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Review on bacterial biofilm: An universal cause of contamination

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ABSTRACT

Biofilms contain cluster of microorganisms that are found to be associated with the biotic and abiotic surfaces. Biofilm formation is a dynamic process and different mechanisms are involved in their attachment and growth. The formation of microbial biofilms is an important reason for failure of antimicrobial therapy. Biofilm-associated infections represent one of the major threats of modern medicine. Consequently, various preventive and control strategies like mechanical, physical and chemical methods can be appropriately applied for controlling biofilm formation or eradicate mature biofilm. The present review will focus on describing the effective bio control and removal of biofilms. These newer bio control strategies are considered as ecofriendly and cost effective method in terms of therapeutic.

Contents

1. Introduction

Biofilms can be either single or multilayered. Biofilms contain either homogenous or heterogeneous populations of bacteria which remain in the matrix made up of extracellular polymeric substances secreted by component population of the biofilm. Costerton, one of the founding fathers of biofilm research, described a biofilm as a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface (Costerton et al., 1999). Bacterial biofilms are widely distributed and play important roles in many industrial activities. In dairy industry biofilm formation can lead to serious hygiene problems and economic losses due to food spoilage and equipment impairment (Gram et al., 2007). A huge significant number of reports have appeared on the persistence of some

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foodborne pathogens on food contact surfaces and biofilms, affecting the quality, quantity and safety of the food products. From a medical perspective, biofilms can form on different medical implants such as catheters, artificial hips and contact lenses, these infections can often only be treated by removal of the implant, thus increasing the trauma to the patient and the cost of treatment. It has been estimated that biofilms are associated with 65% of nosocomial infections and that treatment of these biofilm-based infections costs $>$ $1 billion annually (Licking, 1999; Potera, 1999). Microorganisms in biofilms catalyze chemical and biological reactions causing metal corrosion in pipelines and tanks, and they can reduce the heat transfer efficacy if biofilms become sufficiently thick at plate heat exchangers and pipelines (Mittelman, 1998; Vieira et al., 1993). Some populations of biofilm-associated bacteria exhibit antibiotic resistance (Vasudevan, 2014). Biofilm also enables gene transfer among bacteria which can lead to increase in the number of virulent strains (Lewis, 2001). After more than 70 years of the first report on biofilms (Zobell, 1943), still an alarm in a broad range of areas, like food, environmental and biomedical fields (Flint et al., 1997; Maukonen et al., 2003; Sihorkar and Vyas, 2001). In this current review, we have tried to put light upon the biofilms, its structure and formation, pathogenesis and green strategy for biofilm control.

2. Biofilm development

In most biofilms formation, unicellular organisms come together to form a community that is attached to a solid surface and covered in an exo-polysaccharide matrix. The microorganisms account for less than 10% of the dry mass, whereas the matrix can account for over 90%. There are a variety of mechanisms by which different microbial species are able to come into closer contact with a surface, attach firmly to it, promote cell–cell interactions and grow as a complex structure (Breyers and Ratner, 2004; Verstraeten et al., 2008). Presently five simple generalized stages are shown for formation of biofilm (Fig. 1). Step-1 planktonic cell attaches with the substrate by adhesion mechanism, Step-ll cell starts adsorption and multiplication, Step-lll early development of biofilm architecture, production of cell-cell signaling molecule and finally produce firmly mature biofilm architecture with extracellular polymeric substances (EPS) and Step-V dispersion of single cell from the biofilm. Literature review showed that both genetic and environmental factors contribute towards the microbial biofilm formation (Maric and Vranes, 2007). EPS have been called 'the dark matter of biofilms' because of the large range of matrix biopolymers and the difficult to analyzed (Flemming et al., 2007). EPS mainly consist of polysaccharides and other biomolecules like proteins, lipids and nucleic acids etc. (Cortes et al., 2011). Polymers like glycopeptides, lipids and lipopolysaccharides form a scaffold and hold the biofilm together (Flemming and Wingender, 2010). The complexity of biofilm structure and metabolism has led to the analogy of biofilms to tissues of higher organisms (Costerton et al., 1995). The comparison between planktonic and sessile biofilm interaction represents in Fig. 2.

