Received: 24 February 2024 | Revised: 15 April 2024 | Accepted: 22 May 2024 | Published online: 29 May 2024

REVIEW

Medinformatics
2024, Vol. 00(00) 1–12
DOI: 10.47852/bonviewMEDIN42022687

BON VIEW PUBLISHING

Fighting Biofilm Bearing Microbes, Global Challenges, Initiatives, and Current Novel Therapeutics/ Antibiofilm Strategies: A Narrative Scientific Record

Bright E. Igere[1],* and Morenike O. Adeola[1]

[1]*Department of Biological Sciences, Dennis Osadebay University, Nigeria*

Abstract: Microbial survival against diverse anti-biocidal agents has advanced beyond single organism interaction into intricate sessile cells consisting of dynamic three-dimensional extracellular complex matrix of water channels. Such complex architecture is built with heterogeneous and variable components that encourage failure of antimicrobial-chemotherapeutic strides especially among biofilm bearing/expressing microbes (BBM). This is a noteworthy public health concern as such occurrence has welcomed global attention in recent times with focus on fighting BBM as well as exploration of novel therapeutic strategies. A narrative scientific description of biofilm as a community of microbes wrapped in extracellular polymeric substances (EPS) was reviewed. The challenges of disease/infection recalcitrance, the risk to public health, and the necessity to develop novel therapeutics for the management/control and suppression of biofilm-linked infections were emphasized. It also summarized potential approaches including the use of antibiofilm/anti-adhesion agents, antimicrobial proteins, aptamers, nano-particulates, quorum sensing inhibitors, and peptide or protein-based nucleic acids while discussing the agents' efficient potential ability. Such antibiofilm agents/mechanisms and their target-specific-therapeutic relevance promise a future for the management/control of biofilm-associated microbial infections. Its application may also herald a generational effective combination therapy against illnesses/infections caused by BBM and serve as a potential source for BBM global control.

Keywords: extracellular complex matrix bearing organisms, antibiofilm strategies, microbial infections, biofilm, novel therapeutics

1. Introduction

Biofilm, a complex and aggregated (encapsulated) community of stable microorganisms in an extracellular matrix, has been produced/developed in a multitude of biological, ecological, and environmental materials by diverse clinical/environmental microbial strains [1, 2]. Such capacity has created in strains the propensity to withstand antibiotic resistance, thwart host immune responses, withstand high environmental stress, and be linked to chronic and recalcitrant infections, making biofilms bearing strains pose a serious global health risk [3]. Morbific bacteria as well as biofilm bearing/expressing microbes (BBM) possess the potential to create biofilms in tissues and biomaterials, which may result in persistent infections that are difficult to manage/control [4]. Over the years, diverse related investigators have reported various strains which include *Proteus mirabilis* [5], *Klebsiella pneumonia* [6], *Streptococcus viridians* [7], *Pseudomonas aeruginosa* [8], *Staphylococcus epidermidis* [9], *Enterococcus faecalis* [10], *Staphylococcus aureus* [11, 12], and *Escherichia coli* [13], which harbor such potential. Yet the menace of BBM has remained one of the concerns in the control of B-bearing strains especially among common bacteria strains in diverse nexus. The ability of bacteria to thrive in the presence of high doses of antibiotic agents (also called resistance) has also been linked with the recalcitrance of BBM-associated infections [14, 15], which has resulted in failure of treatment and recurrence of infections. In addition, it has been demonstrated that, in comparison to the population of planktonic cells, the microorganisms contained within any formed biofilm are more resistant to traditional antibiotic therapy [15]. This has aroused high risk among biofilm-based nosocomial infections in patients especially with implanted medical devices such as cardiac pacemakers, joint prostheses, prosthetic heart valves, catheters, dental implants, and contact lenses [16]. Such implanted foreign objects offer a model surface on which bacterial cells may adhere, which promote nonspecific adherence to elements and create shear pressures, hydrophobicity, and electrostatic interactions [17].

The concerns arising from BBM have also extended onto oral-pharyngeal bacteria which are shown to attach to hydrophobic and hydrophilic abiotic surfaces including rough surfaces than smooth ones. This is a common occurrence among BBM as it covers/

*Corresponding author: Bright E. Igere, Department of Biological Sciences, Dennis Osadebay University, Nigeria. Email: igere.esegbuyota@dou.edu.ng

clogs abiotic surfaces on dental restorative and implant materials [18]. This may result damage or destruction of inflammatory conditions around the oral-dental region after surface implantation known as periimplantitis (this involves a microbial infection and an excruciating damage to the hard and soft tissues around dental implants and may even cause the implantation failure) [19].

The development of biofilm by various strains may also be traced to exposure to subinhibitory antibiotic concentrations (SIAC) (also described as exposure to antibiotic/antimicrobial agent concentrations lower than the minimum inhibitory concentration), thereby reducing the strains' susceptibility to antibiotics [20, 21]. Such has been the recent demonstration among clinical *Enterococcus faecalis* strains' as they speedily acquire the ability to form biofilms on exposure to subinhibitory antibiotic dosages [22]. It was theorized that the SIAC may have occurred in hard-to-reach areas, such as dental root canal, or it may have been introduced by administering antibiotic incorrectly. Such observations have necessitated a search for novel control strategy and management of BBM especially in an infection-based case. The search for novel antibiofilm drugs and tactics has intensified due to the incapacity, inability, failure, and poor success in the antibiotic/antimicrobial treatments and therapy to eradicate bacterial biofilms at subinhibitory and/or inhibitory concentrations. In the light of the aforementioned concerns of BBM and the need to control, the emergence and reemergence of such superbugs, this study was conducted to appraise the need for a research-based BBM control strategy. This scientific record discusses the formation of biofilms and potential inhibition methods. It also explores potential antibiofilm agents and techniques that could be used in the fight against antimicrobial drug resistance and BBM.

2. Methods

The study applied standard search terms such as "biofilm formation and novel management and control strategies" and "antibiotic resistance among biofilm bearing microorganisms and strategies for eradication in clinical and environmental nexus." Documents from PubMed, Scopus, and Web of Science (WoS) were searched, while published documents that do not conform to the terms applied in searching and/or those documents that do not describe the applied terms were not included. Descriptions, definitions, mechanisms, strategies of activity, and research-based suggested approaches for BBM control in clinical and environmental nexus from all retrieved documents were collated and applied in this narrative scientific record. Other related study details from global investigators which were appropriately cited were also re-emphasized and discussed following our previous experience and studies [23].

2.1. Criteria of inclusion

Articles that only focus on bacterial "biofilm formation and novel management and control strategies" and "antibiotic resistance among biofilm bearing microorganisms and strategies for eradication in clinical and environmental nexus" which were reported by previous investigators were applied. Other documents that do not conform to the above criteria were excluded.

2.2. Data analysis

Recovered documents were read and summarized, while necessary details were collated and analyzed with presentation in tables and figures as nonconforming details were removed. Such scientific records details and narrative summary on "biofilm formation and novel management and control strategies" and "antibiotic resistance among biofilm bearing microorganisms and strategies for eradication in clinical and environmental nexus" were chronologically arranged as presented below [23].

2.3. Biofilm formation

Biofilm formation has been described as a dynamic process that involves sets of sequential matrixes between an organism that is trying to survive within a nexus (surface or liquid) and a phase of other biotic agents available to survive on [24]. The bacterial strain approaches the surface to begin the process of forming a biofilm and intercalate with other biomolecular agents. Planktonic single cells and sessile biofilms are the two forms that most bacteria may transition between. The physical, physiological, and gene expression characteristics of planktonic cells and biofilms differ greatly from one another. Extracellular polysaccharides (EPS) encase the sessile cells, which exhibit enhanced surface adherent formation, intrinsic resistance to antibiotics, and remarkable resilience to environmental stressors that are also involved in the interplay as shown in the biofilm formation process (Figure 1) below.

