



Harnessing Bacteriophages: A Promising Approach to Combat Foodborne Pathogen Biofilms

Ananda Sekar Kinanti ¹, Asep Awaludin Prihanto ^{2*}, Yoga Dwi Jatmiko ³, Rovina Kobun ⁴ and Wen Xia Ling Felicia ⁴

¹Department of Aquaculture, Faculty of Fisheries and Marine Science, Brawijaya University, Jl. Veteran, Malang 65415, Jawa Timur, Indonesia

²Department of Fishery Product Technology, Faculty of Fisheries and Marine Science, Brawijaya University, Jl. Veteran, Malang 65415, East Java, Indonesia

³Department of Biology, Faculty of Mathematics and Natural Science, Brawijaya University, Jl. Veteran, Malang 65415, East Java, Indonesia

⁴Food Security Research Lab, Faculty of Food Science and Nutrition, Universiti Malaysia Sabah, Kota Kinabalu 88400, Malaysia

*Corresponding author: asep_awa@ub.ac.id

ABSTRACT

A biofilm is a community of microorganisms that adhere to surfaces and are protected by a polymeric matrix they produce. Several pathogenic bacteria that form biofilms, such as *Clostridium perfringens*, *Staphylococcus aureus*, species of *Vibrio sp.*, *Bacillus cereus*, *Salmonella sp.*, *Clostridium botulinum*, *Shigella sp.*, *Escherichia coli*, *Campylobacter sp.*, *Yersinia sp.*, *Listeria sp.*, and *Aeromonas sp.* can cause foodborne disease outbreaks. The formation of biofilms by these pathogens increases their resistance to extreme environmental conditions and cleaning agents, posing significant challenges in the food industry. Biofilms not only threaten food safety but also increase production and handling costs. Conventional methods for eliminating biofilms are often ineffective, necessitating alternative approaches. The use of bacteriophages, viruses that specifically attack bacteria, shows excellent potential as antibiofilm agents. Bacteriophages can significantly reduce the number of biofilm-forming bacteria through lytic mechanisms on surfaces such as stainless steel, rubber, and fresh vegetables. Therefore, bacteriophages are expected to be implemented as innovative solutions to control biofilms in food and non-food industries, enhancing overall food safety. This review aims to explain in detail the potential of bacteriophages in combating biofilms of foodborne pathogens.

Keywords: Biofilm, Foodborne diseases, Food safety, Bacteriophage

Article History

Article # 24-792

Received: 01-Sep-24

Revised: 02-Oct-24

Accepted: 08-Oct-24

Online First: 17-Oct-24

INTRODUCTION

The prevalence of unsafe food due to contamination by pathogenic bacteria leads to various foodborne diseases (Gallo et al., 2020). According to the World Health Organization (WHO), foodborne diseases are infectious or toxic diseases caused by consuming contaminated food or water. These diseases include intoxication (food poisoning caused by toxins produced by pathogens), infection (ingestion of food containing pathogens), and toxicoinfection (toxin production when pathogens grow in the human intestine) (Lennard, 2020;

Gourama, 2020; Abebe et al., 2020). Several bacteria commonly contaminating food sources include *Clostridium perfringens*, *Staphylococcus aureus*, species of *Vibrio sp.*, *B. cereus*, *Salmonella sp.*, *Clostridium botulinum*, *Shigella sp.*, *E. coli*, *Campylobacter sp.*, *Yersinia sp.*, *Listeria sp.*, and *Aeromonas sp.* (Odo et al., 2021; Balta et al., 2021; Sheng & Wang, 2021; Bendary et al., 2022).

Pathogenic bacteria can survive in extreme conditions by forming biofilms (Liu et al., 2023). Biofilms are defined as accumulations of microbial cells that adhere to and grow on abiotic or biotic surfaces (Kumar et al., 2020).

Cite this Article as: Kinanti AS, Prihanto AA, Jatmiko YD, Kobun R and Felicia WXL, 2024. Harnessing bacteriophages: a promising approach to combat foodborne pathogen biofilms. International Journal of Agriculture and Biosciences xx(x): xx-xx. <https://doi.org/10.47278/journal.ijab/2024.172>



A Publication of Unique Scientific Publishers

Typically, biofilms adhere to solid surfaces of materials such as stainless steel, rubber, or plastic (Carrascosa et al., 2021). The structure of biofilms consists of various components, including extracellular polysaccharides (EPS), proteins, and DNA (Treccani, 2023). In an industrial context, biofilm removal is often carried out using chemicals or antibacterial agents to lysing the biofilm. However, this approach presents new challenges, as bacteria can resist these agents and leave residues that are unsafe for consumption and harmful to the environment (Amankwah et al., 2021; Tushik et al., 2022). Therefore, there is a need for alternative solutions that are safer and more environmentally friendly, such as the use of bacteriophages (Tian et al., 2021; Stefani et al., 2021; Figueiredo et al., 2021). Bacteriophages, specific viruses that target bacteria, offer the potential as a more effective and safer method for biofilm control (Łusiak-Szelachowska et al., 2020).

