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VIOLACEIN FROM BACTERIA AND ITS APPLICATION

Worku Dereje Garoma

Abstract

Violacein is a water-insoluble violet or purple pigment found in Chromobacterium violaceum, a versatile pigment that exhibits several biological activities and, at present, has gained increasing importance in industrial markets, such as in medicine, cosmetics, and textiles. In this review paper different types of applications of Violacein such as antibacterial, anticancer, antinematode, antimalarial, as a marker of quorum sensing (QS) activities, textile dying, cosmetics and food industries are discussed below.

Key words: **Violacein, Antibacterial, Antinematode, Anticancer cell, Antimalarial, and Quorum sensing.**

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1. INTRODUCTION

The production of bioactive secondary metabolite is an essential defense mechanism and/or competitive strategy for many bacterial species (Duran *et al*., 2007). One of the bacterial secondary metabolites are pigments, compounds that are widely used in industries that come in a wide variety of colors, some of which are water-soluble (Usman *et al*., 2017).

In food, cloth, painting, cosmetics, pharmaceuticals, and plastics Pigments are widely used. A serious hazard to human health and a potential environmental disaster may result due to uncontrolled industrial applications of synthetic pigments. Natural pigments are alternative pigment to synthetic pigments and their source can be plants, microorganisms, animals, and minerals and can be biodegradable and easily accessible at a cheaper production. Bacteria is one of the pigment-producing microbial species, offer certain advantages based on its flexibility, short life cycle, and simple propagation technique (Ahmad *et al*., 2012).

Different varieties of colors such as Yellow, Pink-red, Golden, Purple, red, Creamy and yellow colors are produced by *Chromobacterium violaceum, Agrobacterium aurantiacum*, *Staphylococcus aureus*, *Serratia marcescens*, *Bacillus Spp.* and *Flavobacterium sp*. respectively (Usman *et al*., 2017).

Chromobacterium is, a gram-negative bacterium belonging to the Rhizobiaceae family, is as a saprophyte (Ahmad *et al*., 2012), that inhabits the soil and water (Soliev *et al*., 2011), tropical and subtropical areas produce violet pigment violacein which is an indole derivative compound *(Batista et al., 2017).*

Violacein is a water-insoluble violet or purple pigment found in *Chromobacterium violaceum*, first isolated from the Amazon River in Brazil (Azman *et al*., 2018), a versatile pigment that exhibits several biological activities and, at present, has gained increasing importance in industrial markets, such as in medicine, cosmetics, and textiles. Violacein from bacteria has assorted biological properties in a pharmacological context, including its antioxidant, immunomodulatory, antitumoral, and antiparasitic activities. In addition, it uses in the fields of cosmetics, textiles, food, toys, and insecticides (Duran *et al*., 2012). Violacein has also become a useful indicator of quorum sensing due to its ease of visualization (Azman *et al*., 2018), and in nature, it might be responsible for protection against UV radiation.

Diverse genera of bacterial strains, including Collimonas, Duganella, Janthinobacterium, Microbulbifer sp., and Pseudoalteromonas produce violacein. These violacein producers are varied phylogenetically and so are the locales from which they have been isolated. These include quite a selection of environs as these bacteria have been found associated with the surfaces of sea sponges and the rhizosphere of olive groves and even within glaciers. Perhaps the best known genus, however, is Chromobacterium which includes the strain *C. violaceum* (Choi *et al*., 2015).

Objective

The objective of this review is: To gather information on application of violacein from bacteria.

2. Violacein from *Chromobacterium violaceum* and its Applications

Violacein: is a water-insoluble violet or purple pigment extracted from the gram-negative bacterium Chromobacterium violaceum (Azman *et al*., 2018).

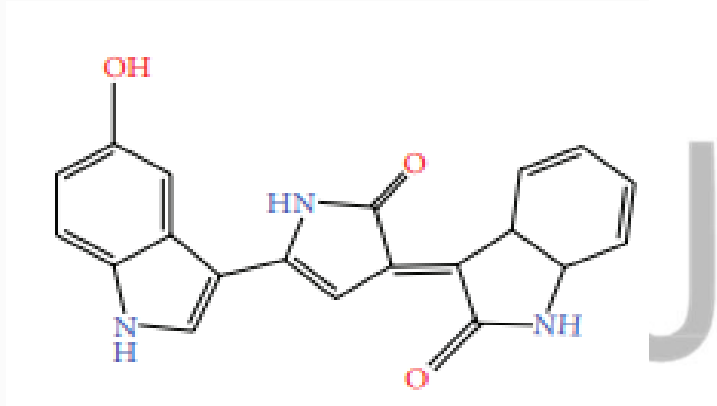

Figure 1: Structure of violacein

2.1 Anticancer activity of Violacein

Currently, due to non-specific targeting cancer treatments of solid tumors such as chemotherapy and radiotherapy have yet to produce effective therapeutic results. Complications, such as toxicities in cancer patients may occur. The natural compounds have ability in inducing programmed cell death (apoptosis), a process dysregulated in cancer cells and under normal and hypoxic conditions, Violacein has anti-proliferative activity on a number of human cancer cell lines (Hashimi *et al*., 2015).

