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Quorum Sensing Inhibitor and its Inhibition Mechanism: Mushroom Derived Agents

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Abstract – **Bacteria communicate with one another using chemical signal molecules. The bacterial communication system (quorum sensing, QS) is a process by which bacteria produce and detect signal molecules and thereby coordinate their behavior in a cell-density dependent manner. In bacteria, chemical communication involves producing, releasing, detecting, and responding to small hormone-like molecules termed auto inducers. Three main QS systems can be distinguished: the acylhomoserine lactone (AHL) QS system in Gram-negative bacteria, the auto inducing peptide (AIP) QS system in Gram-positive bacteria and the autoinducer-2 (AI-2) QS system in both Gram-negative and - positive bacteria. This process, termed quorum sensing, allows bacteria to monitor the environment for other bacteria and to alter behavior on a population-wide scale in response to changes in the number and/or species present in a community. Quorum sensing in food processing environments can lead to post-treatment contamination, thereby reducing product shelf life and disease transmission. The ability to control quorum sensing is a significant problem because of health problems and economic losses. There is a quest to find a natural product rather than a synthetic product that can be used as generally recognized as safe. Mushrooms produce a huge number of natural products. Many mushroom extracts contain phenol derivatives, terpenes, flavonoids, etc., which have the ability to suppress attachment to microbial cells. This mini-review combines most of the recently published work on quorum sensing inhibition (mushroom inhibitor) and figure out the inhibition mechanism which can be safely used in food safety and human health issues.**

Keywords – **Quorum Sensing, Extract, Mushroom, Biofilm.**

I. Introduction

Quorum sensing (QS) is a regulatory mechanism that allows bacteria to control their gene expression in response to the population density. To be able to sense the population density, the bacteria produce AI molecules that accumulate in the environment. The QS signal is produced during specific stages of growth, although the production level is also influenced by the environmental conditions. When a threshold concentration is reached, the AI activates a transcription regulator by binding to it and the activated regulator can induce or repress the expression of target genes. This leads to the activation of a cellular response that extends beyond physiological changes required to metabolize or detoxify the molecule [1], [2]. Usually, the processes that are regulated by QS are not worthwhile when undertaken as an individual cell but they are beneficial when a group of bacteria acts together [3]. QS was first described in the marine bacterium *vibrio fischeri*, where it regulates luminescence in the squid light organ. One individual cell producing luminescence would be a waste of energy, but when a whole community of cells works together, the resulting light production is worth the effort. Similary, QS gene regulation can be used as a strategy to invade hosts successfully: when just one bacterium express its virulence genes, it is easily detected and dealt with by the host's immune response. If the bacteria wait before attacking until they are present in sufficient numbers, they may be able to overwhelm an unexpecting host before it gets a chance to defend itself. Many species of bacteria use QS for gene regulation and many aspects in bacterial life are QS regulated, like biofilm formation, bioluminescence, virulence, DNA exchange, sporulation, etc. [4], [5]. Diffusion sensing would allow the bacteria to assess the cell's environment that does not allow the produced enzymes to diffuse away. The concepts of QS as population density sensing and diffusion sensing have been unified in the concept of efficiency sensing [6].

The microbial populations communicate with each other by production, release, and subsequent detection of chemical signaling molecules called autoinducers (AI). This process is called Quorum Sensing (QS). It allows bacteria to regulate gene expression in response to changes in cell-population density [4], [7], [8]. Acyl homoserine lactone (AHL) and auto inducing peptide (AIP) QS system are used in gram-negative bacteria (G^-) and gram-positive bacteria (G^+), respectively. Autoinducer-2 (AI-2) QS system can be used by both G^- and G^+ bacteria [4], [9]. Bis-(3-5) -cyclic dimericguanosine monophosphate (c-di-GMP) is also considered as second messenger in many bacteria [10]. In an opportunistic pathogen *Pseudomonas aeruginosa*, two AHL signaling systems *las* and *rhl* are co-existed. These two QS systems are arranged in a hierarchical fashion as the LasR-LasL system activates the RhlR - RhlI system [3], [4]. Thus, using QS mechanism bacteria work like multicellular organisms and express different virulence factors such as biofilm formation, bioluminescence, sporulation, pathogenesis etc [11].