Bacteriophages (phage) are viruses that specifically infect bacteria based on genus, serotype, or strain. Bacteriophages can be found in various environments, including soil, water, meat products, dairy products, and vegetables (Au et al., 2021). All bacteriophages are obligate parasites, meaning their survival depends on their bacterial hosts for growth and reproduction (Węgrzyn, 2022). Lytic bacteriophages, in particular, are used as biocontrol agents due to their ability to rapidly lyse bacterial cells without integrating into the bacterial DNA (Kassa, 2021; Elois et al., 2023). According to Chegini et al. (2020), bacteriophages can be used as antibiofilm agents against *Pseudomonas aeruginosa*, replacing ciprofloxacin antibiotics, which are often ineffective due to increasing resistance. Danis-Włodarczyk et al. (2021) demonstrated the use of bacteriophages to destroy biofilms formed by *Staphylococcus aureus* on orthopaedic implants, as bacteriophages can replace ceftazolin antibiotics that only target the biofilm surface. Kim et al. (2024) utilized bacteriophage pVa-21 as an anti-biofilm agent for *Vibrio alginolyticus*, providing an alternative to antibiotics. Additionally, Wu et al. (2024) used bacteriophages to eliminate biofilms of antibiotic-resistant *E. coli* and *Salmonella enteritidis*, replacing the commonly used Quaternary Ammonium Chloride (QAC) cleaning agents. This review highlights the importance of bacteriophages as antibiofilm agents that can contribute to combating antibiotic resistance and offer effective alternatives for biofilm control.

Biofilm

Biofilm is a collection of bacteria adhering to solid surfaces and encapsulated in an extracellular polymeric substance (EPS) matrix (Hooshdar et al., 2020). Biofilms can form on nearly any surface, including medical equipment, industrial machinery, and other solid substrates (Caldara et al., 2022). The biofilm matrix consists of EPS, which serves various functions, including adhesion, bacterial cell aggregation, biofilm cohesion, water storage, protection, absorption of organic compounds and inorganic ions, enzymatic activity, nutrient provision, genetic information exchange, electron donation and acceptance, export of cell components, storage of excess energy, and enzyme binding (Karygianni et al., 2020; Telegdi et al., 2020; Naaz

et al., 2023). EPS is a hydrated biopolymer composed of polysaccharides, proteins, nucleic acids, and lipids secreted to envelop and immobilize cells. This biopolymer is often called slime (Priyadarshane and Das, 2023).

Bacteria in biofilms exhibit higher antibiotic resistance than bacteria in their planktonic form. This increased resistance can be attributed to several factors, including the slow penetration of antibiotics through the extracellular polymeric matrix of the biofilm, reduced bacterial growth rates, increased genetic transfer, and the expression of resistant genes within the biofilm (Abushaheen et al., 2020; Pinto et al., 2020; Roy et al., 2022). The biofilm's maturation level also significantly affects bacterial resistance to antibiotics (Grande et al., 2020). A study by Chen et al. (2020) found that *Pseudomonas aeruginosa* biofilms grown for 5-12 hours remained sensitive to gentamicin, while biofilms grown for 24 and 48 hours showed high resistance to the same antibiotic. Aquaculture farmers often rely on the preventive use of antibiotics in farmed fish to reduce pathogenic *Vibrio* and its biofilm, which has gradually led to the emergence of *Vibrio* resistance and increased the burden on the aquaculture industry. Matamp & Bhat (2019) identified a characteristic lysin in *Vibrio parahaemolyticus* phage with lytic activity against various *Vibrio* species, making it a promising bio-bactericide for treating *Vibrio* resistance and addressing the problem of antibiotic overuse in the aquatic industry.

Formation and Biofilm Role

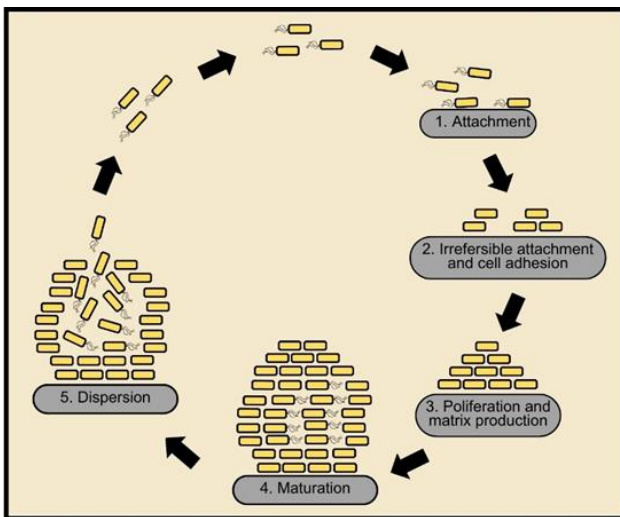
Bacteria living in biofilms are protected from conditions that can damage cells, making this a crucial factor in the disease cycle caused by pathogenic bacteria in both animals and plants (Vestby et al., 2020). Biofilms have specific functions and roles for each microorganism (Table 1).

