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REVIEW ARTICLE

Impact of Biofilm Infection and its Treatment

[*]P.M Diaz[1]

[1]Ponjesly College of Engineering, Nagercoil, Kanyakumari, India.

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ABSTRACT

Microorganisms are generally attached to the environment and create an extracellular matrix of polysaccharide material which finally leads to the formation of biofilms. These biofilms occur as a result of interaction between the extracellular polysaccharide material and microbial cells. They have several advantages and disadvantages. The drawbacks of these biofilms are that it causes chronic bacterial infection, infection on medical devices, contamination of food, deterioration of water quantity etc. This leads to serious problems for living and non-living organisms. It is due to the fact that the augmented resistance of biofilm associates with the organisms to form antimicrobial agents and these organisms have the potential to cause infections in patients with inherent medical devices. In hospital, the formation of biofilms on medical equipment and vents allow group of microscopic organisms to persist as reservoirs that can readily cause diseases by directly attacking the body tissues which spread to other patients too. Biofilm infections have a major role to play in the clinical decision-making process. This paper describes about the analysis of biofilm formation and also reviews the existing and propagative mechanisms of biofilms in the natural environment. The possible therapeutic approaches and antibiotics treatment in order to overcome the harmful effects of microbial biofilms are also reviewed.

Keywords: Biofilms, Microorganisms, Antimicrobial agents**,** Planktonic cells, Chronic inflammatory diseases.

1. INTRODUCTION

Bacteria that produce a structure of multicellular communities are known as biofilms. This biofilm contains large number of microorganisms which stick to each other on the environmental surface. It produces a matrix source of Extracellular Polymeric Substance (EPS). Normally, it is a polymeric composite which is composed of extracellular polysaccharides, DNA and proteins. It is usually seen in floating mats on liquid surfaces and also on the surface of leaves particularly during highly humid climates. Biofilm can also form solid substrates. It may be formed on the body of living or non-living things and can be widespread in hospital, natural and industrial environment [1, 2]. The microbial cells growing in a biofilm are physiologically separated from similar planktonic organic cells. These biofilms may contain cellular recognition of specific or non-specific attachment sites on the surface [3, 4]. It undergoes a phenotypic shift in cell behaviour when it changes the biofilm growth mode where large number of genes are controlled differentially. [5] These biofilms protect the bacteria. They are more resistant to traditional antimicrobial treatments causing serious health risks. Biofilms are normally produced through various kinds of infrastructure such as oil refineries, plumbing, paper mills, medical implants, building HVAC systems and heat exchangers [6]. It also contaminates certain polymers like lipopolysaccharides, lipids and glycopeptides in order to form a scaffold. Apart from that, microbial biofilm has been widely used for heavy metal remediation. Marine fouling is one of the processes of microbial biofilm in which it leads to the growth of algae, plants, animals and microorganisms on ship hulls. It is followed by the increase of higher marine organisms and raise of fuel expenditure of pilgrim ships up to 60% [7]. In the medical field, these biofilms

*Corresponding author. Tel.: +919443558554
Email address: pauldiaz71@gmail.com (P.M.Diaz**)**
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cause unpredictable infections which may lead to dangerous diseases, triggers immune response and even obstructs indwelling catheters. Finally, patients in the hospital acquire infections leading to death. [8] The population of biofilms is increasing because of several reasons such as bacterial resistance against bacteriophages and antibiotic resistance. Secretion of diverse surface molecules decreases the development rate, virulence factors, chemical biocides, amoebae, etc. Therefore the environment must be protected from the effects of biofilms by following various precautions such as exterior assaults and other chemical treatments including antibiotics.

2. FORMATION OF BIOFILMS

[9] The biofilm formation is quite an intricate process, but can be generally described very shortly in four basic steps as follows.

- Conditioning film deposition on the surface,
- Attachment of microorganisms to the conditioning film,
- Growth and colonization of bacteria.

This results in biofilm formation. According to [10], at first the conditioning films change the environmental properties of the substrate and allow microorganisms to get deposited on the surface. The next step is the microorganism attachment which is still unidentified. The thermodynamic interaction mechanisms and DLVO theory are the two methods that have been used to explain the initial microbial attachment. [11] A cell has several parts such as pili, flagella, fimbriae or glycocalyx that may have an impact on the microbial attachment rate. The next process is the growth and colonization. In this stage, polysaccharide production anchors the bacteria to the surface and allows the colonies to grow on the surface. The method of colonies growth is the most important step in biofilm accumulation. A fully developed biofilm contain interstitial spaces that separate vertical structures from EPS matrix. These fully developed biofilms have a heterogeneous structure and has the capability for mass internal transport. [12] Moreover the polysaccharides may also contain certain materials from the surrounding environment including soil particles, minerals and blood components that are not limited. The last step of biofilm formation is known as dispersion and in this final stage the biofilm is completely developed. This may contain slight changes in its size and shape. Figure A1 represents the formation of biofilms [13].