It has been suggested that inactivating the QS system of pathogen can result in a significant decrease in virulence factor production. In fact, an anti-QS approach has already shown promise in the battle against pathogenic microorganisms [3]. The QS system can be interfered with a number of ways, including (i) inhibition of AHL molecule

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biosynthesis, (ii) degradation of AHL molecules by bacterial lactonases, and (iii) use of small molecules to block the activation of AHL receptor protein [1], [11].

Multiple reports have discussed the involvement of QS in biofilm formation and conflicting conclusions have been drawn regarding the importance of QS in bacterial biofilm formation [12], [13]. These inconsistencies might have resulted from the use of different biofilm models and/or different bacterial strains. Although much remains to be learned about the involvement of QS in biofilm formation, maintenance, and dispersal, QS inhibitors (QSI) have been proposed as promising antibiofilm agents. QS inhibition can be achieved by inhibiting signal synthesis or direct degradation of the signal, inhibition of binding of the signal molecule to the receptor and/or inhibition of the signal transduction cascade. Given the promise of anti-QS compounds, efficient screening for these agents becomes imperative.

The discovery of QS might have open a new era of action against microbial pathogensis. Anti-QS and anti-biofilm are fundamental strategy to combat against foodborne pathogenesis and microbial spoilage rather than killing. According to the regulations for producing and labelling natural foods by United States Department of Agriculture (USDA), the application of artificial flavorings, chemical and synthetic preservatives are prohibited in the United States [14]. Nowadays, all over the world, consumers are more concern about carcinogenic issues. Consequently, researchers are trying to find alternative source which are less toxic and popular as generally recognized as safe (GRAS) [15], [16]. Considering the harmful effect of synthetic compounds on human health, it is necessary to screen QS and biofilm inhibitors from natural source.

Therefore, the QS mediated formation is a safety problem which needs to be solved in food industries.

There are many quorum sensing inhibitor in market. Most of them are synthetic compounds. To ensure environmen--tally friendliness, less toxic and more specific natural products have been the aim of most current research. The aim of this mini review is to outline the mushroom derived quorum sensing inhibitor and indicate the mode of action based on recent published articles.

II. Mechanism of Quorum Sensing

One alternative approach is targeting the bacterial communication system (quorum sensing, QS). QS is a process by which bacteria produce and detect signal molecules and thereby coordinate their behavior in a cell-density dependent manner [17]. Three main QS systems can be distinguished**:** the acylhomoserine lactone (AHL) QS system in Gram-negative bacteria, the autoinducing peptide (AIP) QS system in Gram-positive bacteria and the autoinducer-2 (AI-2) QS system in both Gram-negative and -positive bacteria (***Figure 1***). Many Gram-negative bacteria use AHL signalling molecules (***Figure 1***) which are produced by a LuxI-type synthase and are perceived by a DNA-binding LuxR-type transcriptional activator [17]. The QS system of Gram-positive bacteria typically consists of signalling peptides (***Figure 1***) such as Agr and RNA-III activating/inhibiting peptides (RAP/RIP) in *Staphylococcus aureus*, and a two-component regulatory system made up of a membrane-bound sensor and an intracellular response regulator [18]. A third QS system is shared by many Gram-positive and Gram-negative bacteria and is based on a mixture of interconvertible molecules collectively referred to as AI-2 (***Figure 1***) [17], [19]. A key enzyme in the production of AI-2 is LuxS. LuxS catalyzes the cleavage of S-ribosylhomocysteine to homocysteine and 4, 5-dihydroxy -2, 3-pentanedione (DPD). DPD will subsequently undergo spontaneous rearrangements and modifications, forming a mixture of molecules, collectively called AI-2. Although LuxS is encoded in many sequenced bacterial genomes, AI-2 receptors and signal transduction systems have only been described in *Vibrio* spp., in *Salmonella enterica* serovar Typhimurium and in *Escherichia coli* [19], [20]. In *Vibrio* spp., binding of AI-2 to LuxP, a periplasmic AI-2 receptor associated with the LuxQ sensor kinase, results in the production of LuxR and ultimately changes in gene expression. In *S. enterica* serovar Typhimurium and *E. coli* AI-2 is first transported into the cell prior to initiating a signalling cascade [19].