Bacteria can adapt based on their environment, transitioning between single cells (planktonic) and forming biofilms consisting of more than 1,000 bacterial cells. The biofilm formation process occurs in five stages, as illustrated in Fig. 1. The first stage involves the initial attachment of cells to solid surfaces such as iron, rubber, or plastic. The second stage is characterized by the production of extracellular polymeric substance (EPS), which results in more robust, more "irreversible" bonds. The third stage marks the early development of the biofilm. The fourth stage involves the maturation of the biofilm. In the fifth stage, single cells are dispersed from the biofilm to form new biofilms. Environmental and physiological triggers influence the transition from single cells to biofilm formation, such as quorum sensing, nutrient availability, and cell stress levels (Chirathanamettu & Pawar, 2020).

The formation and spread of biofilms are regulated by three main factors: quorum sensing (QS), bis-(3'-5')-cyclic diguanosine monophosphate (c-di-GMP), and various small RNAs (sRNAs) (Sionov & Steinberg, 2022). QS involves molecular signals known as autoinducers. When bacterial populations reach a critical density and autoinducer concentrations exceed a threshold, bacteria respond by repressing or activating specific target genes.

Table 1: Differences in the function/role of biofilms for each microbe

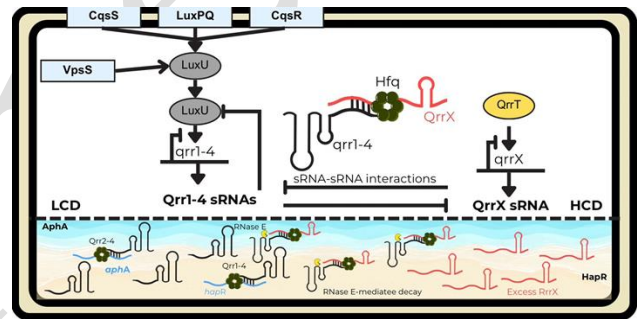
| Microbes | Function/Role | Source |
|-------------------------------|--|---|
| <i>Listeria monocytogenes</i> | a. Self-defense from antibiotics and cleaners b. Media for sticking to surfaces c. Intercellular communication d. Chemical sensing e. Balancing nutrients and toxins in cells | Balaure & Grumezescu (2020); Byun & Kim (2023) |
| <i>Salmonella</i> spp | a. Protection from the environment, antibiotics, disinfectants, and the immune system b. Has the ability to adapt to an environment without a host c. Protection from UV, osmotic changes, dehydration, pH variations and metal toxins | Harrell et al. (2021) Pradhan et al. (2023) |
| <i>Escherichia coli</i> | a. Producing amyloid called curli is useful for stabilizing the environment, producing pigment b. Adapt to extreme environments c. Perform quorum sensing d. Produces autoinducers that can secrete virulent factors, modulate the host immune system, and produce genetic changes | Li et al., (2022) Ballén et al., (2022) |
| <i>Staphylococcus</i> | a. Can survive in environments with limited nutrients b. Can be attached to biotic and abiotic surfaces c. Has adhesin intercellular polysaccharides which can produce enzymes | Nandhini et al., (2022) Schilcher & Horswill, (2020) |
| <i>Pseudomonas aeruginosa</i> | a. Has amyloid as a building material and strengthens the extracellular matrix and prevents the spread of chemical and mechanical substances b. Increases resistance to antibiotics c. As a place for quorum sensing d. Amyloid fibrils in biofilms can polymerize in the absence of an energy source and can function as a molecular scaffold with limited resources | Li et al., (2022) Tuon et al., (2022) |

**Fig. 1:** Biofilm formation process (Source: Canva)

QS plays a crucial role in developing and disseminating biofilms (Tan et al., 2020). The second regulatory factor in biofilm formation is c-di-GMP, which influences bacterial transcription, enzyme activity, and the formation of larger cellular structures (Liu et al., 2022). c-di-GMP regulates the synthesis of exopolysaccharides, adhesive pili, adhesins, and extracellular DNA (eDNA) secretion and modulates cell death and motility, forming three-dimensional biofilm structures. The third factor is sRNA, which is involved in post-transcriptional gene regulation in bacteria. sRNAs participate in metabolic processes, stress adaptation, and microbial pathogenesis (Quendera et al., 2020; Felden & Augagneur, 2021).

Fig. 2 illustrates biofilm formation in *Vibrio cholerae*, highlighting the roles of QS, c-di-GMP, and sRNA. At low cell density, the concentration of autoinducers is also low. Under these conditions, the histidine kinases LuxP and CpqS undergo phosphorylation and can phosphorylate the regulator LuxO. LuxO-P activates the expression of Qrr 1-4 RNA, which represses HapR by inhibiting c-di-GMP synthesis and increasing the production of enzymes synthesising c-di-GMP. Subsequently, c-di-GMP activates

the proteins VpsR and VpsT, which regulate biofilm-related genes, leading to mature biofilm formation (Teschler et al., 2022).

**Fig. 2:** Biofilm formation process in *Vibrio cholerae* (Source: Canva)

Foodborne Bacteria-Forming Biofilm

Pathogenic bacterial biofilms are one of the biggest challenges in the food industry. Biofilms are thin layers formed by communities of microorganisms that adhere to various surfaces and are enclosed within an extracellular matrix. Forming biofilms on equipment, processing facilities, and food products can lead to persistent and difficult-to-eliminate contamination (Carrascosa et al., 2021). Table 2 details various pathogenic bacteria commonly found in biofilm form in food, the types of media that support biofilm growth, optimum conditions for biofilm formation, and effective mitigating strategies to prevent and control contamination.