3. SPREADING OF BIOFILMS IN PATHOGENIC AND NORMAL ENVIRONMENTS

In the protected growth mode, bacterial population creates planktonic cells, which decreases the survival chances. These separated cells may settle on new surfaces in order to form huge planktonic population in the rare environment. A common exception to the overall trend happens in the tremendous oligotrophic environments of deep groundwater and deep ocean, where bacteria would be in a progressive starvation stage [14]. Since, cells change their cell surface and their peptide synthesis patterns in response to hunger, they do not spend their scarce metabolic resources to exopolysaccharide synthesis. Particularly, insoluble substratum of nutrient is quickly consumed by bacteria within these aquatic environments. A consistent presence of these materials in an aquatic system motivates the growth resulting in large and severe population of biofilm. The availability of high nutrient levels and the large surface area in numerous industrial aquatic systems has made the formation of biofilm much easier. [15] Adherent population is the industrial system which includes filter insertion and injection faces, fouling products and destructive metabolites. Bacteria are slowly settled down in the water-cooled side of metal surfaces in heat exchangers and as a result, the biofilm is formed over the surface spreading gradually around the nature and pathogenic environment [16].

4. BIOFILMS AND INFECTIOUS DISEASES

The causes of biofilms have been found to be complicated among the wide range of microbial infections in the human body. [17] Biofilm contains certain number of microorganisms which can even modulate the pathogenic bacterial potential as it is evident from cariogenic bacteria in plaque biofilms. According to the statement of current public system, National Institutes of Health (NIH) has declared that the microbial infections caused by biofilms are more than 70%. So the

infection causing rate of biofilm is very high, excluding common problems such as urinary tract infections, common dental plaque formation, child middle-ear infections, catheter infections and gingivitis. It is similar to the way the E. coli, staphylococcus aureus, gram-positive pathogens and haemophilus influenzae cause biofilms. All these infections are often hardly treated. [18] These infections affect human body by way of using contact lenses as well. Some of the deadly infections are infections in cystic fibrosis and endocarditis. Biofilm infections also occur by means of permanent usage of indwelling medical devices in the heart valves and joint prostheses of human body. Some of the biofilms associated with other infections have been discussed [19].

4.1. Dental plaque

Dental plaque is one of the biofilm infections that occur on the surface of teeth. It is a yellowish biofilm that is formed on teeth surfaces. The growth of microorganisms occurs over the teeth and gingival tissues due to high bacterial metabolic concentration which leads to dental diseases affecting teeth. Biofilms include groups of disease-causing bacteria and these bacteria produce cavities and gum diseases in teeth. The formation of dental plaque biofilms exist on various surfaces of tooth including tissues, gingival crevices, smooth surfaces and stagnant sites of crevices and fissures as these sites are hidden from the forces of removal like a toothbrush clean [20]. Moreover, the growth of plaque biofilm process and changes of microbial composition produce a gram-positive biofilm. In-order to overcome these problems, streptococcus-rich structure filled with gram-negative anaerobes is employed in its extra mature state.

4.2. Kidney stones

One of the reasons for the formation of kidney stones is the impact of biofilm caused by bacteria. They cause diseases in kidneys by blocking urine flow and causing inflammation that can result in kidney failure. According to [21], these stones are generated by the interaction between infecting bacteria and mineral substrates that are derived from the urine. This interface results in a severe biofilm composed of bacteria, mineralized stone material and bacterial exo products [22].

4.3. Ear infections

According to [23], the formation of ear infections is mainly caused by biofilms. These infections can be either long-lasting or severe. Children are prone to ear infections as they are easily affected by various viruses leading to infection. Children's body structure is entirely different from adults. The area inside the child's eardrum is shaped almost horizontally. Bacteria flourish like fluid and this fluid builds-up in the child's eardrum. Stagnant motion is common. In adults, these bacterial fluids are normally emptied out because the area behind the ear tubes slope downward, thus preventing bacteria from settling and breeding. Extreme bacterial fluid can lead the eardrum to fracture because of the pressure inside it.

4.4. Chronic inflammatory infections

Scientific researches confirm that chronic inflammatory diseases are caused by biofilms. These diseases cause infection by large micro biota of chronic biofilms and L-form bacteria. In recent years, it was found that bacterial biofilm results in chronic wounds [24], especially in the setting phase of the inflammatory condition of wound repair**.** The bacterial biofilm causes urinalysis infections. To overcome these infections, antibiotic therapy is been used and it is an important element that plays a major role in the treatment of chronic inflammatory diseases.

5. TREATMENT OF BIOFILM INFECTIONS

[25] Treatment given to the patients who are affected by the biofilm infections is currently a complex and complicated challenge for clinicians and microbiologists. The affected patients due to biofilm infections are very difficult to treat and usually antibiotic treatment is insufficient. The nature of microbial biofilms has helped to overcome the biofilm infections. Now, treatment of biofilm causing infections requires cooperation from surgery, clinical microbiology, interior medicine, pharmacology and basic science. In some other cases, only biofilm reduction is possible followed by the treatment of chronic biofilm suppressive to relapse with an exacerbation. [26] Recently, the treatment of biofilm consists of selection of antibiotics as sensitive and well penetrating. It should also be dealt with the removal of infected indwelling devices, supplementation of the treatment of

anti-QS or agents of biofilm dispersal and early administration of high dosage antibiotics.