3. Molecular basis of biofilm formation

The development of a biofilm and the release of cells (either individually or in clusters) can be regulated by population density-dependent gene expression controlled by cell-to-cell signaling molecules such as acylated homoserine lactones (AHLs) for Gram-negative bacteria (Davies et al., 1998) and specific peptides for Gram-positive bacteria (Yarwood et al., 2004). There is evidence that during this attachment phase of biofilm development, perhaps after micro colony formation, the transcription of specific genes is activated. In particular, studies with *Pseudomonas aeruginosa* algC, algD, and algU::lacZ reporter constructs show that the transcription of these genes, which are required for synthesis of the extracellular polysaccharide (alginate in this case), is activated after attachment to a solid surface (Davies and Geesey, 1995). However, in *Escherichia coli* does produce a receptor-like protein (SdiA), similar to the LuxR-type transcriptional activator in AHL-dependent quorum-sensing (Ahmer, 2004). Secondary messengers like c-di-GMP (cyclic guanosine monophosphate) are also involved in triggering biofilm formation (Jonas et al., 2009). Extra cytoplasmic function (ECF) signaling pathway and quorum sensing (QS) events play a pivotal role in biofilm formation. Two component systems of GacS (HK)/GacA (RR) are generally involved in the formation of *Pseudomonas aeruginosa* biofilm (Rasamiravaka et al., 2015). Two-component system of GraS (HK)/GraR (RR) has been found to be active in biofilms formed by *Staphylococcus aureus* (Boles et al., 2010), PIA is polysaccharide intercellular adhesin that helps in biofilm formation and is encoded by Ica operon (Cramton et al., 1999; Archer et al., 2011). The IcaR (regulatory) and Ica ADBC (biosynthetic) genes are important for the formation of biofilms and impart virulence to the bacteria (Archer et al., 2011).

4. Biofilm challenge

It has now been established that most biofilm growing bacteria

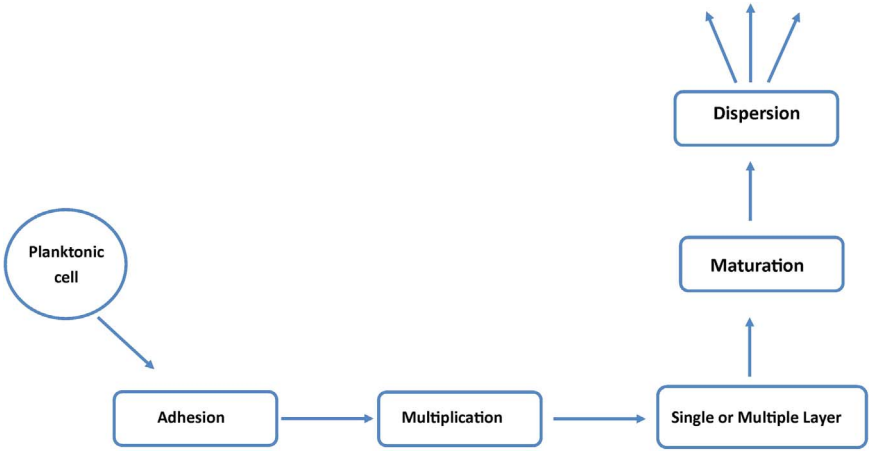


Fig. 1. Schematic diagram of stage wise formation.

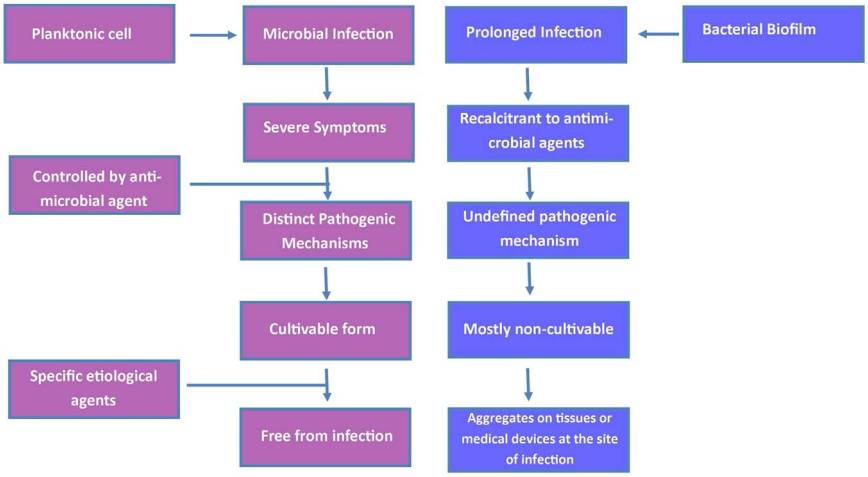


Fig. 2. Comparison of important features of infection between Planktonic and Sessile aggregates.

