Antimicrobial-Resistant Microorganisms and the Possibility of Using Microbial Fuel Cell Technology to Reduce Their Transmission in the Environment

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Abstract Antimicrobial resistance (AMR) is a severe problem in Malaysia and worldwide; the World Health Organization (WHO) ranks AMR among the top ten global threats to public health and development. Malaysia's Antimicrobial Resistance Action Plan (MyAP-AMR) 2017–2021 describes AMR as a One Health concern requiring multidisciplinary collaboration across all sectors: humans, animals, plants, and the shared environment. Thus, it is vital to understand how it spreads in the environment and, concurrently, to discover feasible measures for reducing its spread. Among the environmental drivers of AMR is wastewater or sewage sludge. It is well established that exposure to sewage can promote the intake of AMR bacteria, resulting in the development of life-threatening infections such as sepsis in humans. As a result, prompt action is required to ensure the sludge is safe for human use. One possibility is to treat sludge with microbial fuel cell (MFC) technology, a bio-electrical device that uses the natural metabolic activity of electrogenic bacteria (EB) to generate electricity. Current research in the laboratory focuses on the use of EB like Bacillus subtilis to catalyse the conversion of carbon sources in sludge to sustainable energy. However, no study has been conducted to determine the benefits of MFC technology in preventing the spread of AMR in the environment. Nonetheless, due to its potential to trigger the production of bacteriocins that can kill or deactivate AMR microorganisms, it is expected that MFC-treated sludge will reduce AMR transmission to the environment and eventually to humans. In general, this chapter

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will discuss the fundamentals of AMR and MFC and the additional benefits of MFC technology in reducing AMR transmission.

Keywords Antimicrobial resistance · Microbial Fuel cell · Infections

1 Introduction

Rapid urbanisation and industrialisation have contributed significantly to environmental pollution and human dangers due to their hazardous contents, which include pathogens, irritants, carcinogens, flammable, explosive, and oxidising agents [1]. Thus, proper and efficient waste management should be a major priority today, as it has the potential to have a detrimental influence not only on the environment but also on our society [1]. Fortunately, current wastewater treatment appears to be one of the most effective methods for reducing environmental pollution and health hazard. Additionally, the treated sludge has also been regarded as a critical biological resource for managing successful agriculture by improving crop yields and benefiting society and the economy [2]. However, although the sludge has been sufficiently treated before being applied to the soil, it does not completely eliminate the pathogen, heavy metals, organic chemicals, or chemical irritants present in the sewage sludge. For example, while sewage treatment is known to reduce pathogens, some pathogens such as *Clostridium perfringens* and hepatitis A virus (HAV) persist in the treated sewage sludge for an extended length of time and are resistant to existing wastewater treatment methods [3–5].

Additionally, numerous studies have demonstrated the importance of wastewater as an important reservoir of antimicrobial resistance (AMR), as it provides an excellent setting for the survival of AMR bacteria (ARBs) and AMR genes (ARGs). While the treatment process can assist in eliminating or reducing the ARB load, it has a negligible effect on ARGs. ARGs are not biodegradable and can be transferred through horizontal gene transfer to other bacteria, especially the Gram-negative bacteria [6]. Ultimately, it will promote the spreading of pathogenic AMR or ARBs to animals and humans via consumption of infected vegetables or water, inhalation, or direct skin contact, negatively harming their health [7–9]. Thus, it is vital to develop novel strategies for limiting the spread of AMR or ARB to the environment, such as by the employment of viruses, bacteriocins, or predatory bacteria. Interestingly, these alternatives can be applied using microbial fuel cell (MFC) technology, a bio-electrochemical system that employs microorganisms as catalysts to convert chemical energy stored in organic or inorganic substances to electrical energy [10, 11]. Thus, the review will evaluate the adverse effects of ARB on humans and the potential for risk reduction through the application of MFC technology.

2 Antimicrobial Resistance Microorganisms in the Environment and Its Implication to Humans

AMR, often known as drug resistance, is widely recognised as a global threat to human health that demands immediate action in countries worldwide. AMR is a major concern because it could lead to a post-antibiotic era where antibiotics are no longer effective. AMR refers to resistance in a variety of microorganisms to various antimicrobials, including antibacterial, antiviral, antiparasitic, and antifungal medications [12]. It happens when bacteria, viruses, fungi, and parasites acquire resistance to most antimicrobials used to treat infections [13]. Antibiotics and other antimicrobial treatments become ineffective due to the formation and spread of drug-resistant bacteria, resulting in antimicrobial resistance, which continues to undermine the ability to treat illnesses [14].

