The eminence status of bacterial pigments under different aspects

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Summary

Several bacteria such as *Flavobacterium*, *Serratias*, *Chromobacterium* and *Streptomyces* that produce different pigments are playing a significant role in various fields of sciences. Alternatively, current knowledge about bacterial pigments is limited to medical bacteriology, for instance their importance in virulence factors and protective features, however recently the investigators have revealed the supplementary consequence of pigments in food, textile and pharmaceutical aspects.

Introduction

The pigments play a critical aspect amongst various organisms in environmental interactions fields, difference in gender and the presence of some special features. However, the existence of pigments' variation in micro-organisms is considered to be in relation with the evolution of the selective pressures (18). Pigments have an important role in physiology and molecular process of microorganisms; for example, assist in adapting to environmental conditions, sunlight protection, photosynthetic or in the classification and taxonomy of bacteria (54). The name of bacterial pigments is often derived from the microorganism's name, in which Rosenbach (1884) proposed the golden pathogen and non-pigmented staphylococci as *S. aureus* and *Staphylococcus albus* respectively. Also, the rarely found blue-green *Pseudomonas* species in cystic fibrosis patients were called *Pseudomonas aeruginosa*, which is mainly Latina and means a rusty copper color (18). The purpose of this review is about pigments various roles in bacterial function and also in different sciences such as chemistry, biotechnology and pharmaceutical industry.

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The chemical composition of pigments and growth conditions

Pigments diversity depends on differences in their chemical structure and also the presence of special chromophores (10). An unsaturated organic molecule contains a group of single or double bonds that serves the changes of light absorption to lower frequencies (longer wave lengths). The presence of these substances, results in the creation of the desired color. Indeed, the assortment of these materials, which is commonly called root color, creates the extended spectrum colors like Beta Carotene, Lycopene and Anthocyanin (64). Pigment production and biosynthesis are associated with a variety of factors like the environmental and culture conditions, PH, inorganic phosphate concentration, temperature, etc. (75). For instance production of prodigiosin pigment will increase in Peptone Glycerol Broth and Nutrient Broth from 28°C up to 30°C (20,37).

Pigment-producing bacteria

Some of the most important pigment-producing bacteria are: *Agrobacterium aurantiacum, Serratia marcescens, Chromobacterium violaceum*, *Micrococcus spp. and Pseudomonas aeruginosa*. According to the conducted investigations, Gram-negative bacilli produce a wide range of bacterial pigments (57).

Important pigments produced by bacteria

Some of considerable pigments which are produced with bacteria are as follow: Zeaxanthin, the yellow pigment of *Flavobacterium sp*, Astaxanthin the pinkish pigment of *Agrobacterium aurantiacum*, Yellow carotenoid pigment of *M. varians* and *M. luteus*, Orange carotenoid pigments in *M. nishinomiyaensis*, Pink carotenoid pigment in *M. roseus* and *M. agilis*, Prodigiosin, the red pigment in *Serratia marcescens* and other bacteria, Violacein, the purple pigment in *Iodobbacter*, *Chromobacterium violaceum*, *Janthinobacterium*, Pyocyanin, the blue-green pigment in *Pseudomonas aeruginosa* and Actinorhodin, the blue pigment in *Streptomyces coelicolor* (4,36,53,62,73).

The pigments performance and features

Recently, the usages of pigments in a several range of industries (food industry, intinction and drug production) have been increased (70). Natural colors can be obtained from sundry sources, including ore, insects, plants and microbes in which the plants and microorganisms are the most useful, because of their sustainability in color production and culture situation (3,29,35). Among microbes, bacteria are especially regarded for their highest potential. So producing and also using of bacterial pigments as natural colors have been studied by many researchers, although this issue is currently considered as one of the studied fields for different industrial purposes (13,16,24).

Protective aspect

Protecting against heat and cold, UV ray and also containing anti-microbial, anti-cancer and anti-oxidant properties (30).

Food industry

Usage of natural colors in the food industry has been increased generally. These pigments have been replaced by synthetic dyes (5). Some microorganisms that are capable for producing high efficiency pigments are as follow: *Monascus*, *Serratia*, *Paecilomyces*, *Cordyceps* and Streptomyces (60). It should be noted that Riboflavin, Beta-Carotene and Phycocyanin have high performances in traditional fermented food industry (63).