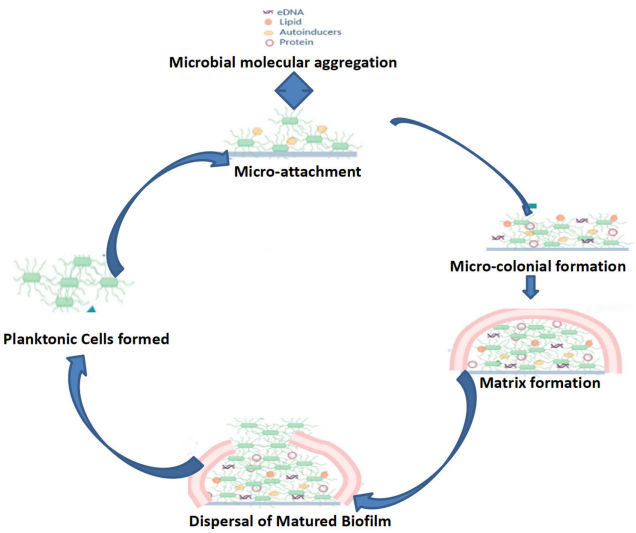

Figure 1. Phases and processes involved in biofilm formation

2.3.1. Reversible attachment

In the presence of suitable conditions, a single planktonic cell may move and attach itself reversibly to a surface, thus commencing the initial phase of the biofilm biogenetic process [25]. This attachment, which is reversible, is facilitated by some electrochemical force and weak contacts including hydrophobic, van der Waals, and electrostatic interactions. Rigidity and stickiness to the surface of attachment are provided by cell appendages such as pili, flagella, and fimbriae. The cells are encased with extracellular polymeric-sugar substances (EPS) which enhance the attachment, and upon attachment, other cellular component activities progress until a mature biofilm is formed [26, 27].

2.3.2. Quasi-irreversible adhesion, cellular organization, and microcolony formation

At this stage, the planktonic cells exhibit a conspicuous increase in layering and organize into a systematic microcolony, accompanied by water channels that create an irreversible attachment. One of the main characteristics of biofilms is colonization, which is essential to their pathogenicity and dormancy. Numerous microbes assemble and

release extracellular polymeric substances (EPS), which serve as a sealant to fix the organisms/strains, as soon as the cells firmly attach to the suitable surface. The microbial colonies are created following these coordinated stages as previously described by some related investigators [28].

2.3.3. Biofilm matrix formation

The adherent's EPS creates a matrix in which the cells establish their community and reach their maximal density. A variety of components, including extracellular DNA (eDNA), sensing and autosensing molecules, polysaccharides, proteins, lipids, and persister cells, combine to form the extracellular matrix (EPS) that encases the cells in a biofilm [29]. The adhesion, protection, and structural rigidity of the cells inside the biofilm are all made possible by the polysaccharides in the matrix [30]. Aggregative polysaccharides, which function as glue and shield the cells from physical strains caused by the flowing fluid depriving them of nutrition, promote colonization [31]. Various polysaccharides that play important roles in maintaining the integrity of biofilms are inherited by organisms (Table 1). Nucleic acids such as ribosomal DNA, eDNA, and other extracellular ribonucleic acids interact with various components of EPS to provide the structural stratification/moiety, nutrition, and defense against gene transfer among BBM. The biofilm is given structure and stability by the proteins in the matrix [32, 33]. A tiny population of latent cells with the highest level of resistance to antibiotics is constituted by persister cells [34, 35].

2.3.4. Maturation of the biofilm and detachment

When nutrition and ideal circumstances are available, the exposed and surviving cells differentiate and proliferate to become mature biofilms bearing strains with a spatial architecture/matrix. This generated biofilm is similar to a collective group that is mediated by chemical signaling molecules released by the biofilm's bacterial residents. It is noteworthy that as the exposed cellular microcolonies mature, specific individual planktonic cells are released into the environment which may migrate depending on environmental conditions to a new surface, causing the bacterial infestation to spread [36].

2.4. Antibiotic resistance among biofilm bearing microorganisms

Antibiotic resistance among biofilm bearing microorganisms is a significant concern in healthcare settings and various industries. Biofilms have remained specifically formed complex communities of organisms that are encased in a self-produced matrix. Such a matrix provides protection against antibiotics/antimicrobial agents and host immune responses in infection cases. Formed biofilm by bearing strains has shown difficult-to-treat potential using antibiotics which implies and enhances microbial resistance through various mechanisms, including reduced antibiotic penetration, altered gene expression, horizontal gene transfer, and the presence of persister cells [37, 38]. These mechanisms contribute to the decreased efficacy of antibiotics against biofilm-associated infections. Biofilm-associated infections are implicated in various medical and public health systems, such as chronic wounds, urinary tract infections, medical device-related infections (e.g., catheters, implants), and respiratory tract infections (e.g., cystic fibrosis). The presence of biofilms often results in recurrent infections and treatment failure [39].

Microbial ability to thrive and/or survive even in the presence of diverse antibiotics/antimicrobial agents has been described as multiple antibiotic resistance (MAR) [37, 40]. Recently, the Centre for Disease Control and Management (CDC) and the European Centre for Disease Prevention and Control have described such strains as extensive antibiotic-resistant bacterial strains (XARB) and pan-antibiotic-resistant bacterial strains (PARB) since such organisms have evolved to become non-susceptible to more than one antimicrobial agent among multiple antimicrobial categories [41]. Such increased phenomenon of resistance among bacteria strains has also been linked with the recalcitrance of BBM-associated infections [15, 42], while others have been termed as superbugs. Such strains, in infection cases, have shown difficulty and resulted in failure of diverse therapeutic and antibiotic treatment strategies, as well as in the recurrence of related microbial infections. Furthermore, diverse related investigators have reported that major BBM strains have demonstrated higher MAR, XARB, and PARB potential in comparison with other antibiotic-resistant strains among a population of planktonic microorganisms contained within any formed system or community using traditional antibiotic therapy [15]. This is an additional contributor to the various suggested potential risks of BBM strains and other biofilm-based infections in patients. When such strains are observed among cases of abiotic implanted medical devices (such as cardiac pacemakers, catheters, joint prostheses, dental implants prosthetic heart valves, and contact lenses) as reported previously by Khatoon [16], there is a possibility of higher case spread and infection case mortality. Suffice it to say that such implanted foreign objects have remained a hub or potential model surface for bacterial cells to adhere and promote nonspecific adherence to elements while creating shear pressures, hydrophobicity, and electrostatic interactions as reported by Connaughton et al. [17]. Table 1 below shows the description of biofilm bearing microbial strains, region of detection, and strategy of detection. However, very few studies have reported and emphasized on the relevance of extensive and pan-antibiotic-resistant potential of diverse strains.

2.5. Infections associated with biofilms

Bacterial bearing biofilms are said to be responsible for more than 80% of persistent and recurring microbial infections in humans [58]. Compared to planktonic cells, BBM have demonstrated 10–1000 times greater genotypic/phenotypic antibiotic resistance [58] both among strains from different environmental niches, such as deep-sea vents, rocks, freshwater streams, rivers, hydrothermal hot springs, etc. Infections linked to BBM may be roughly classified into two categories, namely, native biofilm infections (biofilm that develops on abiotic surfaces) of host tissue [59] and infections linked to indwelling medical devices [60]. It was reported that such biofilms that were first developed on medical implants, such as heart valves, catheters, contact lenses, joint prosthesis, intrauterine devices, and dental units, may increase bloodstream and urinary tract infections. The only control strategy of these infections is to remove the implants, which raises the expenses of care and causes concerns for patients. Chronic and delayed healing lung infections after antibiotic therapy especially among cystic fibrosis patients, chronic rhinosinusitis, chronic prostatitis, chronic otitis media, chronic osteomyelitis, chronic wounds, endocarditis, periodontitis, dental caries, and recurrent urinary tract infections are listed among the host tissue-related biofilm infections which are of frequent emerging concern [59]. Other major biofilm-associated infections which are causing human related disease cases are listed in Table 2 below.