AMR is a natural occurrence aided by several variables: (a) Misuse and overuse of antimicrobials in clinics and animals' healthcare; (b) poor access to clean water, sanitation, and hygiene for both humans and animals; (c) inadequate infection and disease prevention in healthcare facilities and farms; and (d) lack of awareness and knowledge of antimicrobials usage among the public are all driving factors in the development of antimicrobial-resistant pathogens [15, 16]. Increased antimicrobial resistance can lead to many issues: (a) some severe infections being more difficult to control; (b) remaining inside the body for long periods; and (c) more extended hospital stays, all of which significantly impact patients' quality of life and place a strain on medical care, which is directly linked to high expenditures and high risk of infection-related mortality [17, 18].

3 Mechanism of Resistance

AMR has multiple key mechanisms, including drug uptake restriction, drug target alteration, drug inactivation, and active efflux of a drug [19]. These processes can be classified as innate resistance and acquired resistance. Intrinsic resistance is the innate ability of bacteria to resist the efficacy of a certain antibiotic through inherent structural or functional characteristics, and the mechanisms involved are drug uptake limitation, drug inactivation, and active efflux of a drug [19, 20]. Whereas acquired resistance can be acquired through mutational alterations or horizontal gene transfer, the processes involved are drug target modification, drug inactivation, and active efflux of a drug [19, 21].

3.1 Restricting drug's Entry

Antimicrobial chemicals must gain access to the bacterial cell to disrupt the bacteria's regular functions. Microbes may acquire resistance mechanisms by restricting antimicrobial drug uptake [21] (Fig. 1). This method is frequent in gram-negative bacteria and involves changes in the outer membrane's lipid composition, porin channel selectivity, and porin channel concentrations [19]. Lipopolysaccharide (LPS) is typically found in gram-negative bacteria to act as a barrier to particular compounds [19]. This layer gives inherent resistance to a subset of large antibacterial agents. However, the main pathway by which these antibiotics typically cross the Gram-negative bacteria with large outer membranes is via porin channels [22]. Porin channels allow access to hydrophilic compounds such as β-lactam, tetracyclines, and certain fluoroquinolones in gram-negative bacteria [21]. However, porin alterations can impair drug uptake in two ways: decreased porin protein expression or mutations that alter the porin channel's selectivity. For instance, gram-negative bacteria typically impede the uptake of certain antibiotics, such as aminoglycosides and ß-lactams, by altering porin channels' frequency, size, and selectivity in the cell membrane [19]. Enterobacteriaceae and *Pseudomonas aeruginosa* develop resistance by altering the expression of the porin protein, whereas, in *E. aerogenes*, porin mutations were shown to alter the shape of the porin channel, imparting resistance to imipenem and some cephalosporins [19]. All these changes are necessary to prevent antibiotics from accessing the drug binding sites, such as ribosomes and penicillin-binding proteins (PBPs).

3.2 Modification of Drug Targets

Antimicrobial agents are typically directed against specific targets, and structural alterations might impair drug binding, rendering the drug ineffective. Certain resistant bacteria have the ability to change the antimicrobial drug's target, hence conferring resistance. They may resist antimicrobials by reprogramming or concealing binding target sites to avoid detection. Additionally, bacteria have an evolutionary advantage in that they can gain drug resistance due to spontaneous genes modification, promoting structural changes of these antimicrobial binding sites [22]. For example, genetic mutations will influence the active sites of PBPs, which are transpeptidases involved in the synthesis of peptidoglycan in the cell wall [19] (Fig. 1). As a result, this can impede the binding of β-lactam antibiotics and result in multidrug resistance, which is frequently observed in gram-positive bacteria such as *Streptococcus pneumoniae* [19, 22].

On the contrary, Methicillin-resistant *Staphylococcus aureus* (MRSA) by gaining a new low-affinity PBP rather than structurally changing their existing PBPs [23]. Other examples of this type of resistance mechanism include alteration of peptidoglycan subunit peptide chains, which confers resistance to glycopeptides; prevent

drug interaction with the ribosome by affecting ribosomal subunits via ribosomal mutation or ribosomal protection, conferring resistance to macrolides, tetracyclines, and aminoglycosides; alteration in LPS structure of gram-negative bacteria, giving resistance to polymyxins; alterations in RNA polymerase, which provide resistance to fluoroquinolones; and alteration in metabolic enzymes, giving resistance to sulfa drugs, sulfones, and trimethoprim [19, 22]. As a result, the antimicrobial drugs' capacity to bind to their target molecules will be diminished.