Food Safety Concern

Food contamination by pathogenic microorganisms is a significant public health issue and a major cause of economic loss worldwide (Abebe et al., 2020). Microbial biofilms, which include food-damaging bacteria and pathogens, can lead to contamination after processing, reducing product quality and shelf life and potentially spreading disease (Bhadra et al., 2023). The formation of biofilms on both biotic and abiotic surfaces increases risk by exacerbating pathogen circulation in food production

Table 2: Various Pathogenic Bacteria Commonly Found in Biofilm Form in Food

| Bacteria | Material | Optimum condition | Mitigating strategy | Reference |
|--------------------------------|---|------------------------------------|--|----------------------|
| <i>Listeria monocytogenes</i> | Stainless steel and polycarbonate | Temperature up to 30-37°C and pH 7 | increases The use of CDC Biofilm Reactors represents a new approach to assist in the implementation of sanitation control strategies | Mendez et al. (2020) |
| <i>Salmonella enterica</i> | Stainless steel | Temperature up to 30-37°C | increases The tolerance to sanitizers and ability to form biofilm | Chaves et al. (2024) |
| <i>Pseudomonas aeruginosa</i> | Stainless steel surfaces | Temperature up to 11-47°C | increases The efficiency of sanitizers used in the food industry against the biofilms formed was also evaluated | Castro et al. (2021) |
| <i>Escherichia coli</i> | Glass and stainless-steel surfaces | Temperature up to 30-37°C | increases Alternative therapy that uses enzymes to degrade biofilms | Nahar et al. (2021) |
| <i>Bacillus cereus</i> | Can form biofilms on food contact surfaces or in food-processing environments | Temperature up to 30-37°C | increases Biofilm inhibition or removal using enzymes | Lim et al. (2021) |
| <i>Campylobacter jejuni</i> | Stainless steel, copper, glass, and plastic surfaces | Temperature up to 30°C | increases By reducing the adhesion of microorganisms | Šilha et al. (2021) |
| <i>Staphylococcus aureus</i> | Stainless steel and plastic | Temperature neutral pH | 30-37°C, Good hygiene practices, temperature control, use of biocides | Argudin (2021) |
| <i>Vibrio</i> spp. | Stainless steel and plastic | Warm saline conditions | temperature, Thorough cooking, cold storage, use of antimicrobials | Su et al. (2022) |
| <i>Clostridium perfringens</i> | Stainless steel and plastic | Warm anaerobic conditions | temperature, Rapid cooling, adequate heating, good sanitation practices | McClane (2023) |
| <i>Enterococcus</i> spp. | Stainless steel and plastic | Warm humidity | temperature, high Good sanitation, use of probiotics, temperature control | Giraffa (2021) |

environments, thereby causing severe contamination (Araújo et al., 2024). Biofilms formed by pathogenic bacteria harm food, processing operations, and other areas directly impacting human health (Guzmán et al., 2020; Nikolaev et al., 2022). Pathogenic microorganisms adhering to surfaces that come into contact with food can pose sanitation problems because they can persist for extended periods in hostile conditions and serve as sources of contamination (Mazaheri et al., 2021; Sehgal et al., 2024). Biofilm formation on stainless steel surfaces in food processing plants, which can lead to foodborne illness outbreaks, occurs due to pathogens adhering and getting trapped in microscopic cavities with rough surfaces. Microorganism attachment to food processing surfaces facilitates the formation of biofilms that become sources of contamination (Abebe, 2020).

Additionally, biofilms can reduce production efficiency and the use of materials in food processing (Yuan et al., 2020). Since biofilms embedded in extracellular polymeric substances (EPS) are difficult to remove from food production facilities (Huang et al., 2022), developing effective methods to prevent, reduce, control, and eliminate biofilm formation on food surfaces and processing equipment is crucial. Food contaminated by foodborne pathogens due to biofilm formation can be seen in Table 3.

Bacteriophage as AntiBiofilm

Bacteriophages are viruses that replicate inside bacterial cells. The first scientist to discover these viruses was French researcher Félix d'Hérelle. Bacteriophages have a more complex structure than other viruses, consisting of several meticulously arranged parts (Letarov, 2020). Their structure includes a hexagonal-shaped head, a neck, and a tail. The head contains two twisted strands of DNA (Farooq et al., 2022). The neck connects the head and tail, while the tail functions to inject the viral DNA into the host cell (Zinke et al., 2022). The tail portion of a bacteriophage features receptor-binding proteins, which can be located on tail fibres, tail spikes, or the tail tip. These structures

enable the bacteriophage to recognize receptors on the host, such as lipopolysaccharides, teichoic acids, and porins (Dunne et al., 2021; Filik et al., 2022; Leprince & Mahillon, 2023). The structure of a bacteriophage is illustrated in Fig. 3.