Table 1. Description of biofilm bearing strains, detection country, and control initiatives

Biofilm bearing strain	Source of isolate	Any detected gene	Place of detection	Strategy of detection	Strategic test relevance	Reference
Staphylococcus epidermis		IcaA, icaD, icaC, and icaB	United States of America	According to Richards method		[43]
Staphylococcus aureus	Raw shrimp	IcaA; icaB; icaC	China	Microtiter plate assay as described by Vasudevan *et al*. (2003)	Uninoculated wells containing Brain Heart Infusion Broth	[44]
Escherichia coli	Biomedical materials: silicone, stainless steel	Curl genes, type 1 fimbriae	United States of America	Microtiter and surface hydrophobicity test	Glasswares used control	[45]
Klebsiella pneumonia	Urine	bla_{NDM-1} and $bla_{OXA-181}$	UK	Supplemented tryptic soy broth described by Cusumano *et al*. (2019)	Detection	[46]
Pseudomonas aeruginosa	Medical devices	*lasB*; *toxA*;	Cameroon	Congo red agar	Detection	[47]
Acinetobacter baumannii	Medical devices and surfaces	*blaOXA*; *adeABC*; *ompA*	Nepal	Microtiter plate assays, flow cell biofilm assays	Glasswares used control and assay	[48]
Enterococcus faecalis	Water sample and slaughterhouse	*cylA*	Nigeria	Microtiter plates and crystal violet staining	Glasswares used control and assay	[49]
Candida albicans	Clinical samples	*ALS3*; *HWP1*	Nepal	Microtiter plates and crystal violet staining	Glasswares used control and assay	[50]
Streptococcus mutans	Tooth surfaces	*gtfB*; *gtfC*; *gtfD*; *gbpB*	Poland	Microtiter plate assay and tube method	Glasswares used control and assay	[51]
Salmonella enterica	Food processing surfaces	*BapA*		Crystal violet staining	Detection	[52]
Listeria monocytogenes	Food processing environments	*bap*	Egypt	Microtiter plate assay	Glasswares used control and assay	[53]
Vibrio cholerae	Freshwater	*hlyA*	Southern and Eastern Slovakia	Congo red agar assay, microtiter plate assay	Detection, glasswares used control and assay	[54]
Mycobacteria tuberculosis	Lungs	*Mtb H37Rv*	Poland	Microtiter plate assay	Glasswares used control and assay	[55]
Legionella pneumophila	Water systems	*FlaA*; *Lqs*; *CsgG*	Australia	Culture-based methods	Isolation, glasswares used assay	[56]
Haemophilus influenzae	Respiratory tract	*Hif KR494*		Microtiter plate assay	Glasswares used control and assay	[57]

Table 2. Bacterial species involved in biofilm-associated infection and their adherent surface

S.No.	Bacterial species	Infection/diseases	Surface	References
1	*Streptococcus mutans*	Dental caries Endocarditis	Tooth surface Vascular grafts	[61]
2	*Enterococcus faecalis*	Endocarditis Root canal infection	Heart valves Urinary catheters Tooth Central venous catheter	[62]
3	*Klebsiella pneumonia*	Pneumonia Respiratory tract infection Urinary tract infection Pyogenic liver abscess	Lungs Liver	[63]
4	*Pseudomonas aeruginosa*	Nosocomial infection Otitis media Cystic fibrosis	Central venous Catheters Middle ear Prostheses Lungs Contact lenses	[8]
5	*Staphylococcus sp. (Staphylococcus aureus; Staphylococcus epidermidis)*	Nosocomial infections Chronic wounds Endocarditis Musculoskeletal infections Otitis media	Sutures Central venous catheters Arteriovenous shunts Prostheses Surfaces/deep skin Prostheses Heart valves Bones Middle ear	[64]
7	*Escherichia coli*	Bacterial prostatitis Urinary tract infection Otitis media	Prostheses Urinary tract Urinary catheters Middle ear	[13]
8	*Haemophilus influenzae*	Otitis media	Middle ear	[65]
9	*Burkholderia cepacia*	Cystic fibrosis	Lungs	[66]
10	*Mycobacterium tuberculosis*	Tuberculosis	Lungs	[67]

2.6. Alternative control approaches for biofilm-related infections

Because of the high level of antibiotic resistance observed among the aforementioned BBM and formed bacterial communities, treating biofilm-associated illnesses successfully has become problematic. The center portion of the biofilm contains bacterial cells that are difficult to eliminate with traditional antibiotics and chemotherapy, which exacerbates the situation worldwide. Thus, different approaches (Figure 2 and Table 3) as well as diverse novel control alternatives have been suggested by related investigators [68–70] in order to overcome the drug resistance nature of bacterial biofilm populations and BBM. One notable approach is the use of antibiofilm agents with activity based on enzyme inhibition, disruption, disorganization of community, etc., as previously reported by investigators. One notable physical approach applied in previous studies includes the application of vapor bubbles which are induced by laser. This technique has shown potential in destroying biofilm matrix/complex, preventing attachment of BBM from surfaces while reducing the density of formed biofilm cells on surfaces beyond 1.01–1.10 log10 CFU/ml within a very short time ranging from 2 to 5 mins [71]. Other strategies that possess similar potential include the use of nonthermal cold plasma among seafood sources [72, 73], treatment with high-intensity ultrasound at low frequency in dairy food sources and dairy production lines [74], treatment of production machine surfaces with high hydrostatic pressure, treatment with *ultraviolet-C* [75], and treatment with photodynamic inactivation [76] as depicted in Figure 2 below.

Some suggested strategies over the years include the use of small natural and biological products, the application of quorum sensing (QS) signaling genes and their products, mixed or co-microbial culture products, the use of nano-based particles, the application of CRISPR, etc.

2.6.1. Naturally produced small biological molecules

These are produced among BBM and their related communities. Specific examples include poly-amino radicals (such as D-amino acids and polyamine norspermidine) which encourage the induction of antibiofilm biomolecules and dispersal of mature biofilms complex which may prevent biofilm formation among strains of *S. aureus* and *E. coli* [68]. These compounds may find application as antibiofilm agents in the method for dispersing biofilms. They may also serve as antibiofilm compounds (NAC/N-acetyl cysteine and Tween 80) both by themselves and/or in conjunction with antibiotics as they were found to be effective against nonpigmented rapid growing mycobacterium biofilms [79]. Furthermore, cell walls of mycobacterial strains and their extracellular matrix have a high lipid content which may also be harnessed with other compounds such as Tween 80. Tween 80 has shown increased effectivity against mycobacterial biofilm than NAC suggesting their potential for combined usage as antibiofilm agents. It may also be beneficial in the treatment of infections linked to mycobacterial biofilm communities. Another effective antibiofilm strategy is the degradation of the biofilm complex by EPS degrading enzymes. Some examples given are DNase I, Dispersin B (DspB), and a-amylase. Antibiotic effectiveness is boosted when biofilm structural components are degraded, allowing for greater antibiotic penetration. The degradation of eDNA, biofilm complex, and EPS is caused by DNase I, DspB, and α-amylase, respectively [84]. These enzymes not only prevent the

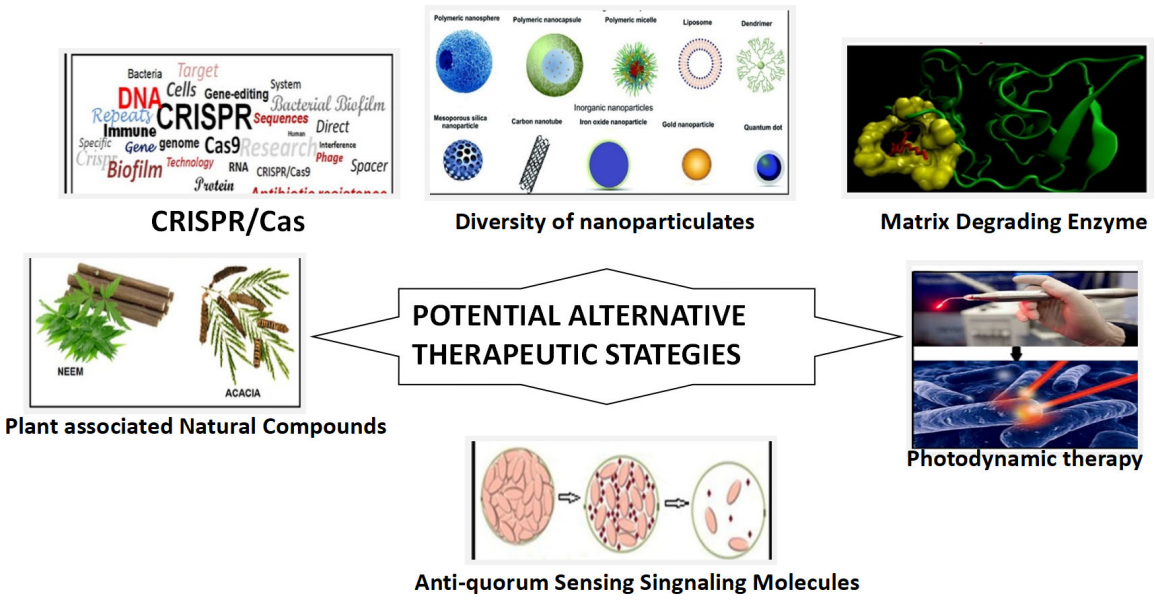

Figure 2. Representation of potential alternative approach to control of biofilm bearing microbes

formation of biofilms but also break down established biofilms in a variety of bacteria, including *S. aureus*, *Vibrio cholerae*, and *P. aeruginosa* [77].

