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Exploring the Bacteriophage in Malaysia: An Overview of Applications and Challenges

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ABSTRACT

Antibiotic resistance is a worldwide concern as more drugs are losing efficacy and fewer candidates are being developed in the pipeline. As a result, there is growing attention towards alternative applications of microbial control, and bacteriophages have come to the forefront of research. However, there is limited data and experimental studies in Malaysia. The well-documented use of these viruses to overcome the problem of antimicrobial resistance and multi-drug resistance is still scarce in the country and warrants exploration. Here, we discuss the potential of bacteriophage applications in healthcare, animal husbandry, aquaculture and agriculture in Malaysia. The challenges faced in doing so and reception among the country's researchers, clinicians and healthcare authorities are also discussed. Although the use of bacteriophages in this capacity is just beginning to unfold, it is hoped that there will be a shift in perception towards a positive reception, especially with the looming threat of antibiotic resistance.

INTRODUCTION

Antimicrobial resistance is a public health concern in Malaysia as it is in many countries. Recently, in April 2021, the World Health Organization (WHO) published a report on the diminishing effectiveness of antibiotics available for clinical use and the lack of new candidates being developed (WHO, 2021a).

The misuse and overuse of antibiotics, together with the slow pace of new drug development, have exacerbated the problem of resistance, forcing researchers to focus on alternative antimicrobial therapeutics. Many ASEAN countries, including Malaysia, have begun exploring ways to combat antimicrobial resistance, and bacteriophage research is one of the promising options (Binte et al., 2020; Chu et al., 2022). Mostly comprising large DNA-bearing viruses, bacteriophages need to infect a specific bacteria host to replicate and survive. Upon activation of the lytic cycle, the virus progeny will form and be released into the environment through rupture of the bacterial cell wall which will destroy the host in the process. Phage therapy and antibiotic therapy differ in their modes of action and dose administration. Antibiotics target broad bacterial processes, often affecting both harmful and beneficial bacteria, which can lead to resistance. In contrast, phage therapy uses bacteriophages that specifically infect and lyse certain bacterial strains, minimizing the impact on the microbiota and evolving alongside bacteria to reduce resistance. While antibiotics are administered in fixed doses, phages replicate at the infection site, potentially reducing the need for repeated doses.

With its abundance in the environment, the only challenge is to isolate the most effective phages to destroy pathogens without affecting the functions of human and animal cells. Bacteriophages potentially have a variety of applications, and some of them have been approved by the United States Food and Drug Administration. They include medicine (to treat wound infection), agriculture (to control plant pathogens) and food safety (to control contamination).

Anti-Microbial Resistance

Poor monitoring and rampant misuse of antibiotics in ASEAN countries are resulting in a huge public health threat: the rise of antimicrobial-resistant (AMR) and multidrug-resistant (MDR) bacteria. This may be demonstrated by the persistent increase in tuberculosis (TB) infections known as MDR-TB in the region (WHO, 2021b). Worldwide pathogen monitoring has recorded a rise in the prevalence of such bacteria against a number of antibiotics, including sulfonamides and phenicols (Hendriksen et al., 2019). The global prevalence of single-drug resistance and cross-resistance in bacterial species varies significantly across ASEAN countries, influenced by local healthcare practices, antibiotic usage, and surveillance systems (Vilaichone et al., 2018; Chua et al., 2021). In Malaysia, the antibiotic prescription rate in hospitals and primary care settings remains high (between 70 % and 80 %), which results in higher mortality, morbidity and treatment cost as common pathogens begin to develop resistance (Akhtar et al., 2020).

