Trends in Food Science & Technology 43 (2015) 189–204

TRENDS IN FOOD SCIENCE & TECHNOLOGY

Review

Plant food extracts and phytochemicals: Their role as Quorum Sensing Inhibitors

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Traditionally, plant food extracts and phytochemical compounds have been used as remedies against microbial infections with the added benefit that most of them are safe for human consumption. These compounds have been also highlighted as *Quorum Sensing* Inhibitors (QSI). *Quorum Sensing* (QS) is a regulatory mechanism that enables bacteria to make collective decisions with respect to the expression of a specific set of genes which can be related to virulence factors. Among all the available studies, most of them use biosensor to demonstrate the role of plant foods and phytochemicals as QSI and only few of these studies focus on their mechanisms of action. This review summarizes the published scientific work on the use of plant food extracts and phytochemicals as QSI, highlighting the techniques used to identify their biological activity and their mechanisms of action.

Introduction

Since ancient times, plant food extracts and phytochemicals have been used in nutrition and medicine mostly because of their range of beneficial effects against human chronic diseases such as cardiovascular diseases and inflammation as well as their antimicrobial activity. Plant food extracts and phytochemicals have been recognized as effective treatments against microbial infections with the added benefit that most of them are harmless for human health. However, in the last years, plant food extracts and phytochemicals have also been highlighted as *Quorum Sensing* Inhibitors (QSI). *Quorum Sensing* (QS) is a regulatory mechanism that enables bacteria to make collective decisions with respect to the expression of a specific set of genes (Kalia, 2013). Several authors have demonstrated that QS regulate bacterial pathogenesis by controlling competence development, sporulation, antibiotic synthesis, virulence factor induction, cell differentiation, and nutrient flux along with other physiological events in pathogenic bacterial infections (Greenberg, 2003). Atkinson and Williams (2009) demonstrated that QS mechanisms amplify bacterial virulence by stimulating the expression of disease causing attributes, such as motility, biofilm formation, and secretion of virulence factors. In QS systems, bacteria produce low-molecular-weight signaling compounds, known as autoinducers that are released into the environment. The most widely studied signaling compounds include fatty acid derivatives, generally *N*-acylhomoserine lactones (AHLs) used by Gram-negative bacteria, and a furanosyl borate diester, autoinducer-2 (AI-2), which is used in interspecies communication (Kalia, 2013). However, other molecules such as autoinducer-3 (AI-3), which activates enterohemorrhagic *Escherichia coli* (EHEC) virulence genes, and amino acids and short peptides used by Gram-positive bacteria have been also identified as signaling molecules (Kalia, 2013). QS signaling molecules serve to inter or intra bacteria species communication but also modulate the host immune response. Previous exposure of the host organism to QS

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http://dx.doi.org/10.1016/j.tifs.2015.02.009

molecules facilitated the survival of the infected host organism that is able to increase the clearance of infecting bacteria (Bjarnsholt *et al.*, 2005). In other cases, exposure to QS signals before infection can extend the survival of the host but also the persistence of the infection (Bandyopadhaya *et al.*, 2012).

Many research studies have reported the capacity of plant extracts and phytochemicals to interfere in intra- and inter-species QS communication systems (Teplitski, Robinson, & Bauer, 2000; Vandeputte *et al.*, 2010; Vattem, Mihalik, Crixell, & McLean, 2007). Actually, the ability of plants to interrupt QS systems may serve as a defense mechanism to fight against bacterial invasion. One of the keys of success of plant food extracts and phytochemicals could be their similitude to what is considered the ideal QSI, which includes being chemically stable, highly effective low-molecular-mass molecules and harmless for human health (Rasmussen & Givskov, 2006). In fact, the consumption of these extracts and phytochemicals are rarely associated with any side-effect as seen in many antibiotic regimes. Additionally, plant food extracts and phytochemicals have also been recognized to serve as novel food preservation techniques, although their use must be selected in the specific system in which they are to function, as they cannot easily be transferred from one QS system to another (Rasch *et al.*, 2007).