2.6.2. Quorum sensing inhibition

The formation of biofilms may be controlled by QS signaling gene inhibition and their products. A variety of chemicals and inhibitors have shown abilities to disrupt the QS signaling cascade, making them useful as alternative therapies for illnesses linked to biofilms [78]. The bacterial QS signaling is disrupted by halogenated furanone that was isolated from sea algae, *Delisea pulchra* [85]. In addition, acyclic diamine (ADM 3) was recently reported by Kaur et al. [85] to have improved antibacterial and antibiofilm activities. Azithromycin, usnic acid, ginseng extract, and garlic extract all have inhibitory effects on bacterial and fungal biofilms through attenuation of bacterial QS signaling [86]. By stimulating the enzyme phosphodiesterase that breaks down c-di-GMP, nitric oxide (NO), a signaling molecule, disperses the biofilms in *P. aeruginosa* and increases the activity of antimicrobial drugs, causing a switch to planktonic growth [87]. In order to suppress biofilm-mediated infections, CRISPRi technology has most recently been employed to knock down the fimbriae-associated gene (fimH) and the luxS gene of QS signaling [78, 88].

2.6.3. Extracellular polysaccharide disrupting agents

As earlier discussed, major extracellular polymeric-sugar substances (EPS) which are formed in biofilm encourage the protection of BBM from antimicrobial therapy. Any novel agent that may encourage disorganization of EPS complex possesses potential of exposing biofilm bearing cells to various agents. Some of such antibiofilm agents that acts enzymatically to disrupt exo-polysaccharides are categorized as DNases, polysaccharide lyases, etc., with examples as DNase I and DspB [89]. While DNase I aids the digestion of eDNA in the biofilm structure, DspB aids in glycosidic hydrolysis of the EPS that facilitates bacterial aggregation using hydrolyase to cleave polymers of β 1–6 N-acetylglucosamine. This activity disrupts and disperses EPS layers allowing effective action of antimicrobial agents in health systems. It is suggested that the aforementioned antibiofilm agents or enzymes be applied in combination with antimicrobial substances for efficient and effective results on BBM [81].

2.6.4. Bacterial and actinomycetes co-microbial cultural strategies

It is not gainsaying that diverse bacteria possess the potential of producing bioactive agents of natural origin and natural biomolecules with antibiofilm potentials. Such potentials have been reported in methanolic preparation from actinomycete which is associated with corals. The agent has shown inhibition potential against the development of biofilm by strains of *S. aureus* [83]. Furthermore, 4-phenylbutanoic acid, which is another naturally occurring compound, has also shown strong antibiofilm potential/ effectivity against some strains of both gram-positive and gram-negative organisms [80]. Extracts of *Acacia* and *Azadirachta indica* (neem) have also demonstrated antibacterial activity against *S. mutans* and *S. faecalis* strains which were reported to be positive biofilm producers.

2.6.5. Plant-based essential oils

These are plant-related extracts that possess antibiofilm potential and may inhibit or repress biofilm cells or matrix in addition to other effector protein's function (such as T3SS), QS genes, flagella motility, and attachment on surfaces and disruption-dispersion of microbial biofilm matrix. One well-studied source of plant-related essential oil following the study of diverse related investigators is the citrus peel [84].

2.6.6. Nanoparticles

In recent times, specific particulates have been considered as alternative antimicrobial source agents to combat multidrug resistance and treatment of biofilm-based infections [90]. Their biocompatible nano-formulations have been able to overcome the limitations of traditional antibiotic therapies, such as decreased penetration and retention in cells or biofilms. Different types of nanoparticles, such as metal nanoparticles with antibacterial and antibiofilm properties, organic nanoparticles, green nanoparticles, and their mixtures, have been employed in recent years [91].

Table 3. Biofilm bearing strains, resistant nature, applied antibiofilm, and activities

Biofilm bearing strain	Source of isolate	Strain nature of antibiotic resistance	Antibiofilm and related control strategy	Strategy of activities	Reference
Staphylococcus epidermis and other gram-negative strains	Surface of materials	Multiple antibiotic resistance	Vapor bubbles and nonthermal cold plasma	A physical approach involving cellular disruption, disorganization, etc.	[71]
Staphylococcus aureus	Raw shrimp	Resistant to gram-positive antibiotics	Naturally produced small biological molecules, vapor bubbles, and nonthermal cold plasma	Biomolecules and physical approach	[73]
Escherichia coli	Biomedical materials: silicone, stainless steel	Pan-drug resistance	Naturally produced small biological molecules, vapor bubbles, and ultrasound at low frequency	Biomolecules, physical and light approach	[74]
Klebsiella pneumonia	Urine	Multiple antibiotic resistance	High hydrostatic pressure and *ultraviolet-C*	Physical and radio-rays	[75]
Pseudomonas aeruginosa	Medical devices	Resistance to antibiotics	Photodynamic inactivation, extracellular polymeric-sugar substances, quorum sensing (QS)	Photo-illumination, enzyme inhibition, biomolecules and chemicals	[76–78]
Acinetobacter baumannii	Medical devices and surfaces	Multiple antibiotic resistance	Naturally produced small biological molecules	Biomolecules	[68]
Enterococcus faecalis	Water sample and slaughterhouse	Extended-spectrum beta-lactamase	Naturally produced small biological molecules	Biomolecules and chemicals	[79]
Candida albicans	Clinical samples	Antifungal resistance	QS	Chemicals and inhibitors	[78]
Streptococcus mutans	Tooth surfaces	Multiple antibiotic resistance	Bacterial and actinomycetes co-microbial cultural strategies, enzyme inhibition	Biomolecules, inhibitors, and chemicals	[80]
Salmonella enterica	Food processing surfaces	Multiple antibiotic resistance	Enzyme inhibition and extracellular polysaccharide disrupting agents		[80, 81]
Listeria monocytogenes	Food processing environments	Antibiotic resistance	Nanoparticles and enzyme inhibition		[77, 82]
Vibrio cholerae	Freshwater	Multiple antibiotic resistance	Naturally produced small biological molecules, nanoparticles, and extracellular enzymes	Enzyme inhibition	[77, 82]
Mycobacteria tuberculosis	Lungs	Multidrug resistance	Naturally produced small biological molecules	Biomolecules and chemical	[79]
Legionella pneumophila	Water systems	Antibiotics resistance	Naturally produced small biological molecules		[83]
Haemophilus influenzae	Respiratory tract	Antibiotic resistance	Naturally produced small biological molecules, plant-based essential oils, nanoparticles	Surfaces disruption and dispersion	[82, 84]

There is a panel of publications on the removal of bacterial biofilm communities using nanoparticles [82]. According to Kulshrestha et al. [69], CaF2-NPs possess suppressive and inhibitory effects on genes linked to major *S. mutans* pathogenesis or virulence indices (vicR, gtfC, ftf, spaP, and comDE). They also suggest that enzymatic activity related to cell adhesion, glucan synthesis acid tolerance, acid production and QS is suppressed, which inhibits the formation of biofilms. Photodynamic treatment (PDT) has been utilized to treat a variety of infections in the past few years, including those caused by bacteria, fungi, viruses, protozoa, and even parasites. Previous researchers have also indicated that PDT has effectively decreased the number of clinically significant microorganisms, including antibiotic-resistant and drug-resistant gram-positive and gram-negative bacteria [92]. Because PDT can selectively adhere to the membranes of pathogenic cells and precisely deliver light to the afflicted tissue, it can maximize microbe damage while minimizing host injury, which gives it a major advantage over traditional treatment [93]. Our team has recently demonstrated that PDT may be utilized to resolve biofilm-related concerns in *S. mutans* infection cases [94].

3. Conclusion

One of the effects of bacterial bearing biofilm in any nexus is its capacity to fuel chronic illnesses, command/control bacterial antibiotic resistance, and bacterial survival. Compared to planktonic communities, these biofilms or BBM express an extra resistance mechanism that limits the effectiveness of therapies and promotes the re-establishment and spread of persistent harmful organisms. The global situation has gotten worse due to the emergence and spread of strains of *Mycobacterium tuberculosis* that have totally become highly multidrug-resistant strains. The level of resistance to antibiotics among biofilm or BBM dynamics and the potential alternative therapeutic control approaches on persistent/recalcitrant infections bearing biofilm strains were addressed and have been covered in this timeline scientific record. Other alternative potential mechanisms and strategies that may be applied for treating and/or controlling infections implicated by multidrug-resistant (pan or extreme antibiotic-resistant and potential superbug) strains may include novel antibiofilm agents, enzyme-based biofilm inhibition, inhibition of recalcitrant bacterial response, cell wall and EPS cleavage, lipopolysaccharide disassembly, CRISPRi gene editing technologies, photodynamic therapy, membrane perforation/permeability, target-specific probe, and antibiotics-based nanoparticles. The application of the aforementioned strategies above may not only advance the control of BBM and multidrug-resistant strains in infection cases but also herald a generational effective combination therapy against illnesses/infections implicated by BBM and serve as a potential source for controlling bacterial bearing biofilms in the future.