According to the 2017 Malaysian National Surveillance of Antibiotic Resistance (NSAR) study, there has been an alarming rise in the spread of antimicrobial-resistance and multidrug-resistance genes (Institute for Medical Research, 2020). These genes confer microbes the ability to neutralise the active site of antibiotics or an enhanced efflux of drugs. For example, resistance to all antibiotics in Acinetobacter baumanii has increased by 42.4 % in 2021 compared to the year before. In many public hospitals, the rise of extended spectrum beta-lactamase (ESBL) feature in Enterobacteriaceae species has become a major problem. Klebsiella pneumoniae, one of the most common nosocomial pathogens, has been found to have increased resistance towards cefotaxime and ceftazidime (a third-generation cephalosporin introduced in the 1980s) from 22.6 % and 20.6 % in 2020 to 24.5 % and 22. 5 % in 2021. Resistance to cefotaxime in Escherichia coli has also increased from 15 % in 2010 to 23.4 % in 2016. The presence of the New Delhi metallo-B-lactamase-1 (NMD-1) gene in carbapenem-resistant K. pneumoniae (CRKP) was identified at a Malaysian hospital in 2010. Since then, its prevalence has increased dramatically from 0.3 % in 2011 to 2.8 % in 2015. The increasing usage of carbapenems in Malaysia has led to a steady rise of carbapenem resistance, as these antibiotics are advised for the treatment of ESBL infections (Paterson et al., 2004; Institute for Medical Research, 2020). Vancomycin-resistant Enterococcus faecium also reportedly increased from 8.7 % in 2012 to 14.9 % in 2016.

The indiscriminate use of antimicrobials in animal husbandry and poultry production is another key contributor to the spread of antimicrobial resistance in Malaysia. Many current antibiotics used in human healthcare are also being used in veterinary production, including third and fourth generation cephalosporins, macrolides, fluoroquinolones, aminoglycosides and penicillin. They are frequently used to stimulate growth or to prevent infection in livestock and poultry kept in congested and unsanitary conditions. These antimicrobial residues accumulate in muscle tissues, blood and internal organs (Hossain et al., 2022), which may be passed on via the food chain, potentially resulting in foodborne infections that cannot be treated with routinely used antibiotics. E. coli and K. pneumoniae are two common bacteria found in farm animals and are usually resistant to a range of antibiotics (Brennan et al., 2016; Harada et al., 2016). Cases of Salmonella, Campylobacter, Methicillin-resistant Staphylococcus aureus (MRSA) and Vancomycin-resistant S. aureus (VRSA) are also on the rise in food animals, with serious consequences for public health (Friese et al., 2013; Schmithausen et al., 2015; Hassali et al., 2019; Gahamanyi et al., 2020; Grant et al., 2016).

The excessive use of antibiotics has added pressure on the national healthcare system, where precious resources have to be allocated to control the spread of AMR and MDR bacteria, besides increasing treatment cost for patients. Antimicrobial resistance is expected to surpass all other causes of death by 2050, so it is critical to find a safe and effective solution to mitigate this impending threat.

Potential Applications in Malaysia

Bacteriophages, which are viruses that selectively kill bacteria, offer an effective alternative for treating drug-resistant bacterial infections. Phages can be found anywhere where there is an abundance of host bacteria, and this has made them a potentially rich resource for the discovery of new antibacterial agents to complement existing treatments (Derensinski et al., 2009). Phages have demonstrated their potential as a viable alternative to antibiotics. However, the adoption of phage therapy and its research vary by country and may be influenced by healthcare infrastructure, legislation, funding and reception among clinicians. Although the boom of synthetic antibiotics in the mid-20th century had somewhat diminished interest in phage therapy, some researchers, particularly those in Eastern Europe, had continued to explore its potential. In Malaysia, there is very little interest and research in the use of bacteriophage, even for non-human applications. This indicates that the country’s healthcare, research and industry players still have many alternatives to deal with bacterial infection and may rather avoid the manipulation of viruses due to safety fears.

Phage therapy is indeed difficult to develop as the high specificity of the virus requires it to be used as a cocktail that is tailor-made for the host population. This means a “phage bank” has to be established to produce the cocktail of different bacteriophages to treat the same disease, as pathogen components may vary between patient and location. The host pathogen needs to be studied to determine if they bear receptors that allow the correct bacteriophage to infect them. Furthermore, bacteria can evolve and change their receptors, allowing the host pathogen to develop resistance against phage infection just like antimicrobials (Dimitriu et al., 2022; Oechslin et al., 2018; Labrie et al., 2010).