Pharmaceutical industry

Many of bacterial pigments have been respected as antibiotics and immunosuppressive agents due to their high clinical and research potentials or for treating a variety of diseases such as cancer, leukemia, diabetes that can be noticed as below.

Anthocyanins

A flavonoids water-soluble pigment, with a wide range of biological activities consists of antioxidant, reduction of the risk of cancer, regulation of the immune response as well as reduction of inflammation (25,50,59).

Prodigiosin

A pinkish linear trypyrrole pigment with cytotoxic and T cell suppressive activities (56,67).

Metacyclo-prodigiosin

Desmethoxy prodigiosin and Prodigiosin 25-C: This pigment has anti-malarial, antibiotic, immunosuppressive and anti-biofilm activities (11,78). Yoshida and colleagues have showed that cycloprodigiosin hydrochloride; similar to other prodigiosins can promote H^+/Cl^- symport which may lead to cytosol acidification and resulting in cell death process (8,72). Other hypotheses about the pigment's functions were suggested by Songia *et al.* (44). They found that the rise of preventing of human lymphocytes proliferation is conducted by inhibiting the retinoblastoma phosphorylation and suppression depending on kinase 2 and 4. Scientists have found that this pigment stimulates apoptosis in sw-620 and DLD-1 that causes mutations or defects in the p53 function (39).

Astaxanthin

A red-orange pigment that is produced by the fungus, yeast, *Agrobacterium aurantiacum*, and *Xanthophyllomyces* dendrorhous (76). This pigment has health benefits in the prevention of cardiovascular diseases, enhancing the human immune system, bioactivity against *H. pylori* and prevention of cataracts due to its high antioxidant activity (38,74).

Violacein

A purple pigment that can be produced by several bacterial species. This pigment has the antitumor, antiparasitic, antiprotozoal, anti-cancer, antiviral, antibacterial and furthermore antioxidant activities (12,23,40). The antitumor mechanism of this pigment is still being studied, and it has been recently shown that the mentioned pigment activates the apoptosis in HL60 (leukemia) cell line and p38 MAPK through the activation of caspase-8 and transcription of NF-KB. The pigment's toxicity in colorectal cancer cell line, (HT29) has been evaluated. In addition, blocking the G1 phase, up-regulation in p53, p27, and p21 levels, decrease cyclin D1 expression in the cell cycle are the violacein pigment other consequences (42). Anti-mycobacterial activity of violacein pigment produced from *Janthinobacterium sp*. and yellow-orange Flexirubin pigment gained from *Flavobacterium sp*. were studied by Mojib *et al*. (12,40,42,47).

As an inhibitor

The following pigments can be mentioned as a number of those which are respected as an inhibitor factor: i) The yellow-orange flexirubin pigment produced by *Flavobacterium sp.* with the bactericidal activity against *E .coli* and *B. cereus*. It seems that this antibacterial activity is more effective in Gram positive bacteria (48). ii) Pyocyanin and Pyorubin produced by *P. aeruginosa* have antibacterial effects on *Citrobacter sp* (68). iii) The orange pigment produced by *Exiguobacterium aurantiacum* that has antimicrobial activity against *E. coli, Klebsiella sp., S. aureus* and *Erwinia sp* (49). iv) Melanin, a dark color, water insoluble and resistant to concentrated acid, pigment by antimicrobial properties and also protecting against UV, solar and gamma rays (17,21). The antibacterial function of melanin in protecting bacteria is still unknown. Recently a recombinant plasmid containing tyrosinase gene has been manipulated in *E. coli* that induces the melanin in tyrosine supplemented medium, whereas this role of melanin hasn't been proved yet in *P. aeroginosa* in in-vitro (6,15,52).

Textile industry purposes

Microorganisms produce a large variety of stable pigments like Carotenoids, Flavonoids, and Quinones. In addition, some natural colors, especially anthraquinones compounds, show the significant antibacterial activity, so they are capable to be used as anti-microbial dyes in textile industries. Alihosseini *et al*. described that the red prodigiosin pigment achieved from Vibrio strains is used as the color for wool, nylon, silk and acrylic fibers (1,43,66). A study conducted by Yusof demonstrated that the *Serratia marcescens* prodigiosin is applied for dyeing in acrylic fabric, micropolyester, polyester, silk and cotton (51). Ahmad *et al.* described that violacein pigment produced by *Chromobacterium violaceum* is used as different fabric dyes like silk, cotton, acrylic and polyester (24).