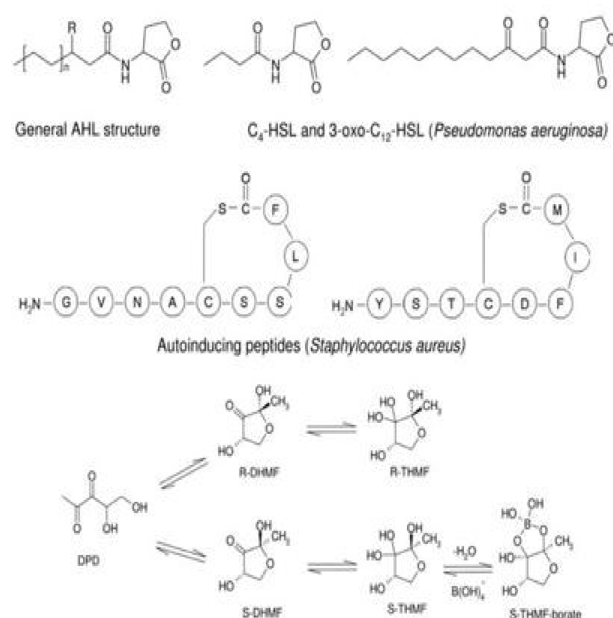

Fig. 1. Quorum sensing signal molecules [16].

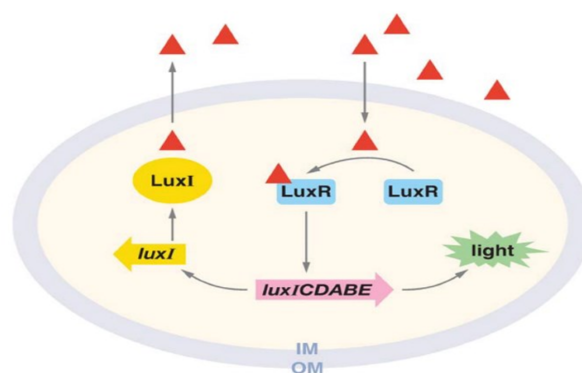

Fig. 2. Quorum sensing in Gram-negative bacteria.

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Quorum sensing in *Vibrio fischeri*; a LuxIR signaling circuit. Red triangles indicate the autoinducer that is produced by LuxI: OM, outer membrane; IM, inner membrane [17].

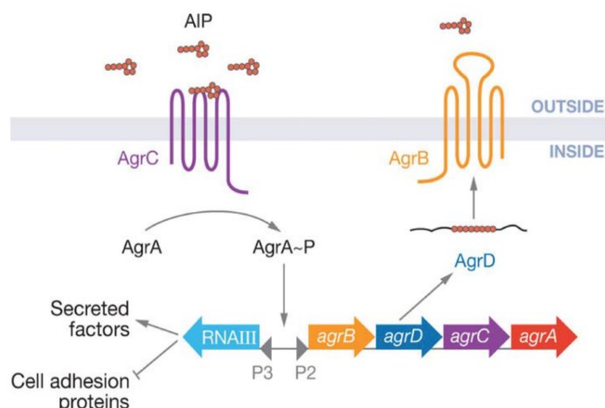

Fig. 3. Quorum sensing in Gram-positive bacteria.

