and Drug Administration (FDA), European Food Standards Authority (EFSA), and Food Safety and Standard Authority of India (FSSAI) have conclusive and specific guidelines for using synthetic artificial dyes in the food industry. As per FSSAI guidelines, the permissible limit of these synthetic dyes in food products is 100 ppm only in the final product. But unregulated use of these dyes has been proven to be detrimental to human health,[3] mostly due to the presence of unidentified impurities which could not be removed even after purification procedure.[4] Excessive consumption of synthetic dyes may lead to abdominal pain, asthma, and renal failure.[5] It was reported that consumption of such synthetic pigments above 50 mg per day may elevate allergic and hypersensitive reactions and also lead to several neurological disorders.[6] Other risks associated with synthetic food dyes involve disruption of the natural immune system, increased inflammation, and oncogenicity.[7] Synthetic food colours are also toxic to liver, kidney, and testes in human.[8] They lower the level of high-density lipoprotein cholesterol, secretion of glutathione and alternatively increase the level of low-density lipoprotein cholesterol, plasma urea, cretin, creatinine and blood glucose. Simultaneously these synthetic food dyes significantly increase the activities of alkaline phosphatase, acid phosphatase, and lactate dehydrogenase enzymes.[9] Tartrazine and Carmoisine-derived food colours are toxic against normal microflora of human beings, like *Escherichia coli*, and *Staphylococcus albus* also.[10] As a consequence, most of the European countries have banned the use of synthetic dyes as food colouring agents.

In this background, natural dyes have got their importance to be used as food colorant again. Initially, different plants derivatives like lycopene, β-carotene, anthocyanin, chlorophyll were used as colouring agents for various packaged food particles. All these chemicals are extracted and processed from different plants parts for which a regular supply of sufficient amount of raw materials are necessary. Moreover, the plant-derived pigments are sensitive to various weather conditions like light, temperature, and pH. As a result, the focus of the research regarding the bio-colouration of foods has shifted towards microorganisms. Microorganisms are considered as the most industrially beneficial organic colour producers due to their neutral effects on seasonal variation, ease of handling, high growth rate, genetically and metabolically modifiable nature, greater stability than their synthetic counterparts and last but not the least highly cost-effective production rate.[11] By monitoring various cultural conditions like carbon/nitrogen source, rate of aeration, temperature, pH, one can regulate pigment production according to his/her need. By using the genetic modification technique, pigment production capacity per microbial cell can be increased many folds. Not only by minimizing the health hazards, but microbial pigments have also proved their efficiency as anti-cancerous, antioxidant, antimicrobial, antitumor and antifouling agents.[12,13] Different microbial pigments like carotenoids, melanin, flavins, quinines, monascin, violacein are widely being used in the food industry for colouring different food products, nowadays.[14] A list of commercially available food-grade dyes of microbial origin is mentioned in Table 1.

Microbes that can produce food grade pigments

Pigment production by microorganisms is quite common in nature. A diverse range of microorganisms like bacteria, fungi, and algae produce pigments as primary or secondary

Table 1. List of synthetic colours and their biological counterpart

Colour	Commercially Available Synthetic Colour	Biological colour from plant source	Biological colour from microbial source
Yellow	Yellow FCF	• Curcumin (Indian saffron) from *Curcuma longa* • Riboflavin	• Pigment from *Aspergillus niger* • Riboflavin produced by *Bacillus subtilis*
Red	Red No. 3, Red No. 40	• β-Carotene from *Daucus sativus* • Betalain from Beta vulguris	• Astaxanthene from different microbial sources • Phycobilins from Cyanobacteria
Green	Fast Green FCF	Chlorophyll from plant leaves	• Chlorophylls of photosynthetic bacteria • Zeaxanthene
Brown	Carmoisin/ Chocolate Brown	Caramels from heat treated sugar	Melanin from different microbes
Blue	Brilliant Blue/ Indigo Carmine	Purple Cabbage + baking soda	Modified phycocyanin pigments from *Spirulina natans*
Black	Black PN	Activated charcoal	Concentrated Melanin

metabolitesby-products which play a crucial role in the survival of producing organisms in many aspects.

Bacteria

In many bacteria, pigment production occurs to activate photoreactive mechanisms to overcome DNA damages caused by UV rays,[15] to give protection against oxidative damage[16] and many others. Pigments like melanin are produced by a few strains of *Pseudomonas stutzeri,*[17] *Azotobacter chroococcum,*[18] *Burkholderia cenocepacia,*[19] and many species of *Actinobacteria,*[20] *Aeromonas, Alteromonas, Bacillus,* and *Vibrio.*[17] Other than melanin, many pigments like chinonenes, phenazines, flavins, carotenoids, and heterocyclic compounds like prodigiosins from *Serratia marcescens*[21] and many other bacteria are produced as secondary metabolites, which help the bacteria to overcome different environmental and physiological stresses.[13] Photosynthetic pigments of bacteria like Phycocyanin, Allophycocyanin, Phycoerythrin, bacteriochlorophyll[22] are also being used in the food industry. Beside photosynthesis, these bacterial pigments also have antiviral, antibacterial and antifungal activities.[23] Zeaxanthene and lutein, two carotenoids produced by *Flavobacterium* sp. are widely used in the food industry for the yellow or orange colouration of many common foods like pasta.[24] Many carotenoid pigments are known for their antioxidant, antitumorigenic activities. The azaphilone pigment produced by *Monascus* sp. is commercially sold in dry powder form which is widely used in the food industry.[25] Pyocyanin produced by *Pseudomonas aeruginosa* is currently used as colouring agent in confectionaries, cakes, puddings, and beverages.[26]

Fungi

Fungi including yeasts and molds are more industrially economical than other microorganisms for pigment production. Pigmentous fungi have been isolated from a diverse range of habitats including marine to mangrove sediments, endophytic to invertebrate inhabitant, and geothermal to halophilic soil. *Monascus purpureus*, commonly known as 'Red Yeast' produces three types of pigments- yellow-coloured ankaflavin and monascine, orange-coloured rubropunctatine and monascorubrine and purple coloured rubropunctamine[27] and monascorubramine.[28] This yeast is widely used as a colour intensifier and food additive in the food industry. Commercially used 'Natural Red' (chemically anthraquinone) is the product of the fungi *Penicillium oxalicum.*[29] The use of fungi for production of different edible pigments is an age-old practice. Pigments like azaphilone, anthraquinones, chromene, hydroxyanthraquinone, napthoquinone, carotenoids, and many others are produced as secondary metabolites by different classes of fungi (Table 2). Though the initial research regarding the industrial use of fungi was restricted within the

Table 2. List of common fungi and pigments produced by them

Name of the fungi	Group of the fungi	Pigment produced	Class of the pigment
Aspergillus niger	Ascomycota	Azangerone C[32]	Azaphilone
Monascus purpureus	Ascomycota	Ankaflavin, Monascine Rubropunctatine, Monascorubrine, Rubropunctamine[27] Monascorubramine[28]	Azaphilone
Penicillium rubrum	Ascomycota	Mitorubrin[33]	Azaphilone
Alternaria sp. ZJ9 6B	Ascomycota	Alterporriol K[34]	Anthraquinone
Aspergillus sp. 05F16	Ascomycota	Bostrycin[35]	Anthraquinone
Penicillium bilaii	Ascomycota	Citromycin[36]	Chromene
Penicilium frequentans	Ascomycota	Questin[37]	Hydroxyanthraquinone
Fusarium oxysporum	Ascomycota	5-O-methyljavanicin[38]	Napthoquinone
Fusarium fujikuroi	Ascomycota	β-carotene[39]	Carotenoides
Phycomyces blakesleeanus	Mucoromycota	β-carotene[40]	Carotenoides

Basidiomycetes group, however, the Ascomycetes group of fungi exhibit better potency of pigment production than the former.[30] While selecting a fungus for industrial production of edible biopigment, it is necessary to assay the toxicity of the fungus, if any. For example, commercial production of food-grade pigment is avoided from *Penicillium* and *Fusarium* as they have been detected with some toxicity.[31]

Algae

Among all the pigments of microbial origin, microalgae are the most reliable, easily extractable and industry-friendly source. The practice of consumption of whole microalgae as a potential source of all essential amino acids[41] and highly digestible mono and polysaccharides[42] is quite primitive. But the use of microalgae as a food colorant flourished when the use of biocolorant gained importance in the food sector. Algae are reliable and primary sources of phycobilin and phycobiliproteins. Though commercially extracted from plants, algae can also act as an alternative for commercial chlorophyll production. In chlorophyta group of algae, the biomass-to-pigment ratio is equivalent to that of the seed plant.[43] *Spirulina platensis*, *Chlorella vulgaris*, *Dunaliella salina*, and *Haematococcus pluvialis* are widely used in the food industry as a potential sources of different biocolorants namely phycocyanin, carotenoids, astaxanthin, lutein, lycopene etc.[44] *Chlorella vulgaris* is used to provide a green tone in butter cookies.[45] Combination of these phycobilin varies in different members of Glaucophyta, Cryptophyta and Rhodophyta.[46] Besides phycobiliproteins, microalgal pigments like carotenoids, xanthophyll, and chlorophyll have high commercial utilization and market value. Algal pigments have been widely used as supplements of synthetic food colours and are additionally preferred for their anti-inflammatory, antidiabetic, and anticarcinogenic activity.[47]

Types of microbial pigments used in food industry

Whatever be the source, most commercially produced microbial pigments can be broadly categorized as melanin, phycobiliproteins, xanthenes and its derivatives, quinone and its derivatives, and carotenoids.