cause chronic infections (Costerton et al., 2003). *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* can cause overwhelming chronic infections in compromised hosts (Costerton et al., 1995). Biofilm growth occurs on natural surfaces such as heart valves (endocarditis) (Høiby et al., 1986), periodontitis (Kolenbrander and Palmer, 2004) in the lungs of cystic fibrosis (CF) patients causing chronic bronchopneumonia (Bjarnsholt et al., 2009), teeth, (Palmer et al., 2010), in the middle ear in patients with chronic and secretory otitis media (Hall-Stoodley et al., 2006; Homøe et al., 2009), urinary tract infections (Skandamis et al., 2009), in chronic rhinosinusitis (Sanderson et al., 2006). Recent analyses from chronic wounds have identified the presence of biofilm-growing bacteria, thereby explaining why these wounds persist (Bjarnsholt et al., 2008).

Diagnosing biofilm infections is extremely difficult (Hall-Stoodley et al., 2012). Even in individuals with excellent cellular and humoral immune reactions, biofilm infections are rarely resolved by the host defense mechanisms (Khoury et al., 1992). Sessile bacterial cells release antigens and stimulate the production of antibodies, but the antibodies are not effective in killing bacteria within biofilms and may cause immune complex damage to surrounding tissues (Cochrane et al., 1988). Biofilms that cause inflammation rarely grow to sizes larger than 100.

Mm (Bjarnsholt et al., 2013). Many wound pathogens are very difficult to culture (even if grown anaerobically) and persistent cells from the biofilm might even be impossible to culture (Pasquaroli et al., 2013). Antibiotic therapy typically reverses the symptoms caused by planktonic cells released from the biofilm, but fails to kill the biofilm (Marrie et al., 1982). For this reason biofilm infections typically show recurring symptoms, after cycles of antibiotic therapy, until the sessile population is surgically removed from the body (Costerton et al., 1995).

There is an urgent need to rethink both the diagnosis and treatment strategies about biofilm. When studying the impact of biofilms and their treatment in patients, it is important to combine several methods of detection to avoid false negatives (Hall-Stoodley et al., 2012). Eradicating biofilm-forming bacteria is almost impossible, and the best option is to remove the infected area if possible (Høiby et al., 2010). Different methods in microscopy extended considerable attention in the study of biofilms such as scanning electron microscopy (Zottola, 1991), epifluorescence microscopy (Holah et al.,1989), Interference reflection microscopy (Ladd and Costerton, 1990), atomic force microscopy (Caldwell et al., 1992), confocal laser scanning microscopy (Beech, 1996) and other technique such as Fluorescent in situ hybridization (Waar et al., 2005), Micromanipulation (Chen et al., 1998), Optical Tweezers (Mehta et al., 1999), shearing techniques (Bryers, 1987).

5. Biofilm battle to antimicrobial agents

One major problem caused by biofilms is their increased tolerance towards antimicrobial agents that impairs the treatment of biofilm-related infections in clinical settings (Lebeaux et al., 2014). Several mechanisms are thought to be involved in biofilm tolerance and resistance, including slow penetration of the antimicrobial agent through the biofilm, changes in the chemical microenvironment within the biofilm. One mechanism of biofilm resistance to antimicrobial agents is the failure of an agent to penetrate the full depth of the biofilm. Polymeric substances like those that make up the matrix of a biofilm are known to retard the diffusion of antibiotics (Nickel et al., 1985). Mathematical models predict that a formidable penetration barrier should be established if the antimicrobial agent is deactivated in the outer layers of the biofilm faster than it diffuses (Vrany et al., 1997). Sometimes, if the antibiotic gets degraded while penetrating the biofilm, the antibiotic action declines rapidly. Antibiotics may get adsorbed on the extracellular polymeric surfaces of the biofilm which can decrease the penetration of the antibiotic (aminoglycosides) (Shigeta et al., 1997). Occasionally, antibiotics which are positively charged in nature can bind to the negatively charged molecules of the biofilm matrix. This interaction thereby hampers the passage of the antibiotic to the biofilm depth (Nichols et al., 1988). Another mechanism is that rapid change the microenvironment of the biofilm which leads the malfunction of the antibiotics. In subterranean layers of the biofilm, there is no consumable oxygen and becomes anaerobic environment (de Beer et al., 1994). The environmental heterogeneity generated within biofilms represents in Fig. 3. It has been proved that a class of antibiotics namely aminoglycosides are not active in anaerobic environmental condition (Tack and Sabath, 1985). In response to *anti*biotics, bacteria can accumulate high levels of beta-lactamases. Scanning confocal laser photomicrographs of Pseudomonas aeruginosa PAO1-J32 biofilms have shown beta-lactamase gene (ampC) promoter activity via expression of the green fluorescent protein (GFP) reporter gene, 6 days after exposure to high dose ceftazidime (100 mg/ ml for 4 h) (Bagge et al., 2004). DNA-binding regulatory protein (brlR) involved in the biofilm-specific antibiotic tolerance of *P. aeruginosa* (Liao and Sauer, 2012). BrlR acts as a repressor of phoPQ expression with increased colistin susceptibility (i.e. higher membrane susceptibility) and tobramycin resistance (Chambers and Sauer,