As a virulence factor

There is a proven relationship between pigments and virulence factors in several bacteria, so the most important ones are mentioned as below.

Staphyloxanthin

Is a carotenoid pigment which is produced in the biosynthetic pathway by *S. aureus*. Many studies have shown that deletion of the gene encoding the CrtM enzyme in the initial biosynthesis of

Staphyloxanthin produces the bacteria without pigments and more sensitivity to death by human neutrophils respectively (51). The gene which encoding this pigment is regulated by operon CrtOPQMN (45). It is noteworthy that 4', 4'-diaponeurosporene is considered as a secondary biosynthetic compound. Transferring of both CrtM and CrtN genes from *S. aureus* to other genus of bacteria will lead to synthesis of the 4', 4'-diaponeurosporene. This topic has been investigated in mouse models (51). Compared to wild strains, non- pigmented mutants of *S. aureus* are more sensitive to death by hydrogen peroxide, superoxide, hydroxyl radicals, hypochlorite and oxygen (45,51).

Pyocyanin

Many species of *Pseudomonas spp.* produce blue, green pigment of Pyocyanin (41). Many studies indicate that non-pigmented mutant of *P. aeruginosa* is mostly ineffective on both acute and chronic lung infection model in mice. This pigment has considerable toxic properties in a wide range of target organisms, comprising bacteria, yeasts, insects, nematodes, and plants (33,69). One of these mechanisms is inhibition of cellular respiration (46). On the other hand, the ability of changing redox cycle and increasing oxidative stress causes harmful varied effects on the host cells, for instance disturbing the Ca^{2+} homeostasis in human respiratory epithelial cells. While, Ca^{2+} is important for ion transport regulation and mucus secretion, it is more likely to develop *P. aeruginisa* lung related infections (34). Other toxic effects of this pigment are respiratory cell disorders, inhibition of epidermal cell growth factors, prostaglandin release from epithelial cells and changing the balance of protease and anti-proteases activity in cystic fibrosis (2).

Violacein

Oxidation and bounding of two L-tryptophan molecules by VioA and VioE enzymes produce pyrrolidone and, eventually, Violacein (7). This pigment has powerful antioxidant properties and may protect lipid membrane against peroxidation that induced by hydroxyl radicals (75). Evaluating of this pigment as a chemotherapeutic agent shows that it is capable to induce leukocytes apoptosis (7).

Granadaene of group B Streptococcus

Granadaene is one of the main causes of neonatal infections is Group B streptococcus, which can produce the red-orange pigments (31). Though, recent reports have shown that ornithine rhamno-polyene pigment structure with 12 conjugated double bonds is called granadaene and increases survival in macrophages (65). Additionally related studies demonstrated that, Streptococcus pigmented strains may lead to systematic related infections. Also the mentioned pigment may have the virulence function (50,77).

As a marker

The emergence of violacein pigment with *Flexibacter* and *Sporocytophaga* imply on water contamination (14,22). As well the non-blue pigment of *Vogesella indigofera* illustrates the chromium contaminated sites because this bacterium produces blue pigment in normal conditions but in Cr^{6+} contaminated areas, the related encoding genes expression is inhibited which is defined as a bacterial defense system (19,71).

Currently, pigment biosynthesis can be regulated by molecular techniques and genetic engineering with expression and inhibition of responsible genes (9). A blue actinorhodin pigment produced by *Streptomyces coelicolor* can be lead to the production of bright yellow Kalafungin by using of genetic modification techniques (61). This method is performed for modification of actinorhodin pigment to Anthraquinones (26,28). Production of bacterial pigments such as Prodigiosin and Violacein is controlled by the Quorum sensing system (32,58). Finally it should be noted that pigments produced by bacteria are removable by using different solvents and their features are detectable with various techniques: Thin-layer chromatography (TLC), Ultraviolet–visible spectroscopy (UV-Vis), Fourier transform infrared spectroscopy (FTIR), Electrospray ionization mass spectrometry (ESI-MS), Nuclear magnetic resonance (NMR), and High performance liquid chromatography (HPLC). Moreover the spectroscopy of various pigments is available by Raman Spectroscopy. Nowadays, extracting the pure and concentrated bacterial pigments is a major challenge of technology (27,55).

Conclusions

In conclusion, despite of our hypothesis about bacterial pigments, these components have both pathogenesis factors and beneficial aspects.

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