Melanin

Melanin is a universally occurring dark polymeric pigment (oxidized phenolic/indolic compound). In our system produced in the melanosomes of the melanocytes. The ratio of two of its naturally occurring forms- eumelanin and pheomelanin regulates the type of pigmentation of hair and skin.[48] The pigment is produced from its precursor L-tyrosine[49] by enzymatic modification where the enzyme tyrosinase is a product of the *tyr* gene present in chromosome number 11 of humans. The tyrosinase enzyme converts L-tyrosine to L-DOPA which is then oxidized to produce dopachrome. Melanin is a polymerized product of this dopachrome.[50] Not only in pigmentation, but melanin is also well known for its free radical scavenging activity,[51] anti-inflammatory activity by inhibiting *cox* and *lox* genes, protective activity against anti-microbial drug,[52] anti-cancer activity[53] and many others. Recent studies have shown that different melanin derivatives can interact with SARS-CoV-2 spike protein and can act as antiviral compounds.[54]

Though direct melanin-containing food grains are unavailable, but, Vitamin C[55] and Vitamin D[56] rich foods and other antioxidants can increase melanin production in our system. Industrial production of melanin is principally done using *Aeromonas media* and *Pseudomonas maltophila*.[53] Genetically modified bacteria are now being considered to increase the yield of melanin in industries. Recombinant *E. coli* has been prepared by cloning two melanin-producing genes *mel* and ORF438 from *Streptomyces antibioticus.*[57]

Chlorophyll

Chlorophyll, the major photosynthetic pigment of plants and algae largely prevails in its different forms like Chlorophyll a, Chlorophyll b, Chlorophyll c, and Chlorophyll d. A modified form of chlorophyll, known as Chlorophyllides is produced by different Cyanobacteria.[58] The pigment is highly soluble in organic solvents like ether and alcohol due to its long hydrocarbon chain attached to the central porphyrin ring. With the overgrowing urge to use biopigments in food stuffs, industrial production of chlorophyll gets hyped to give green colouration to the foods. Chlorophyll is not only being used to imply green colour to foods like cakes and beverages but it is also being added to retain the colour of many packaged foods.[59] Initially, ethanolic extraction of chlorophyll from plants was used for this purpose but with due course of time it was found that the chlorophyta group of algae can produce an almost equivalent amount of chlorophyll compared to seed plants but in less time. As maintenance of algal culture is easier than seed plants, it is preferred over the second for commercial chlorophyll production.

Use of chlorophyll as a food colour is beneficial for human health also. Reports in favour of chlorophyll as an antitoxin, anticancer and anti-inflammatory compound have already published. Chlorophyll protect the liver and intestine by reducing and/or neutralizing the toxicity of certain toxic compounds. Besides that, chlorophyll can regulate the blood pressure, the pancreas, and abnormal release of thyroid hormone. The healing effect of chlorophyll against chronic ulcers has also been established.[60]

Commercially chlorophyll is available in the market as Semi-synthetic sodium copper chlorophyllins (SCC). In this compound the magnesium ion of the chlorophyll's tetrapyrrole ring is replaced by copper and the hydrocarbon chain is deleted to increase the stability and water solubility.[61] However, the bioavailability of this modified form may not be similar to that of the natural one we get from our diet.[62] For chlorophyll production large scale cultivation of filtered microalgae like *Chlorella*, *Dunaliella*, and *Spirulina* is done either in an 'Open Air System' or in a 'Photobioreactor' depending on the availability of nutrients, sunlight, carbon dioxide, and water. However, construction, maintenance and handling of the first one is easier than the second one.[63] After cultivation, the cells are lysed by homogenization, sonication, or grinding, and chlorophyll is extracted using organic solvents like acetone or ethanol. However, dimethyl formamide (DMF) shows best extraction ability than other solvents. However, the use of DMF is restricted due to its toxic nature. Usually, extraction is performed in multiple steps and the degree of extraction depends on several physical parameters.[64] Nowadays, Supercritical Fluid Extraction (SFE) has gained importance to overcome the negative impact of organic solvent extraction in nature. In this method, liquid carbon dioxide is used for extraction purposes at around 31 °C temperature and 7.38 MPa pressure in a specially designed apparatus. After the extraction, the fluid is removed from the extract by keeping the mixture at atmospheric pressure.[65]

Phycobiliproteins and phycobilin

Phycobiliproteins are water-soluble protein-bound forms of phycobilin, a group of light-harvesting pigments, located within the phycobilisome of Cyanobacteria and red algae and help the host organism to capture the light of specific wavelength (usually higher than that of the chlorophyll) and transfer the same

Table 3. Different phycobiliproteins and their producer algae

Producer algae	Group of algae	Name of the pigment
Arthrosporia platensis & *Arthrosporia maxima*	Cyanobacteria	Phycocyanin and Phycoerythrin
Porphyridium cruentum	Rhodophyta	Phycoerythrin
Porphyridium aerugineum	Rhodophyta	Phycocyanin
Galdieria sulphuraria	Rhodophyta	Phycocyanin
Oscillatoria quadripunctulata	Cyanobacteria	Phycocyanin

into photosynthetic reaction center with high efficiency. Depending upon the wavelength of light they absorb, phycobiliproteins are classified into four major groups - phycocyanin, phycoerythrin, phycoerythrocyanin, and allophycocyanin.[66] Among them, phycocyanin has extensive nutraceutical and pharmaceutical value due to its anticarcinogenic, antioxidative, and anti-inflammatory activities.[67] Phycocyanin is commonly produced from chlorophyll A containing dried cyanobacteria *Arthrospira platensis*. The first report of extraction of phycobilin was done from *Oscillatoria* sp. for industrial production of Brilliant blue.[68] Later on, phycobilin extraction was started from the cell culture of different cyanobacteria and red algae (Table 3) to fulfil the needs of the food and cosmetic industry.[46]

Metabollically phycobilin is produced from heme which is obtained from its precursor protoheme IX by the action of the enzyme ferrochelatase. The heme is then converted into biliverdin IXα by heme oxygenase. Phycobilin is the reduced product of biliverdin IXα which is catalyzed by the enzyme ferrodoxin-dependent bilin reductase. Covalent attachment of phycobilin with apoprotein produces phycobiliproteins by phycobiliprotein reductase.[69]

Phycoerythrin is used in the food industry as a natural red colorant and is preferred over anthocyanin due to its stability in a wide range of pH. This pigment is extensively used in the preparation of candy, lollipops, and decoration of cakes at lower pH.[70,71] Another phycobiliprotein, phycocyanin is used as a natural non-toxic blue colorant of chewing gum, various soft and alcoholic beverages, milkshakes and many other milk products.[70] In the USA, increasing demand for natural blue colorants for preparing candy and chewing gum, *Spirulina* extract, another source of phycobiliprotein is currently being used.[72] Antioxidant and anti-cancerous effects of phycocyanin have been successfully tested *in vitro* on liver cells, renal cells, cardiac cells, blood cells, macrophages, neuronal cells, and other.[73]

For industrial production of phycobilin and phycobiliproteins, the cells are disrupted by maceration, sonication and freeze-thaw technique[74] and sometimes by enzymatic hydrolysis. To increase the yield of the product in fewer cases both the mechanical technique and enzymatic hydrolysis are used in combination.[75] Extraction of the pigments are commonly done in water and 100 mM acetate buffer of pH 6.0.[76] However, whatever the means of extraction, the purity obtained after extraction is poor, and purified phycobilin and phycobiliproteins which should be used in the food industry are highly expensive. The stability of phycobilin and phycobiliproteins are major concern as these pigments are readily degradable under adverse environmental and physical conditions. To increase the stability of phycocyanin, the extract is mixed with 20% glucose, 20% sucrose or 2.5% sodium chloride.[77] Mixing of high sugar concentrations increases the stability of phycocyanin for about 2 months. The addition of benzoic acid, citric acid, and sucrose increases the thermal stability of the pigments.[78]

Carotenoids

Carotenoids are another group of important accessory light-harvesting pigments used by photosynthetic microorganisms. It implies yellow, orange, or red colouration on the food staffs like cakes, cheese, ice cream, and many non-alcoholic beverages. Carotenoids act as the precursor of Vitamin A. In addition, the role of carotenoids in minimizing oxidative damage by neutralizing the superoxide radicals is also well established. Metabolically carotenoids are derivatives of isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP). In archaebacteria and fungi, IPP is produced enzymatically in cytosol from Acetyl CoA via mevalonate (MVA pathway). IPP is then isomerized to form DMAPP and both these molecules act as a conjugant to produce lycopene and β-carotene.[79,80] On the other hand, in eubacteria, malarial parasites, and microalgae, carotenoid precursor IPP is produced from pyruvate and glyceraldehyde 3 phosphate via the intermediate methylerythritol 4 phosphate (MEP pathway).[81]

Microbial carotenoids include β-carotene, astaxanthin, zeaxanthin, etc. β-carotene, commonly sold as CI Natural yellow 26, should contain all trans β-carotene and no cis β-carotene in the mixture. However, no such regulation has still been implied for other carotenoids. Increased production of commercial β-carotene has been achieved by the implementation of Recombinant DNA Technology. The highest recombinant β-carotene production was reported from a fungus *Yarrowia lipolytica* under defined environmental and culture condition.[82] Other microbes reported for commercial production of β-carotene include *Blakeslea trispora, Dunaliella salina,* and *Dunaliella bardawil.*

Lycopene is another lipophilic carotenoid which structurally intermediate between β-carotene and Xanthophyll. Industrially, lycopene is produced by modifying β-carotene biosynthetic pathway in filamentous fungi like *Blakeslea trispora*. In this fungus, lycopene accumulation is directed by the addition of imidazole as an inhibitor of the fermentation of glucose via MEP pathway.[83] In a different study, the efficacy of different inhibitors of the enzyme lycopene cyclase has been evaluated for accumulation of lycopene in the system where it has been established that around 270 mg/L of lycopene accumulation can be obtained at 100 to 1000 ppm of inhibitors concentration.[84]

Astaxanthin is a red coloured carotenoid that belongs to the Xanthophyll sub class and is well known for its antioxidant activity. Commercial production of astaxanthin is done from the yeast *Xanthophyllomyces dendrorhous,*[85] *Phaffia rhodozyma,*[86] and also from a few microalgae like *Haematococcus pluvialis*, *Chromochloris zofingiensis*, etc.[87] For commercial production of astaxanthin, yeast cells are lysed by the enzyme Accellerase or Glucanex under optimum conditions. The fermentation was best reported at 20 °C, pH 6 at a constant aeration rate of 1 L/min. Biomass and product formation both can be increased by increasing the agitation speed upto 600 rpm at controlled environment. In addition to Accellerase or Glucanex, the extraction of astaxanthin can be more intensified using supercritical CO_2.[88]