This requires the phage bank to be regularly updated so it can expand its collection and maintain the effectiveness of its viruses in treating infections. The maintenance of the virus bank, together with constant regulatory tests for safety, require a heavy investment. In a developing country like Malaysia, where funding is limited and broad economical methods are in top demand, the government and industry players have little to no appetite in establishing complicated healthcare facilities like a phage bank.

The safety aspect is also a challenge, especially when the country lacks knowledge and researchers to utilise phage therapy. Unlike Western countries that have been studying bacteriophage therapy for the past 100 years, there is still very little literature on the subject produced by Malaysian scientists. Bacteriophage research in Malaysia is still developing, with studies such as those on bacteriophages from water samples effective against Vibrio cholerae (Al-Fendi et al., 2014) and those targeting colibacillosis in broiler chickens (Lau et al., 2010) marking important contributions. However, the overall scope of research in this area remains limited compared to more established fields of microbiology or regions with a longer tradition of bacteriophage studies. Basically, the bacteriophage used in a therapy only infect prokaryotes and does not infect the patients' eukaryotic cells. However, bacteriophage can have potential concerns related to the human immune response. For example, the human immune response may recognize bacteriophages as foreign entities and may produce antibodies against it. In addition to this, as with any foreign substance injected into the human body, some people may develop allergic reactions to phage preparations. These allergic reactions might range from mild skin irritation to life-threatening complications.

Despite the concerns, phage therapy has mostly been observed to be safe and effective. Most reported complications like fever, diarrhoea, nausea and inflammation among patients are attributed to endotoxins formed by the rupturing and lysis of bacterial cell walls in the lytic phase and it is a transient response indicating that the therapy is working (Ujmajuridze et al., 2018; Ooi et al., 2019). These conditions were often milder and less common than the side-effects observed in antibiotic-treated patients.

Although there are many challenges in bacteriophage research, the number of local researchers who are interested in the field is growing, with the primary goal of isolating and characterising viruses against key AMR and MDR pathogens, such as Salmonella spp., K. pneumonia and Enterococcus spp. (El-Telbany et al., 2021; Baqer et al., 2021) (Table 1). The recent alarming report on the rise of antimicrobial resistance in ASEAN countries has begun to open the eyes of scientists and stakeholders on the importance of developing novel agents and therapeutic strategies that not only overcome the cases, but also prevent their rise in the first place (Center for Disease Dynamic, Economics and Policy, 2021).

Phage as Anti-Bacterial Therapy

Phage therapy is the use of phages or their derivatives as bioagents to cure or prevent infectious diseases caused by bacteria (Matsuzaki et al., 2005). Despite the low enthusiasm in the medical community, efforts are still made to consider applying phage as a treatment option. Sourcing for bacteriophage is never a problem as they may be found in abundance where their hosts reside, such as in jungles, dairy products, seafood, vegetables, meat samples and sewage (Tan et al., 2021; Premaratne et al., 2017; Thung et al., 2017).

Although Malaysia has not approved any clinical trials on phage therapy, in vivo pre-clinical investigations have been reported. For example, an intraperitoneal phage administration study was reported to be efficient in reducing Burkholderia pseudomallei infection in mice experiment

Table 1: The list of bacteriophages studies in Malaysia included in this article.

