STM JOURNALS

Research & Reviews: A Journal of
Microbiology & Virology

https://journals.stmjournals.com/rrjomv/

ISSN: 2230-9853 (Online)
ISSN: 2349-4360 9(Print)
Volume 16, Issue 2, 2026
May–August
DOI (Journal): 10.37591/RRJOMV

Review RRJOMV

A Review of Biofilm: Mechanism of Dispersal and Eradication Strategies for Medical Devices

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Abstract

Biofilm is formed by the adhesion of different microorganisms with each other and to the surface forming a matrix-like structure. Biofilm on medical devices forms over a period which causes severe infections and is harmful to immune-suppressed patients. Therefore, removal from the medical devices is required to get rid of it. These biofilms can be removed by various methods such as scrubbing or high-pressure spraying, steam removal, and usage of chemicals or disinfectants, etc. However, it has been seen that microbial biofilms are highly resistant to these substances. Therefore, we need new methods to eradicate biofilms from the surfaces of medical devices. These ways may include the coating of different medical devices with polymers, paints, and the application of nanoparticles of different metals. Furthermore, advanced approaches – such as nanotechnology-based coatings and surface modifications – have shown promising potential for preventing microbial adhesion and biofilm formation. Nanoparticles, particularly those of silver, copper, zinc oxide, and titanium dioxide, may exhibit strong antimicrobial properties and can interfere with microbial growth and biofilm development. Polymer-based coatings can also provide a protective barrier that reduces the attachment of microorganisms to medical device surfaces. These approaches may improve the durability and safety of medical devices while reducing the risk of device-associated infections. Therefore, the development of effective, bio-compatible, and environmentally safe anti-biofilm strategies is essential for controlling persistent biofilm-associated infections and improving patient outcomes.

Keywords: Antibiotics resistance, biofilm, biofilm eradication, biofilm on medical devices, nanoparticles combating strategies

INTRODUCTION

Biofilms are complex structured communities of microorganisms that form inside the extracellular matrix or by adhering to the surfaces of materials. This structure protects them from nutrition deficiency or severe conditions such as dehydration [1].

Biofilms are the leading cause of hospital infections, particularly in patients with weakened immune systems. Catheters, contact lenses, heart valves, pacemakers, dentures, and joint implants offer an ideal surface for biofilm growth. Biofilms are responsible for around 50% of hospital-acquired illnesses [2].

Biofilms can be controlled with antibiotics, such as imipenem and colistin, but they are difficult to eradicate at low concentrations and can be harmful at large doses. Treatment is challenging because greater MIC and MBC are needed to eradicate biofilm bacteria [3].

Additionally, biofilm bacteria are shielded from the immune system. As a result, the complement

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Received Date: July 18, 2026
Accepted Date: August 20, 2026
Published Date: August 21, 2026

Citation: Ayushi Sharma, Anupam Singh. A Review on Biofilm: Mechanism of Dispersal and Eradication Strategies for Medical Devices. Research & Reviews: A Journal of Microbiology and Virology. 2026; 16(2): 51–56p.

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system and phagocytosis are less active. Numerous elements, including structure, oxygen and nutrition availability, metabolic activity, and genetic resistance, affect biofilm resistance [4].

Oxygen also plays a key role; antibiotics are only effective in oxygen-rich biofilm regions. High exposure can increase the rate of mutation and resistance in bacteria [5].

Some biofilms are not immediately adhered to the surface but rather develop clusters within the matrix (like cystic fibrosis in patients). This also leads to chronic infections by preventing the immune system and medications from working [6].

Several techniques are utilized to cure or control biofilms, including removing infected implants, targeting cyclic di-GMP, and suppressing quorum sensing [7].

Research is currently underway to develop new anti-biofilm drugs. These developments are designed to improve treatment efficacy and reduce biofilm-related infections. Scientists hope to develop more effective therapeutic techniques that can be used in clinical settings by acquiring a better knowledge of the mechanisms involved in biofilm formation and persistence [8].