Using a two-component response regulatory system, *Staphylococcus aureus* detects and responds to an extracellular peptide. Small red circles indicate the AIP. P2 and P3 designate the promoters for *agr BDCA* and RNAIII, respectively [17].

III. Quorum Sensing Inhibition

The process of QS can be disrupted by different mechanisms: (i) reducing the activity of AHL cognate receptor protein or AHL synthesis, (ii) inhibiting the production of QS signal molecules, (iii) degradation of the AHL, and (iv) mimicking the signal molecules primary by using synthetic compounds as analogues of signal molecules (AHLs) has been appreciated and applied the most. Antibodies and decoy receptors to inhibit QS signals have been suggested as novel approaches for anti-infective therapy [16], [21], [22]. One of the most important prerequisites for circumventing the pathogenicity issues related to QS is its detection. The need for biosensors was realized quite early primarily because of the increasing variation in the QS signals produced by divers organisms. In order to establish the link between cause and effects AHL and AI-2 reporters were developed over a period of time by different researchers [1], [23]. These biomonitor strains allow sensitive, quantitative and real time detection of QS signals such as AHLs. In most of the biomonitor strains known so far, the QS regulated promoter is fused to the lux operon or lacZ. Although, these reporter strains have a functional regulator protein, they lack the AHL syntheses enzyme. The promoter activity gets induced by exogenous QS signals. Here, the receptor gets activated by the presence of AHLs, which binds to its cognate LuxI promoter and initiates the expression of certain genes. The expression of the relevant genes is proportional to the concentration of the signal molecules. In brief, it mimics the natural QS system with certain easily identifiable phenotypes. Although each reporter strain detects a set of QS signals, their complemen--tarities allow detection of a wide range of AHLs and even AHL analogues or mimics. *Chromobacterium violaceum* has high sensitivity for QS signal compounds with 4-6 carbon acyl side chains, *E.coli* harbouring pSB410 is effective for 6-8 carbon side chains and pSB1075 is sensitive for detecting AHLs with 10-14 carbon side chains lengths. The inability of *C. violaceum* CV026 biosensor to detect 3-hydroxy derivatives of AHL can prove helpful in elucidating potential cases where *P.fluorescens* may be present. Another equally effective biosensor for long chain AHL inhibitor screening is *Agrobacterium tumefaciens* NT1 (traR, tra: :lacZ749). It contains a lacZ fusion in the tra1 gene of pTiC58, which is induced to produce the enzyme β-galactosidase. The degradation of 5-bromo-4-chloro-3-indoylβ-D-galactopyranoside (X-gal) results in the appearance of blue color. The best part of this biosensor strain is its ability to respond to a wide range of AHLs at very low concentration. The third class of reporter strain needed for identifying QSIs which may target long-chain AHLs - C16 - C20 is represented by *S. meliloti* Rm41sinI: :lacZ (pJNSinR). A more recent addition to reporters for detecting long-chain AHLs is *C. violaceum* VIR24, which was derived from *C. violaceum* type strain ATCC124 [24]. In vitro methods including high throughput genetic tools have proven effective in screening of non-toxic QSIs from natural sources and for elucidating their effects [25], [26].

IV. Criteria for Selecting QSIs

For selecting an effective QSI, it has been proposed that it should meet at least the following few criteria: (a) a small molecule with ability to efficient reduction of the QS regulated gene expression, (b) high specific for a given QS regulator with no adverse effects on the bacteria or the host, (c) chemical stability and resistant to degradation by various host metabolic system, and (d) preferably longer than the native AHL. As a consequence of these characteristics of a QSI, the bacteria are not likely to become resistant to such drugs, which generally exerts selection pressure during treatment of infections and these compounds are not likely to affect the population of beneficial bacteria present in the communities harbouring the host. Finally, these QSIs which do not show antigenicity due to their low molecular weights are expected to expedite drug discovery against infectious diseases.