The most commonly recognized mechanisms of action of plant food extracts and phytochemicals are related to their similarity in chemical structure to QS signals and also their ability to degrade signal receptors (Kalia, 2013). In the case of AHLs, the proteins that act as receptors or regulators are known as the LuxR family of transcriptional regulators, whereas AI-2-type QS is dependent on the activity of LuxP/Q-type proteins. In this case, LuxP is a periplasmic-binding protein that binds AI-2 (Reading & Sperandio, 2006). Nevertheless, there are other potential mechanisms of action that plant food extracts and phytochemicals might use to inhibit bacterial QS (Fig. 1). However, only few of the available studies focus on the role of plant food extracts and phytochemicals as QSI deals with the potential mechanisms of action (Kalia, 2013). Therefore, the main objective of this review is to summarize all the scientific work focused on the use of plant food extracts and phytochemicals as QSI, highlighting the

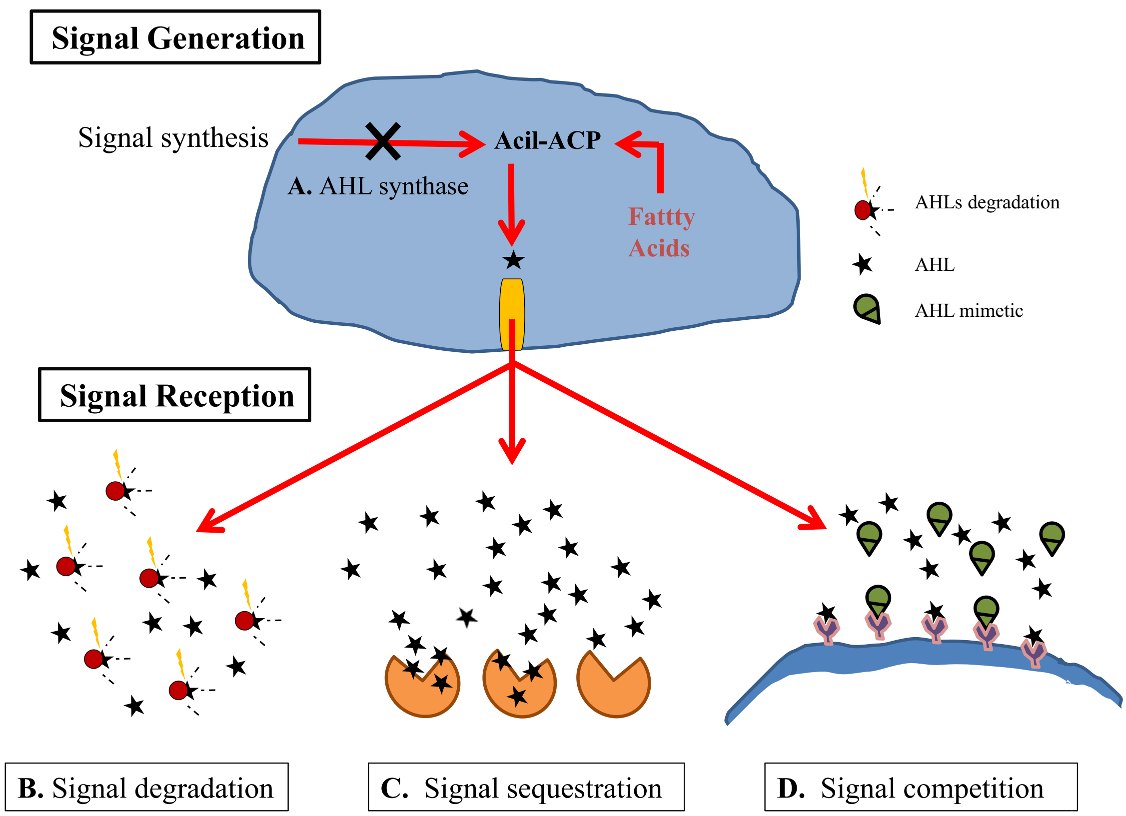

Fig. 1. Scheme of the potential mechanisms of action of plant food extracts and phytochemicals as QSI. The process of QS can be disrupted by reducing the activity of AHL cognate receptor protein and/or AHL synthase (A) or inhibiting the production of QS signal molecules by different mechanisms such as; (B) degradation of the AHL, (C) sequestration of the AHL (D) mimicking the signal molecules primarily by using plant food extracts and phytochemicals as analogues of signal molecules.