NATURE AND FORMATION OF BIOFILM

Biofilms are very sensitive to their environment; that is, they can transform to changes in their environment and the bacterial colonies can easily separate themselves from the biofilm colony [9]. When these detach from their colony, they can easily be removed by chemicals. It is often observed when they detach in form of clumps, they persuade the protective property and are difficult to kill (as shown in Figure 1) [10].

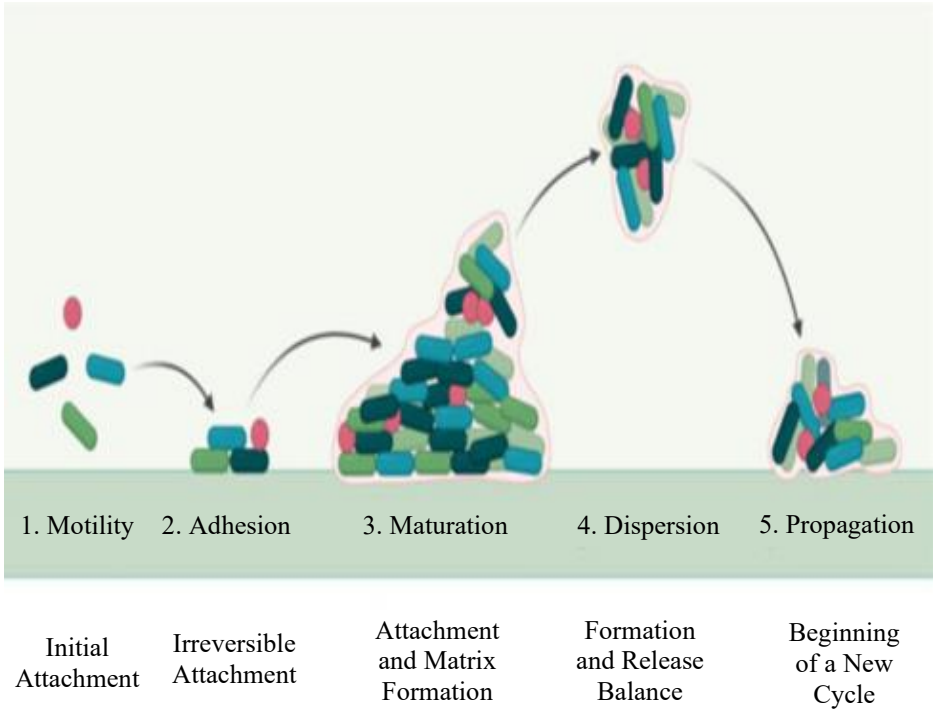

Figure 1. Representation of biofilm production.

In a few cells, it is observed that cells produce chemical signals and which causes a change in the genetic expression in the extracellular polymeric substances (EPS). Initially, a bacterium is introduced to a surface driven by gravitational force or Brownian motion and suffers attractive and repelling forces that depend on temperature, pH, property of the medium, level of nutrients, etc. [11].

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BIOFILM ON MEDICAL DEVICES

It has been observed that several biofilms are developed on different medical devices which cause infection in patients when used. Bacteria – such as *Corynebacterium* spp., *Acinetobacter* spp., *Candida* spp., and *Enterococcus* spp. – were isolated from biofilm present on central venous catheters. These bacteria present in biofilms are tough to eradicate as they possess a protective sheet for the resistance of antibiotics. Multiple tests are being used currently for the detection of biofilms includes, DNA based method (PCR, Sequencing), Fluorescence In-Situ Hybridization (FISH), and confocal scanning laser microscopy, etc. [12].