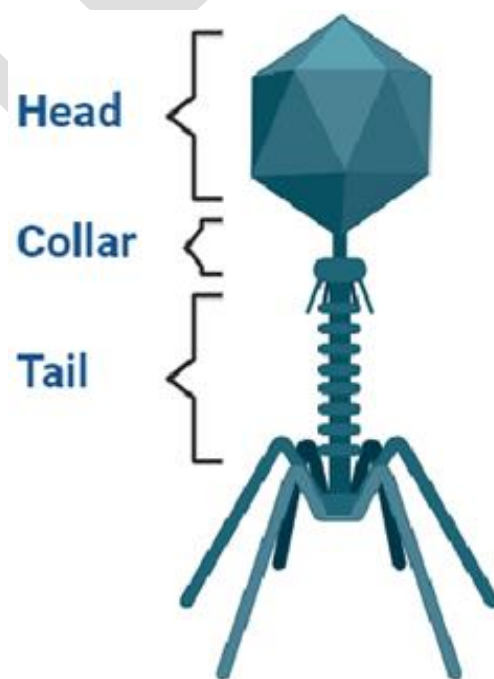


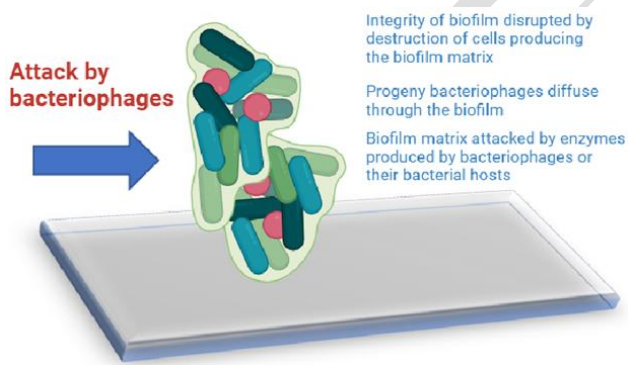
Fig. 3: Bacteriophage structure (Source: BioRender).

Mechanism of Action

One application of bacteriophages is their use as biocontrol agents against biofilm-producing bacteria, also known as antibiofilm agents (Amankwah et al., 2021). This is because bacteriophages are viruses that infect bacteria in a specific manner. Moreover, bacteriophages are readily available in nature, given their abundance. All bacteriophages are obligate parasites, meaning they depend on their hosts for survival (Naureen et al., 2020). The Biofilm destruction by bacteriophages can be seen in Fig. 4.

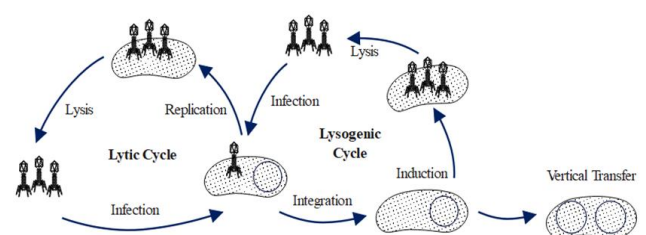
Table 3: Food contaminated by foodborne pathogens as a result of biofilm formation

| Foodborne Pathogens | Characteristics | Contaminated Food | The Main Symptoms of Food Poisoning | Examples of Harmful Effects | Spoilage | References |
|--------------------------------|---|---|---|--|----------|---------------------------|
| <i>Listeria monocytogenes</i> | Gram-positive, facultative anaerobic bacterium | Soft cheeses, pate, and unpasteurized milk | Gastroenteritis, fever, and severe cases, bacteraemia and encephalitis, especially in high-risk individuals | Decreased product quality and shelf life, potential fatal listeriosis | | Valenti et al. (2021) |
| <i>Salmonella enterica</i> | Gram-negative, rod-shaped, facultative anaerobic, flagellate, non-spore forming | Poultry and produce | Gastroenteritis, abdominal cramps, bloody diarrhea, fever, and vomiting | Spoilage of fresh produce and animal products, economic loss | | Ehuwa et al. (2021) |
| <i>Pseudomonas aeruginosa</i> | Gram-negative, rod-shaped, motile, aerobic, endospore negative, oxidase and catalase positive | Fruits, vegetables, meat, low-acid dairy products | Nausea, vomiting, and diarrhea | Spoilage of raw vegetables and dairy products, economic losses | | Urganci et al. (2022) |
| <i>Escherichia coli</i> | Gram-negative, rod-shaped, non-spore metabolically active | Consuming undercooked meat, unpasteurized milk, or contaminated water | Characterized by symptoms such as nausea, abdominal cramps, diarrhea, vomiting, headache, and fever | Gastrointestinal infections, urinary tract infections, hemorrhagic colitis, hemolytic uremic syndrome, thrombotic thrombocytopenic purpura, kidney failure | | Guptaa & Chaudhary (2022) |
| <i>Bacillus cereus</i> | Bacteria that can live in both oxygen-rich (aerobic) and low-oxygen (facultatively anaerobic) environments, and it forms spores, which are tough, dormant forms that can survive harsh conditions | Spices, dairy products, meats, food products, ready-to-eat foods, and dairy products | Nausea and vomiting, diarrhea, abdominal pain and cramps, fever, weakness of Appetite, Muscle aches | Meningitis, brain abscess, cellulitis, endophthalmitis, pneumonia, endocarditis, and osteomyelitis | | Jelena et al. (2021) |
| <i>Campylobacter jejuni</i> | Gram-negative, rod-shaped, microaerophilic, flagellate, non-spore forming, motile | Undercooked poultry, unpasteurized milk, and contaminated water | Diarrhea, abdominal pain, fever, and vomiting | Gastrointestinal acute enteritis, meningitis, arthritis, pelonephritis | | Manaa et al. (2022) |
| <i>Staphylococcus aureus</i> | Gram-positive, facultative anaerobic, spherical, flagellate, non-spore forming, non-motile | Foods such as meat, milk products, poultry, eggs, fish, salads, and pastries due to poor food handling practices. | Nausea, vomiting, abdominal cramps, and diarrhea | Osteomyelitis, endocarditis, chronic wound infection, eye infection, multimicrobial biofilm infection, renal abscess | | Pal et al. (2022) |
| <i>Vibrio</i> spp. | Gram-negative, rod-shaped, halophilic bacteria | Quality of water and seafood, especially in high-risk environments like oyster production | Gastroenteritis to sepsis | Contamination of seafood, potential for severe illness | | Martins et al. (2021) |
| <i>Clostridium perfringens</i> | Gram-positive, spore-forming, anaerobic bacterium | Meat and meat products | Diarrhea, necrotic enteritis, gangrene in humans | Production of toxins leading to enterotoxemia, and food poisoning, spoilage of meat products | | El Bayomi et al. (2020) |
| <i>Enterococcus</i> spp. | Gram-positive, lactic acid bacteria | Cheese, fermented foods | Opportunistic infections, particularly in immunocompromised individuals | Spoilage of cheese and fermented foods, potential health risks | | Giraffa (2021) |

