Microbial Pathogenesis 148 (2020) 104457

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

Short communication

Rhodethrin and Rubrivivaxin as potential source of anti-biofilm agents against vancomycin resistant *Enterococcus faecalis* (ATCC 19443)

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ARTICLE INFO

Keywords:
Antimicrobial
Biofilm
Motility
Enterococcus faecalis
Rhodethrin and Rubrivivaxin

ABSTRACT

Enterococcus faecalis is frequently present in the hospital environment and readily forms a biofilm that protects from antibiotics and resistance against environmental stress conditions, thereby increasing nosocomial chronic infections. This study aims to assess antimicrobial and antibiofilm activities of two novel terpenoid derivatives Rhodethrin (Rdn) and Rubrivivaxin (Rbn) against vancomycin resistant *Enterococcus faecalis* strain (ATCC19443). Both terpenoids effectively prevent biofilm formation with >75% attenuation in cell biomass and significantly decrease the production of exopolysaccharides (EPSs) ($p = 0.005$) and besides their expansion on different surface media. The findings provide new evidence that such terpenoid derivatives could be developed as novel antibacterial drugs.

1. Introduction

Enterococci are a common causes of endocarditis, surgical wound infections, bacteremia, and infections associated with intravenous (or) urinary catheters and other medical devices [1–4]. The recent reports from the World Health Organization (WHO) [5] ranked vancomycin resistant *Enterococci* (VRE) as a major hospital acquired pathogen. The main cause in rapid emergence and spread of vancomycin resistance [6–8]. However, *Enterococci* are emerged as an increasingly important cause of nosocomial infections in the last decade. The dozens of *Enterococcus* species have been identified as *Enterococcus faecalis* and *Enterococcus faecium* are responsible for the majority of human infections. According to previous studies [9], *Enterococcus faecalis* is responsible for about 80–90% of all enterococcal infections. The most prominent enterococcal virulence determinants are the surface adhesins, whose production is governed by its well defined Quoram sensing (QS) network that complement the formation of biofilm.

However, most of the microorganisms could become pathogenic by communicating through Quoram Sensing (QS) and biofilm formation [10]. Furthermore, the microorganisms commonly use two component signal transduction system (TCST) as a core mechanism to regulate the expression of virulence factors in response to ecological fluctuations during several phases of infection [11]. Similarly, several biological activities including biofilm formation, replication, initiation, stress response [12] inter and intracellular virulence, motility, and cell growth are regulated by the signal transduction mechanisms [13,14]. To shirk the stress, and also the host immune system, these bacterial cells acquire a thick biomolecule layer. Such matured biofilms could resist antibiotics by 100 times compared to that of planktonic cells [15], which represent a complex adaptation of bacterial existence that further safeguards from the conservational stresses.

Indole and phenol terpenoids contain a large class of structurally diverse natural products from anoxygenic phototrophic bacteria (APBs) and plant systems [16]. Such natural products may serve as novel drugs for various opportunistic infectious pathogens and microbes exhibiting drug resistance [17]. However, many of them are being used as potential biological molecules [16–19]. They also serve as an alternative source for eradication and prevention of biofilm formation. Herein, we report the antibacterial and antibiofilm activities of novel terpenoid derivatives, Rhodethrin and Rubrivivaxin, against *Enterococcus faecalis* strain (ATCC19443).

2. Methods

2.1. Bacteria strain and culture preparation

Enterococcus faecalis (ATCC 19443) was obtained from American Type Culture Collection (ATCC), USA. The culture was revived and grown aerobically in brain heart infusion (BHI) (Himedia, India) media at 200 rpm, 37 °C for 8 h. The grown culture was centrifuged and

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https://doi.org/10.1016/j.micpath.2020.104457
Received 12 May 2020; Received in revised form 14 August 2020; Accepted 14 August 2020
Available online 20 August 2020