Acknowledgment

The authors wish to appreciate the contribution of Associate Professor Abeni T Beshiru and Associate Professor Cyrus T Ekundayo for their instructive support and criticism in ensuring that this study becomes an excerpt. The study benefited from the funding from the African-German Network of Excellence in Science.

Ethical Statement

This study does not contain any studies with human or animal subjects performed by any of the authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest to this work.

Data Availability Statement

The data that support this work are available upon reasonable request to the corresponding author.

Author Contribution Statement

Bright E. Igere: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Morenike O. Adeola**: Methodology, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Project administration.

References

[1] Høiby, N. (2017). A short history of microbial biofilms and biofilm infections. *Journal of Pathology, Microbiology and Immunology*, *125*(4), 272–275. https://doi.org/10.1111/apm.12686

[2] Flemming, H. C., & Wuertz, S. (2019). Bacteria and archaea on Earth and their abundance in biofilms. *Nature Reviews Microbiology*, *17*(4), 247–260. https://doi.org/10.1038/s41579-019-0158-9

[3] Vasudevan, R. (2014). Biofilms: Microbial cities of scientific significance. *Journal of Microbiology & Experimentation*, *1*(3), 84–98. https://doi.org/10.15406/jmen.2014.01.00014

[4] Martens, E., & Demain, A. L. (2017). The antibiotic resistance crisis, with a focus on the United States. *The Journal of Antibiotics*, *70*(5), 520–526. https://doi.org/10.1038/ja.2017.30

[5] Wasfi, R., Hamed, S. M., Amer, M. A., & Fahmy, L. I. (2020). *Proteus mirabilis* biofilm: Development and therapeutic strategies. *Frontiers in Cellular and Infection Microbiology*, *10*, 414. https://doi.org/10.3389/fcimb.2020.00414

[6] Nirwati, H., Sinanjung, K., Fahrunissa, F., Wijaya, F., Napitupulu, S., Hati, V. P., . . . , & Nuryastuti, T. (2019). Biofilm formation and antibiotic resistance of *Klebsiella pneumoniae* isolated from clinical samples in a tertiary care hospital, Klaten, Indonesia. *BMC Proceedings*, *13*, 20. https://doi.org/10.1186/s12919-019-0176-7

[7] Kennedy, H. F., Morrison, D., Kaufmann, M. E., Jackson, M. S., Bagg, J., Gibson, B. E. S., . . . , & Michie, J. R. (2000). Origins of *Staphylococcus epidermidis* and *Streptococcus oralis* causing bacteraemia in a bone marrow transplant patient. *Journal of Medical Microbiology*, *49*(4), 367–370. https://doi.org/10.1099/0022-1317-49-4-367

[8] Gellatly, S. L., & Hancock, R. E. W. (2013). *Pseudomonas aeruginosa*: New insights into pathogenesis and host defenses. *Pathogens and Disease*, *67*(3), 159–173. https://doi.org/10.1111/2049-632X.12033

[9] Fey, P. D., & Olson, M. E. (2010). Current concepts in biofilm formation of *Staphylococcus epidermidis*. *Future Microbiology*, *5*(6), 917–933. https://doi.org/10.2217/fmb.10.56

[10] Zheng, J. X., Lin, Z. W., Chen, C., Chen, Z., Lin, F. J., Wu, Y., . . . , & Deng, Q. W. (2018). Biofilm formation in *Klebsiella pneumoniae* bacteremia strains was found to be associated with CC23 and the presence of *wcaG*. *Frontiers in Cellular and Infection Microbiology*, *8*, 21. https://doi.org/10.3389/fcimb.2018.00021

[11] Kong, C., Chee, C. F., Richter, K., Thomas, N., Rahman, N. Abd., & Nathan, S. (2018). Suppression of *Staphylococcus aureus* biofilm formation and virulence by a benzimidazole derivative, UM-C162. *Scientific Reports*, *8*(1), 2758. https://doi.org/10.1038/s41598-018-21141-2

[12] Adeola, M. O., Akinnibosun, F. I., & Imade, O. S. (2022). Occurrence of community-acquired Panton-Valentine leukocidin-producing and enterotoxin-producing methicillin-resistant *staphylococci* in companion dogs. *Studia Universitatis Babeș-Bolyai Biologia*, *67*(1), 23–48. https://doi.org/10.24193/subbbiol.2022.1.02

[13] Bellion, M., Santen, L., Mantz, H., Hähl, H., Quinn, A., Nagel, A., . . . , & Jacobs, K. (2008). Protein adsorption on tailored substrates: Long-range forces and conformational changes. *Journal of Physics: Condensed Matter*, *20*(40), 404226. https://doi.org/10.1088/0953-8984/20/40/404226

[14] Aggarwal, S., Stewart, P. S., & Hozalski, R. M. (2015). Biofilm cohesive strength as a basis for biofilm recalcitrance: Are bacterial biofilms overdesigned? *Microbiology Insights*, *8*, MBI-S31444. https://doi.org/10.4137/MBI.S31444

[15] Boudarel, H., Mathias, J. D., Blaysat, B., & Grédiac, M. (2018). Towards standardized mechanical characterization of microbial biofilms: Analysis and critical review. *npj Biofilms and Microbiomes*, *4*(1), 17. https://doi.org/10.1038/s41522-018-0062-5

[16] Khatoon, Z., McTiernan, C. D., Suuronen, E. J., Mah, T. F., & Alarcon, E. I. (2018). Bacterial biofilm formation on implantable devices and approaches to its treatment and prevention. *Heliyon*, *4*(12), e01067. https://doi.org/10.1016/j.heliyon.2018.e01067

[17] Connaughton, A., Childs, A., Dylewski, S., & Sabesan, V. J. (2014). Biofilm disrupting technology for orthopedic implants: What's on the horizon? *Frontiers in Medicine 1*, 22. https://doi.org/10.3389/fmed.2014.00022

[18] Busscher, H. J., Rinastiti, M., Siswomihardjo, W., & van der Mei, H. C. (2010). Biofilm formation on dental restorative and implant materials. *Journal of Dental Research*, *89*(7), 657–665. https://doi.org/10.1177/0022034510368644

[19] Ranieri, M. R. M., Whitchurch, C. B., & Burrows, L. L. (2018). Mechanisms of biofilm stimulation by subinhibitory concentrations of antimicrobials. *Current Opinion in Microbiology*, *45*, 164–169. https://doi.org/10.1016/j.mib.2018.07.006

[20] Rainer, F., Horvath, A., Sandahl, T. D., Leber, B., Schmerboeck, B., Blesl, A., . . . , & Stadlbauer, V. (2018). Soluble CD163 and soluble mannose receptor predict survival and decompensation in patients with liver cirrhosis, and correlate with gut permeability and bacterial translocation. *Alimentary Pharmacology and Therapeutics*, *47*(5), 657–664. https://doi.org/10.1111/apt.14474

[21] Vasilchenko, A. S., & Rogozhin, E. A. (2019). Sub-inhibitory effects of antimicrobial peptides. *Frontiers in Microbiology*, *10*, 1160. https://doi.org/10.3389/fmicb.2019.01160

[22] Bernardi, S., Anderson, A., Macchiarelli, G., Hellwig, E., Cieplik, F., Vach, K., & Al-Ahmad, A. (2021). Subinhibitory antibiotic concentrations enhance biofilm formation of clinical *Enterococcus faecalis* isolates. *Antibiotics*, *10*(7), 874. https://doi.org/10.3390/antibiotics10070874

[23] Igere, B. E., Onohuean, H., & Nwodo, U. U. (2022). Water bodies are potential hub for spatio-allotment of cell-free nucleic acid and pandemic: A pentadecadal (1969–2021) critical review on particulate cell-free DNA reservoirs in water nexus. *Bulletin of the National Research Centre*, *46*(1), 56. https://doi.org/10.1186/s42269-022-00750-y

[24] Floyd, K. A., Eberly, A. R., & Hadjifrangiskou, M. (2017). Adhesion of bacteria to surfaces and biofilm formation on medical devices. In Y. Deng & W. Lv (Eds.), *Biofilms and implantable medical devices* (pp. 47–95). Woodhead Publishing. https://doi.org/10.1016/B978-0-08-100382-4.00003-4