**Fig. 4:** Biofilm destruction by bacteriophages (Source: BioRender).

The mechanism by which bacteriophages eliminate biofilms differs from chemical antibiotics or biocides due to their co-evolution with host bacteria (Singh et al., 2022). Bacteriophages attack host bacteria with at least four distinct mechanisms (Hussain et al., 2021; Teklemariam et al., 2023). As illustrated in Fig. 5, the first mechanism involves replicating bacteriophages inside the host cell, increasing the number of bacteriophages (amplification). Once dispersed within the biofilm and targeting bacteria that produce extracellular polymeric substances (EPS),

bacteriophages progressively dismantle the biofilm and reduce the likelihood of its regeneration. The second mechanism involves bacteriophages carrying depolymerase enzymes that can degrade EPS. The third mechanism includes bacteriophages inducing depolymerase enzymes from the host genome, contributing to EPS degradation. The fourth mechanism addresses persister cells. Although bacteriophages cannot replicate or destroy these inactive cells, they can remain inside until the cells become active again. Once reactivated, bacteriophages can initiate a productive infection that ultimately destroys these cells (Dennehy & Abedon, 2021).

**Fig. 5:** Mechanism of bacteriophage in lysing bacterial cells (Source: BioRender).

Bacteriophages have two types of life cycles: the lytic cycle and the lysogenic cycle. However, the lytic cycle is the most effective antibiofilm agent (Latka & Drulis-Kawa, 2020; Amankwah et al., 2021; Singh et al., 2022). The lytic cycle consists of several stages. Initially, the bacteriophage undergoes adsorption, attaching to the host cell's surface. During this stage, the bacteriophage tail fibres bind to specific receptors on the cell surface. Next, the bacteriophage injects its nucleic acid into the host cell's cytoplasm. The phage genome then replicates and increases in number within the cytoplasm. The early genes expressed regulate the host cell's metabolism to facilitate bacteriophage replication. Subsequently, new bacteriophages are formed, with the late genes directing their assembly. These new virions assemble by joining the head and tail, encapsulating the nucleic acid within the head, and undergoing virion maturation. Finally, the bacteriophages lyse the host cell, releasing new bacteriophages ready to infect other cells within the biofilm and initiate a new lytic cycle (Elois et al., 2023).

Isolation of Bacteriophages

Bacteriophages can be isolated from various samples, as summarised by several literature sources in Table 4.

Based on the examples in Table 4, isolating bacteriophages, viruses that specifically infect bacteria, is a crucial step in developing phage therapy as a potential alternative to antibiotics, particularly in combating drug-resistant bacteria. As concerns about antibiotic resistance continue to grow, research in this field has expanded, and various studies have successfully demonstrated the effectiveness of bacteriophage isolation using various methods. These methods are designed to target various types of bacterial pathogens, including highly resistant ones, thereby opening up new possibilities for treating infections that are difficult to manage with conventional approaches.