Phage Application	Phage strain	Phage family	Isolation source	Host pathogen	Reference
Clinical	vB_ZEFP	*Podoviridae*	Hospital wastewater plant	*Enterococcus faecalis*	(El-Telbany et al., 2021)
	KP	*Podoviridae* *Myoviridae* *Siphoviridae*	Sewage water and cockles	*Klebsiella pneumonia*	(Baqer et al., 2021)
	C34	*Myoviridae*	Sea water	*Burkholderia pseudomallei*	(Guang-Han et al., 2016)
	ΦNUSA-1	*Myoviridae*	Raw sewage wate	*Staphylococcus aureus*	(Tan et al., 2020)
	ΦNUSA-10	*Siphoviridae*			
Agriculture	No strain name	Not reported	Sewage and soil sample	*Escherichia coli*	(Tan and Tony, 2014)
	pPM_01	*Siphoviridae*	Sewage treatment facility	*Proteus mirabilis*	(Wirjon et al., 2016)
	NΦ-1 and NΦ-3	*Podoviridae*	Termite infected rice	*Xanthomonas oryzae* In rice	(Liu et al., 2021)
	ΦKpaV03 ΦKpaVa10 and ΦKpaV12	*Myoviridae*	Domestic sewage facility	*Klebsiella pneumoniae*	(Paran et al., 2020)
	ΦKpaV03 and ΦKpaVa10	*Podoviridae*			
Livestock	SE07	*Podoviridae*	Retail chicken meat	*Salmonella Enteritidis*	(Thung et al., 2017)
	SE01-SE14 ST01-ST04 CJ01-CJ04 VP01 and VP02 EC01-EC05	Not reported	Various food types and sewage water	*Salmonella Enteritidis* *SalmonellaTyphimurium* *Camphylobacter Jejuni* *Vibrio parahymolyticus* *Escherichia coli*	(Thung et al., 2017) (Thung et al., 2020)
	ΦLM1-ΦLM05 ΦEC1-ΦEC3 ΦSA1 and ΦSA2 ΦMRSA1 ΦCC1 ΦCj1-ΦCJ5	Not reported	Food product (Beef, chicken, vegetable, clam, cockles and shrimps) and environmental samples (water and sewage)	*Camphylobacter jejuni, Escherichia coli, Staphylococcus aureus, Listeria monocytogenes*	(Premarathne et al., 2017)
	EC1	Not reported	Chicken faeces	*Escherichia coli*	(Lau et al., 2010)
	VPUSM	*Myoviridae*	Environmental water samples: rivers, lakes, sewage, fish farms, ditches, ponds	*Vibrio cholerae*	(Al-Fendi et al., 2014)
	CJ01	*Myoviridae*	Retail chicken meat	*Camphylobacter jejuni and Camphylobacter lari*	(Thung et al., 2020)
Aquaculture	Vp33, Vp22, Vp21, Vp02 Vp08 and Vp11	*Podoviridae* *Siphoviridae*	Seafood samples	*Vibrio parahaemolyticus*	(El-Telbany et al., 2021)
	vB_Sags-UPM1	*Siphoviridae*	Infected tilapia	*S. agalactiae*	(Megat et al., 2023)
	VpKK5	*Siphoviridae*	Coastal sand sediment	*Vibrio parahaemolyticus*	(Lal et al., 2016)
	VhKM4	*Myoviridae*	A diseased culture Barramundi Perch Lates calcarifer	*Vibrio harveyi and Vibrio parahemolyticus*	(Taylor and Reeder, 2020)

(Guang-Han et al., 2016). Although the formulation is tolerable to mice, the safe dose and immunological interactions have yet to be properly characterised in humans. Using the agar overlay method, Tan et al. (2021) tested the lytic activity of multiple phages against S. aureus strains recovered from sewage (Tan et al., 2021). Excitingly, they discovered that two phages from the Myoviridae and Siphoviridae families had an extraordinarily broad host range against >80 % of methicillin-resistant S. aureus (MRSA) and its susceptible counterpart (MSSA). Because of their broad and outstanding antibacterial properties, these phages have been proposed as a potential novel therapeutic option for S. aureus clinical infection (Tan et al., 2020).

Another study by Wirjon et al. (2016) found that Phage pPM_01 isolated from a sewage treatment facility in Penang was a good candidate to treat Proteus mirabilis, which caused urinary tract infection in humans (Wirjon et al., 2016). This was due to the phage's high lytic capabilities and virulence against P. mirabilis. The genome analysis showed neither virulence factors nor potentially known toxins were present in the phage pPM_01 genome (Wirjon et al., 2016). Another host-specific phage C34 belonging to the Myoviridae family was isolated from a seawater sample and found to be potent against clinical B. pseudomallei (Guang-Han et al., 2016). The efficacy of C34 phages had been evaluated an in vivo model, resulting in significant reduction of bacterial burden in B. pseudomallei-infected mice compared with untreated control. Phage therapy for melioidosis is currently being reviewed in clinical trials, but it has not yet been licensed for industrial use. The findings of phage C34 and several other phages reported elsewhere (Kvitko et al., 2012; Wang et al., 2022) strongly implied their potential to be developed as a therapeutic agent for melioidosis.