3.3 Drug Inactivation

Antimicrobial resistance genes or ARGs may encode enzymes capable of chemically altering or degrading the drug via hydrolysis (Fig. 1). Bacteria inactivate drugs in two ways: either by degrading the drug or by transferring a chemical group to the drug, so inactivating it. A common example is the hydrolytic deactivation of the ß-lactam ring in penicillins and cephalosporins by ß-lactamases, a drug hydrolysing enzyme [22]. When the ß-lactam bond is broken, the antimicrobial drug's antibacterial activity is lost. On the contrary, drug inactivation via enzymatic transfer of a chemical group to the drug can result in drug inactivation by interrupting the drug's interaction with its bacterial target. Acetyl, phosphoryl, and adenyl groups are the most common chemical groups implicated in this resistance mechanism [19, 22], with acetylation is the most diversely employed mechanism, and its efficacy against aminoglycosides, chloramphenicol, streptogramins, and fluoroquinolones have been demonstrated [19].

3.4 Active Efflux of a Drug

Certain bacteria have membrane proteins that operate as an export or efflux pump for certain antimicrobials (Fig. 1), actively transporting the drug out of the cell and preventing the drug from building up in the cells to a level that would be harmful to the bacterium [19, 22]. This mechanism has been observed in *E. coli* and other Enterobacteriaceae against tetracyclines, Enterobacteriaceae against chloramphenicol, Staphylococci against macrolides, and *Staphylococcus aureus* and *Streptococcus pneumoniae* against fluoroquinolones [19, 24]. There are five leading families of efflux pumps, classified according to their structure and energy source in bacteria. These five families are as follows: the ABC family; the multidrug and toxic compound extrusion (MATE) family; the small multidrug resistance (SMR) family; the major facilitator superfamily (MFS) family; and the resistance-nodulation-cell division (RND) family. Most of these efflux pump families are composed of a single component and function by transporting substrates through the cytoplasmic membrane [19].

The transfer of ARGs between bacteria has been described, and this process may contribute to the rapid spread of ARGs between bacteria [25, 26]. The majority

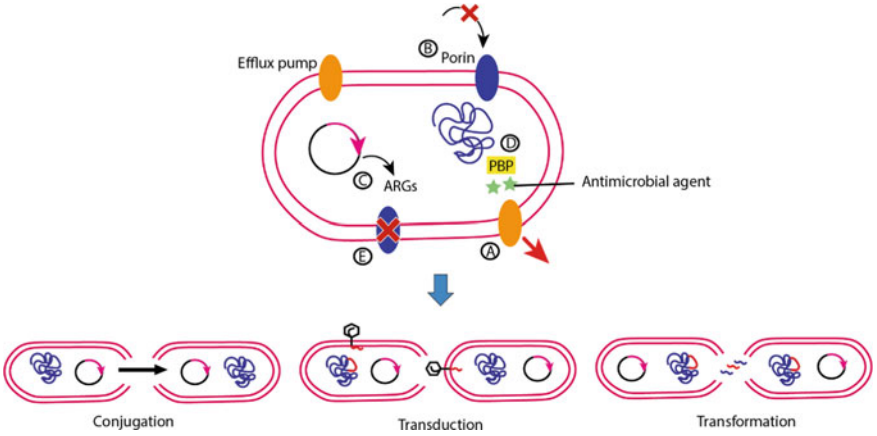

Fig. 1 Possible mechanism of antimicrobial resistance. (A) Altered affinity or increased expression of efflux pump, (B) decreased membrane permeability through modified porins, (C) increased production of antimicrobial resistance genes (ARGs), (D) structural changes or mutations of PBPs, and (E) modification of drug targets may promote ABR among bacteria. Transfer of ARGs between bacteria can occur via conjugation, transduction, and transformation

of ARGs are found on mobile genetic elements like plasmids or transposons, and they are transferred between bacteria via various mechanisms, including transformation, transduction, and conjugation [26–28] (Fig. 1). In transformation, bacteria acquire and incorporate an extracellular DNA segment, previously released into the environment by other organisms [29, 30]. Transduction involves the transmission of a DNA segment or plasmid harbouring ARGs between bacteria by a phage [31]. Finally, conjugation facilitates genetic exchange by elongating a pilus in Gram-negative bacteria or producing sex pheromones in Gram-positive bacteria [32]. Once resistant, a bacterium can rapidly multiply and pass on the resistance determinants to its progeny [33].