The violacein, a blue pigment extracted from Chromobacterium violaceum, is able to induce apoptosis in a variety of cancer cells, plus those leukemia cell lines. During the apoptotic colon cancer cell death, violacein has effect on reactive oxygen species (ROS) production. Violacein mediates ROS production followed by activation of Caspase-3, release of cytochrome c, and calcium release to cistosol in human colon carcinoma cell line cells. Violacein-induced ROS are

collectively key mediators of mitochondrial membrane collapse, leading to cytochrome **c** release, and culminate in tumor apoptosis (De Carvalho *et al*., 2006).

2.2 Violacein as Antinematode Activity

Violacein is well known for its several biological activities including antinematode effects. At the present time, the marine bacterium *Microbulbifer* sp. D250 produces the antinematode agent purple pigment violacein, thereby extending the target range of this small molecule. Heterologous expression of the violacein biosynthetic pathway in *E. coli* and experiments using pure violacein demonstrated that this secondary metabolite facilitates bacterial accumulation in the nematode intestine, which is accompanied by tissue damage and apoptosis (Ballestriero *et al*., 2014).

Bacterial communities are often heavily consumed by micro faunal predators, such as protozoa and nematodes. To defend themselves against predation, bacteria evolve various defence mechanisms. Violacein which is an antinematode compound is toxic to *Caenorhabditis elegans* which are major predators for bacteria (Jousset, 2014).

2.3 Violacein as Antibacterial activity

Violet pigment Violacein, produced by *Chromobacterium violaceum*, has antibacterial activity and concerned much attention in recent time due to its pharmacological properties. The possible antibacterial mode of action of violacein from *C. violaceum* UTM5 is against *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA) strains. The mode of action of violet pigment violacein fraction on the cell membrane integrity of both strains causes release of protein, K^+, and extracellular adenosine 5′-triphosphate (ATP). The disruption the membrane integrity of *S. aureus* and MRSA strains is due to a strong antibacterial activity of violet fraction from *Chromobacterium violaceum* (Aruldass *et al*., 2018).

Priya et al (2018), reported that concurrently violacein has also been shown to have antibacterial properties particularly towards Gram-positive bacterial strains. Violacein is an expectant molecule for the development of an antimicrobial drug for the eradication of S.aureus biofilm infection. Volacein is also present in cells with reduced metabolism while its action is enhanced by the active cell metabolism (Batista et al., 2017). Violacein (VIO) has also an antimicrobial potential on *Staphylococcus epidermidis* biofilm (Dodou *et al*., 2019).

Violacein also shows antibacterial activity against gut microbiome such as *Bacillus licheniformis, Bacillus subtilis, Bacillus megaterium, Mycobacterium tuberculosis, Pseudomonas aeruginosa*, and others. The mechanism involved in violacein antibacterial activity remains

unclear. However, it has been suggested that this molecule can affect cell viability by decomposing components essential for life maintenance inside the cell, since this violet pigment leads to cell death, not only inhibition of bacterial growth (Pauer *et al*., 2018).

2.4 Antimalarial Activity of Violacein

As a report of Bisland *et al* (2018), wild-type and drug-resistant strains of the malaria parasite, *Plasmodium falciparum* are killed by violacein and it is therapeutically against malaria. Violacein pigment able to inhibit the growth of mouse and human derived plasmodium parasites and is effective against young and mature forms of the human parasite and its activity extended to chloroquine-sensitive and chloroquine resistant of *plasmodium falciparum* (Azman *et al*., 2018). Additionally violacein has in vitro activity against Plasmodium falciparum and in vivo activity against *Plasmodium chabaudi chabaudi* (Lopes *et al*., 2009).

2.5 Violacein as Quorum Sensing (Qs) Marker

Quorum Sensing is defined as the most important adaptive response of bacterial communities to the environment occurs by cooperative and coordinated metabolic arrangements produced by specific molecules. The QS system of Chromobacterium violaceum ATCC 31532 comprise four main components: CviI synthase, AHLs diffusible molecule, a CivRtype signal receptor and some target genes which involve the activation of lytic activity such as chitinases, and exoproteases, virulence factor like type VI secretion related gene, and genes related to a transcriptional regulator, a guanine deaminase and cviI responsible for the AHL synthesis and the violacein operon (vioABCDE) among others (Stauff and Bassler, 2011).