[25] Berne, C., Ducret, A., Hardy, G. G., & Brun, Y. V. (2015). Adhesins involved in attachment to abiotic surfaces by gram-negative bacteria. In M. Ghannoum, M. Parsek, M. Whiteley, & P. K. Mukherjee (Eds.), *Microbial biofilms* (pp. 163–199). Wiley. https://doi.org/10.1128/9781555817466.ch9

[26] Lee, C. K., de Anda, J., Baker, A. E., Bennett, R. R., Luo, Y., Lee, E. Y., . . . , & Wong, G. C. L. (2018). Multigenerational memory and adaptive adhesion in early bacterial biofilm communities. *Proceedings of the National Academy of Sciences*, *115*(17), 4471–4476. https://doi.org/10.1073/pnas.1720071115

[27] Armbruster, C. R., & Parsek, M. R. (2018). New insight into the early stages of biofilm formation. *Proceedings of the National Academy of Sciences*, *115*(17), 4317–4319. https://doi.org/10.1073/pnas.1804084115

[28] Petrova, O. E., & Sauer, K. (2012). Sticky situations: Key components that control bacterial surface attachment. *Journal of Bacteriology*, *194*(10), 2413–2425. https://doi.org/10.1128/jb.00003-12

[29] Hooshdar, P., Kermanshahi, R. K., Ghadam, P., & Khosravi-Darani, K. (2020). A review on production of exopolysaccharide and biofilm in probiotics like lactobacilli and methods of analysis. *Biointerface Research in Applied Chemistry*, *10*(5), 6058–6075. https://doi.org/10.33263/BRIAC105.60586075

[30] Limoli, D. H., Jones, C. J., & Wozniak, D. J. (2015). Bacterial extracellular polysaccharides in biofilm formation and function. In M. Ghannoum, M. Parsek, M. Whiteley & P. K. Mukherjee (Eds.), *Microbial biofilms* (pp. 223–247). Wiley. https://doi.org/10.1128/9781555817466.ch11

[31] Maunders, E., & Welch, M. (2017). Matrix exopolysaccharides; the sticky side of biofilm formation. *FEMS Microbiology Letters*, *364*(13), fnx120. https://doi.org/10.1093/femsle/fnx120

[32] Dunsing, V., Irmscher, T., Barbirz, S., & Chiantia, S. (2019). Purely polysaccharide-based biofilm matrix provides size-selective diffusion barriers for nanoparticles and bacteriophages. *Biomacromolecules*, *20*(10), 3842–3854. https://doi.org/10.1021/acs.biomac.9b00938

[33] Colvin, R. B., Traum, A. Z., Taheri, D., Jafari, M., & Dolatkhah, S. (2014). Granulomatous interstitial nephritis as a manifestation of Crohn disease. *Archives of Pathology and Laboratory Medicine*, *138*(1), 125–127. https://doi.org/10.5858/arpa.2012-0224-CR

[34] Xavier, J. B., & Foster, K. R. (2007). Cooperation and conflict in microbial biofilms. *Proceedings of the National Academy of Sciences*, *104*(3), 876–881. https://doi.org/10.1073/pnas.0607651104

[35] Abraham, T., Schooling, S. R., Nieh, M. P., Kučerka, N., Beveridge, T. J., & Katsaras, J. (2007). Neutron diffraction study of *Pseudomonas aeruginosa* lipopolysaccharide bilayers. *The Journal of Physical Chemistry B*, *111*(10), 2477–2483. https://doi.org/10.1021/jp066012+

[36] Matilla-Santander, N., Valvi, D., Lopez-Espinosa, M. J., Manzano-Salgado, C. B., Ballester, F., Ibarluzea, J., . . . , & Vrijheid, M. (2017). Exposure to perfluoroalkyl substances and metabolic outcomes in pregnant women: Evidence from the Spanish INMA birth cohorts. *Environmental Health Perspectives*, *125*(11), 117004. https://doi.org/10.1289/EHP1062

[37] Igere, B. E., Igolukumo, B. B., Eduamodu, C., & Odjadjare, E. O. (2021). Multi-drug resistant *Aeromonas* species in Annelida: An evidence of pathogen harbouring leech in recreation water nexus of Oghara Nigeria environs. *Scientia Africana*, *20*(2), 145–166. https://doi.org/10.4314/sa.v20i2.13

[38] Maikalu, R. B., Igere, B. E., & Odjadjare, E. E. O. (2023). Enterobacter species distribution, emerging virulence and multiple antibiotic resistance dynamics in effluents: A countrified spread-hub and implications of abattior release. *Total Environment Research Themes*, *8,* 100074. https://doi.org/10.1016/j.totert.2023.100074

[39] Lebeaux, D., Ghigo, J. M., & Beloin, C. (2014). Biofilm-related infections: Bridging the gap between clinical management and fundamental aspects of recalcitrance toward antibiotics. *Microbiology and Molecular Biology Reviews*, *78*(3), 510–543. https://doi.org/10.1128/mmbr.00013-14

[40] Igere, B. E., Okoh, A. I., & Nwodo, U. U. (2022). Lethality of resistant/virulent environmental *Vibrio cholerae* in wastewater release: An evidence of emerging virulent/antibiotic-resistant-bacteria contaminants of public health concern. *Environmental Challenges*, *7*, 100504. https://doi.org/10.1016/j.envc.2022.100504

[41] Magiorakos, A. P., Srinivasan, A., Carey, R. B., Carmeli, Y., Falagas, M. E., Giske, C. G., . . . , & Monnet, D. L. (2012). Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. *Clinical Microbiology and Infection*, *18*(3), 268–281. https://doi.org/10.1111/j.1469-0691.2011.03570.x

[42] Igere, B. E., Peter, W. O., & Beshiru, A. (2022). Distribution/spread of superbug and potential ESKAPE-B pathogens amongst domestic and environmental activities: A public health concern. *Discovery*, *58*(313), 1–20. http://www.discoveryjournals.org/discovery/current_issue/v58/n313/A1.pdf?

[43] Nowicka, J., Janczura, A., Pajączkowska, M., Chodaczek, G., Szymczyk-Ziółkowska, P., Walczuk, U., & Gościniak, G. (2023). Effect of Camel peptide on the biofilm of *Staphylococcus epidermidis* and *Staphylococcus haemolyticus* formed on orthopedic implants. *Antibiotics*, *12*(12), 1671. https://doi.org/10.3390/antibiotics12121671

[44] Dai, J., Huang, J., Wu, S., Zhang, F., Li, Y., Rong, D., . . . , & Wu, Q. (2023). Occurrence, antibiotic susceptibility, biofilm formation and molecular characterization of *Staphylococcus aureus* isolated from raw shrimp in China. *Foods*, *12*(14), 2651. https://doi.org/10.3390/foods12142651

[45] Gomes, L. C., Araújo, P. A., Teodósio, J. S., Simões, M., & Mergulhão, F. J. (2014). The effect of plasmids and other biomolecules on the effectiveness of antibiofilm agents. In K. P. Rumbaugh & I. Ahmad (Eds.), *Antibiofilm agents: From diagnosis to treatment and prevention* (pp. 161–174). Springer. https://doi.org/10.1007/978-3-642-53833-9_8

[46] Lim, S., Choi, M., Kim, H., & Kim, J. M. (2023). Sleep quality and related factors among liver transplant recipients in Korea: A cross-sectional study. *Journal of Nursing Research*, *31*(4), e286. https://doi.org/10.1097/jnr.0000000000000567

[47] Madaha, E. L., Gonsu, H. K., Bughe, R. N., Fonkoua, M. C., Ateba, C. N., & Mbacham, W. F. (2020). Occurrence of bla_{TEM} and bla_{CTXM} genes and biofilm-forming ability among clinical isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in Yaoundé, Cameroon. *Microorganisms*, *8*(5), 708. https://doi.org/10.3390/microorganisms8050708

[48] Ghimire, U., Kandel, R., Neupane, M., Shrestha, S., Sudeep, K. C., Khanal, S., & Joshi, D. R. (2021). Biofilm formation and blaOXA genes detection among *Acinetobacter baumannii* from clinical isolates in a tertiary care Kirtipur Hospital, Nepal. *Progress in Microbes & Molecular Biology*, *4*(1), 1–17. https://doi.org/10.36877/pmmb.a0000245