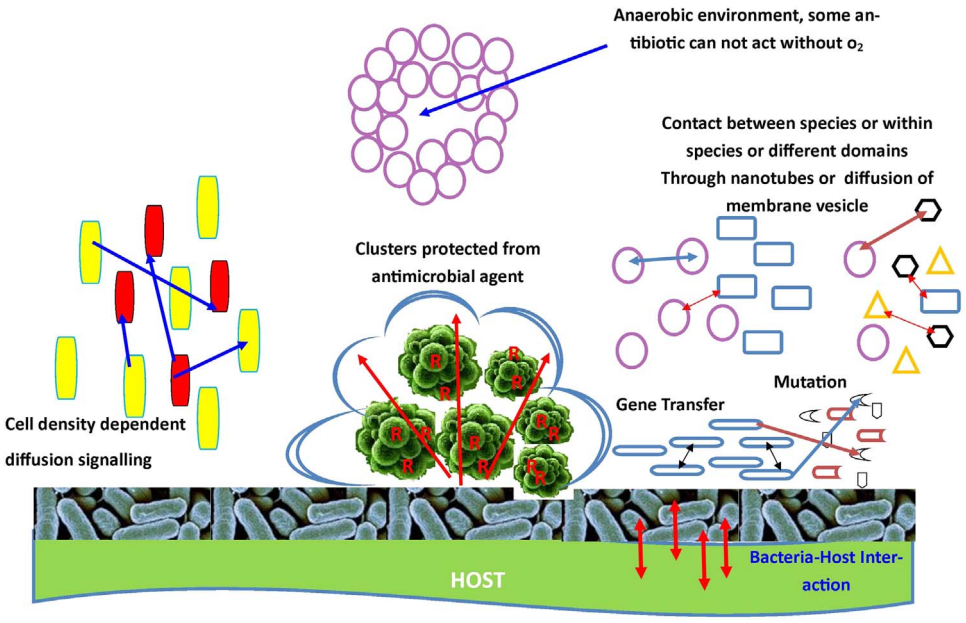


Fig. 3. Schematic representation of interaction of individual, within species, between species and multiple domain in biofilm.

2013). Sigma factor (sigma 22) encoded by algT/algU which is inhibited by the anti-sigma factor MucA and activated in response to cell wall stress, which contributes to antibiotic tolerance. In biofilms, a small subpopulation of bacteria can reversibly enter a slow-growing or starved state. These cells are known as persisters or dormant cells and highly resistant to killing by antibiotics (Lewis, 2012). There are now growing evidences that one of the main factors leading to persisters formation is nutritional stress, with a major effector molecule, ppGpp, the mediator of stringent response (Nguyen et al., 2011). Biofilms are not only recalcitrant to antibiotics, but also evade host immune-responses (Hanke and Kielian, 2012). Phagocytic cells seem not only to be unable to physically engulf the biofilm structures but also to be impaired in their activities (Scherr et al., 2015). Even though there are several outstanding reviews on antimicrobial resistance in biofilms (Bjarnsholt et al., 2013; Lewis, 2010; Soto, 2013; Mah, 2012; Fux et al., 2005), most of these focus on a specific organism, a specific mechanism, or both.

6. Common process for biofilms control

Searching remedy for biofilm infection is one of the most difficult and challenging tasks in antibacterial drug development, because different bacteria were used chemically diverse molecules to establish biofilms. Thus, there is a great problem with marketability, even if such an approach could succeed, because only specific bacteria could be targeted. Strategies to plan against bacterial biofilm must be achieved by prevention of biofilm formation rather than dispersal of the formed biofilm. The biofilms can be eliminated by adopting different strategies like Mechanical, physical and chemical methods.