4 Antimicrobial Resistance Transmission in the Environment Through Wastewater

AMR has emerged as a significant global concern in recent years, affecting humans, animals, and the environment. The inappropriate and excessive use of antibiotics in a variety of sectors, including agriculture, veterinary medicine, and healthcare, is at the root of the global epidemic that has emerged in AMR transmission in the environment [34], implying that the environment serves as an AMR reservoir and is critical for transmitting AMR microorganisms with ARGs to animals and humans [34, 35]. AMR is facilitated by several factors, including antibiotics, antimicrobial genes, heavy metals, and biocides [34], and it can be transmitted to the environment

in a variety of ways, including through wastewater from hospitals, healthcare-related companies, livestock farms, and agriculture [36].

Antibiotics are frequently used to treat human illnesses in the healthcare sector [37]. Antibiotic abuse and overuse in humans, on the other hand, may result in the selection of resistant strains [38]. Additionally, veterinary drugs used in animal husbandry were originally intended to prevent animal diseases but are now being inappropriately used for other purposes, such as feed additives and growth stimulants [39]. As a result, humans and animals expel biologically active antibiotics in their urine and faeces, which are then discharged into wastewater treatment facilities (WWTPs) [40] (Fig. 2). Additionally, the pharmaceutical industry's inappropriate disposal of unused or expired medicines may also contribute to the discharge of antibiotics and AMR microorganisms into the environment. Besides, antibiotics have a half-life of a few hours to hundreds of days, which means they will linger in wastewater and be considered persistent pollutants in the environment [41]. To survive and grow in sewage, bacteria will develop resistance mechanisms to AMR drugs. Susceptible bacteria will be killed, or their activity will be suppressed under the impact of these antibiotics. Meanwhile, bacteria that are intrinsically or acquired resistant to antibiotics have a better chance of survival and expansion [42]. The surviving AMR microorganisms with ARGSs will spread the genes to other microbes, thereby making wastewater a reservoir for AMR microorganisms. Besides, due to the antibiotic's slow decomposition, it may find its way into groundwater or aquatic systems throughout the wastewater treatment process [35], where it can be disseminated to humans, animals, and the environment.

AMR microorganisms can be transmitted to the sewage system through infected human secretion, clinical or industrial settings. The ARBs will then transfer to the wastewater treatment plants (WWTPs) and eventually transmitted to sewage workers and residents who live near the WWTPs. This can be occurred either through drinking infected water, consume infected vegetables, or via recreational use

Additionally, biocides are a factor in AMR. Biocides are antimicrobial chemical compounds frequently used in the home, industry, and healthcare to control infections and microbiological contamination [43]. Ethanol, formaldehyde, chlorhexidine, triclosan, and quaterium ammonium compounds (QACs) are all examples of common biocides [34]. Improper biocide disposal in WWTPs can increase the number of biocides entering the environment, raising the likelihood of causing AMR in microorganisms residing in the WWTPs [40]. For example, chlorine resistance in Salmonella typhi demonstrates how improper biocide use can exert selective pressure on bacteria, which then respond by developing resistance mechanisms [43]. When mixed with other biocides such as QACs and chlorhexidine, triclosan has been proven to cause antibiotic resistance in microbes. Additionally, sub-lethal doses of biocides contribute to selecting mutations conferring antibiotic resistance [34].

Heavy metals are also a vector for AMR transmission in the environment. Heavy metals are non-antibiotic antimicrobial compounds that have been extensively used in agricultural and industrial applications for a variety of purposes [44]. Interestingly, they can also act as a selector for ARGs, possibly by physically associated with plasmids or chromosomes containing ARGs [45]. For example, MRSA