Characterization of Bacteriophages

The obtained bacteriophages are then characterized to determine their properties in Fig. 6. According to Abdelrahman et al. (2022), who isolated *E. coli* specific bacteriophages, various types of characterization can be performed. This characterization includes morphological observation using an electron microscope, determination of host range by testing several bacterial species in a double-layer medium, and creating a one-step growth curve by infecting bacteria in the exponential phase using

a Multiplicity of Infection (MOI) value of 1.0 (Lukman et al., 2020). Additionally, phage resistance testing is conducted by culturing phages on bacteria in the exponential phase and testing at MOIs of 0.01, 0.1, 1, and 10, as well as pH and temperature stability testing at various temperatures and pH values. In the study by Jamal et al. (2019) on *Enterobacter cloacae*-specific bacteriophages, characterization involved assessing the phage's effect on calcium and magnesium adsorption by adding CaCl_2 and MgCl_2 to determine adsorption capacity and the number of non-adsorbed phages. Protein expression characterization was also performed using ultracentrifugation at 187,000xg for 4 hours and mixed with PBS (pH 7). This study also involved DNA isolation, which resulted in a genome size of 40kb. Chen et al. (2020) focused on expressing and purifying depolymerase enzymes produced by specific *E. coli* bacteriophages. Therefore, bacteriophage characterization should be tailored to the specific research objectives, but general characterization such as morphology, host range, pH and temperature stability, and growth curve should be included (Zurabov & Zhilenkov, 2021; Abdelsattar et al., 2022; Karaynir et al., 2022).

The morphology of bacteriophages can be observed using a specialized tool called Transmission Electron Microscope (TEM), as shown in Fig. 6. Fig. 6 (A) depicts the morphology of bacteriophage JBP901, which infects *Bacillus cereus*. This bacteriophage, isolated from various traditional fermented foods, is classified in the Myoviridae family with a capsid dimension of 95 ± 5 nm and a tail length of 170 ± 5 nm (Matamp & Bhat, 2020). Fig. 6 (B) presents the appearance of bacteriophage LPST94, which infects *Salmonella*, isolated from aquatic environments. This bacteriophage features an icosahedral head and a long tail, with a head diameter of 67.60 ± 2.30 nm and a tail length of approximately 116.30 ± 4.10 nm. Based on its morphology, this bacteriophage belongs to either the Ackermannviridae or Myoviridae family (Islam et al., 2020). Fig. 6 (C) illustrates the morphology of bacteriophage PS5, which targets both *E. coli* and *Salmonella* isolated from poultry products. This bacteriophage is classified in the Myoviridae family and has an isometric head with a diameter of 84 nm and a tail of 106 nm (Duc et al., 2020). Fig. 6 (D) shows the commercial bacteriophage Listshield™ that targets *Listeria monocytogenes*. The image indicates that the commercial bacteriophage Listshield™ belongs to the Myoviridae family (Wintachai & Voravuthikunchai, 2022).

Table 4: Effectiveness of isolation method on the bacteriophage recovery

| Bacteriophage method | Bacteria | Sample | References |
|---|--|---|-----------------------------|
| Double agar layer method | <i>Campylobacter sp</i> | Chicken skin | Nafarrate et al. (2020) |
| Agar overlay assay method | <i>Bacillus cereus</i> , <i>Bacillus subtilis</i> , <i>enterotoxigenic Escherichia coli</i> (ETEC), and <i>enterohemorrhagic Escherichia coli</i> (EHEC) | Soil | Artawinata et al. (2023) |
| Double-layer agar method | <i>Vibrio Parahaemolyticus</i> | Clam (<i>Meretrix meretrix</i>) | Cao et al. (2021) |
| Double-layer agar (DLA) | <i>Pseudomonas Aeruginosa</i> | Wastewater | Sharma et al. (2021) |
| Double agar overlay plaque assay | <i>Vibrio parahaemolyticus</i> | Seafood samples | Tan et al. (2021) |
| Hydrodynamic counter-current chromatography | <i>Escherichia coli</i> | Water sources, effluent, or fecal samples | Friedersdorff et al. (2022) |
| Membrane chromatography | <i>Escherichia coli</i> | Wastewater | Roshankhah et al. (2023) |
| Double-layer agar method | <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Acinetobacter sp</i> , <i>Pseudomonas aeruginosa</i> | Wastewater Treatment | Alilesh et al. (2024). |
| Plaque assay | <i>Staphylococcus spp.</i> , <i>Escherichia coli</i> , and <i>Klebsiella pneumoniae</i> | Pasteurized milk and wastewater | Imklin et al. (2024) |
| Plaque assay | <i>Bacillus cereus</i> | Such as soil, water, or food samples | Wang et al. (2024) |

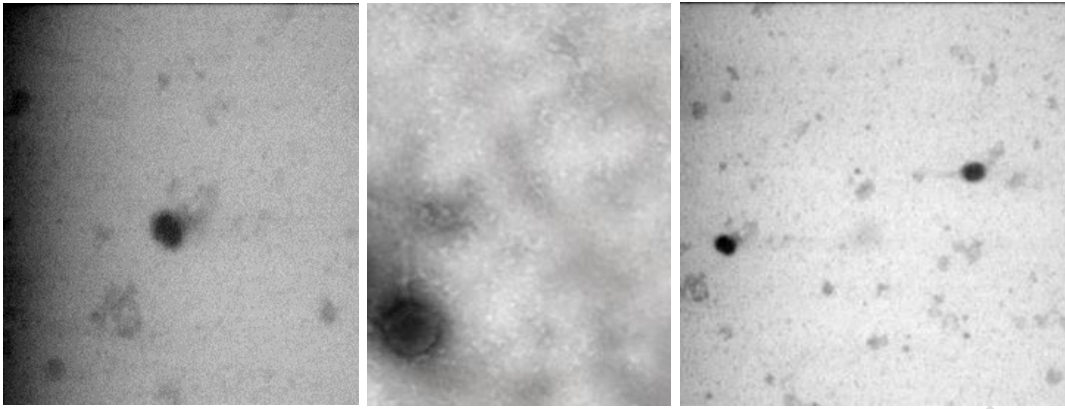


Fig. 6: The morphology of bacteriophages was observed using TEM ordo *Caudovirales* (Source: Personal Results).