Zeaxanthin is an orange-coloured modified β-carotene commercially being produced by genetically engineered *Escherichia coli*. Besides that, other bacteria of the family *Flavobacteriaceae* and *Sphingomonadaceae*[89] family are also used for commercial Zeaxanthin production. These cells are not only engineered for overexpression of related genes but also metabolically engineered to modify the existing biochemical pathway that leads towards increased production of Zeaxanthin.[90]

Fucoxanthin is another important Xanthophyll type of carotenoid that is being used in the food industry to give brownish colour to the food stuffs. Fucoxanthin is produced by different types of Brown algae like *Sargassum*, *Laminaria*, *Undaria,* and some other microalgae like diatoms.[91] Around 420 µg/g Fucoxanthin can be commercially extracted from the brown algae *Eisenia bicyclis,* in 90% ethanol at 110 °C under 1500 psi pressure.[92]

In most cases, carotenoids are extracted by non-polar or organic solvents from different plant sources like Kabocha pumpkin, Cassava leaves, Marigold flowers and many others.[93] Extraction can be done using either the Soxhlet, Supercritical fluid extraction or Green method.[94] However, industrial production of carotenoids from microbes like cyanobacteria, microalgae, and bacteria are preferred over the plants due to lower overall production cost. These microbes, not only use low-cost agricultural wastes as substrate for fermentation, but also the extraction of pigments from the microbes are relatively cheaper than that of the plant sources.[95] For large-scale production of carotenoids, microbes like *Dunaliella salina*, *Xanthophyllomyces dendrorhous*, *Haematococcus pluvialis*, *Blakeslea trispora*, *Bradyrhizobium* sp., *Paracoccus zeaxanthinifaciens, Chlorella zofingiensis* and *Brevibacterium aurantiacum* are currently being used extensively.[96]

Riboflavin

Riboflavin, commonly known as Vitamin B12, is a dietary supplement used in baby foods, dairy products, and packaged fruit juices.[7] In addition to being used as a nutritional supplement, it also imparts a yellow colour to the food. Metabolically, riboflavin is used as a precursor of flavin, an important co-enzyme required in different dehydrogenation reactions. Industrially riboflavin is produced mostly by submerged fermentation of simple sugar by *Bacillus subtilis*, *Candida famata*, *Ashbya gossypii,*[97] *Eremothecium ashbyii, Debaryomyces subglobosus, Clostridium acetobutylicum.*[98] However, genetically modified *Escherichia coli*, *Corynebacterium ammoniagenes* are also used for riboflavin production nowadays.[99] Though mostly purified (97%), as per FSSAI guidelines, a marketable purified riboflavin may contain 5 ppm of arsenic and 20 ppm of lead as metallic impurities.

Other smaller groups

Apart from these major classes, bacteria produce a few other pigments also, which are known to have antimicrobial properties and hence used as food pigments, as well as, protect related food from being contaminated by other microbes. Prodigiosins produced by *Serratia marcescens* and *Hahella chejuensis* are widely used in food industry as immunosuppressants, anti-cancer, and antibiotic agents.[100,101]

Factors that regulate pigment production in microbes

All pigments are metabolic products/by-product of certain biosynthetic pathways. So, pigment production mostly depends on the smooth running of the concerned metabolic pathway. To regulate the quantitative extent of pigment, the concerned metabolic pathway should properly be directed. For industrial production of microbial pigments to be used in the food industry, the nature of fermentation, media composition, temperature, pH, moisture content, aeration and the incubation period play crucial roles.

Carbon and Nitrogen source

For fungal growth and pigmentation, the selection of mono/poly/oligosaccharides is essential. In most cases Glucose is preferred over other carbon sources like maltose, fructose, etc.[102] The carbon requirement also varies from species to species. For *Rhodotorulla glutinis*, it has been reported that sucrose is preferred over other carbon sources.[103] Sometimes, it may happen that the carbon requirement for biomass production does not match the carbon requirement of pigment production per cell. In those cases, a suboptimum condition may be maintained concerning both biomass and pigment production. For β-carotene production from the fungi *Blakeslea trispora* Glucose and corn strip liquor served as best carbon and nitrogen source,[27] however, if strains are acclimatized with lactose, then whey can also be used.[104]

Nitrogen, one of the key components for microbial growth and biomass production, can also influence the extent of pigments produced by certain organisms. It has been reported that glutamic acid and 6-furfurylaminopurine convincingly increase monascin in a specific strain of *Monascus.*[105] The effect of different nitrogen sources on the growth and pigment production by *Serratia nematodiphila* was studied where yeast extract was reported as the best nitrogen source from all the view point.[106] Though reports are very few in support of the utilization of nutrients by every individual microbe in association with their pigment production, the optimization of carbon and nitrogen sources during fermentation still needs standardization.

Temperature

All the biochemical processes are best performed at their optimum temperature where their concerned enzymes show maximum activity. Most of the pigment production so far reported is done at mesothermal temperature. During fermentation, the temperature is controlled by the exposure to light where the time and intensity of exposure are directly proportional to the temperature. Similarly in a few bacteria and fungi like *Myxococcus xanthus*, *Mycobacterium marinum*, *Rhodotorulla glutinis* positive carotenoid production was evident in the light.[107] A psychrotolerant *Paenibacillus* was reported to grow maximum at 25 °C and its pigment was successfully extracted with a lab scale bioreactor.[108] Few cold-adopted bacteria and fungi are found to produce FDA-approved colour at psychrophilic temperature, however, the absence of proper policies regarding the utilization of resources from psychrophilic areas, appears as a challenge.

pH

Maintenance of proper pH of the medium is not only required for the growth of the concerned microorganism, but it also influences the stability of the pigment depending upon its acidic or basic nature. Lycopene production gets promoted at neutral to slightly alkaline pH, while acidic pH facilitates β-carotene production.[109] An orange pigment produced by halophile *Salinococcus roseus* changes to yellow when grown at acidic pH.[110] Similarly, the green pigment produced by *Pseudomonas aeruginosa* at neutral pH will be turned into dark red and yellow if grown at pH 2 and pH 13, respectively.[111] Not only the stability, but pH also influences the overall pigment production concerning the control. *Micrococcus luteus* produces a carotenoid pigment at pH 7, however, drifting the pH from pH 7 will decrease the pigment production by lowering the overall biomass.[112]

Besides these major physical regulators of pigment and biomass production, many other minor parameters like dissolved oxygen, humidity, and availability of different micronutrients also regulate microbial pigment production.

Improving the production of microbial pigment

Every industrial production aims to increase the yield of the product cost-effectively. Basic improvements in the strategy of industrial production of any commercial microbial product involve the modification of the producer organism so that it can produce increased amount of target product than the original. So screening and selection of the desired microbial strain followed by subsequent genetic modifications are important for improving its production threshold.

Screening of pigment producing microorganisms

Numerous screening strategies have been employed to select the desired producer organisms. Microbes that can produce edible pigments can be isolated using bioprospecting programs. Source microorganisms are allowed to grow in an optimum environment for pigment production in a selective media. Bacteria like *Micrococcus* sp., *Serratia* sp., *Salinococcus* sp., etc. are optimized for maximum pigment production in the presence of 1% glucose, 0.1% yeast extract, 2-6% NaCl at 30 °C-37 °C at pH 7.[113] Phycobilin-producing cyanobacteria like *Anabaena*, *Nostoc*, *Oscillatoria*, *Chrococcus,* etc. can be screened out using BG11 and CFTRI media at 30 °C in the presence of light intensity of 25 L mol photons/m^2 /s following 12:12 hour light/dark regime for 27 days.[114] The screening strategies also involve prior knowledge about any toxic by-product, and should be selected accordingly. For example, the producer organism of commercial bio colour Quoron TM, *Fusarium venenatum* produces a cytotoxin 4, 15-diacetoxyscirpenol.[115] Modern biophysical and spectrophotometric techniques like LCMS, NMR, and UV VIS spectroscopies are employed for the detection and screening of microbial pigments.[116]

Strain improvement strategies

Traditional techniques related to the genetic modification of microbes are the key strategy for increasing the production of pigments. Plenty of chemical mutagens like 1-methyl-3-nitro-1-nitrosoguanidine (NTG), ethyl methane sulfonate (EMS), and physical mutagens like UV rays of specific wavelength have widely been employed as mutagens.[117] Recent developments in molecular biological techniques and biological databank and data management systems play a crucial role in the identifying and revealing genetic information of the producer organism, which in turn helps in modifying the strain for better production. The entire PKS-FAS gene cluster of *Monascus purpureus* was identified for azaphilone pigment production including the pivotal enzymes MppR1 and MpPKS5. This information helps to modify the organism at the genetic level which lead to better azaphilone production.[118] Mining and reconstructing metabolic pathways by insertions and deletions of certain genes also improve the overall pigment productivity of certain organisms. Modifications of the promoter, RBS region of the pivotal enzyme of pigment producing pathways may guide the efficiency and amount of the enzyme produced and thereby control the pigment production.[119]

Modification of cultural conditions

Not only with modification of producer organism but enhanced production of commercial grade microbial pigment also requires the modification of culture conditions aiming towards the increased production of desired pigment. Pigments are produced both by solid-state fermentation and submerged fermentation technique. The media compositions and associated physical, chemical, and environmental factors can be modified to get the product at optimum concentration. Pigment production by different molds can be optimized by implying suitable immobilization techniques that minimize the cell loss and increase cost-effective production of desired pigment. Controlling other physical and environmental factors like moisture content, temperature, pH of the medium, etc. can also affect pigment production. Choosing a suitable substrate for the fermentation technique also plays an important role in pigment production. Apple pomace is used in solid-state fermentation for the production of pink shed from *Rhodotorula*, red shed from *Chromobacteria*, yellow pigment from *Micrococcus.*[120] *Penicillium purpurogenum* normally produce a brick red pigment, however by modifying the culture condition, one can channel the production towards violet and orange pigment.[121] Designing new metabolic pathways and modification of existing pathways are also being employed to bypass the blockage in production due to feedback inhibition of traditional biosynthetic pathways. For example, β-carotene production in *Escherichia coli* can be increased by introducing a novel mevalonic acid pathway where the first part of the pathway resembles that of *Streptococcus pneumoniae* and the end part resembles that of *Enterococcus faecalis.*[122] In recent years, multiple pigment-producing genes have been identified by advanced biotechnological techniques and biosynthetic pathways for pigment production have been discovered using isotope labelling.[123] Most of the pigments produced by the microbes are insoluble. However, chemical modifications have been done to make them soluble in various solvents like aminoacetic acid, and aminobenzoic acid, so that, they can be used as food colorants.