Another study by Paran et al. (2020) used a lytic bacteriophage cocktail isolated from a domestic sewage plant to treat clinical K. pneumoniae (Paran et al., 2020). The phage was observed to lyse a gentamycin-resistant strain of the bacteria. Significantly, because mono-phage treatment is more personalised and time demanding, this discovery sheds light on the effectiveness of using phage cocktail treatments (Paran et al., 2020).

Phage in the Livestock and Aquaculture

The use of bacteriophages is not confined to human healthcare. It may be used in livestock and poultry protection to reduce animal mortality. The aquaculture is rapidly growing industry and livestock farming is a significant part of the economy in ASEAN regions. The traditional reliance on antibiotic has led to rising concerns on antibiotic resistance and threatens the sustainability of the industry. Studies on the effectiveness of phage in controlling pathogens such as Vibrio and Aeromonas which are responsible for significant mortality in shrimp and fish population have been reported. For example, a study demonstrated that phage treatment significantly protected shrimp from Acute Hepatopancreatic Necrosis Disease (AHPND) caused by Vibrio parahaemolyticus (Jun et al., 2018). Additionally, the isolation of specific phages, like vB_AdhS_M4 against Aeromonas dhakensis, indicates the feasibility of targeted phage therapy for biocontrol in aquaculture (Sawaengwong et al., 2023).

Malaysia's livestock industry is growing, and it includes both ruminants and non-ruminant animals, such as dairy, poultry and porcine (Rosali et al., 2015). Population and wealth growth have increased demand for meat and poultry, which resulted in farms overusing antibiotics to enhance the growth of animals and supply stock in the fastest time possible. As a result, increasing levels of AMR and MDR bacteria and residual antibiotics have been detected in dairy and poultry products (Hassali et al., 2018; Geidam et al., 2012). Intensive livestock farming can facilitate disease transmission as these animals often have low genetic diversity and are reared in large and dense populations (WHO, 2016). Campylobacter spp., Salmonella spp., Listeria spp. and E. coli are examples of food-borne pathogens frequently associated with the livestock industry (WHO, 2016). Bacteriophages may thus be utilised to prevent and controlling pathogenic bacterial growth and proliferation in these animals.

While many studies have isolated phage against MDR pathogens and investigate their efficacy in vitro, local researchers are screening for potential bacteriophages to tackle the degree of antimicrobial resistance in the food chain (Lisha et al., 2017; Mohammad Jajere et al., 2020). Recently, phage against Campylobacter jejuni and Salmonella which are common food pathogens have been isolated by local scientists (Thung et al., 2017; Thung et al., 2020). Some of these phages may act as a biocontrol agent to selectively reduce or eliminate pathogen-susceptible organisms from animal environments (e.g., Intestinal flora).

A local study at Universiti Putra Malaysia has also reported the isolation of phages specific for C. jejuni, E. coli, S. aureus and Listeria monocytogenes from various environments to combat food-borne diseases (Thung et al., 2017). The study suggested that people do frequently ingest phages in their food and can be isolated from food products. Previously, Lau et al. (2010) documented the efficiency of bacteriophage isolated from chicken faeces in combating pathogenic strains of E. coli that caused colibacillosis in chickens (Lau et al., 2010). They demonstrated that the phage could reduce the severity of E. coli infection, bacterial loads (septicaemia) and mortality rate in farmed chickens. In another Malaysian study, Al-Fendi et al. (2014) successfully recovered 11 vibrio-phages from a variety of sources, including rivers, lakes, sewage, fish farms, ditches and ponds (Al-Fendi et al., 2014). They went on to characterise three of them, three of which were lytic phages with a narrow host range and recommended them as good candidates for use as biological control agents against cholera (Tan and Tony, 2014).