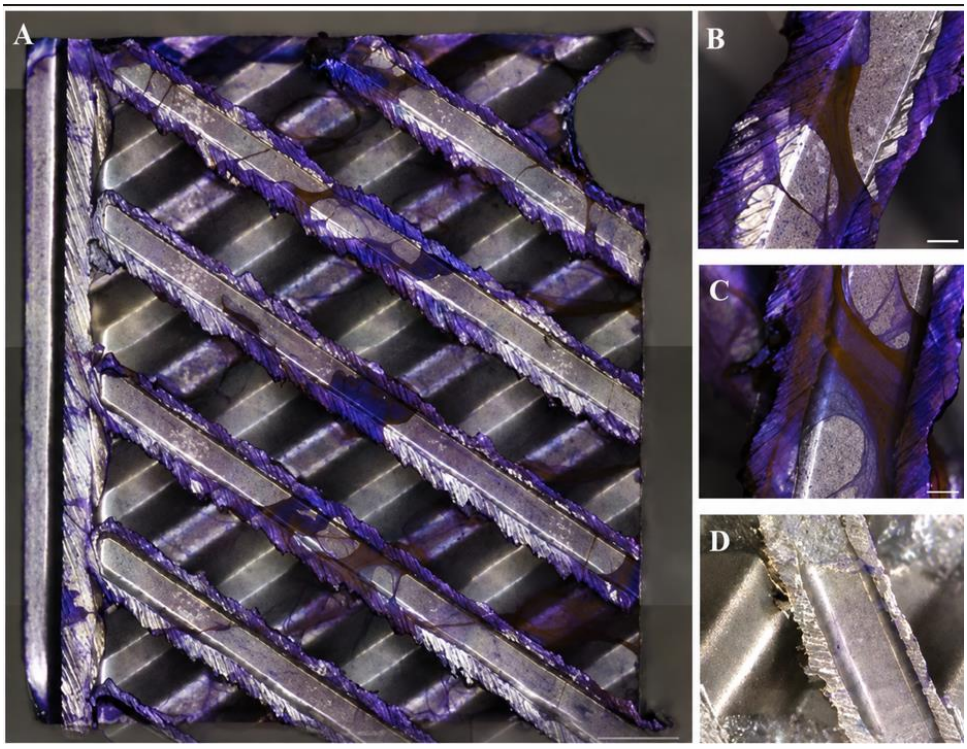

Figure 2. Crystal violet staining (purple) [13].

Some essential medical devices are given following on which biofilms developed [13]:

- Central venous catheters.
- Contact lenses.
- Endotracheal tubes.
- Intrauterine devices.
- Mechanical heart valves.
- Pacemakers.
- Peritoneal dialysis catheters.
- Prosthetic joints.
- Tympanostomy tubes.
- Urinary catheters.
- Voice prostheses.

METHODS FOR ERADICATION OF BIOFILM

When technology wasn't so developed, people were hooked into pure nature and natural resources for combating bacterial biofilms. Those methods include the usage of plant extracts (Icartin and Resveratrol), honey, cumin oil, vegetable, and essential tea tree oil. During a recent study, it's found that a compound (methyloxycarbonylselenoesters) is effective in inhibiting the activity of bacterial biofilm [14].

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Using Direct Current (DC) & Pulsed Corona Discharge

Cold air plasmas of DC and pulsed corona discharges were used for disinfection of *Streptococci* biofilm and *Bacillus cereus* spores. The curbing of the number of bacteria in the biofilm by DC & pulsed corona reached 2.4 logs with 10 min treatment time and 3.3 logs with water spraying by 2-minute treatment. This shows that both methods can productively reduce the bacterial population in the biofilm on plastic surfaces [15].

Using Nitroxoline (Anti-Bacterial Agent)

Recent discoveries have been made which shows "Nitroxoline," an anti-bacterial agent was found to stand against drug-resistant pathogens like *Acinetobacter baumannii* and *Staphylococcus aureus.* It is used to cure urinary tract infections. The ability of nitroxoline to chelate different bivalent metallic ions is primarily responsible for its antimicrobial activity mode of action. It's been suggested that it interacts with Mg^{2+}, stabilizing the lipopolysaccharide molecules that make up the bacterial membrane's outer layer [16].

As a result, the bacterial surface becomes more hydrophobic, reducing bacterial adhesion to the catheter. The fact that nitroxoline's antibacterial activity is decreased in the presence of Mn^{2+} and Mg^{2+} but not of Ca^{2+}, Na^{+}, or K^{+} supports this mechanism [17].

