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Gene Silencing with Herbal Compounds against Bacteria

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Abstract

Quorum sensing (QS) is an important process involved in bacterial survival and infections, recent research has focused on the development of therapeutic agents which prevent or manage bacterial pathogenesis by inhibiting bacterial QS. Inhibition of quorum sensing offers an alternative to antibiotic mediated bactericidal or bacteriostatic approach and reduces the risk for development of resistance. Inhibition of bacterial quorum sensing by attenuating the signals can prevent the development of bacterial and fungal virulence and successful establishment of infections. Understanding the quorum sensing inhibition activity of natural bioactive phytochemicals can lead to the discovery of novel compounds and development of more effective strategies in preventing and managing microbial infections. In this study the effect of *Satureja khuzestanica* extract, an endemic plant of Iran, on the expression level of QS gene in *P. aeruginosa* and *A. baumanii* were investigated.

Keywords: RT-PCR; *Satureja khuzestanica*; *Pseudomonas aeruginosa*; MIC; Carvacrol

Introduction

For this purpose first is necessary expose organism with MIC concentration of herbal extracts. Then, microorganisms were treated with extract before and after treatment using genomic and proteomic techniques. Surprisingly, in this study the expression level of QS gene was decreased in the presence of *S. Khuzestanica*. However, the expression of gyrAgene (Housekeeping gene) that was used as an internal control was not altered before and after treatment with this herb. Based on the results, *S. Khuzestanica* could play a, major role in lowering the *P. aeruginosa* resistance to drugs, by reducing QS gene expression. According to results of current research we hope in future be used it to the clinic with a wider range as a complementary therapy and also for surgery operation.

Materials and Methods

For many years, control of bacterial infections by inhibiting microbial growth has been a primary approach of antimicrobial chemotherapy. An emerging problem associated with continual in discriminant use of this therapeutic strategy is the selection of resistant bacteria with higher levels of tolerance against broad-spectrum antibiotics.

Development of novel antibiotics that interfere with metabolism coupled with continued in discriminant use of antibiotics will only lead to evolution of new resistance mechanisms and pathways by bacteria. Recently, it has been recognized that there is a need for a strategy that can block very basic mechanisms of bacterial communication that appear to control bacterial virulence factors leading to pathogenicity. Emerging research has suggested that functions including swarming, biofilm formation, secretion of virulence factors and acquiring competency play an important role in successful and recurrent establishment of bacterial infections in living systems. These processes common to several bacterial diseases are now shown to be related to a cell density-dependent regulation of gene expression mediated by the recognition of signalling molecules called auto inducers (AI). This process sometimes referred to as 'quorum sensing' (QS) has been shown to modulate the expression of genes involved in processes related to survival, virulence and pathogenicity [1-3] and is mediated by small signalling molecules such as acetylated- homoserine lactones (AHLs).

Results

Opportunistic Gram negative bacteria including Pseudomonas sp. have been shown to employ this type of AHL-mediated quorum sensing to regulate the expression of genes related to survival, virulence and competency [4]. Recently, several inhibitors of QS have been discovered from natural sources and have been produced synthetically. Some natural sources include *Australian macroalga, Deliseapulchra* and *green alga, Ulvalactua* that produce halogenated furanones and furanone-like pigments which interfere with quorum sensing [5,6]. These halogenated furanones synthesized in the laboratory have a high degree of AHL inhibition activity and were able to repress a number of genes controlled by QS. In addition, analogs of *S-adenosylmethionine* (SAM), such as *S-adenosylcysteine* and sinefungin can inhibit LuxI mediated synthesis of AHL but can interfere with eukaryotic pathways that use SAM. Recent studies have shown that interference with *P. aeruginosa* quorum signalling by metabolites from *Penicillium species* can increase susceptibility to these agents [7]. Unfortunately, all these compounds are highly reactive and toxic to the host which has limited their therapeutic applications [8] and potential usage in vivo. The current quest for new antimicrobials is therefore aimed at discovering nontoxic inhibitors of QS that can be used for treatment of bacterial infections in humans [8].

Discussion

Natural products especially plants used in traditional medicines are a promising source for deriving molecules that can potentially inhibit quorum sensing [9-11]. These plants can offer a large and attractive repertoire for the discovery of quorum sensing inhibitors. They are of particular importance as these have been used for thousands of years for the treatment and management of diseases and may have few

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side-effects and toxicity issues as with many antibiotic regimens and currently known QS inhibitors. Herbs, Spices and Medicinal Plants HSMP used in Hispanic cultures have been used for several centuries to treat common ailments, are well known for their antimicrobial effects on a variety of human pathogens [12,13]. However, few studies have investigated their QS related antivirulent activities including in *P. aeruginosa*. The body of literature discussing HSMP from Central/ South American continent as sources of QSI is very limited [14-17]. We believe that some of the antimicrobial properties of HSMP may be contributed by the QS inhibiting phytochemicals present in it.*Satureja khuzestanica*, from Lamiaceae family is an Iranian endemic plant,famous for its medical uses as an analgesic and antiseptic in folk medicine [18]. It is mostly found in western and southern part of Iran [19]. Recently, antiviral, antibacterial, antifungal, and antiprotozoal effects were investigated from various species of Satureja [19,20]. However, the possible effect of *Satureja khuzestanica* on decreasing the resistance of *P.aerogenase* against antibiotics and the mechanisms involved have not yet been studies.

Conclusion

The antibacterial activity of the *S. Khuzestanica'soil* might be due to main phenolic components, Carvacrol and Thymol [21]. Carvacrol is also found in Thyme, However, its high ratio in *S. khuzistanica* has discriminated this plant from other herbs with antimicrobial effects [22,23]. In view of this and with regard to the antimicrobial effect of *S. Khuzestanica* against *p. aerogenase* and also resistance of this strain to variety of antibiotics, this study aimed to test this hypothesis that *S. Khuzestanica* extract may alter the expression of QS gene ,and thus may lead to a lower susceptibility of this strain to antibiotics.

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