The use of phage in aquaculture has also been proposed, especially to control water-borne pathogens. Vibrio spp. and A. hydrophila are two frequent bacterial diseases affecting the aquaculture industry, causing not only high mortality rates but also significant economic losses. Methods to control these pathogens are similar to the livestock industry, which is the use of antibiotics. Tan et al. (2021) reported six bacteriophages isolated from seafood samples (blood clams, prawns, and surf clams) that demonstrated a narrow host specificity, infecting only the V. parahaemolyticus strains, which was commonly found in a variety of seafood (Tan et al., 2021). The isolation of Myoviridae and Siphoviridae phage against Vibrio harveyi were also done in Universiti Malaysia Sabah (Lal et al., 2017; Lal et al., 2016). This bacterium is known to cause gastroenteritis, which is frequently manifested in humans as bouts of abdominal pain, diarrhoea, fever and nausea. A temperate phage was recently reported and employed against Streptococcus agalactiae infection in tilapia fish (Megat et al., 2023). The phage endolysin is observed to destroy two strains of S. agalactiae with variable degrees of efficiency.

Phage in Agriculture

The use of bacteriophage to control plant pathogens has caught the interest of the agricultural industry. With millions of hectares of fertile land, the Malaysian economy is still partially dependent on agricultural production, particularly commodities like rubber and palm oil. Agriculture is also an important industry as the country tries to achieve food security by producing robust crops with better yield and disease resistance. The country's tropical climate is both a blessing and a curse because the warm and humid environment is not only suitable to promote the growth of plants, but it also stimulates the growth of phytopathogens (plant bacteria) like Xanthomonas spp., Dickeya spp. and Ralstonia spp.

The extent of antibiotic use in agricultural production in low- and middle-income countries was recently revealed more extensive than most of the literature reported (Taylor & Reeder, 2020). According to their findings, antibiotics were routinely used in the production of more than 100 crops, with rice topping the list as the most commonly treated product. Five antibiotics are most commonly reported in plant agriculture: streptomycin (the most widely used antibiotic globally), oxytetracycline, kasugamycin, oxolinic acid (OA), and gentamicin (McManus, 2014; Sundin & Wang, 2018; Miller et al., 2022). In Malaysia, a study found that 62.4 % of farms used antibiotics, with broiler chicken being the most treated (78 %) (Teo et al., 2023) and colistin sulphate (a reserved antibiotics) was noted 3.6 % of cases, raising concerns of the resistance.

Although the use of bacteriophage has not been approved for any application in Malaysia, researchers have discovered several phages that can infect common phytopathogens that harm plantations in order to mitigate the heavy dependency on antibiotics and to be applied in agriculture as biocontrol agent. Xanthomonas oryzae pv. oryzae (Xoo), for example, causes bacterial leaf blight (BLB) disease, and it is one of the most destructive pathogens of paddy crops in Malaysia. Two isolated Podoviridae phages from termites found in rice-growing areas were identified and sequenced (Liu et al., 2021). These phages have a short latent period with high burst size, indicating that they are specifically active against a large number of host strains. The detailed analysis of the phage genome showed that the presence of two important genes; holin and lysin, were responsible for bacterial host lysis. Similarly, the suitability of incorporating phage cocktails with fertiliser to treat tomato bacterial wilt caused by Ralstonia solanacearum, and soft rot disease in pitaya (dragon fruit) caused by Xanthomonas campestris, was evaluated (Tan & Tony, 2014). The findings revealed that 80 % of the tomato plants exhibited no wilting symptoms, and disease spread was successfully limited in pitaya plants.