V. Quorum Sensing and Biofilm

Biofilm development and quorum sensing (QS) are closely interconnected processes. Biofilm formation is a cooperative group behavior that involves bacterial popula--tions living embedded in a self-produced extracellular matrix. QS is a cell-cell communication mechanism that synchronizes gene expression in response to population cell density. Intuitively, it would appear that QS might coordinate the switch to a biofilm lifestyle when the population density reaches a threshold level. However, compelling evidence obtained in different bacterial species coincides in that activation of QS occurs in the formed biofilm and activates the maturation and disassembly of biofilm in a coordinate manner.

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VI. Formation of Biofilm

The transition of microorganisms from the planktonic to the sessile (biofilm) state is often described as occurring in a series of steps or phases. The stages of biofilm formation include: i) the formation of a conditioning film; ii) cellular attachment; iii) the formation of microcolonies which eventually merge to become mature biofilms; and iv) biofilm dispersion and recolonization; duration: sec-days.

VII. Combating Against Biofilm

Biofilms constitute a protected mode of growth that allows microorganisms to survival in hostile environments, being their physiology and behavior significantly different from their planktonic counterparts. In dairy, sea food, wine, etc. industry, biofilms may be a source of recalcitrant contaminations, causing food spoilage and are possible sources of public health problems such as outbreaks of food borne pathogens. Biofilms are difficult to eradicate due to their resistant phenotype. Consequently, new control strategies are constantly emerging with main incidence in the use of bio solutions (enzymes, phages, interspecies, interactions and antimicrobial molecules from microbial origin) [27], [28].

VIII. Mushroom as Natural Products

Since ancient times, mushrooms have been valued as both food and medicines. Medicinal mushrooms possess a long history of use, especially in Asian countries. However, they have also played a crucial role in treatment of several diseases affecting rural populations of Eastern European countries. They have been used by preparing hot water extracts, concentrates or in powdered forms [29].

Mushrooms possess high contents of qualitative protein, crude fibre, minerals and vitamins. Apart from their nutritional potentials, mushrooms are also sources of physiologically beneficial bioactive substances that pro--mote good health. They produce a wide range of secondary metabolites with high therapeutic value. Health promoting properties, e.g. antioxidant, antimicrobial, anticancer, cholesterol lowering and immune-stimulatory effects, have been reported for some species of mushrooms.

Both fruiting bodies and the mycelium contain compounds with wide ranging antioxidant and antimicro--bial activities [30], [31], [32], [33].

Various mushrooms species secrete substances that possess QS-inhibitory activity, were found to disrupt QS-regulated behaviors of bacteria. Three wild mushrooms (*Amanita rubescens, Russula delica, Lactarius* sp.) have been reported to have anti-QS properties using *Chromobacterium violaceum* strains as biomonitor [34]. Various mushrooms species secrete substances that possess QS-inhibitory activity. The chloroform extract of *Cordyceps. taii* (CECT), the ethyl acetate extract of *Cordyceps. taii* (EECT) and the acetone extract of *Cordyceps. taii* (AECT) exhibited selective antimicrobial activities against the nine microorganisms tested [35].

Agaricus bisporus forms the most cultivated mushroom in the world. Its methanolic extract revealed MIC = 5 µg/mL against *Bacillus subtilis*, and also shows activity against *Bacillus cereus*, *Micrococcus luteus*, *Micrococcus flavus*, *Staphylococcus aureus*, and *Staphylococcus epidermidis* [36], [37], [38]. Other *Agaricus* species have also demonstrated antimicrobial activity. *Agaricus bitorquis* and *Agaricus essettei* methanolic extracts showed an inhibitory effect upon all the tested gram-positive bacteria [36]. *Agaricus silvicola* methanolic extract also revealed antimicrobial properties against *Bacillus cereus* (MIC = 5 µg/mL), *Bacillus subtilis* (MIC = 50 µg/mL), and against *Staphylococcus aureus* (MIC = 5 µg/mL) [39]. The mycelium of *Agaricus* cf. *nigrecentulus* and *Tyromyces duracinus* (ethyl acetate extracts) showed activity only against *Staphylococcus saprophyticus* [40].