In very recent studies, it has been stated that for large scale production of microbial pigments, agro-industrial waste materials as a substrate for fermentation has been preferred. For producing food-grade pigments from *Monascus ruber*, *Penicillium resticulosum*[124] corn steep liquor obtained from different cereal processing industries can act as a good nitrogen and vitamin source. During carotenoid production from *Rhodotorula glutinis* mung bean waste is being used.[125] Whey protein is used for submerged fermentation by *Rhodotorula rubra* that produces a characteristic yellow pigment.[126] Similarly, waste from the fruit and vegetable industry like jackfruit seed, Kinnow peel, apple pomace, grape waste, etc. are currently being used as substrates for fermentation by various microbes for the commercial production of pigment.[12]

Controlling other physical parameters of fermentation

Besides the screening and strain improvement strategies, the functionality of the fermenter like aeration rate, agitation speed, etc. also play an important role in regulating yield. At an agitation rate of 1000 rpm, more red pigment can be recovered from *Monascus purpureus* than that with a lower agitation rate.[127] In a mathematical model presented in 2002, it has been stated that the aeration and agitation rate play a crucial role in the production of β-carotene by *Blakeslea trispora*. Maximum β-carotene production was reported at lower agitation speed with higher aeration rate.[128] In addition to aeration and agitation, pigment production from edible fungus *Neurospora intermedia* can be enhanced by post-treatment with 95% humidity.[129] However, solid-state fermentation for commercial bio-pigment production is favoured over submerged fermentation due to the ease in isolation of pigment from the reactor.

Advantages and challenges of using microbial pigments

Advantages

Microbial pigments are preferred over their synthetic counterpart mostly due to their availability, non-toxic nature. Microbial pigments are evident for having lower downstream processing costs with higher yield than the synthetic pigments.[130] Microbial pigments also exhibit antioxidant, anticancer, immunosuppressive and inflammatory properties in different cases.

The antioxidant activity of a compound is related to the presence of conjugated systems that are susceptible to electrophilic attack. Staphyloxanthin produced by *Staphylococcus aureus* reduces oxidative stress in Swiss albino mice caused by carbon tetrachloride.[131] Another group of microbial pigments like β-carotene, astaxanthin and zeaxanthin also show some extent of antioxidant properties due to their reactive hydroxyl group.[132] A recent study with carotenoid pigments of *Staphylococcus* sp. and *Pseudomonas* sp. has demonstrated their free radical scavenging activity using DPPH assay. Different red pigments like monascorubramine, lycopene, undecylprodigiosin, orange pigments like orevactaene, neurosporaxanthin, and many others produced by certain groups of fungi, actinomycetes are well evident for their antioxidant nature.[133] The addition of natural microbial pigments produced from whey in the food chelates the free radicals from the body and thus acts as a potential antioxidant.[134]

Anti-cancerous activity of microbially produced pigments is another important advantage of using them as food colorants, whereas synthetic colours are sometimes carcinogenic. Extracted pigment from *Monascus purpureus* mixed with coix seed was tested for its anti-cancerous activity over HEp-2 cell line of human laryngeal carcinoma and it was observed that the IC_{50} value of the pigmented seed was decreased about 42%.[135] Pigments like anthocyanin, and violacein produced by different microbes, can be used as food colorant and have anti-cancerous, anti-inflammatory properties. Prodigiosin produced by *Serratia marcescens* is currently used as a dietary supplement for treating diabetes mellitus. This particular pigment has also been successfully tested as an inducer of the apoptotic pathway and an inhibitor of cell cycle.[136] Cytotoxic activity of different bacterial pigments has been successfully tested against different mammalian and human cell lines. Melanin produced by *Bacillus* sp. and *Pseudomonas* sp. is being used for treating metastatic melanoma. Pigments like prodigiosin and its analogs, violacein and many other carotenoids are reported for their immunosuppressive activities through inhibition of proliferation of T cells. The anti-inflammatory and antiproliferative effect of scytonemin, produced from cyanobacteria, is well established for reducing cytokine production which upregulated during the onset of carcinoma.[14]

Microbial pigments like prodigiosin compounds produced by *Serratia* and *Vibrio*, tambjamines produced by many marine bacteria like *Pseudoalteromonas*, and violacein produced by *Janthinobacterium* and *Chromobacterium* have antibacterial activities against wide range of gram-positive and gram-negative bacteria. They are effective against multiple human pathogens also. Not the antibacterial properties, but all these compounds are also well known for their antifungal activities against a broad range of pathogenic fungi like *Candida*, *Penicillium*, *Aspergillus*, *Cryptococcus*, *Histoplasma,* and many others.[13] Flexirobin, ant342, a yellow pigment produced by *Flavobacterium* sp. is currently being used as a chemotherapeutic agent for the treatment of tuberculosis. Carotenoid pigments from *Staphylococcus* sp. and *Pseudomonas* sp. are evident to exhibit antimicrobial properties against *Bacillus subtilis*, *Streptococcus pyogenes*, *Shigella* sp., *Klebsiella* sp. and *Escherichia coli.*[132] Staphyloxanthin isolated from *Staphylococcus gallinarum* has been reported to have growth inhibition against *Escherichia coli*, *Staphylococcus aureus,* and *Candida albicans.*[137] Similarly, the antimicrobial activity of violacein was successfully tested against a broad range of bacteria namely *Bacillus lichenniformis*, *Bacillus subtilis*, *Bacillus megaterium*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa,* and viruses like polio virus, herpes simplex virus and simian rotavirus SAII.[138,139] Pyocyanin, a blue pigment produced by *Pseudomonas aeruginosa* is widely used as natural food colorant. This compound shows distinct antibacterial efficacy against different food pathogen like *Bacillus spizizennii*, *Escherichia coli*, *Staphylococcus aureus*, *Enterobacter aerogenes,* and even against other strains of *Pseudomonas aeruginosa* also.[140] Pigments produced from endophytic fungi have shown better antimicrobial potential than commercially available streptomycin against many human pathogens.

Few microorganisms that produce edible pigments also possess some nutritional value. *Spirulina*, a widely used algae as green/ blue colorant can act as a potential source of essential amino acids (single cell protein), calcium, potassium, magnesium, iron, and vitamins.[141] Other than *Spirulina*, microalgae like *Chlorella*, *Dunaliella,* and *Aphanizomenon* can also act as rich sources of protein. Microalgae can act as potential source of other macronutrients like polyunsaturated fatty acids, and vitamins also.[142]

Challenges

Although edible pigments of microbial origin are associated with numerous health benefits for consumers, their use in the food industry is not widely accepted by industrialists due to high production and maintenance costs. The use of microbial pigments in the food industry increases the overall production cost by at least five times, while in confectionery items, it can increase up to twenty times.[131] The production and maintenance of raw materials (bacterial culture) and the low yield per unit for the producing organism make these pigments more expensive than synthetic dyes.[143] Additionally, natural pigments often have inherent odors that can affect the quality and palatability of food. Most foods that contain natural pigments as coloring agents require deodorization, a technique used to mask unpleasant odors. Another significant drawback of using microbial pigments in the food industry is their natural instability. These pigments do not maintain the same consistency as synthetic pigments. The quality and stability of microbial pigments are greatly influenced by heat, light, air, water activity, and pH levels, making the use of these pigments in the food industry more challenging. Various modifications have been implemented to enhance the stability of these natural pigments. In many cases, slight changes in media composition can alter the associated structure of the pigments while keeping the skeleton intact, which, in turn, increases their stability under harsh environmental conditions.[144]

Presently most of the fermentation are performed using different synthetic and chemically defined media which needs extreme expertise to formulate and prepare. Additionally, they are costly enough to increase the price of the product. To make these biocolours available to all for use as a food colour, new synthetic or semisynthetic media must be formulated to reduce the production cost.

Isolation and purification of pigments from microbes is another technical challenge. Conventional separation techniques that involve different types of solvents like acetone or ethyl acetate have significant negative effects on human health. Thus, some alternative strategies like spray drying, solid phase extraction may be tested to overcome the challenge. Another disadvantage of using microbial pigment for food coloration is that many microorganisms show their pathogenicity in the human body under some specified condition. Melanin producing organisms like *Vibrio cholerae*, *Cryptococcus neoformans*, *Aspergillus fumigatus* are known for their pathogenicity in human.[13] Organisms like *Serratia marcescens* that produce prodigiosin causes urinary tract infection, *Staphylococcus aureus* that produces staphyloxanthin, *Chromobacterium violaceum* that produce violacein are all known human pathogen.[145] It was reported in a recent publication, that *Stenotrophomonas maltophilia* produces an orange pigment, but the organism causes serious fatal infections in human beings.[146] So, while dealing with these microbes for their pigment production, trials are going on to reduce the pathogenicity of these organisms while being used for industrial purposes. To reduce the microbial toxicity generated from the source of isolation, genetically modified non-toxic non-pathogenic microbes like *Escherichia coli*, *Saccharomyces cerevisiae*, *Candida albicans* and *Zymomonas mobilis* are preferred over other microbial sources.[147]