Using Silver (Ag) Nano-Particles

Several fungi secrete various biologically relevant substances which act as stabilizing agents during the synthesis of colloidal metal nanoparticles including silver nanoparticles. These nanoparticles notably decreased the fatty acid content in the cell membrane of *E.coli* cells. This showed that it can **b**e used to eradicate bacterial biofilm. Microorganisms provide a renewable and versatile solution for the production of value-added items. Fungi secrete large amounts of bioactive compounds that serve as both reducing and stabilizing agents in the synthesis of colloidal metal nanoparticles, like silver nanoparticles, which have strong antimicrobial properties and can be used in a variety of industries [18].

Using Electrical Methods

The removal of biofilm from the surface of a device can be done by using an electrical method. Direct current, Radiofrequency and AC block the attachment of biofilm, as Electrical field increases the efficacy against biofilm known as "bioelectric effect". A study shows that when direct electrical current is applied across the flow cell through Platinum electrodes immersed in seawater will effectively strip pre-grown biofilm from the membrane surface. This successful biofilm removal may be due to a number of conflicting factors [19].

Using Iron Oxide Nano-Particles

An advance research carried out and they concluded that nano-carriers containing super paramagnetic iron oxide nanoparticles (hydrophobic) and antibiotic methicillin (hydrophilic) penetrates 20 μm thick biofilm by the application of external magnetic field with high efficiency. Antibacterial and anti-adhesive properties are proposed for devices coated with iron oxide nanoparticles against microorganisms. It also works on biofilms that have already evolved. Iron oxide nanoparticles produce reactive oxygen species, which increase hydrophobicity and reduce biofilm adhesion to the surface, modifying nano-particles for anti-biofilm properties [20].

Using Carbon Nano Tubes (CNTs)

As studies suggested that CNTs possess antimicrobial and electrical properties and due to which its application over the surface of medical devices will reduce the attachment of spores and bacteria. Multi walled CNTs have shown to be effective in reducing *E. coli* planktonic cells and biofilms. This was the first report where an anionic dye conjugated to CNT was employed to enhance photo destruction activity against Gram negative bacteria. This photodynamic therapy may be a viable solution to currently active antimicrobial treatments for biofilm-related diseases [21].

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BIOFILM CONTROL AND TREATMENT

Biofilm control is a major challenge due to its complex structure and high resistance against conventional treatments. If biofilms are not managed effectively, it may lead to an increase in infection-related mortality and morbidity both. Excessive use of antibiotics there is highly virulent and drug-resistant microbial stains are developing, which highlights the need of advanced therapeutic strategies [22].

In biofilm management, preventive approaches play crucial and important role. There is an involvement of surface modification, preoperative or postoperative precautions, and antimicrobial coating on medical devices in it. Early-stage biofilm formation can be inhibited through antibacterial agents, environmental modifications and surface treatments [23].

But when once biofilm gets mature, it is difficult to eliminate it. Multiple strategies are employed such as enzymatic degradation of EPS (extracellular polymeric substances), mechanical removal, vaccination approaches, and biofilm dispersal techniques. In clinical settings, physical, biological, chemical and combinational approaches are used to disrupt the mature biofilms [24].

Traditional antibiotics show limited effectiveness against biofilms due to poor penetration, altered metabolic state of bacteria, and resistance mechanisms such as efflux pumps and enzymatic degradation. High-doses and combination therapies have been seen to be effective in some cases, but their toxicity and limited success are among major limitations [25].

Natural compounds or bioactive agents also show significant anti-biofilm activity by interfering with microbial communication and gene expression. Probiotics also play important role by inhibiting pathogen adhesion, enhancing immune response, and suppressing the biofilm formation [26].

Engineering technologies – like gene editing (CRISPR-Cas system) – are used for reducing the bacterial virulence and antibiotic resistance. Monoclonal antibody-based therapies were also target biofilm components, although there is a limited clinical application available of them [27, 28].

CONCLUSION

Biofilms pose a risk of slowing wound healing, making it more difficult to cure infections and diseases such as otitis media, endocarditis, cystic fibrosis, periodontitis, and chronic prostatitis. As its eradication of is very tough to perform. Alternative strategies to eradicate biofilms, as described here, offer promising future perspectives for the fight against these recalcitrant high-density infections. As our understanding of those mechanisms continues to enhance, so will our ability to develop compounds which may bypass them.

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