An overview of bacterial quorum sensing inhibition mechanism has been given in ***Table I*** from this table, it is clear that quorum sensing mostly controlled biofilm. In recent years, drug resistance of human pathogenic bacteria has been extensively reported. Moreover, persistent infections were also observed due to improved resistance of bacteria in quorum sensing. This creates a tremendous economic loss and pressure on the medical community to find alternative approaches for the treatment of diseases related with quorum sensing. Therefore, efforts are been applied to discover efficient antimicrobial molecules not so vulnerable as current drugs to bacterial resistance mechanisms, including those in quorum sensing. Some natural products have distinctive properties that make them perfect candidates for these much needed therapeutics. Mushroom produce an enormous array of secondary metabolites (phytochemicals) that are not essential for their normal physiological functions. The importance of diverse natural product has been recognized by humans due to their beneficial properties for health. Inclusively, many classes of mushroom secondary metabolites have demonstrated their potential as antimicrobials or synergists of other products.

Table I. Mushroom extracts with antimicrobial activity against gram- negative, and positive bacteria.

Microorganism	*Mushrooma*	Results	References
Actinomyces naeslundii	*Lentinus edodes*	CFU = 0–3.30 (± 5.48) × 106 MIC = 0.05–20 mg/mL	[41], [42], [43]
Bacillus cereus	*Agaricus bisporus, Agaricus bitorquis, Agaricus essettei, Agaricus silvicola, Armillaria mellea, Boletus edulis, Cantharellus cibarius, Clitocybe alexandri, Clitocybe geotropa, Cortinarius sp., Gloeoporus thelephoroides, Hexagonia hydnoides, Hydnum repandum, Hypholoma fasciculare, Irpex lacteus (M), Lactarius camphorates, Lactarius delicious, Lactarius piperatus, Lactarius volemus, Laetiporus sulphureus, Lentinus edodes, Lepista nuda, Leucopaxillus giganteus (M), Macrolepiota procera, Meripilus giganteus (M), Meripilus giganteus, Phellinus sp., Pleurotus ostreatus (M), Pleurotus ostreatus, Ramaria*	IZD = 5–21 mm MIC = 5 µg/mL – 100 mg/mL	[32], [36], [37], [39], [40], [44], [45], [46], [47, 48]