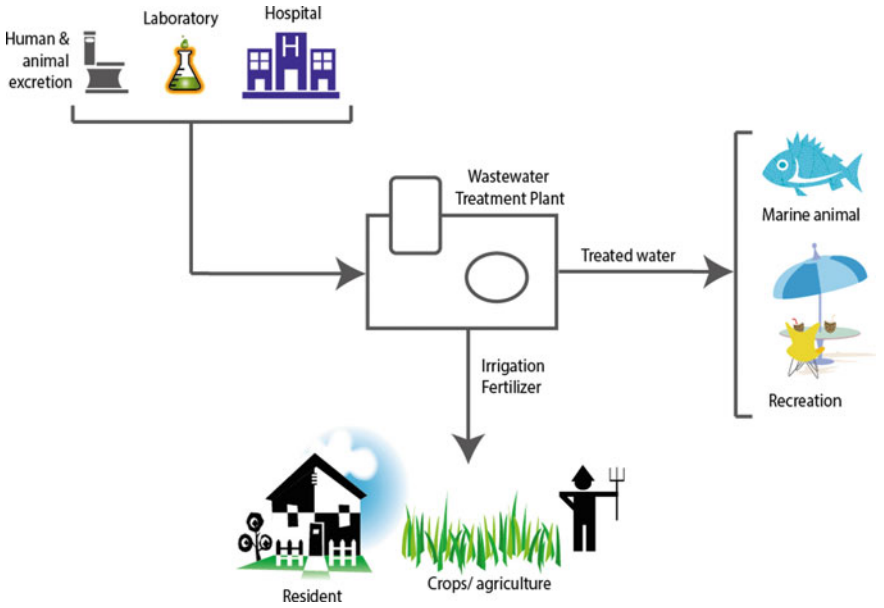

Fig. 2 Potential transmission of antimicrobial resistance microorganisms in the environment.

isolated from livestock possessed plasmids encoding resistance genes to Cu and Cd (*copA*, *cadDX,* and *mco*), as well as numerous antimicrobials such as Macrolides, Lincosamides, Streptogramin B, Tetracyclines, Aminoglycosides, and Trimethoprim (*erm(T)*, *tet(L)*, *aadD,* and *dfrK*) [46, 47]. Thus, incorrect disposal of heavy metals to WWTPs might increase metals entering the environment and the development of AMR microorganisms [40].

The environment is considered a route of transmission for ARBs to humans, facilitated by WWTPs. This finding is consistent with some studies demonstrating the occurrence of antibiotic-resistant bacteria such as *E. coli* against cephalexin, ciprofloxacin, and ampicillin in treated sewage produced by Penang WWTPs [36]. Additionally, humans may be exposed to these bacteria while participating in recreational activities in contaminated surface water, ingesting contaminated drinking water, or consuming fresh fish products [48]. In agriculture, sludge is frequently applied as fertiliser due to its nutritional contents. However, this might also facilitate the spread of AMR microorganisms to animals or humans through the consumption of contaminated crops or direct skin contact [37]. Additionally, the leading cause of AMR emergence worldwide is the improper use of antimicrobial drugs by humans in hospitals to treat infections [13]. Although the primary purpose is to treat the infections caused by pathogenic microorganisms, these microorganisms continually mutate and evolve, enabling them to adapt to their environment and eventually develop resistance to specific antibiotic treatments. As a result, the antimicrobial-resistant bacteria can spread from the infected patients to other people via unclean

hands or contaminated objects. Patients who remain untreated for AMR bacteria will subsequently convey these resistant microorganisms to others, increasing the danger of disease spread, severe sickness, and even death.

5 The Effect of Antimicrobial Resistance Microorganisms on Humans

Usually, antibiotics, one of the antimicrobial agents, are prescribed to treat a wide range of illnesses and surgical procedures, including organ transplants, blood infections, pneumonia, and cancer treatment [13]. However, improper use of this drug may cause pathogenic microorganisms to evolve to become resistant to antimicrobial treatment, making infections more difficult to treat and raising the risk of disease spread, severe illness, and death [13]. In general, the more antibiotics used, the more bacteria adapt and develop new ways to survive, leading to antibiotic resistance. As a result, some bacteria live and multiply rather than being eradicated by antibiotics, causing significantly more harm and may impact patients' quality of life, such as increased healthcare expenses, hospitalisation length, and mortality [49].

MRSA, one of the most well-known examples of AMR, has been linked to high mortality rates across the globe each year, rendering treatment ineffective [50]. Additionally, 4.1% of newly diagnosed tuberculosis cases are multidrug resistant. It is anticipated to grow dramatically by 2040, particularly in nations with a high prevalence of tuberculosis, such as India and the Philippines [49, 51]. Compared to non-resistant bacteria, resistant bacteria quadruple the likelihood of getting a severe medical issue and triple the possibility of dying. Naturally, these negative consequences will be magnified as the severity of resistant infections and the host's sensitivity increase [52, 53]. This is consistent with the increased morbidity and fatality rates experienced by infected patients over time. It is estimated that if significant action against AMR is not taken by 2050, roughly ten million people will die [49, 54].