[49] Igbinosa, E. O., Beshiru, A., & Odjadjare, E. E. O. (2020). Diversity, antimicrobial characterization and biofilm formation of *Enterococci* isolated from aquaculture and slaughterhouse sources in Benin City, Nigeria. *Ife Journal of Science*, *22*(3), 51–63. https://doi.org/10.4314/ijs.v22i3.4

[50] Lamsal, S., Adhikari, S., Raghubanshi, B. R., Sapkota, S., Rijal, K. R., Ghimire, P., & Banjara, M. R. (2021). Antifungal susceptibility and biofilm formation of *Candida albicans* isolated from different clinical specimens. *Tribhuvan University Journal of Microbiology*, *8*(1), 53–62. https://doi.org/10.3126/tujm.v8i1.41195

[51] Staszczyk, M., Jurczak, A., Magacz, M., Kościelniak, D., Gregorczyk-Maga, I., Jamka-Kasprzyk, M., . . . , & Krzyściak, W. (2020). Effect of polyols and selected dental materials on the ability to create a cariogenic biofilm–On children caries-associated *Streptococcus mutans* isolates. *International Journal of Environmental Research and Public Health*, *17*(10), 3720. https://doi.org/10.3390/ijerph17103720

[52] Latasa, C., Roux, A., Toledo-Arana, A., Ghigo, J. M., Gamazo, C., Penadés, J. R., & Lasa, I. (2005). BapA, a large secreted protein required for biofilm formation and host colonization of *Salmonella enterica* serovar Enteritidis. *Molecular Microbiology*, *58*(5), 1322–1339. https://doi.org/10.1111/j.1365-2958.2005.04907.x

[53] Osman, K. M., Kappell, A. D., Fox, E. M., Orabi, A., & Samir, A. (2020). Prevalence, pathogenicity, virulence, antibiotic resistance, and phylogenetic analysis of biofilm-producing *Listeria monocytogenes* isolated from different ecological niches in Egypt: Food, humans, animals, and environment. *Pathogens*, *9*(1), 5. https://doi.org/10.3390/pathogens9010005

[54] Valáriková, J., Korcová, J., Ziburová, J., Rosinský, J., Čížová, A., Bieliková, S., . . . , & Farkaš, P. (2020). Potential pathogenicity and antibiotic resistance of aquatic *Vibrio* isolates from freshwater in Slovakia. *Folia Microbiologica*, *65*, 545–555. https://doi.org/10.1007/s12223-019-00760-w

[55] Bekier, A., Kawka, M., Lach, J., Dziadek, J., Paneth, A., Gatkowska, J., . . . , & Dziadek, B. (2021). Imidazole-thiosemicarbazide derivatives as potent anti-*Mycobacterium tuberculosis* compounds with antibiofilm activity. *Cells*, *10*(12), 3476. https://doi.org/10.3390/cells10123476

[56] Whiley, H., Keegan, A., Fallowfield, H., & Bentham, R. (2014). Detection of *Legionella, L. pneumophila* and *Mycobacterium avium* complex (MAC) along potable water distribution pipelines. *International Journal of Environmental Research and Public Health*, *11*(7), 7393–7405. https://doi.org/10.3390/ijerph110707393

[57] Su, Y. C., Resman, F., Hörhold, F., & Riesbeck, K. (2014). Comparative genomic analysis reveals distinct genotypic features of the emerging pathogen *Haemophilus influenzae* type f. *BMC Genomics*, *15*, 38. https://doi.org/10.1186/1471-2164-15-38

[58] Qiao, G., Li, H., Xu, D. H., & Park, S. I. (2012). Modified a colony forming unit microbial adherence to hydrocarbons

assay and evaluated cell surface hydrophobicity and biofilm production of *Vibrio scophthalmi*. *Journal of Bacteriology and Parasitology*, *3*(1), 1000130. https://doi.org/10.4172/2155-9597.1000130

[59] Burmølle, M., Norman, A., Sørensen, S. J., & Hansen, L. H. (2012). Sequencing of IncX-plasmids suggests ubiquity of mobile forms of a biofilm-promoting gene cassette recruited from *Klebsiella pneumoniae*. *PLOS ONE*, *7*(8), e41259. https://doi.org/10.1371/journal.pone.0041259

[60] Esteban, A., Ferguson, N. D., Meade, M. O., Frutos-Vivar, F., Apezteguia, C., Brochard, L., ..., & Anzueto, A. (2008). Evolution of mechanical ventilation in response to clinical research. *American Journal of Respiratory and Critical Care Medicine*, *177*(2), 170–177. https://doi.org/10.1164/rccm.200706-893OC

[61] Abranches, J., Miller, J. H., Martinez, A. R., Simpson-Haidaris, P. J., Burne, R. A., & Lemos, J. A. (2011). The collagen-binding protein Cnm is required for *Streptococcus mutans* adherence to and intracellular invasion of human coronary artery endothelial cells. *Infection and Immunity*, *79*(6), 2277–2284. https://doi.org/10.1128/iai.00767-10

[62] Minardi, D., Cirioni, O., Ghiselli, R., Silvestri, C., Mocchegiani, F., Gabrielli, E., ..., & Muzzonigro, G. (2012). Efficacy of tigecycline and rifampin alone and in combination against *Enterococcus faecalis* biofilm infection in a rat model of ureteral stent. *Journal of Surgical Research*, *176*(1), 1–6. https://doi.org/10.1016/j.jss.2011.05.002

[63] Chung, P. Y. (2016). The emerging problems of *Klebsiella pneumoniae* infections: Carbapenem resistance and biofilm formation. *FEMS Microbiology Letters*, *363*(20), fnw219. https://doi.org/10.1093/femsle/fnw219

[64] Arciola, C. R., Campoccia, D., Speziale, P., Montanaro, L., & Costerton, J. W. (2012). Biofilm formation in *Staphylococcus* implant infections. A review of molecular mechanisms and implications for biofilm-resistant materials. *Biomaterials*, *33*(26), 5967–5982. https://doi.org/10.1016/j.biomaterials.2012.05.031

[65] Ortiz-Romero, M. D. M., Espejo-García, M. P., Alfayate-Miguelez, S., Ruiz-López, F. J., Zapata-Hernandez, D., & Gonzalez-Pacanowska, A. J. (2017). Epidemiology of nasopharyngeal carriage by *Haemophilus influenzae* in health children: A study in the Mediterranean Coast region. *The Pediatric Infectious Disease Journal*, *36*(10), 919–923. https://doi.org/10.1097/INF.0000000000001625

[66] Zlosnik, J. E., Costa, P. S., Brant, R., Mori, P. Y., Hird, T. J., Fraenkel, M. C., ..., & Speert, D. P. (2011). Mucoid and nonmucoid *Burkholderia cepacia* complex bacteria in cystic fibrosis infections. *American Journal of Respiratory and Critical Care Medicine*, *183*(1), 67–72. https://doi.org/10.1164/rccm.201002-0203OC

[67] Qvist, T., Johansen, I. S., Pressler, T., Høiby, N., Andersen, A. B., Katzenstein, T. L., & Bjerrum, S. (2014). Urine lipoarabinomannan point-of-care testing in patients affected by pulmonary nontuberculous mycobacteria – Experiences from the Danish Cystic Fibrosis cohort study. *BMC Infectious Diseases*, *14*, 655. https://doi.org/10.1186/s12879-014-0655-4

[68] Kolodkin-Gal, I., Cao, S., Chai, L., Böttcher, T., Kolter, R., Clardy, J., & Losick, R. (2012). A self-produced trigger for biofilm disassembly that targets exopolysaccharide. *Cell*, *149*(3), 684–692. https://doi.org/10.1016/j.cell.2012.02.055

[69] Kulshrestha, S., Khan, S., Meena, R., Singh, B. R., & Khan, A. U. (2014). A graphene/zinc oxide nanocomposite film protects dental implant surfaces against cariogenic *Streptococcus mutans*. *Biofouling*, *30*(10), 1281–1294. https://doi.org/10.1080/08927014.2014.983093

[70] Lönn-Stensrud, J., Landin, M. A., Benneche, T., Petersen, F. C., & Scheie, A. A. (2009). Furanones, potential agents for preventing *Staphylococcus epidermidis* biofilm infections? *Journal of Antimicrobial Chemotherapy*, *63*(2), 309–316. https://doi.org/10.1093/jac/dkn501