7. Mechanical control

Few mechanical strategies that are being adopted for removal of biofilm-associated bacteria are: avoidance of attachment of the bacteria to the surface, Surface charge and Hydrophobicity, use of compounds that can disrupt the biofilm formation, induction of dispersion or degradation of the formed biofilm (Yang et al., 2012; Blackledge et al., 2013; Masak et al., 2014). Surface roughness can also affect biofilm adhesion. Rough surfaces are more conducive to biofilm formation and maturation, while smooth surfaces are less susceptible to biofilm adhesion. The roughness of a surface can affect the hydrophobicity or hydrophilicity of the contacting substance, which in turn affects its ability to adhere (Meiron and Saguy, 2007). Modification of the surface charge of polymers has also proven to be an effective means of biofilm prevention. Positively-charged polycationic chains enable the molecule to stretch out and generate bactericidal activity (Jansen, 1995) Hydrophobicity also plays significant role in determining the ability of bacteria to form biofilms. Some species are not able to attach to a surface and are sometimes able to establish themselves directly to earlier colonists (Jansen, 1995).

8. Physical control

Theoretically, biofilm formation on medical devices can be prohibited by altering the device's surface to prevent bacterial attachment, or by including antibacterial therapeutics in the device to prevent early stages of biofilm formation. The physical methods used for the regulator of biofilms include super-high magnetic fields (Pothakamury et al., 1993), ultrasound treatment (Qian et al., 1997), high pulsed electrical on their own (Pothakamury, 1996), low electrical fields both on their own (Davis et al., 1991). Low currents of 200 and 400 mA, using silver, carbon and platinum electrodes killed planktonic cells of Gram-positive and Gram-negative bacteria and *Candida albicans* (Davis et al. (1991). In combination with antibiotics and low electrical currents was successfully employed for biofilm control (Jass et al., 1995; Jass and Lappin-Scott, 1996). Nano-plasma trimethyl silane (TMS) coating can be used on stainless steel or hydrophilic surfaces to prevent *S. epidermis* biofilms (Ma et al., 2012). Silane xerogel coatings can provide super hydrophobic coating and act as anti-adhesion agent against biofilm-forming bacteria (Privett et al., 2011). A technique named antimicrobial lock technique (ALT) can be used to inhibit biofilm formation in catheters (Bordi and de Bentzmann 2011).

Table 1
Plant source and active compound against bacterial biofilm.

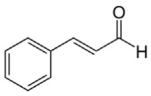
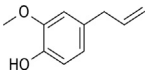
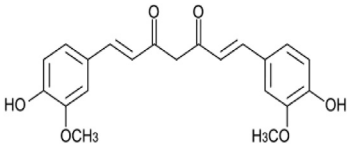
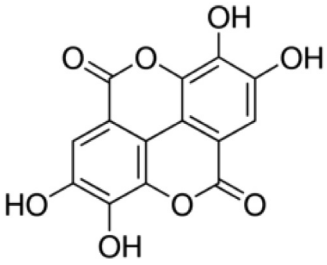
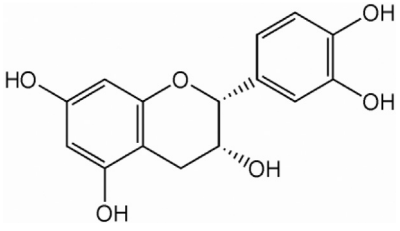
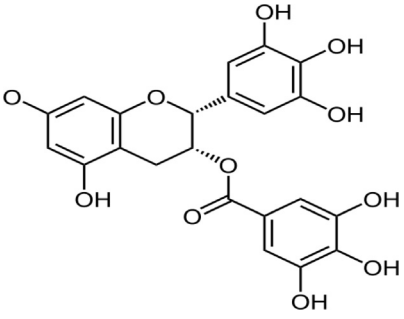
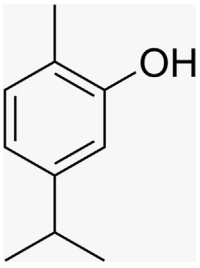
Plant Source	Active Compound	Biological Role	References
		1. Inhibited and inactivated biofilms in *Listeria monocytogenes* 2. Inhibited biofilm formation of *Staphylococcus epidermidis* 3. Inhibit biofilm formation of *Cronobacter sakazakii*	Zhou et al., 2013 Sharma et al., 2014 Amalaradjou et al., 2011
		1. Inhibited and inactivated biofilms in *Listeria monocytogenes* 2. Inhibited biofilm formation of *Klebsiella pneumonia* 3. Decreased biofilm formation of *Pseudomonas aeruginosa*	Zhou et al., 2013 Magesh et al., 2013
		1. Inhibited biofilm formation of *E. coli, P. aeruginosa, P. mirabilis S. marcescens* and *C. albicans* 2. Inhibit biofilm formation of *H.pyroli, S. epidermis* 3. Inhibit biofilm *of E. faecalis* 4. Inhibit biofilm formation of *V. harveyi, V. parahaemolyticus* and *V. vulnificus*	Shahzad et al., 2014 Sharma et al., 2014 Pattiyanthanee et al., 2009 Neelkantha et al., 2013; Packiavathy et al., 2013
		1. Inhibit biofilm formation of *B. cepacia* 2. Inhibit biofilm production of *S. dysgalactiae* 3. Inhibit biofilm production of *S.aureus, E. coli, C. albicans*	Huber et al., 2003 Ta et al., 2014 Durig et al., 2010; Bakkiyaraj et al., 2013
		1. Inhibit biofilm formation of *E. coli*	Borges et al., 2014
		1.Inhibit biofilm formation of B.cepacia 2. nhibit biofilm formation of E. corrodens	Huber et al., 2003 Matsunaga et al., 2010
		1. Inhibit biofilm of *L. monocytogenes* 2. Inhibit biofilm of *P.aeruginosa*	Upadhyay et al., 2013 Soumya et al., 2011