Additionally, AMR may result in inadequate treatment of sepsis, which is among the top cause of death in hospitals, with a mortality rate of 19.7 worldwide [55]. Sepsis is a potentially fatal organ dysfunction caused by an abnormal host response to infection [56]. This is a common complication seen in immunocompromised cancer patients and recipients of hematopoietic stem cell transplants [57]. As a result, the global spread of AMR microorganisms, particularly among immune-deregulated patients, may result in a delay in commencing effective empirical antibiotic therapy, potentially resulting in infection and hence sepsis [57]. Thus, it is vital to decrease AMR transmission in the environment, which can begin with appropriately managing sludge disposal and treatment; and ensuring that it is safe for human application.

6 Microbial Fuel Cell (MFC) technology and Its Application in Minimising Antimicrobial Resistance Transmission in the Environment

MFC technology is a relatively new biotechnology that can remediate wastewater while generating electricity. MFCs enhance electricity generation during wastewater treatment by exploiting residual sludge substrates, such as acetate or glucose, using electrogenic bacteria's (EB's) enzymatic activity [58]. EB is a type of organism capable of transferring electrons extracellularly across the cell membrane to electron acceptors, such as electrodes and oxide minerals, both under anaerobic and microaerobic environments [59, 60]. These bacteria can utilise this extracellular electron transfer (EET) to get energy for development or facilitate cell-to-cell communication [61].

Under aerobic circumstances, microorganisms near the anode decompose organic materials, and the resulting electrons are either transported directly through cell components such as proteases or nanowires on the membrane surface or indirectly via the electron shuttle [62]. The cathode accepts electrons and protons from the anode and initiates a reduction process [63]. The equation below illustrates the reaction of a typical MFC at the anode and cathode when acetate is used [64].

$$\text{Anode reaction}: \ CH_3COO^- + 2H2O \text{ —} > 2CO_2 + 7H^+ + 8e^-$$

$$\text{Cathode reaction}: \ O_2 + 4e^- + 4H^+ \text{—} > 2H_2O$$

MFCs could generate energy from diverse substrates, from pure chemicals to complex mixtures of organic compounds present in wastewater. While substrates with a high concentration of complex organic matter could stimulate the growth of various active microorganisms, simpler substrates are believed to produce more immediate output. Acetate and glucose are often utilised as substrates in MFCs and power generation. Acetate is commonly used as a substrate for benchmarking novel MFC components, reactor designs, or operating conditions due to its inertness to alternative microbial conversions (fermentation and methanogenesis) at ambient temperature [65]. As for glucose, compared to anaerobic sludge with a limited substrate supply, the introduction of glucose can increase power output by up to 161 mW/m2 [66].

There are three basic reactor configurations: (a) uncoupled bioreactor MFC in a bioreactor followed by a chemical fuel cell, (b) integrated bioreactor MFC, and (c) MFC with bacteria-anode interaction (Fig. 3). In an uncoupled MFC, a biofuel, such as methane gas, is created in a bioreactor before a chemical fuel cell takes place. One of the major disadvantages of this configuration is mainly the low conversion efficiencies of the biological substrate to hydrogen and the requirement for high fuel cell temperatures to achieve sufficient hydrogen oxidation. The second design is identical to the first, except that the fermentation (mainly to hydrogen gas) occurs

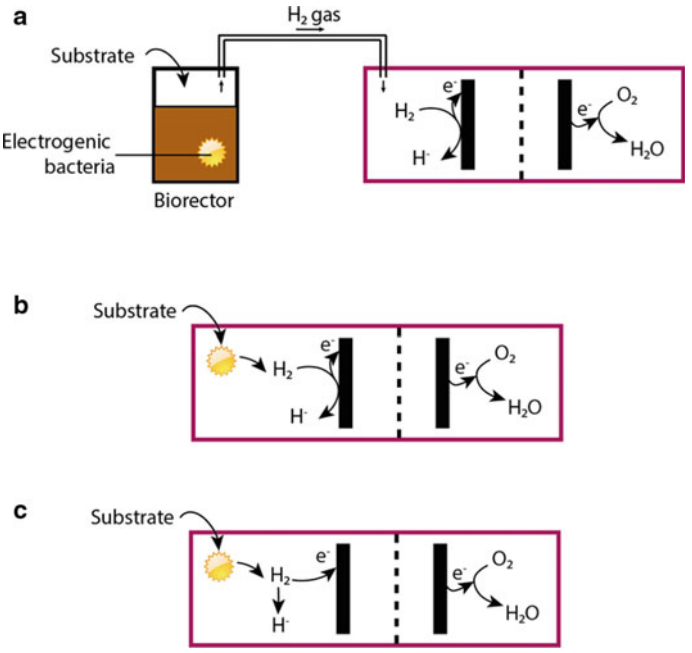

Fig. 3 Three basic reactor configurations: (A) uncoupled bioreactor MFC in a bioreactor followed by a chemical fuel cell, (B) integrated bioreactor MFC, and (C) MFC with bacteria-anode interaction. Adapted with permission from [58](CCBY)

within the fuel cell. This type of MFC frequently employs catalysts to create the best environment for hydrogen gas conversion to electricity. The third configuration, dubbed the genuine MFC, involves direct electron transfer from the bacteria to the anode without an intermediate fermentation product [58].