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	botrytis, Ramaria flava, Rhizopogon roseolus, Sarcodon imbricatus, Sparassis crispa, Tricholoma portentosum		
Enterococcus faecium	*Lentinus edodes*	MIC > 1.5 – > 5 0 mg/mL	[42]
Lactobacillus casei	*Lentinus edodes*	CFU = 5.00 (± 7.07) × 10-1 - 9.28 (± 2 .76) × 102 MIC = 0.05–15 mg/mL	[41], [42], [43]
Listeria innocua	*Lentinus edodes*	IZD = 8 mm	[44]
Listeria monocytogenes	*Lentinus edodes, Pycnoporus sanguineus (M),*	IZD = 11–13 mm	[40], [44], [47]
Staphylococcus sp.	*Lentinus edodes*	IZD = 12 mm	[47]
Staphylococcus aureus	*Agaricus bisporus, Agaricus bitorquis, Agaricus essettei, Agaricus silvícola, Armillaria mellea, Boletus edulis, Cantharellus cibarius, Clitocybe geotropa, Cortinarius sp., Cortinarius abnormis, Cortinarius ardesiacus, Cortinarius archeri, Cortinarius austroalbidus, Cortinarius austrovenetus, Cortinarius austroviolaceus, Cortinarius coelopus, Cortinarius clelandii, Cortinarius [Dermocybe sp, Dermocybe canaria, Dermocybe kula], Cortinarius fulvoiubatus, Cortinarius ianthinus, Cortinarius memoria-annae, Cortinarius persplendidus, Cortinarius sinapicolor, Cortinarius submagellanicus, Cortinarius tricholomoides, Cortinarius vinosipes, Ganoderma lucidum, Hydnum repandum, Hygrophorus agathosmus, Hypholoma fasciculare, Irpex lacteus (M), Lactarius camphoratus, Lactarius delicious, Lactarius piperatus, Lactarius volemus, Laetiporus sulphureus, Lentinus edodes, Lepista nuda, Leucopaxillus giganteus (M), Macrolepiota procera, Meripilus giganteus (M), Meripilus giganteus, Morchella elata (M), Morchella esculenta var. vulgaris (M), Navesporus floccosa, Nothopanus hygrophanus (M), Paxillus involutus (M), Phellinus rimosus, Pleurotus eryngii (M), Pleurotus ostreatus (M), Pleurotus sajorcaju, Pycnoporus sanguineus (M), Ramaria botrytis, Ramaria flava, Sparassis crispa, Suillus collitinus*	CFU = 2.1 × 104 IZD = 8–24 mm MIC = 5 µg/mL - 50 mg/mL IC50 < 0.01 – ≥ 2.00 mg/mL	[36], [39], [42], [44], [47], [48], [49], [50], [51], [52], [53], [54], [55]
MRSA	*Lentinus edodes, Phellinus linteus*	IZD = 12 mm MIC = 500 µg/mL	[47], [56]
Staphylococcus epidermidis	*Agaricus bisporus, Hygrophorus agathosmus, Lentinus edodes, Pleurotus sajor-caju, Suillus collitinus*	IZD = 11–27 mm MIC = 7.81–62.5 µg/mL	[38], [44], [47], [53]
Streptococcus mutans	*Lentinus edodes*	CFU = 2.15 (± 5.58) × 105 MIC = 0.1–10 mg/mL	[41], [42], [43]
Micrococcus luteus	*Agaricus bisporus, Agaricus bitorquis, Agaricus essettei, Clitocybe alexandri, Laetiporus sulphureus, Lentinus edodes, Ramaria flava*	IZD = 10–21 ± 1 mm	[36], [45], [46], [55], [57]
Sarcina lutea	*Armillaria mellea (M), Armillaria mellea, Clitocybe geotropa, Meripilus giganteus (M), Meripilus giganteus, Morchella costata (M), Morchella esculenta var. vulgaris (M), Paxillus involutus (M), Pleurotus ostreatus (M), Sparassis crispa*	IZD = 8–27 mm	[58], [59]
Enterobacter aerogenes	*Agaricus bisporus, Clitocybe alexandri, Hygrophorus agathosmus, Meripilus giganteus (M), Paxillus involutus (M), Pleurotus ostreatus (M), Pleurotus sajor-caju, Rhizopogon roseolus, Suillus collitinus*	IZD = 8–22 mm MIC = 15.62–125 µg/mL	[38], [45], [53], [58]
Enterobacter cloacae	*Armillaria mellea, Clitocybe geotropa, Meripilus giganteus (M), Meripilus giganteus, Paxillus involutus (M), Pleurotus ostreatus (M), Sparassis crispa*	IZD = 10–20 mm	[58], [59]
Escherichia coli	*Agaricus bisporus, Armillaria mellea (M), Armillaria mellea, Boletus edulis, Cantharellus cibarius, Clitocybe alexandri, Clitocybe geotropa, Cortinarius sp., Ganoderma lucidum, Hydnum repandum, Irpex lacteus (M), Lactarius camphoratus, Lactarius delicious, Lactarius piperatus, Lactarius volemus, Laetiporus sulphureus, Lentinus edodes, Lepista nuda, Leucoagaricus cf. cinereus (M), Macrolepiota procera, Marasmius sp. (M), Marasmius cf. bellus (M), Meripilus giganteus (M), Meripilus giganteus, Morchella costata (M), Morchella hortensis (M), Navesporus floccosa, Paxillus involutus (M), Phellinus rimosus, Pleurotus eryngii (M), Pleurotus ostreatus (M), Pleurotus sajor-caju, Rhizopogon roseolus, Sparassis crispa, Suillus collitinus*	IZD = 8–27.40 ± 0.19 mm MIC = 250 µg/mL – > 50 mg/mL	[37], [42], [45], [46], [47], [52], [53], [54], [59], [60]
Klebsiella aerogenes	*Lentinus edodes*	IZD = 9 mm	[47]
Klebsiella pneumoniae	*Agaricus bisporus, Agaricus bitorquis, Ganoderma lucidum, Lactarius piperatus, Lentinus edodes, Lepista nuda, Pleurotus sajor-caju, Ramaria flava*	IZD = 4–31.60 ± 0.10 mm MIC = 0.5 mg/mL	[36], [38], [44], [47], [48], [51], [54], [57], [61]
Neisseria subflava	*Lentinus edodes*	CFU = 9.49 (± 2.60) × 106 – 1.50 (± 0,50)×108	[41], [43]
Pseudomonas aeruginosa	*Agaricus bisporus, Boletus edulis, Cantharellus cibariusCortinarius sp., Cortinarius abnormis, Cortinarius ardesiacus, Cortinarius archeri, Cortinarius austroalbidus, Cortinarius austrovenetus, Cortinarius austroviolaceus, Cortinarius coelopus, Cortinarius clelandii, Cortinarius [Dermocybe sp., Dermocybe canaria, Dermocybe kula], Cortinarius fulvoiubatus, Cortinarius ianthinus, Cortinarius memoria-annae, Cortinarius*	IZD = 6–20 mm MIC = 0.5–100 mg/mL IC50 = 0.04 – > 2.00 mg/mL	[32], [37], [38], [46], [47], [49], [51], [52], [54]