Table 1 (*continued*)

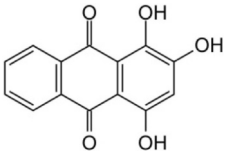
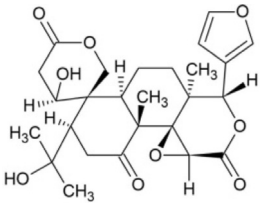
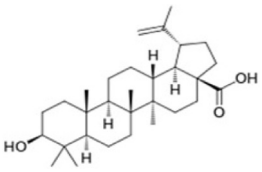
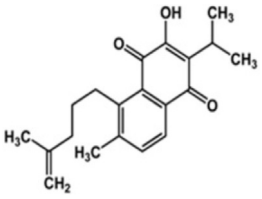
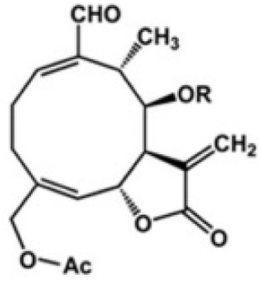
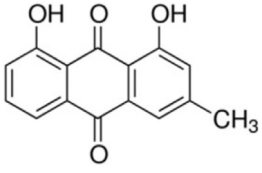
		**Inhibit biofilm formation of *P. aeruginosa***	Walencka et al., 2007
		**Inhibited biofilm formation of *P.aeruginosa* and *S.malophilia***	Ding et al., 2011
		**Inhihibit biofilm of *E. corredens* and *S. epidermidis***	Moran et al., 2014; Matasunga et al., 2010
		**Inhibit biofilm production of *K.pneumoniae* and *S. epidermis***	Magesh et al., 2013; Artini et al., 2012
		**Inhibited *C. albicans* biofilm**	Tsang et al., 2012
		**Inhibit biofilm of *Vibrio harveyi***	Hu et al., 2006

Table 1 (*continued*)

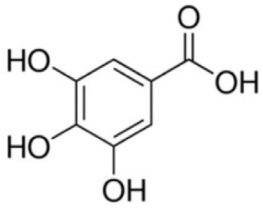
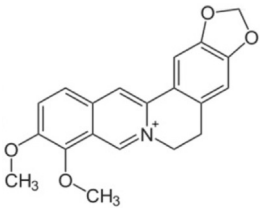
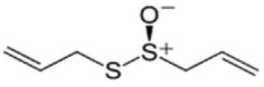
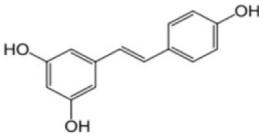
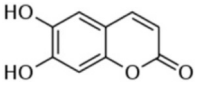
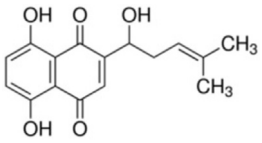
		**Inhibit biofilm of *P. aeruginosa***	Cho et al., 2013
		**Inhibit biofilm production of *S.epidermidis* and *S. aureus***	Kuzma et al., 2007
		**Inhibit biofilm formation of *P. aeruginosa* and *S.epidermis***	Pérez-Giraldo et al., 2003, Ta et al., 2014
		**Inhibit biofilm of *P.acnes* , *P. aeruginosa* and *S. epidermidis***	Coenye et al., 2012, Moran et al., 2014, Cho et al., 2013
		**Inhibit biofilm of *S.aureus* and *E.coli***	Durig et al., 2010, Lee et al., 2014