DISCUSSION

Acceptability of any newly developed processed food in society not only depends on its nutritional value or palatability, but the appearance of the food is also an important criterion for being preferred over other foods. A highly nutritional and palatable food may not be preferred by the consumer due to its pale appearance. Any food, both processed and raw, activates our so-called 'semantic memory' through the excitation of the olfactory and occipital cortex of our brain.[148] On the other hand, food intake controls our gut microflora which in turn controls our neurological and hormonal status. Colour of a food is thus important to increase the intensity of its physical appearance. The relationship between food colour and apprehended taste is well reported. People in their subconscious mind think about the taste of unknown food, simply by seeing its hue and intensity of colour. Any lucrative food increases our appetite by increasing the cortisol level in our system.[149] In addition, to amplify the appearance, food colours also help in keeping the flavor and vitamins away from light-induced damage. Three types of synthetic colours - primary, blended, and lake colours are used for food colouration. Synthetic chemical colours like amaranth, tartrazine, quinoline yellow, allura red, and indigo carmine were initially widely used in the food industry for colouration. Though, these synthetic colours are cost-effective and business-friendly, but the possible health hazards associated with these synthetic colours decrease their acceptability to consumers. A detailed survey has reported that synthetic food colours may result in behavioral changes in children. It may decrease the attention of children. The most common hazards associated with synthetic food colour is cancer and hypersensitivity. Biological colours are thus considered an alternative of these synthetic dyes. Use of different plant parts and extracts for the commercial production of biological colours is an age-old process. However, the high maintenance cost of the producer plants, slower breeding rate and maturation rate, and the complex extraction strategy paved the way for microbial pigment as an alternative. Colours of microbial origin, so, implied as a substitute of synthetic colour. Microbes are easy to cultivate and require lesser space to grow than an equivalent number of plants. The R&D cell of a pigment industry can easily manipulate the strains and culture conditions to increase in the production of desired pigment. Moreover, extraction of the pigment from the microbial cell is comparatively user-friendly and less troublesome. Many pigments like phycobilin, β-carotene, melanin are now being produced using microbial origin. In addition, microbial pigments have been established as beneficial from the perspective of human health. Pigments like β-carotene, Phycocyanin, Violacein, etc. are well known for their antioxidant nature. Phycocyanin is also known for its anti-tumorigenic and immunoregulatory properties. Many pigment-producing microbes like *Spirulina* are also well known for their nutritional value. So, in addition, to impart colour to the food particle, biopigments are also important for their positive effect on human health. As a result, modern food technology supports the use of microbial pigments as a food colour.

CONCLUSION

This review discussed the importance, acceptability, and current scenario of microbial pigments in the food industry. There is a wide diversity of microbes that are able to produce edible pigments. However, certain modifications are necessary to remove the odour of the raw product. These biopigments are also beneficial for human health and in some cases, if not all, they have additional nutritional value also.

Future prospect

New advancements related to the use of microbial pigments as food colour should involve the chemical modification of the extracted colours to intensify their colouring property without deteriorating their nutritional and health values. In addition to the colouring properties, a few microbial pigments like isoprenoids, flavonoids, and alkaloids are also known for imparting fragrance to food products. Another avenue may also involve the research that aims towards the increased production of such colours with minimal input that ultimately leads to a financial profit for the developer without hampering the consumers' purpose.

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DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

Not applicable.

REFERENCES

1. Burrows A. Palette of our palates: a brief history of food coloring and its regulation. *Compr Rev Food Sci Food Saf.* 2009;8(4):394-408. doi: 10.1111/j.1541-4337.2009.00089.x
2. Mittal J. Permissible synthetic food dyes in India. *Resonance.* 2020;25(4):567-577. doi: 10.1007/s12045-020-0970-6
3. Frick D. The coloration of food. *Rev Prog Color.* 2008;33(1):15-32. doi: 10.1111/j.1478-4408.2003.tb00141.x
4. Srivastava S. Food adulteration affecting the nutrition and health of human beings. *J Biol Sci Med.* 2015;1(1):65-70.
5. Kobylewski S, Jacobson MF. Toxicology of food dyes. *Int J Occup Environ Health.* 2012;18(3): 220-246. doi: 10.1179/1077352512Z.00000000034
6. Mahmoud NH. Toxic effects of the synthetic food dye brilliant blue on liver, kidney and testes functions in rats. *J Egypt Soc Toxicol.* 2006;34:77-84.
7. Dafallah AA, Abdellah AM, Abdel-Rahim EA, Ahmed SH. Physiological effects of some artificial and natural food coloring on young male albino rats. *J Food Technol Res.* 2015;2(2):21-32. doi: 10.18488/journal.58/2015.2.2/58.2.21.32
8. Sadar P, Dande P, Kulkarni N, Pachori R. Evaluation of toxicity of synthetic food colors on human normal flora and yeast. *Int J Health Sci Res.* 2017;7(8):110-114. doi: 10.13140/RG.2.216583.60322
9. Rana B, Bhattacharyya M, Patni B, Arya M, Joshi GK. The realm of microbial pigments in the food color market. *Front Sustain Food Syst.* 2021;5:e603892. doi: 10.3389/fsufs.2021.603892
10. Nigam PS, Luke JS. Food additives: production of microbial pigments and their antioxidant properties. *Curr Opin Food Sci.* 2016;7:93-100. doi: 10.1016/j.cofs.2016.02.004
11. Ramesh C, Vinithkumar NV, Kirubagaran R, Venil CK, Dufosse L. Multifaceted applications of microbial pigments: Current knowledge, challenges and future directions for public health implications. *Microorganisms.* 2019;7(7):186. doi: 10.3390/microorganisms7070186
12. Tuli HS, Chaudhary P, Beniwal V, Sharma AK. Microbial pigments as natural color sources: current trends and future perspectives. *J Food Sci Technol.* 2015;52(8):4669-4678. doi: 10.1007/s13197-014-1601-6
13. Wynn-Williams DD, Edwards HGM, Newton EM, Holder JM. Pigmentation as a survival strategy for ancient and modern photosynthetic microbes under high ultraviolet stress on planetary surfaces. *Int J Astrobiol.* 2002;1(1):39-49. doi: 10.1017/S1473550402001039
14. Krinsky NI, Johnson EJ. Carotenoid actions and their relation to health and disease. *Mol Aspects Med.* 2005;26(6):459-516. doi: 10.1016/j.mam.2005.10.001
15. Eskandari S, Etemadifar Z. Isolation and characterization of melanin producing Pseudomonas stutzeri strain Uis2 in the presence of L-tyrosine and survey of biological properties of its melanin. *Iran J Med Microbiol.* 2020;14(1):70-83. doi: 10.30699/ijmm.14.1.70
16. Gospodaryov D, Lushchak V. Some properties of melanin produced by *Azotobacter chroococcum* and its possible application in biotechnology. *Biotechnol Acta.* 2011;4(2):61-69.
17. Keith KE, Killip L, He P, Moran GR, Valvano MA. *Burkholderia cenocepacia* c5424 produces a pigment with antioxidant properties using a homogentisate intermediate. *J Bacteriol.* 2007;189(24):9057-9065. doi: 10.1128/JB.00436-07
18. Manivasagan P, Venkatesan J, Sivakumar K, Kim SK. Actinobacterial melanins:current status and perspective for the future. *World J Microbiol Biotechnol.* 2013;29(10):1737-1750. doi: 10.1007/s11274-013-1352-y
19. Lapenda JC, Silva PA, Vicalvi MC, Sena KXFR, Nascimento SC. Antimicrobial activity of prodigiosin isolated from *Serratia marcescens* UFPEDA 398. *World J Microbiol Biotechnol.* 2015;31(2):399-406 doi: 10.1007/s11274-014-1793-y
20. Saer RG, Blankenship RE. Light harvesting in phototrophic bacteria: structure and function. *Biochem J.* 2017;474(13):2107-2131. doi: 10.1042/BCJ20160753
21. Orlandi VT, Martegani E, Giaroni C, Baj A, Bolognese F. Bacterial pigments:a colorful palette reservoir for biotechnological applications. *Biotechnol.* 2022;69(3):981-1001. doi: 10.1002/bab.2170
22. Abdel-Aal ESM, Akhtar H, Zaheer K, Ali R. Dietary sources of lutein and zeaxanthin carotenoids and their role in eye health. *Nutrients.* 2013;5(4):1169-1185. doi: 10.3390/nu5041169
23. De Carvalho JC, Cardoso LC, Ghiggi V, Woiceichowsky AL, Vandenberghe LPD, Soccol CR. Microbial pigments. Brar S, Dhillon G, Soccol C, editor. Biotransformation of waste biomass into high value biochemicals, New York, NY, USA: Springer. 2014:73-97. doi: 10.1007/978-1-4614-8005-1_4
24. Nagarajan Y, Kalidoss A, Ali MS, Anuradha V. Production of food grade pigments from *Pseudomonas aeruginosa. Int J Curr Res Biol Med.* 2016;1(1):14-18.
25. Dufosse L. Microbial production of food grade pigments. *Food Technol Biotechnol.* 2006;44(3):113-132.
26. Fielding BC, Haws EJ, Holker JAC, et al. Monascorubrin. *Tetrahedron Lett.* 1960;1(26):24-27. doi: 10.1016/S0040-4039(01)82691-5
27. Mapari SAS, Nielsen KF, Larsen TO, Frisvad JC, Meyer AS, Thrane U. Exploring fungal biodiversity for the production of water-soluble pigments as potential natural food colorants. *Curr Opin Biotechnol.* 2005;16(2):31-238. doi: 10.1016/j.copbio.2005.03.004
28. Kalra R, Conlan XA, Goel M. Fungi as a potential source of pigments: harnessing filamentous fungi. *Front Chem.* 2020;8:369-392. doi: 10.3389/fchem.2020.00369
29. Molelekoa TBJ, Augustyn W, Regnier T, da Silva LS. Chemical characterization and toxicity evaluation of fungal pigments for potential application in food, phamarceutical and agricultural industries. *Saudi J Biol Sci.* 2023;30(5):e103630. doi: 10.1016/j.sjbs.2023.103630
30. Zabala AO, Xu W, Chooi YH, Tang Y. Characterization of a silent gene cluster that produces azaphilones

from *Aspergillus Niger* ATCC 1015 reveal a hydroxylation-mediated pyran-ring formation. *Chem Biol.* 2012;19(8):1049-1059. doi: 10.1016/j.chembiol.2012.07.004