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	persplendidus, Cortinarius sinapicolor, Cortinarius submagellanicus, Cortinarius tricholomoides, Cortinarius vinosipes, Ganoderma lucidum, Hydnum repandum, Lactarius camphoratus, Lactarius delicious, Lactarius piperatus, Lactarius volemus, Laetiporus sulphureus, Lentinus edodes, Lepista nuda, Macrolepiota procera, Navesporus floccosa, Phellinus rimosus, Pleurotus sajor-caju, Ramaria flava		
Salmonella typhimurium	*Agaricus bisporus, Armillaria mellea (M), Armillaria mellea, Clitocybe geotropa, Ganoderma lucidum, Hygrophorus agathosmus, Irpex lacteus (M), Lepista nuda, Meripilus giganteus (M), Meripilus giganteus, Morchella costata (M), Morchella elata (M), Morchella esculenta var. vulgaris (M), Morchella hortensis (M), Navesporus floccosa, Paxillus involutus (M), Phellinus rimosus, Pleurotus ostreatus (M), Pleurotus sajor-caju, Sparassis crispa, Suillus collitinus*	IZD = 6–16 mm MIC = 15.62–125 µg/mL	[38], [52], [53], [59], [61]
Klebsiella pneumoniae	*Amanita citrina*	MIC = 2.5mg/ml	[62]
Pseudomona. areuginosa	*Bjerkandera adusta*	MIC = 1.25 mg/ml	[62]
Escherichia coli	*Clavicorona pyxidata*	MIC = 2.5mg/ml	[62]
Staphylococcus. aureus	*Fomitopsis pinicola*	MIC = 5mg/ml	[62]

IX. Conclusion

Most of mechanisms are still not fully understood about, mechanism of quorum sensing and inhibition. But in vitro and vivo we have found many mushroom quorum sensing inhibitor to fight against diseases and spoilage. More research needs to do for screening out the major components from extract.

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Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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