[71] Shiroodi, S., Schwarz, M. H., Nitin, N., & Ovissipour, R. (2021). Efficacy of nanobubbles alone or in combination with neutral electrolyzed water in removing *Escherichia coli* O157: H7, *Vibrio parahaemolyticus*, and *Listeria innocua* biofilms. *Food and Bioprocess Technology*, *14*, 287–297. https://doi.org/10.1007/s11947-020-02572-0

[72] Choi, J. H., Jung, E. H., Lee, E. S., Jung, H. I., & Kim, B. I. (2022). Anti-biofilm activity of chlorhexidine-releasing elastomerics against dental microcosm biofilms. *Journal of Dentistry*, *122*, 104153. https://doi.org/10.1016/j.jdent.2022.104153

[73] Choi, M. S., Jeon, E. B., Kim, J. Y., Choi, E. H., Lim, J. S., Choi, J., & Park, S. Y. (2022). Application of dielectric barrier discharge plasma for the reduction of non-pathogenic *Escherichia coli* and *E. coli* O157: H7 and the quality stability of fresh oysters (*Crassostrea gigas*). *LWT*, *154*, 112698. https://doi.org/10.1016/j.lwt.2021.112698

[74] Pedrós-Garrido, S., Condón-Abanto, S., Beltrán, J. A., Lyng, J. G., Brunton, N. P., Bolton, D., & Whyte, P. (2017). Assessment of high intensity ultrasound for surface decontamination of salmon (*S. salar*), mackerel (*S. scombrus*), cod (*G. morhua*) and hake (*M. merluccius*) fillets, and its impact on fish quality. *Innovative Food Science & Emerging Technologies*, *41*, 64–70. https://doi.org/10.1016/j.ifset.2017.02.006

[75] Roy, P. K., Mizan, M. F. R., Hossain, M. I., Han, N., Nahar, S., Ashrafudoulla, M., ..., & Ha, S. D. (2021). Elimination of *Vibrio parahaemolyticus* biofilms on crab and shrimp surfaces using ultraviolet C irradiation coupled with sodium hypochlorite and slightly acidic electrolyzed water. *Food Control*, *128*, 108179. https://doi.org/10.1016/j.foodcont.2021.108179

[76] Tan, L., Zhao, F., Han, Q., Zhao, A., Malakar, P. K., Liu, H., ..., & Zhao, Y. (2018). High correlation between structure development and chemical variation during biofilm formation by *Vibrio parahaemolyticus*. *Frontiers in Microbiology*, *9*, 1881. https://doi.org/10.3389/fmicb.2018.01881

[77] Kalpana, B. J., Aarthy, S., & Pandian, S. K. (2012). Antibiofilm activity of α-amylase from *Bacillus subtilis* S8-18 against biofilm forming human bacterial pathogens. *Applied Biochemistry and Biotechnology*, *167*, 1778–1794. https://doi.org/10.1007/s12010-011-9526-2

[78] Zuberi, A., Ahmad, N., & Khan, A. U. (2017). CRISPRi induced suppression of fimbriae gene (*fimH*) of a uropathogenic *Escherichia coli*: An approach to inhibit microbial biofilms. *Frontiers in Immunology*, *8*, 1552. https://doi.org/10.3389/fimmu.2017.01552

[79] Muñoz-Egea, M. C., García-Pedrazuela, M., Mahillo-Fernandez, I., & Esteban, J. (2016). Effect of antibiotics and antibiofilm agents in the ultrastructure and development of biofilms developed by nonpigmented rapidly growing mycobacteria. *Microbial Drug Resistance*, *22*(1), 1–6. https://doi.org/10.1089/mdr.2015.0124

[80] Nithya, C., Devi, M. G., & Karutha Pandian, S. (2011). A novel compound from the marine bacterium *Bacillus pumilus* S6-15

inhibits biofilm formation in gram-positive and gram-negative species. *Biofouling*, *27*(5), 519–528. https://doi.org/10.1080/08927014.2011.586127

[81] Darouiche, R. O., Mansouri, M. D., Gawande, P. V., & Madhyastha, S. (2009). Antimicrobial and antibiofilm efficacy of triclosan and DispersinB® combination. *Journal of Antimicrobial Chemotherapy*, *64*(1), 88–93. https://doi.org/10.1093/jac/dkp158

[82] Hernández Sampieri, R., Fernández Collado, C., & Baptista Lucio P. (2014). *Metodología de la investigación*. Mexico: McGraw-Hill.

[83] Bakkiyaraj, D., & Karutha Pandian, S. T. (2010). *In vitro* and *in vivo* antibiofilm activity of a coral associated actinomycete against drug resistant *Staphylococcus aureus* biofilms. *Biofouling*, *26*(6), 711–717. https://doi.org/10.1080/08927014.2010.511200

[84] Sun, Y., Guo, D., Hua, Z., Sun, H., Zheng, Z., Xia, X., & Shi, C. (2019). Attenuation of multiple *Vibrio parahaemolyticus* virulence factors by citral. *Frontiers in Microbiology*, *10*, 894. https://doi.org/10.3389/fmicb.2019.00894

[85] Kaur, L., Khajuria, R., Parihar, L., & Singh, G. D. (2017). Polyhydroxyalkanoates: Biosynthesis to commercial production – A review. *Journal of Microbiology, Biotechnology and Food Sciences*, *6*(4), 1098–1106. https://doi.org/10.15414/jmbfs.2017.6.4.1098-1106

[86] Bjarnsholt, T., Jensen, P. Ø., Rasmussen, T. B., Christophersen, L., Calum, H., Hentzer, M., . . . , & Givskov, M. (2005). Garlic blocks quorum sensing and promotes rapid clearing of pulmonary *Pseudomonas aeruginosa* infections. *Microbiology*, *151*(12), 3873–3880. https://doi.org/10.1099/mic.0.27955-0

[87] Barraud, N., Schleheck, D., Klebensberger, J., Webb, J. S., Hassett, D. J., Rice, S. A., & Kjelleberg, S. (2009). Nitric oxide signaling in *Pseudomonas aeruginosa* biofilms mediates phosphodiesterase activity, decreased cyclic di-GMP levels, and enhanced dispersal. *Journal of Bacteriology*, *191*(23), 7333–7342. https://doi.org/10.1128/jb.00975-09

[88] Zuberi, A., Misba, L., & Khan, A. U. (2017). CRISPR interference (CRISPRi) inhibition of luxS gene expression in *E. coli*: An approach to inhibit biofilm. *Frontiers in Cellular and Infection Microbiology*, *7*, 214. https://doi.org/10.3389/fcimb.2017.00214

[89] Roy, R., Tiwari, M., Donelli, G., & Tiwari, V. (2018). Strategies for combating bacterial biofilms: A focus on anti-biofilm agents and their mechanisms of action. *Virulence*, *9*(1), 522–554. https://doi.org/10.1080/21505594.2017.1313372

[90] Pelgrift, R. Y., & Friedman, A. J. (2013). Nanotechnology as a therapeutic tool to combat microbial resistance. *Advanced Drug Delivery Reviews*, *65*(13–14), 1803–1815. https://doi.org/10.1016/j.addr.2013.07.011

[91] Baek, Y. W., & An, Y. J. (2011). Microbial toxicity of metal oxide nanoparticles (CuO, NiO, ZnO, and Sb_2O_3) to *Escherichia coli, Bacillus subtilis*, and *Streptococcus aureus*. *Science of the Total Environment*, *409*(8), 1603–1608. https://doi.org/10.1016/j.scitotenv.2011.01.014

[92] Carpenter, A. W., de Lannoy, C. F., & Wiesner, M. R. (2015). Cellulose nanomaterials in water treatment technologies. *Environmental Science & Technology*, *49*(9), 5277–5287. https://doi.org/10.1021/es506351r

[93] Plaetzer, K., Krammer, B., Berlanda, J., Berr, F., & Kiesslich, T. (2009). Photophysics and photochemistry of photodynamic therapy: Fundamental aspects. *Lasers in Medical Science*, *24*, 259–268. https://doi.org/10.1007/s10103-008-0539-1

[94] Lamas, A., Regal, P., Vázquez, B., Cepeda, A., & Franco, C. M. (2019). Short chain fatty acids commonly produced by gut microbiota influence *Salmonella enterica* motility, biofilm formation, and gene expression. *Antibiotics*, *8*(4), 265. https://doi.org/10.3390/antibiotics8040265

How to Cite: Igere, B. E., & Adeola, M. O. (2024). Fighting Biofilm Bearing Microbes, Global Challenges, Initiatives, and Current Novel Therapeutics/Antibiofilm Strategies: A Narrative Scientific Record. *Medinformatics*. https://doi.org/10.47852/bonviewMEDIN42022687