MFC technology effectively displaces non-renewable fossil fuels such as natural gas and coal and reduces greenhouse gas emissions that contribute to global warming and climate change [67, 68]. However, despite its benefits in green energy production, no study has been undertaken to determine its role in minimising the transmission of AMR bacteria found in sewage sludge to the environment. Yet, it has been demonstrated that several EB employed in MFC, such as *Bacillus subtilis*, release bacteriocin, which may substantially inhibit AMR transmission in the environment.

6.1 The Application of Microbial Fuel Cells Technology in Reducing Antimicrobial Resistance in the Environment

One possible alternative is to use MFC. As previously said, MFCs are well renowned for their ability to degrade pollutants while simultaneously generating significant amounts of electric energy. Notably, MFC is also known to break down antibiotics

and ARGs, increasing the likelihood that it will help prevent AMR transmission in the environment. For example, MFC was demonstrated to remove 85.1% and 65.5% of sulfamethoxazole (SMX) and norfloxacin (NFLX), respectively [71, 72]. Additionally, the number of ARGs and integrons after MFC treatment was significantly less than that discovered in WWTPs. For example, the relative abundance of the *intI1* is between 63.11 and 652.00 copies/mL(g) in the MFC product, compared to 109 to 1011 copies/mL in WWTPs [62, 73].

There are numerous approaches to increase the rate of AMR bacteria removal by MFC, which can be accomplished by adjusting the conditions that influence antibiotic removal: (a) raising the voltage, (b) selecting suitable substrates, and (c) including some additives into the system. For example, according to Yang et al. (2018), increasing the voltage from 0 to 1.5 V raised the degradation rate of sulfadiazine (SDZ) from 79.3 to 91.9% [74]. This increase in antibiotic removal may be because certain microbial communities, such as *Methylococcus capsulatus, Dechlormonas, Byssovorax cruenta*, *and Longilinea arvoryzae* are positively influenced by electrical stimulation, and this would promote their bacterial activity to accelerate biological metabolism [62, 75].

Additionally, the type of substrate may affect the rate of antibiotic clearance. For example, the addition of acetate accelerates the breakdown of chloramphenicol by up to 96.53% [76]. Consistently, Zeshan and Ullah (2020) observed that acetate-fed MFCs generated maximum voltage and power densities faster than glucose- or sucrose-fed MFCs, implying that different types of substrates may affect MFCs performance and hence their potential to remove antibiotics [77]. Additionally, certain inorganic compounds, such as nitrite and copper aid in reducing ARGs. For example, it has been demonstrated that the addition of nitrite increases sludge's hydrolysis rate and decreases the requirement for carbon sources, encouraging microorganism growth and metabolism and consequently improving MFC performance [78].

The presence of EB in MFC may potentially affect the antibiotic's clearance rate. *Bacillus* species, for example, are capable of creating a variety of antimicrobial compounds (AMCs) that are useful in the food and pharmaceutical industries [79]. Additionally, strains of the *Bacillus subtilis* group have been recognised for decades to produce a vast array of secondary metabolites capable of mediating antibiosis. At least 4–5% of the genome of any strain of *Bacillus subtilis* is projected to be devoted to synthesising AMCs, which are primarily antimicrobial peptides (AMPs) [79]. AMPs are often cyclic and hydrophobic in structure, with unusual moieties such as D-amino acids (AA) or intramolecular thioether linkages. Along with AMPs, volatile metabolites are a wide class of antimicrobials that play a range of metabolic and functional functions [79]. These peptides are referred to as "bacteriocins," which are low molecular weight molecules that can inhibit the growth of bacteria closely related to the generating strain [80]. Alternatively, bacteriocins may operate as antimicrobial or lethal peptides, directly reducing competing strains or pathogens in the environment, such as *Klebsiella* sp., a capsulated bacterium, resulting in decreased AMR transmission/

7 Malaysia's Initiatives for Preventing the Spread of Antimicrobial Resistance in the Environment

Antibiotic resistance is reaching alarmingly high levels all around the globe. New resistance mechanisms are evolving and spreading over the world, posing a danger to the health management to handle common ailments resulting from the AMR infection [81]. In addition to the escalating prevalence of debilitating diseases, augmenting cases of antibiotic resistance also cause major economic burden due to AMR containment and high cost of disease treatment [82]. Consequently, it is projected that AMR would put a total of 24 million people (particularly from the low-income countries) into extreme poverty by 2030 [83], further corroborating the urgency to combat the dissemination of AMR worldwide comprehensively.