Table 1 (*continued*)

		**Inhibited biofilm formation in *P. aeruginosa* and *S. maltophilia***	Artini et al., 2012

9. Chemical control

Chemical modifications are the main strategy for biofilm prevention. Antibiotics, biocides, and ion coatings are commonly used chemical methods of biofilm prevention. N-alkylpyridinium bromide, an antimicrobial agent, was attached to a poly (4-vinyl-N-hexylpyridine), the polymer was capable of inactivating $\geq$99% of *S. epidermidis, E. coli*, and *P. aeruginosa* bacteria (Jansen, 1995). Iron-chelating compounds can be used to disrupt Pseudomonas aeruginosa biofilms if used along with aminoglycosides (Moreau-Marquis et al., 2009; Reid et al., 2009). Sodium citrate inhibited biofilm formation by several Staphylococci species in vitro (Shanks et al., 2006). Some detergents are bactericidal and some disinfectants may even depolymerize EPS like peracetic acid (Holah et al., 1989), hydrogen peroxide (Juven and Pierson, 1996), iodine (Cargill et al., 1992), chlorine (Characklis, 1989). N-acetyl cysteine, a derivative comes from the amino acid L-cysteine, inhibits biofilm formation of *S. epidermis* (Perez-Giraldo et al., 1997).

10. Green technology against biofilm

We have come to understand many things about the unique biology of bacterial biofilms. Biofilms represent microbial societies with their own defense and communication systems. There is good evidence indicating that the biofilm mode of life leads to increased resistance to antimicrobial products (Simoes et al., 2006; Simoes and Vieira, 2009). There is a continuing debate about determining factors that contribute to the formation of biofilms. We have to rethinking alternate diagnosis and treatment process against biofilm. The increase of microbial resistance to antibiotics threatens public health on a global scale as it reduces the effectiveness of treatments and increases morbidity, mortality, and health care costs (Coast et al., 1996). Moreover, the emergence of resistant bacteria to conventional antimicrobials clearly shows that new biofilm control strategies are required (Sidhu et al., 2001). So we have to rethinking alternate diagnosis and treatment process against biofilm. Following are the some green technology to fight against bacterial biofilm.

11. Bacteriophages against biofilm

Bacteria within a biofilm can show high levels of resistance to agents, such as biocides and antibiotics. Bacteriophages are ubiquitous in nature that infects bacteria naturally and may provide a natural, highly specific, non-toxic, feasible approach for controlling several microorganisms involved in biofilm formation (Kudva et al., 1999). They can either coexist with their host by inserting themselves into the bacterial genome (lysogenic bacteriophages) or destroy them (lytic bacteriophages; the type most suited to therapeutic use). Phage T4 and E27 are successfully employed against the infection of *E. coli* and *Pseudomonas aeruginosa* biofilms (Doolittle et al., 1996). *Enterobacter agglomerans* biofilms degraded by the bacteriophage through cell lysed (Hughes et al., 1998). The synergistic effect of an alkaline cleaner and a bacteriophage in the inactivation of *E. coli* O157:H7 biofilms formed on stainless steel (Sharma et al., 2005). It has been reported that phages alone can disrupt biofilm colonies of target organisms, such as *Staphylococcus epidermidis* growing on silicon catheters (Curtin and Donlan, 2006). Phages were efficient in the removal of biofilms in the early stage of development and 5 days old biofilms of *P. fluorescens* (Sillankorva et al., 2004). A bacteriophage (L. monocytogenes phage ATCC 23074-B1) was used successfully in L. monocytogenes biofilm inactivation (Hibma et al., 1997). Genetically modified phages have also been capable to attack biofilm. An *E. coli* phage, T7, was modified to express dispersin B, an enzyme that degrades b-1, 6- N-acetyld-glucosamine (an important component of biofilm) in such a way that the enzyme is released into the extracellular milieu during bacterial cell lysis (Lu and Collins, 2007). The Food and Drug Administration has amended the US food additive regulations to provide for the safe use of bacteriophages on ready-to-eat meat against *Listeria monocytogenes* (Setlow, 1992). About 80% of nosocomial infections caused by *Klebsiella pneumoniae* are due to multidrug-resistant strains. It has been reported that the ability of bacteriophages to treat mice infected with *K. pneumoniae*. Phage SS specific for K. pneumonia B5055 is well characterized, and its potential as a therapeutic agent is evaluated in an experimental model of *K. pneumonia* mediated lobar pneumonia (Cahill et al., 2000). Bacteriophages are a diverse group of viruses which are easily manipulated, and therefore have potential uses in biotechnology, research, and therapeutics. The challenge of bacteriophage manufacturing is an issue. Simultaneous with the advancement of biotechnology, phage manufacturing has increased in sophistication is capable of producing clinical-grade bacteriophage preparations along with complete protocol for the isolation, characterization, manufacturing, purification, and quality control of bacteriophages for clinical use (Merabishvili et al., 2009).