31. Buchi G, White JD, Wogan GN. The structures of mitorubrin and mitorubrinol. *J Am Chem Soc.* 1965;87(15):3484-3489. doi: 10.1021/ja01093a036
32. Huang CH, Pan JH, Chen B, et al. Three bianthraquinone derivatives from the mangrove endophytic fungus *Alternaria* sp. Zj9-6b from the south china sea. *Mar Drugs.* 2011;9(5):832-843. doi: 10.3390/md9050832
33. Xu J, Nakazawa T, Ukai K, et al. Tetrahydrobostrycin and 1-Deoxytetrahydrobostrycin, two new hexahydroanthrone derivatives, from a marine-derived fungus *Aspergillus* sp. *J Antibiot.* 2008;61(7):415-419. doi: 10.1038/ja.2008.57
34. Capon RJ, Stewart M, Ratnayake R, Lacey E, Gill JH. Citromycetins and Bilains A-C: new aromatic polyketides and diketopiperazines from australian marine-derived and terrestrial *Penicillium* spp. *J Nat Prod.* 2007;70(11):1746-1752. doi: 10.1021/np0702483
35. Mahmoodian A, Stickings C. Studies in the biochemistry of micro-organisms. 115 metabolites of penicillium frequentans westling: isolation of sulochrin, asterric acid, (+)-bisdechlorogeodin and two new substituted anthraquinones, questin and questinol. *Biochem J.* 1964;92(2):369-378. doi: 10.1042/bj0920369
36. Tatum JH, Baker RA, Berry RE. Naphthoquinones produced by *Fusarium oxysporum* isolated from Citrus. *Phytochemistry*. 1985;24(3):457-459. doi: 10.1016/S0031-9422(00)80746-3
37. Avalos J, Pardo-Medina J, Parra-Rivero O, et al. Carotenoid biosynthesis in *Fusarium. J. Fungi.* 2017;3(3):39-54. doi: 10.3390/jof3030039
38. Garton G, Goodwin T, Lijinsky W. The biogenesis of beta-carotene in the fungus Phycomyces blakesleeanus. *Biochem J.* 1950;2:35.
39. Guil-Guerrero JL, Navarro-Juarez R, Lopez-Martinez JC, Campra-Madrid P, Rebolloso-Fuentes MM. Functional properties of the biomass of three microalgal species. *J Food Eng.* 2004;65(4):511-517. doi: 10.1016/j.jfoodeng.2004.02.014
40. Becker W. Microalgae in human and animal nutrition. Richmond A, editor. Handbook of microalga culture. Oxford, UK: Wiley-Blackwell. 2007:312-351. doi: 10.1002/9780470995280.ch18
41. Chen Z, Wu W, Wen Y, et al. Recent advances of natural pigments from algae. *Food Prod.* 2023;5(39):1-14. doi: 10.1186/s43014-023-00155-y
42. Yangylar F, Yildiz PO. Microbial pigments and the important for food. *Erz Univ Fen Bil Enst Dergisi.* 2016;.9(2):118-142. doi: 10.18185/eufbed.55880
43. Eriksen NT. Production of phycocyanin—a pigment with applications in biology, biotechnology, foods and medicine. *Appl Microbiol Biotechnol.* 2008;80(1):1-14. doi: 10.1007/s00253-008-1542-y
44. Nwoba EG, Ogbonna CN, Ishika T, Vadiveloo A. Microalgal pigments: a source of natural food colors. In: Alam M, Xu JL, Wang Z, editors. Microalgae biotechnology for food, health and high value products. Singapore: Springer. 2020:81-123. doi: 10.1007/978-981-15-0169-2_3
45. Vandamme EJ, Revuelta JL, editors. Industrial biotechnology of vitamins biopigments, and antioxidants. Weinheim, Germany: Wiley-VCH. 2016. doi: 10.1002/9783527681754
46. Hirt PA, Paus R. *Healthy Hair (Anatomy, Biology, Morphogenesis, Cycling, and Function)*. In:Miteva M, editor. *Alopecia.* 2019:1-22. doi: 10.1016/B978-0-323-54825-0.00001-6
47. Naoi M, Maruyama W, Riederer P. *Melanin*. In: Kompoliti K, Metman LV, editors. Encyclopedia of movement disorders. Academic Press: Oxford. 2010:169-171. doi: 10.1016/B978-0-12-374105-9.00480-9
48. Ito S. A chemist's view of melanogenesis. *Pigment Cell Res.* 2003;16(3):230-236. doi: 10.1034/j.1600-0749.2003.00037.x
49. Kurian NK, Nair HP, Bhat SG. Evaluation of anti-inflammatory property of melanin from marine *Bacillus* spp. BTCZ31. *Asian J Pharm Clin Res.* 2015;8(3):251-255.
50. El-Naggar NE, Saber WIA. Natural melanin: Current trends, and future approaches, with especial reference to microbial source. *Polymers*. 2022;14(7):1339-1367. doi: 10.3390/polym14071339
51. El-Naggar NE, El-Ewasy SM. Bioproduction, characterization, anticancer and antioxidant activities of extracellular melanin pigment produced by newly isolated microbial cell factories *Streptomyces glaucescens* NEAE-H. *Sci Rep.* 2017;7:e42129. doi: 10.1038/srep42129
52. Vijayababu P, Kurian NK. Melanin and its precursors as effective antiviral compounds: with a special focus on SARS CoV2. *Mol Biol.* 2021;10(6):1-3.
53. Sanadi RM, Deshmukh RS. The effect of vitamin C on melanin pigmentation - a systematic review. *J Oral Maxillofac Pathol.* 2020;24(2):374-382. doi: 10.4103/jomfp.JOMFP_207_20
54. Al Ghamdi K, Kumar A, Moussa N. The role of vitamin D in melanogenesis with an emphasis on vitiligo. *Indian J Dermatol Venereol Leprol.* 2013;79(6):750-758. doi: 10.4103/0378-6323.120720
55. Martinez LM, Martinez A, Gosset G. Production of Melanins with Recombinant Microorganisms. *Front Bioeng Biotechnol.* 2019;7:285-299. doi: 10.3389/fbioe.2019.00285
56. Wang YT, Yang CH, Huang KS, Shaw JF. Chlorophyllides: preparation, purification, and application. *Biomolecules.* 2021;11(8):1115-1140. doi: 10.3390/biom11081115
57. Yasuda M, Tabata M. Effect of emulsifiers on the discoloration of chlorophyll and their potential for use in green beverages. *J Food Sci.* 2021;86(7):3033-3045. doi: 10.1111/1750-3841.15782
58. Cady JB, Morgan WS. Treatment of chronic ulcers with chlorophyll:review of a series of fifty cases. *Am J Surg.* 1948;75(4):562-569. doi: 10.1016/0002-9610(48)90367-5
59. Viera I, Perez-Galvez A, Roca M. Green natural colorants. *Molecules*. 2019;24(1):154-171. doi: 10.3390/molecules24010154
60. Martins T, Barros AN, Rosa E, Antunes L. Enhancing