During an ASEAN meeting in 2017, it was recognised that anti-AMR efforts were still insufficient, and that multi-sectoral collaborations from different stakeholders were required. During the summit, ASEAN leaders agree to tackle AMR using the One Health approach which is aimed to enhance the AMR containment activities, actively engage relevant stakeholders, develop defined objectives, and to implement monitoring and evaluation (M&E) systems [84]. In compliance with the declaration, Malaysia has implemented several actions to cut the AMR distribution by implementing different progressive approaches. These include the initiation of One Health concept involving pharmacist, physicians, patients, and other professionals that was established to allow effective communication among the communities thus achieving better public health outcomes for humans, animals, and the environment [85]. Malaysia government with the help from Ministry of Health (MOH) also initiated the "National Surveillance of Antibiotic Resistance (NSAR)" [86] to monitor the occurrence of AMR in Malaysia as well as the protocol on Antimicrobial Stewardship (AMS) Programme in the healthcare facilities to promote an appropriate utilisation of antibiotics in terms of right choice, route of administration, dosage, and duration for antibiotic prescription.

Following the NSAR programme, the "National Surveillance on Antibiotic Utilisation (NSAU)" was also performed to assess the quantity and trajectory of antibiotic use in Malaysian hospitals of various settings and the potential links that contribute to specific antibiotic use. These statistics have aided local health workers in their clinical practice, particularly in the application of antimicrobial stewardship, at the hospital level [87]. In addition to those policies, the Malaysian Action Plan on Antimicrobial Resistance (MyAP-AMR) 2017–2021 has been conducted in collaboration with numbers of constituents and stakeholders including the Ministry of Health (MOH), Ministry of Agriculture and Agro-based Industry (MOA), Ministry of Higher Education (MoHE), Ministry of Defence (MINDEF), hospitals, professional organisations, the animal food industry, private healthcare facilities, community pharmacists, academic institutions, the private sectors, international partners, NGOs, and civil society [88]. The action plan on antimicrobial resistance (MyAP-AMR) is aimed to decelerate the emergence of AMR and prevent its dissemination via

four priority areas: (i) public awareness and education, (ii) surveillance and research, (iii) infection prevention and control, and (iv) appropriate use of antimicrobials.

While there is currently scarce or no report on the clinical assessment of the MFC function in reducing the AMR dissemination, its potential on the accomplishment of AMR reduction is still promising. The inclusion of EB which simultaneously functioning as bacteriocin producer may antagonistically inhibit the resistant bacteria in the wastewater substrate hence attenuating the possibility of resistance genotype transmission among the microbial populations. This action will not only benefit the environment in terms of green renewable electricity generation, but it also represents as a contribution from the engineering sector (other than the healthcare organisation) to decelerate the AMR widespread as has been underlined in the MyAP-AMR that promotes the involvement and collaboration from multiple stakeholders in combating this threatening circumstance. Indeed, restricting the AMR distribution in the community and environment via the function of MFC is interesting, however, an in-depth investigation is required to validate its potential in diminishing the AMR incidents.

8 Conclusion

Antimicrobial resistance (AMR) is a significant global public health problem, ranking among the top ten. This study covers the fundamentals of AMR and the possibility for wastewater to act as a carrier of AMR in the environment. Compared to other conventional wastewater treatment procedures, MFCs can help minimise AMR by boosting antibiotic removal rates. These antibiotics, which are frequently generated from hospitals, are greatly concentrated in sludge, favouring the growth of ARGs among the bacteria that live there. Additionally, this chapter discussed strategies to increase the performance of existing MFCs, primarily by increasing electrical stimulation, selecting appropriate substrates, and incorporating some additives, all of which influence the microbial population and its metabolic activities. It is hypothesised that boosting antibiotics' clearance efficiency may help prevent the creation of ARGs. Nonetheless, it is vital to improve the current design of MFCs and comprehend their operation, and by doing so will reduce AMR transmission in the environment.

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