C. violaceum can be considered to be a bacterium famous in the research community. The single largest factor contributing to the research community's attention to this bacterium is presence of the purple pigment violacein, which is a very useful marker trait during QS assays. Violacein itself has been a molecule of sufficient interest owing a large variety of biological activities reported in it. Though alteration in violacein producing capacity of C. violaceum is often associated with activity of its QS circuit, it should be noted that violacein production in this bacterium is not exclusively controlled by the QS machinery (Kothari *et al*., 2017).

It is essential to accurate interpretation of assay relying largely on quantification of violacein as a measure of QS activity. QS signals may not be the sole control strategy in *C. violaceum* for violacein production. Another important point to be considered while assaying different test products for their potential anti-QS activity against *C. violaceum* is that many of these test substances are dissolved in solvents like DMSO, which itself can affect QS-regulated violacein

production in this bacterium and/or can potentiate or mask the effect of the test formulation. Future research on *C. violaceum* can expand its utility to areas of research other than QS too, such as its use as a model bacterium for studying bacterial stress response, in bioleaching, bioremediation, biosensors (Chaudhari *et al*., 2014).

2.6 Application of Violacein in textile dyeing

Natural dyes and pigments are emerged as an important option to potentially harmful artificial dyes (Venil *et al*., 2016). According to Saxena & Raja (2014), natural dyes are considered eco-friendly as these are renewable and biodegradable and may also provide health benefits to the wearer; textiles colored with natural dyes are preferred by environmentally aware consumers and today there is a niche market for such textiles.

The violet pigment Violacein from *Chromobacterium violaceum* UTM5 has the dyeing potential on different fabrics, i.e. pure cotton, pure silk, pure rayon, jacquard rayon, silk satin, cotton and polyester were tested using mordants and colour fastness tests were performed. The violet pigment has ability of dyeing both natural fibres and synthetic fibres and it can be used as an alternative to synthetic dye. (Venil *et al*., 2016).The textile industry also was interested in violacein application as it is a purple pigment. As example, we can point the lightfast dyed fibers that have been prepared by treating fibers dyed with violacein, deoxyviolacein, or mixtures of their aqueous solutions in the presence of thio-urea, producing a woven silk fabric with bluish purple color (Durán et al., 2012).

2.7 Application of violacein in cosmetics and food industries

In the cosmetic industry, violacein is used as trans-hydroxy violacein, desoxyviolacein, deoxyviolacein or their derivatives, triacetylviolacein and diacetyl (di) methyl violacein and/or furan analogs, in combination with lipophilic and/or hydrophilic substances. Accordingly, cosmetics contain natural microbicides comprising violacein from C. violaceum in a medium containing salts, wool hydrolysate, anthranilic acid or containing yeast extract. Since violacein exhibits an important antibiotic activity against S. aureus and also an antioxidant effect on linoleic acid, a cosmetic lotion containing violacein has also been formulated (Kallmayer *et al*. 2007).

Violacein can be used in a wide range of food industry products as a colorant in the food model systems, where yogurt and jelly have been selected to test the produced violet colorant. In the first food model system, powdered violacein added to the plain yogurt and sweetened yogurt, and color intensity increased in both samples. The samples were kept in the

refrigerator at 4 °C for 30 days and aliquots were taken to evaluate color variation. Yogurt and jelly colored with this powder colorant produced foods of a vivid violet color and their color remained unchanged after one month of storage. These results are incentives for the development of a cost-effective natural colorant that appears as attractive to consumers (Venil *et al*., 2015)

3. Conclusion

Violacein pigment from bacteria has different applications in its pharmacological properties and in textile industries. Pharmacological applications of Violacein provide to triggering of apoptotic tumor cell death in human colon cancer cell or have anti-proliferative activity on a number of human cancer cell lines, defend bacteria against predation, disrupt the membrane integrity of *S. aureus* and MRSA strains, *Bacillus licheniformis*, *Bacillus subtilis*, *Bacillus megaterium*, , *Mycobacterium tuberculosis*, *Pseudomonas aeruginosa* and kill *Plasmodium falciparum*. It is also used as a marker of Quorum sensing (QS). In textile industry Violacein pigment has ability of dyeing both natural fibres and synthetic fibres and it can be used as an alternative to synthetic dye. Violacein can be used in a wide range of cosmetics industry to make lotion and food industry products as a colorant in the food model systems.

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