health benefits through chlorophylls and chlorophyll-rich agro-food: a comprehensive review. *Molecules.* 2023;28(14):5344-5365. doi: 10.3390/molecules28145344
61. Ugwu CU, Aoyagi H, Uchiyama H. Photobioreactors for mass cultivation of algae. *Bioresour Technol.* 2008;99(10):4021-4028. doi: 10.1016/j.biortech.2007.01.046
62. Hosikian A, Lim S, Halim R, Danquah MK. Chlorophyll extraction from microalgae: a review on the process engineering aspects. *Int J Chem Eng.* 2010;2010(1):1-11. doi: 10.1155/2010/391632
63. Brunner G. Supercritical fluids: Technology and application to food processing. *J Food Eng.* 2005;67(1-2):21-33. doi: 10.1016/j.jfoodeng.2004.05.060
64. Li W, Su HN, Pu Y, et al. Phycobiliproteins: molecular structure, production, applications, and prospects. *Biotechnol Adv.* 2019;37(2):340-353. doi: 10.1016/j.biotechadv.2019.01.008
65. Manirafasha E, Guo L, Jing K. Nutraceutical and pharmaceutical applications of phycobiliproteins. In: Jacob-Lopes E, Queiroz M, Zepka L, editors. Pigments from microalgae handbook. Switzerland: Springer: Cham. 2020:575-584. doi: 10.1007/978-3-030-50971-2_23
66. Mysliwa-Kurdziel B, Solymosi K. Phycobilins and phycobiliproteins used in food industry and medicine. *Mini Rev Med Chem.* 2017;17(13):1173-1193. doi: 10.2174/1389557516666160912180155
67. Stanic-Vucinic D, Minic S, Nikolic MR, Velickovic TC. Spirulina phycobiliproteins as food components and complements. Jacob-Lopes E, Zepka LQ, Quiroz MI, editors. Microalgal biotechnology. Techopen. 2018. doi: 10.5772/intechopen.73791
68. Sekar S, Chandramohan M. Phycobiliproteins as a commodity: trends in applied research, patents and commercialization. *J Appl Phycol.* 2008;20(2):113-136. doi: 10.1007/s10811-007-9188-1
69. Wrolstad RE, Culver CA. Alternatives to those artificial FD&C food colorants. *Annu Rev Food Sci Technol.* 2012;3:59-77. doi: 10.1146/annurev-food-022811-101118
70. Bomgardner MM. Food Additives. *Chem Eng News*. 2014;92(6):10-13. doi: 10.1021/cen-09206-cover
71. Fernandez-Rojas B, Hernandez-Juarez J, Pedraza-Chaverri, J. Nutraceutical properties of phycocyanin. *J Funct Foods.* 2014;11:375-392. doi: 10.1016/j.jff.2014.10.011
72. Martins M, Ventura SPM. Emerging seaweed extraction techniques using ionic liquids. In: Torres MD, Kraan S, Dominguez H, editors. Sustainable seaweed technology. Amsterdam, Netherlands: Elsevier. 2020:287-311. doi: 10.1016/B978-0-12-817943-7.00011-1
73. Martinez JM, Delso C, Alvarez I, Raso J. Pulsed electric field permeabilization and extraction of phycoerythrin from *Porphyridium cruentum. Algal Res.* 2019;37:51-56. doi: 10.1016/j.algal.2018.11.005
74. Hemlata V, Afreen S, Fatma T. Extraction, purification and characterization of phycoerythrin from *Michrochaete* and its biological activities. *Biocatal Agric Biotechnol.* 2018;13:84-89. doi: 10.1016/j.bcab.2017.11.012
75. Chaiklahana R, Chirasuwana N, Bunnaga B. Stability of phycocyanin extracted from *Spirulina* sp.: influence of temperature, pH and preservatives. *Process Biochem.* 2012;47(4):659-664. doi: 10.1016/j.procbio.2012.01.010
76. Kannaujiya VK, Sinha RP. Thermokinetic Stability of phycocyanin and phycoerythrin. *J Appl Phycol.* 2016;28(2):1063-1070. doi: 10.1007/s10811-015-0638-x
77. Saha SK, Ermis H, Murray P. Marine Microalgae for Potential Lutein Production. *Appl Sci.* 2020;10(18):6457. doi: 10.3390/app10186457
78. Patel AK, Albarico FPJB, Perumal PK, et al. Algae as an emerging source of bioactive pigments. *Bioresour Technol.* 2022;351:e126910. doi: 10.1016/j.biortech.2022.126910
79. Paniagua-Michel J, Olmos-Soto J, Ruiz MA. Pathways of carotenoid biosynthesis in bacteria and microalgae. *Methods Mol Biol*. 2012;892:1-12. doi: 10.1007/978-1-61779-879-5_1
80. Jacobsen IH, Ledesma-Amaro R, Martinez JL. Recombinant β-carotene production by Yarrowia lipolytica - assessing the potential of micro-scale fermentation analysis in cell factory design and bioreaction optimization. *Front Bioeng Biotechnol.* 2020;8:2296-4185. doi: 10.3389/fbioe.2020.00029
81. Lopez-Nieto MJ, Costa J, Peiro E, et al. Biotechnological lycopene production by mated fermentation of *Blakeslea trispora*. *Appl Microbiol Biotechnol.* 2004;66(2):153-159. doi: 10.1007/s00253-004-1669-4
82. Almanza HA, Montanez J, Martinez G, Aguilar-Jimenez A, Contreras-Esquivel JC, Aguilar CN. Lycopene: progress in microbial production. *Trends Food Sci Technol.* 2016;56:142-148. doi: 10.1016/j.tifs.2016.08.013
83. Rodriguez-Saiz M, de la Fuente JL, Barredo JL. *Xanthophyllomyces dendrorhous* for the industrial production of astaxanthin. *Appl Microbiol Biotechnol.* 2010;88(3):645-658. doi: 10.1007/s00253-010-2814-x
84. Mussagy CU, Silva PGP, Amantino CF, et al. Production of natural astaxanthin by *Phaffia rhodozyma* and its potential application in textile dyeing. *Biochem Eng J.* 2022;187:108658. doi: 10.1016/j.bej.2022.108658
85. Niizawa I, Espinaco BY, Zorrilla SE, Sihufe GA. Astaxanthin production by autotrophic cultivation of *Haematococcus pluvialis*: a success story. IGokare AR, Rao AR, editors. Global perspectives on astaxanthin. Cambridge, MA, USA: Academic Press. 2021:71-89. doi: 10.1016/B978-0-12-823304-7.00005-2
86. Harith ZT, de Andrade Lima M, Charalampopoulos D, Chatzifragkou A. Optimised of production and extraction astaxanthin from the yeast *Xanthophyllomyces* dendrorhous. *Microorganisms.* 2020;8(3):430-448. doi: 10.3390/microorganisms8030430
87. Asker D, Beppu T, Ueda K. *Nubsella zeaxanthinifaciens* gen. nov., sp. 516 Nov., a zeaxanthin-producing bacterium of the family Sphingobacteriaceae isolated from freshwater. *Int J Syst Evol Microbiol.* 2008;58(Pt 3):601-606. doi: 10.1099/ijs.0.65493-0
88. Zhang Y, Liu Z, Sun J, Xue C, Mao X. Biotechnological production of zeaxanthin by microorganisms. *Trends*

Food Sci Technol. 2018;71:225-234. doi: 10.1016/j.tifs.2017.11.006

89. Lourenco-Lopes C, Carreira-Casais A, Corral MF, et al. Carotenoids as natural colorful additives for the food industry. IPrieto MA, Otero P, editors. Natural food additives. IntechOpen. 2022. doi: 10.5772/intechopen.101208
90. Shang YF, Kim SM, Lee WJ, Um BH. Pressurized liquid method for fucoxanthin extraction from *Eisenia bicyclis* (Kjellman) setchell. *J Biosci Bioeng.* 2011;111(2):237-241. doi: 10.1016/j.jbiosc.2010.10.008
91. Wahyuni FD, Shalihah IM, Nurtiana W. Caroteinoids as natural colorant: a review. *Food SciTech J.* 2020;2(2):94-102. doi: 10.33512/fsj.v2i2.9940
92. Saini RK, Keum WS. Carotenoid extraction methods: A review of recent developments. *Food Chem.* 2018;240:90-103. doi: 10.1016/j.foodchem.2017.07.099
93. Di Salvo E, Lo Vecchio G, De Pasquale R, et al. Natural pigments production and their application in food, health and other industries. *Nutrients.* 2023;15(8):1923. doi: 10.3390/nu15081923
94. Sanchez S, Ruiz B, Rodriguez-Sanoja R, Cotera-Flores LB. Microbial production of carotenoids. McNeil B, Archer D, Giavasis I, editors. Microbial production of food ingredients. enzymes & nutraceuticals. Mexico: Woodhead ublishing. 2013:194-233. doi: 10.1533/9780857093547.2.194
95. Gouveia L, Batista AP, Miranda A, Empis J, Raymundo A. *Chlorella vulgaris* biomass used as coloring source in traditional butter cookies. *Innov Food Sci Technol.* 2007;8(3):433-436. doi: 10.1016/j.ifset.2007.03.026
96. Das A, Yoon SH, Lee SH, Kim JY, Oh DK, Kim SW. An update on microbial carotenoid production: application of recent metabolic engineering tools. *Appl Microbiol Biotechnol.* 2007;77(3):505-512. doi: 10.1007/s00253-007-1206-3
97. Averianova LA, Balabanova LA, Son OM, Podvolotskya AB, Tekuteyva LA. Production of vitamin B2 (riboflavin) by microorganisms: an overview. *Front Bioeng Biotechnol.* 2020;8:e570828. doi: 10.3389/fbioe.2020.570828
98. Williamson NR, Fineran PC, Leeper FJ, Salmond GPC. The biosynthesis and regulation of bacterial prodiginines. *Nat Rev Microbiol.* 2006;4(12):887-899. doi: 10.1038/nrmicro1531
99. Gulani C, Bhattacharya S, Das A. Assessment of process parameters influencing the enhanced production of prodigiosin from *Serratia marcescens* and evaluation of its antimicrobial, antioxidant and dyeing potentials. *Malays J Microbiol*. 2012;8(2):116-122. doi: 10.21161/mjm.03612
100. Lee BK, Park NH, Piao HY, Chung WJ. Production of red pigments by *Monascus purpureus* in submerged culture. 2001;6:341-346. doi: 10.1007/BF02933003
101. El-Banna AA, El-Razek AMA, El-Mahdy AR. Some factors affecting the production of carotenoids by *Rhodotorula glutinis* var. glutinis. *Food Nutrition Sci.* 2012;3(1):64-71. doi: 10.4236/fns.2012.31011
102. Lampila LE, Wallen SE, Bullerman LB, Lowry SR. The effect of *Blakeslea trispora* strain and type of whey on the production of b-carotene and other parameters. LWT. 198518:366-369.
103. Zhang XW, Wang JH, Chen MH, Wang CL. Effect of nitrogen sources on production and photostability of Monascus pigments in liquid fermentation. *IERI Procidia.* 2013;5:344-350. doi: 10.1016/j.ieri.2013.11.114
104. Gondil VS, Mohammad A, Tek Chand B. Optimization of physicochemical parameters influencing the production of prodigiosin from *Serratia nematodiphila* RL2 and exploring its antibacterial activity. *3 Biotech.* 2017:7(5):338. doi: 10.1007/s13205-017-0979-z
105. Sajjad W, Din G, Rafiq M, et al. Pigment production by cold-adapted bacteria and fungi: colorful tale of cryosphere with wide range applications. *Extremophiles.* 2020;24(4):447-473. doi: 10.1007/s00792-020-01180-2
106. Padhan B, Poddar K, Sarkar D, Sarkar A. Production, purification, and process optimization of intracellular pigment from novel psychrotolerant *Paenibacillus* sp. BPW19. *Biotechnol Rep.* 2021;29:e00592. doi: 10.1016/j.btre.2021.e00592
107. Rather LJ, Shaheen MS, Ali GS, Islam S, Qing L. Research progress, challenges, and perspectives in microbial pigment production for industrial applications - a review. *Dyes Pigm.* 2023;210:110989. doi: 10.1016/j.dyepig.2022.110989
108. Usman HM, Farouq AA, Baki AS, Abdulkadir N, Mustapha G. Production and characterization of orange pigment produced by halophilic bacterium *Salinococcus roseus* isolated from abattoir soil. *J Microbiol Exp.* 2018;6(6):238-243. doi: 10.15406/jmen.2018.06.00222
109. Benjamin S, Surekha Y, Dhanya P, Josh MKS, Pradeep S. *Micrococcus luteus* Strain BAA2, a novel isolate produces carotenoid pigment. *Electron J Biol*. 2016;12(1):83-89.
110. Fatima M, Anuradha K. Isolation, characterization, and optimization studies of bacterial pigments. *J Pure Appl Microbiol.* 2022;16(2):1039-1048. doi: 10.22207/JPAM.16.2.28
111. Hizbullah MU, Farouq AA, Baki AS, et al. Studies on bio-color production by *Pseudomonas aeruginosa* isolated from soil. *J Adv Miicrobiol.* 2018;12(1):1-12. doi: 10.9734/JAMB/2018/43068
112. Hemlatha, Fatma T. Screening of cyanobacteria for phycobiliproteins and effect of different environmental stress on its yield. *Bull Environ Contam Toxicol.* 2009;83(4):509-515.doi: 10.1007/s00128-009-9837-y
113. Nielsen KF, Smedsgaard J, Larsen TO, Lund F, Thrane U, Frisvade JC. Chemical diversity of fungi:metabolite profiling and metabolomics. Arora DK, editor. Fungal biotechnology in agricultural, food, and environmental applications. New York: Marcel Dekker Inc. 2004:19-35
114. Elyashberg ME, Blinov KA, Williams AJ, Martirosian ER, Molodtsov SG. Application of a new expert system for the structure elucidation of natural products from the 1D and 2D NMR data. *J Nat Prod.* 2002;65(5):693-703. doi: 10.1021/np0103315
115. Lyu X, Lyu Y, Yu H, Chen W, Ye L, Yang R. Biotechnological advances for improving natural pigment production:a state-of-the-art review. *Bioresour. Bioprocess.* 2022;9:1-38. doi: 10.1186/s40643-022-00497-4