According to [27], biofilm infection treatment needs antibiotics to improve adequate effective antibiotic concentration at the biofilm infection site. Altogether indication agents for the treatment of complicated urinary infections include rifamycins, quinolones, macrolides, fusidic acid, nitroimidazole, lincosamides, tetracyclines, sulfonamides and oxazolidinones, glycopeptide, aminoglycosides and polymyxin. This produces results in faster metabolism and significant oxygen consumption systematically. If oxygen supply could not meet the demand, glycolysis method is opted which leads to acidosis and the effects of antibiotics could be affected by pH values. [28] reports that very low value of pH could rise rifamycin SV effects and reduce the effects of β-lactam antibiotics. Hence biofilm infection treatment using antibiotic and acid-base balance correction is used to treat disorders and it could be the most important factor for the biofilm infection treatment. As a result, microbial biofilm can be managed by either breaking the biofilm structure or by preventing the attachment of the microorganism to the biofilm surface, where the biofilm is formed. [29] highlighted that therapeutic methods are the most significant technique to be focused for providing good treatment and prevention of such biofilm-intermediated infections. Currently, methods which do not contain microbial approaches are also being discovered for further inhibition of biofilm.

6. CONCLUSION

In this review, it is concluded that the treatment for biofilm infections are very complicated due to the antibiotic resistance and risk factors for biofilm formation. The well-known omnipresent nature and new medical technologies continue to reveal their major role in generating remedies for various infectious diseases. The treatment provided for biofilm infected patients require further advancement in clinical, surgery, pharmacology and multidisciplinary cooperation which may contribute in the prevention of biofilm infections. Moreover, the scientists from scientific and medicinal field should take collaborative efforts to explore these difficult tasks of the microbial biofilms. It is expected that in future, the clinical and medicinal field may adopt several techniques regarding the molecular mechanisms. New approaches are yet to be discovered in order to manage the formation of biofilm, their toxicity and drug resistance. Therefore further research must be required for the awareness of biofilm infections. Effective strategies on both control and treatment of biofilm infections must be followed.

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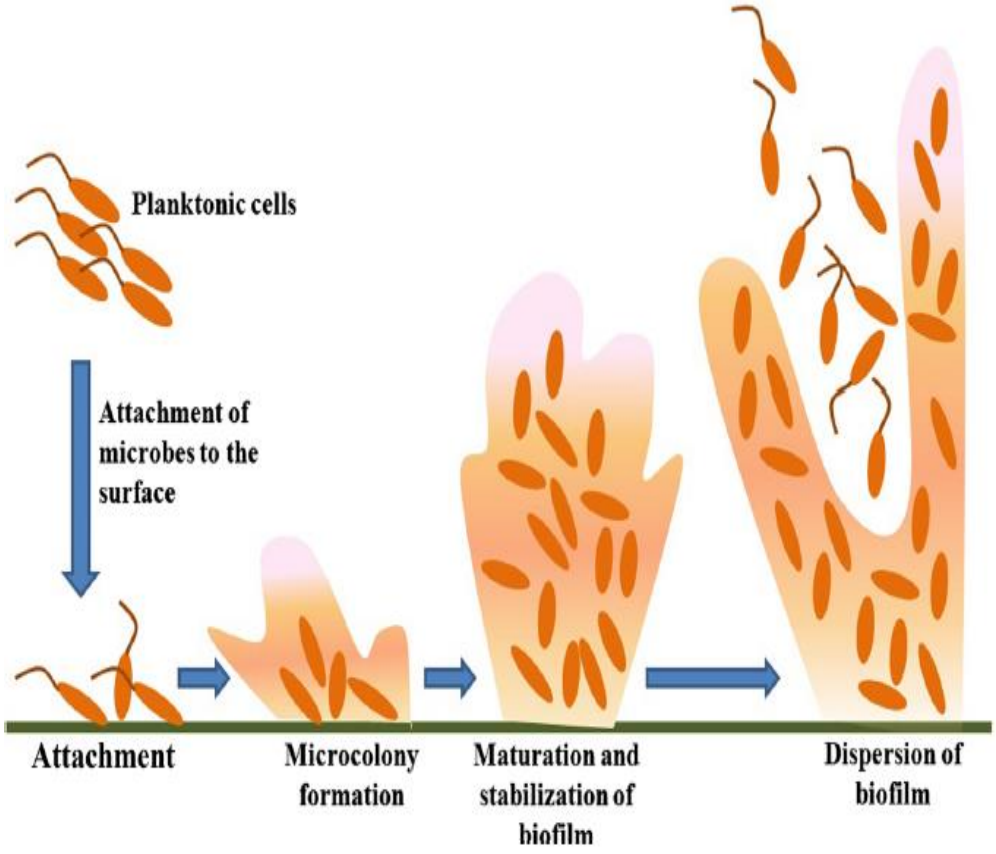
APPENDIX A



Adapted from [13]

Figure A1.Biofilm formation