12. Enzyme against biofilm

Enzymes have also proved effective in cleaning the extracellular polymers form the biofilm matrix (Kumar, 1997). Application of enzymatic cleaning products against biofilms formed by microorganisms commonly found in dairy products (*Lactobacillus bulgaricus*, *Lactobacillus lactis*, *Streptococcus thermophilus*) (Augustin et al., 2004). Cocktail of enzyme mixture of α-amylase, β-glucanase and protease were found effective in cleaning a

simulated industrial biofilm formed during paper pulp manufacture (Wiatr, 1991). An enzymatic product consist of exopolysaccharide-degrading enzymes particularly the colanic acid-degrading enzymes derived from a Streptomyces isolate was reported for the removal and prevention of biofilm formation (vanSpeybroeck et al., 1996). Cellulase from *Penicillium funiculusum* was effective in degrading mature biofilms of *Pseudomonas aeruginosa*; and it was also found to be useful in degrading the exopolysaccharides of *Pseudomonas fluorescens* (Loiselle et al., 2003; Vickery et al., 2004). The treatment of biofilms with proteases that have broad specificity, such as Proteinase K and Trypsin, leads to biofilm disassembly (Mootz et al., 2013). The serine proteases proteinase K (from *Tritirachium album*) and trypsin have frequently been used as efficient biofilm removal agents (Gilan and Sivan, 2013). Proteases like trypsin and proteinase K can disrupt biofilms produced by *S. aureus* (Chaignon et al., 2007). Proteins reached biofilms formed by *S. aureus* with the help of Bap proteins were susceptible to Proteinase K mediated detachment and dispersal (Shukla and Rao, 2013). It has been reported that bacteria use extracellular DNA to form biofilms. To disrupt such kind of biofilms, DNase I can be used to degrade the e DNA released by *S. aureus* (Izano, et al. 2008). The combination of proteolytic enzymes with surfactants increased the wettability of biofilms formed by a thermophilic *Bacillus* species and, therefore, enhanced the cleaning efficiency (Parkar et al., 2004). Synergistic action of enzymes in combination with surfactants and phenolic antimicrobials (Jacquelin et al., 1994). Besides, the use of enzymes in biofilm control is still inadequate due to the low prices of the generic chemicals used today compared with the costs of the enzymes. New formulations containing several different enzymes seem to be fundamental for a successful biofilm control strategy.

13. Plant extract against biofilm

The increase of microbial resistance to antibiotics threatens public health on a global scale as it reduces the effectiveness of treatments and increases morbidity, mortality, and health care costs (Coast et al., 1996). Several researchers have suggested that the plants do exhibit antibiofilm activity. Nowadays, plant products have found widespread application in the medical and food industries as alternatives to conventional therapy (Shan et al., 2007). Plant extracts from a variety of plant species, including common culinary herbs, are under extensive study in an effort to isolate and characterize their bioactive compounds. Table 1 summarizes some plant active component against specific biofilm control.

14. Conclusion

In view of the increased resistance of bacterial biofilms to antimicrobial treatments, new strategies should be implemented for the control of biofilms. Current therapeutic approaches for prevention of biofilms is limited to use of antimicrobial agents and post infection remedy lies in surgical removal of the biofilm followed by continued antibiotic administration. Bio control strategy against biofilm should be considered as a supplement to the present treatment process. Multidisciplinary approaches like Scientist, Biofilm researchers, Doctor, Health profession, Instrument engineers etc. will be necessary in the years to come to translate the data obtained from various biofilm researches to clinic to overcome biofilm associated infection. Such multidisciplinary communication can hope that prevention and inhibition of biofilms by bacteria can be achieved in near future.

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