Additionally, recent studies highlight the increasing adoption of bacteriophages as a biocontrol method against phytopathogens in ASEAN countries (Nawaz et al., 2023; Wang et al., 2024). A study in China reported that increasing the frequency of phage applications can significantly reduce the density of pathogens like Ralstonia solanacearum, leading to lower incidences of diseases such as bacterial wilt in crops (Wang et al., 2024). Similarly, the researchers at university in Jember, Indonesia had recently isolated phages from soybean soil against Pseudomonas syringae pv. glycenia that cause several destructions on the soybean stem, leaf and pod. Their study showed all the phages have double stranded deoxyribonucleic acid (dsDNA) with different propagation ability in the bacterial host (Addy & Wahyuni, 2016).

Phage Challenges and Limitations in Malaysia

The limitation and challenges of bacteriophage application can vary from country to country. Among the major challenges in Malaysia is the availability of financial resources for infrastructure development. The experimental and clinical trials conducted for phage therapy can be costly and time-consuming. Phage therapy exhibits notable host specificity, primarily targeting specific bacterial strains, which contrasts with the broader action of traditional antibiotics. In terms of dose administration, repeated intravenous (IV) doses have been shown to lead to faster phage clearance, activating host immune responses without significant toxicity (Tan et al., 2023; Spek & Smithyman. 2016). Therefore, a sustainable infrastructure is a pressing need for the phage development in clinical, animal husbandry, and agriculture. Laboratories, research facilities and phage banks are needed to develop standardized protocols and their successful execution. Phage applications may require isolation, characterisation, and selection of specific phages to target particular bacterial strains by expertise for its effective use.

The lack of extensive data and inconsistent outcomes have impeded the broader acceptance among the public, medical community and regulatory agencies. For example, the direct influence of phage has not been comprehensively investigated particularly in the context of its application and very few reported by local researchers. The concerns about the safety of phage on the human immune response such as allergic response has prevented phage therapy from becoming a mainstream medical treatment and create hesitation to adopt phage therapy in animal husbandry and food production. Furthermore, the scarcity of comprehensive genetic data on phages limits the ability to accurately predict their behaviour and effectiveness against specific bacterial strains, which is essential for developing personalised treatment strategies (Culqui Molina et al., 2024).

The journey to bringing phage therapy to the forefront in Malaysia and combating pathogenic bacteria with AMR and MDR properties is indeed lengthy and challenging. However, with concerted efforts in research, regulation, public awareness, and collaboration, phage therapy has the potential to play a significant role in addressing the global health challenge posed by drug-resistant bacteria.

CONCLUSION

To summarise, a phage revolution targeting pathogenic bacteria with AMR and MDR properties in Malaysia is indeed a significant endeavour that will be the key for bringing phage therapy out of the shadow. The growing involvement of dedicated local scientists in phage research has make it a promising avenue and it is of the utmost importance because they will play the role of pioneers and lay the foundation for such applications. Phage therapy will be futile in the region without the input of these experts. It is anticipated that there will be more scientific publications covering phage biology, systematics and anti-MDR organism potential as more phage experts emerge. Eventually, there will also be more clinical trials focusing on the use of phage against MDR organisms.

The development of phage interest may be increased by creating an inaugural conference on phage and phage-derived technologies or phage consortium, such as the recent Protein Engineering and Phage Display Conference in Malaysia, as a source of continuing education and providing an avenue where the exchange of ideas and knowledge can occur. It is also critical to hone the complementing skills in the implementation of phage therapy, such as electron microscopy, whole genome sequencing, phage formulation procedures and delivery methods. The molecular characterisation of phages is crucial in designing an effective therapy, i.e., the range of bacterial strains the viruses can target and understanding the molecular basis of bacterial resistance mechanisms, such as CRISPR-Cas systems or surface receptor mutations.

The existing facilities, such as university-based phage collections or current virological institutes may be utilised as the foundation for the development of crucial phage facilities, such as phage banks and testing centres. These existing collaborations can be revisited and modified using the regulatory models from other countries; after these changes, regulatory agencies can accommodate more investigational and personalised therapeutic options. Therefore, the sooner the region begins discussing the issue, the sooner policymakers may begin implementing phage therapy to bring the problem of AMR and MDR cases under control.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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