116. Balakrishnan B, Karki S, Chiu SH, et al. Genetic localization and in vivo characterization of a *Monascus azaphilone* pigment biosynthetic gene cluster. *Appl Microbiol Biotechnol.* 2013;97(14):6337-6345. doi: 10.1007/s00253-013-4745-9
117. Xu S, Gao S, An Y. Research progress of engineering microbial cell factories for pigment production. *Biotechnol Adv.* 2023;65:108150. doi: 10.1016/j.biotechadv.2023.108150
118. Heer K, Sharma S. Microbial pigments as a natural color: A review. *Int J Pharm Sci Res.* 2017;8(3):1913-1922. doi: 10.13040/IJPSR.0975-8232.8(5).1913-22
119. Kojima R, Arai T, Matsufuji, H, Kasumi T, Watanabe T, Ogihara J. The relationship between the violet pigment pp-v production and intracellular ammonium level in *Penicillium purpurogenum.* 2016;6(1):43-50. doi: 10.1186/s13568-016-0215-y
120. Yoon SH, Lee SH, Das A, et al. Combinatorial expression of bacterial whole mevalonate pathway for the production of beta-carotene in *E. Coli. J Bacteriol.* 2009;140(3-4):218-226. doi: 10.1016/j.jbiotec.2009.01.008
121. Dong Y, Feldberg L, Rogachev I, Aharoni A. Characterization of the production of anthocyanin pigment 1 arabidopsis dominant mutant using DLEMMA dual isotope labeling approach. *Phytochemistry.* 2021;186:e112740. doi: 10.1016/j.phytochem.2021.112740
122. Sopandi T, Wardah A, Surtiningsih T, Suwandi A, Smith JJ. Utilization and optimization of a waste stream cellulose culture medium for pigment production by *Penicillium* spp. *J Appl Microbiol.* 2013;114(3):733-745. doi: 10.1111/jam.12110
123. Tinoi J, Rakariyatham N, Deming RL. Simplex optimization of carotenoid production by *Rhodotorula glutinis* using hydrolyzed mung bean waste flour as substrate. *Process Biochem.* 2005;40(7):2551-2557. doi: 10.1016/j.procbio.2004.11.005
124. Kaur B, Chakraborty D, Kaur H. Production and stability analysis of yellowish pink pigments from *Rhodotorula rubra* MTCC 1446. *Internet J Microbiol.* 2008;7(1):1-7. doi: 10.5580/245b
125. Musaalabakri AM, Ariff A, Rosfarizan M, Ismail AKM. Aeration and agitation strategies for the improvement of red pigment production by *Monascus purpureus* FTC 5391. *J Trop Agric Fd Sci.* 2015;34(1):89-102.
126. Mantzouridou F, Roukas T, Kotzekidou P. Effect of the aeration rate and agitation speed on β-carotene production and morphology of *Blakeslea trispora* in a stirred tank reactor: mathematical modeling. *Biochem Eng J.* 2002;10(2):123-135. doi: 10.1016/S1369-703X(01)00166-8
127. Gmoser R, Ferreira JA, Taherzadeh MJ, Lennartsson PR. Post-treatment of fungal biomass to enhance pigment production. *Appl Biochem Biotech.* 2019;189(1):160-174. doi: 10.1007/s12010-019-02961-y
128. Sen T, Barrow CJ, Deshmukh SK. Microbial pigments in the food industry- challenges and the way forward. *Front Nutr.* 2019;6(7):1-14. doi: 10.3389/fnut.2019.00007
129. Kaliwal BB, Sanakal RD, Kurjogi MM. Antibiotic susceptibility and antioxidant activity of *Staphylococcus aureus* pigment staphyloxanthin on carbon tetrachloride (ccl4) induced stress in swiss albino mice. *Int J Biotechnol Appl.* 2010;2(2):33-40. doi: 10.9735/0975-2943.2.2.33-40
130. Chandra P, Sharma RK, Singh AD. Antioxidant compounds from microbial sources: A review. *Food Res Int.* 2019;129:e108849. doi: 10.1016/j.foodres.2019.108849
131. Vishnupriya S, Bhavaniramya S., Baskaran D, Karthiayani A. Microbial pigments and their application. In: Vaishnav A., Choudhary DK, editors. Microbial polymers. Springer: Singapore. 2021:193-214. doi: 10.1007/978-981-16-0045-6_9
132. Zeng H, Qin L, Liu X, Miao S. Increases of lipophilic antioxidants and anticancer activity of coix seed fermented by *Monascus purpureus. Foods.* 2021;10(3):566-578. doi: 10.3390/foods10030566
133. Pandey R, Chander R, Sainis KB. Prodigiosins: a novel family of immunosuppressants with anti-cancer activity. *Indian J Biochem Biophys*. 2007;44(5):295-302.
134. Poonia A, Pandey S. Production of microbial pigments from whey and their applications: A review. *Nutr Food Sci.* 2022;53(2):265-284. doi: 10.1108/NFS-02-2022-0055
135. Barretto DA, Vootla SK. *In vitro* anticancer activity of staphyloxanthin pigment extracted from *Staphylococcus gallinarum* KX912244, a gut microbe of *Bombyx mori. Indian J Microbiol.* 2018:58(2):146-158. doi: 10.1007/s12088-018-0718-0
136. Duran N, Justo GZ, Ferreira CV, Melo PS, Cordi L, Martins D. Violacein: properties and biological activities. *Biotechnol Appl Bioc.* 2007;48(3):127-133. doi: 10.1042/BA20070115
137. Duran M, Ponezi AN, Faljoni-Alario A, Teixeira MFS, Justo GZ, Duran N. Potential applications of violacein:a microbial pigment. *Med Chem Res.* 2012;21(7):1524-1532. doi: 10.1007/s00044-011-9654-9
138. Saleem H, Mazhar S, Syed Q, Javed MQ, Adnan A. Bio-characterization of food grade pyocyanin bio-pigment extracted from chromogenic *Pseudomonas* species found in Pakistani native flora. *Arab J Chem.* 2021;14(3):e103005. doi: 10.1016/j.arabjc.2021.103005
139. Gutierrez-Salmean G, Fabila-Castillo L, Chamorro-Cevallos G. Nutritional and toxicological aspects of Spirulina (Arthrospira). *Nutr Hosp.* 2015;32(1):34-40. doi: 10.3305/nh.2015.32.1.9001
140. Soletto D, Binaghi L, Lodi A, Carvalho JCM, Converti A. Batch and fed-batch cultivations of *Spirulina platensis* using ammonium sulphate and urea as nitrogen sources. *Aquaculture.* 2005:243(1-4):217-224. doi: 10.1016/j.aquaculture.2004.10.005
141. Sigurdson GT, Tang P., Giusti MM. Natural colorants: Food colorants from natural sources. *Annu Rev Food Sci T.* 2002;8:261-280. doi: 10.1146/annurev-food-030216-025923
142. Joshi VK, Attri D, Baja A, Bhusan S. Microbial pigments. *Indian J Biotechnol*. 2003:2(3):362-369.
143. Liu GY, Nizet V. Color me bad: microbial pigments as virulence factors. *Trends Microbiol.* 2009;17(9):406-413. doi: 10.1016/j.tim.2009.06.006
144. Ryan RP, Monchy S, Cardinale M, et al. The

versatility and adaptation of bacteria from the genus *Stenotrophomonas. Nat Rev Microbiol.* 2009;7(7):514-525. doi: 10.1038/nrmicro2163
145. Rolls ET. Taste, olfactory, and food texture processing in the brain, and the control of food intake. *Physiol Behav.* 2005;85(1):45-56. doi: 10.1016/j.physbeh.2005.04.012
146. Ans AH, Anjum I, Satija V, et al. Neurohormonal regulation of appetite and its relationship with stress: a mini literature review. *Cureus.* 2018:10(7):e3032. doi: 10.7759/cureus.3032
147. Dufosse L. Microbial pigments from bacteria, yeasts, fungi, and microalgae for the food and feed industries. In: Grumezescu AM, Holban AM, editors. Handbook of food bioengineering: natural & artificial flavoring agents & food dyes. Academic Press: Amsterdam. 2018:113-132. doi: 10.1016/B978-0-12-811518-3.00004-1
148. Dey S, Nagababu BH. Applications of food color and bio-preservatives in the food & its effect on the human health. *Food Chem Adv.* 2022;1:e100019. doi: 10.1016/j.focha.2022.100019
149. Miller MD, Steinmaus C, Golub MS, et al. Potential impacts of synthetic food dyes on activity and attention in children:a review of the human and animal evidence. *Environ Health Glob.* 21(1):45-64. doi: 10.1186/s12940-022-00849-9