Application of Bacteriophage as Antibiofilm

Bacteriophages play a significant role in molecular biology and biotechnology, with a range of developed applications. They are commonly used in agriculture, healthcare, disease diagnosis, livestock biocontrol, and food safety. Examples of bacteriophage applications include their use as therapeutic agents, pathogen detection tools, and biocontrol agents in the food industry (Wang & Zhao, 2022). Bacteriophages have been applied therapeutically in plants, animals, and humans, with varying degrees of success. The benefits of using bacteriophages as therapeutic agents include their narrow antibacterial spectrum, which makes them highly specific to targeted bacteria, their applicability to both gram-negative and gram-positive bacteria, fewer side effects compared to traditional antibiotics, increased efficacy, and cost-effectiveness (Huang et al., 2021; Liu et al., 2022; Ahmed et al., 2023).

Bacteriophages can also detect pathogenic bacteria due to their specificity in infecting bacterial host cells. This detection process may involve using green fluorescence or reporter genes to visualize bacteria that bacteriophages have infected. Additionally, bacteriophages are used as biocontrol agents to replace antibiotics, considering many bacteria have developed resistance to various antibiotics. Several studies have demonstrated the success of bacteriophages in reducing the number of bacteria such as *Salmonella* sp., *Listeria* sp., and *Pseudomonas* sp. Certain bacteriophages have been commercialized and are considered safe (GRAS) by regulatory bodies like the FDA and USDA, including products such as Agriphage™, Ecoshield™, ListShield™, Listex™ P100, and Salmonellex™ (Costa et al., 2023). To effectively eradicate bacterial biofilms, it is recommended to use a combination therapy approach with phages, either simultaneously or sequentially, along with other alternative antibiofilm agents. This combination therapy involves phages and/or phage-derived enzymes with nanoparticles, chemical compounds, antimicrobial peptides, and disinfectants (Table 5).

One application of bacteriophages is as antibiofilm or biocidal agents that effectively lyse biofilm-forming bacteria. According to Tian et al. (2021), using bacteriophages as antibiofilm agents can be categorized into two main areas: medical and industrial applications. In

the medical field, biofilms often form on medical equipment, increasing patients' risk of significant infections. Bacteriophages can target these biofilm-forming bacteria, disrupt the biofilm matrix, and reduce infection risks (Ferriol-González & Domingo-Calap, 2020). In industrial settings, bacteriophages are commonly applied to stainless steel surfaces, as biofilm-forming bacteria can adhere to various surfaces, both biotic and abiotic, including stainless steel (Jamal et al., 2019; Figueiredo et al., 2021; Lila et al., 2023). Bacteriophages can infect biofilm and planktonic bacteria and disrupt the stability of extracellular polymeric substances (EPS) by producing enzymes (Azeredo et al., 2021).

Future Concern

a. Specificity

Bacteriophages typically have a narrow host range, meaning they infect only specific strains or species of bacteria. This specificity can pose a challenge in clinical applications due to the limited ability of phages to target a wide variety of pathogenic bacteria. To address this issue, one approach being explored is using phage cocktails containing multiple phages, each capable of simultaneously targeting several bacterial strains. Research by Glonti et al. (2024) successfully identified and classified phages targeting *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, demonstrating various host specificities. Testing these phage cocktails on different bacterial strains effectively inhibited phage-resistant mutants. Therefore, using phage cocktails containing diverse phages to combat antibiotic-resistant bacterial infections is a promising strategy.

Genetic engineering techniques are also being developed to broaden the host range of phages, enabling them to treat a broader range of bacterial infections more effectively. Research by Lewis et al. (2024) has demonstrated that genetic engineering can expand the host range of phages by creating phage variants optimized for increased infectivity or broader host specificity. Advances in genetic engineering play a crucial role in paving the way for more efficient phage therapies by allowing the development of phages that can target a broader spectrum of bacterial species, ultimately enhancing the effectiveness of phage therapy against antimicrobial-resistant strains.

Table 5: Examples of combination of phages or phage-derived products and antimicrobials applications against bacterial biofilm formation

| Bacteriophage | Antimicrobial Agent Used | Biofilm-Bacteria | Biofilm Reduction | Reference |
|---|--|---|---|----------------------------|
| Environmental phage-based cocktail | Antibiotics (Ciprofloxacin, sulfamethoxazole/ trimethoprim, Gentamicin, Tobramycin, Meropenem, Imipenem) | <i>Acinetobacter baumannii</i> in a human urine mode | Reduction of biofilm biomass and clearance of persister cells | Grygorcewicz et al. (2021) |
| Bacteriophage Brsv | Amikacin | <i>Proteus mirabilis</i> 3059 | Eradication of biofilm | Maszewska et al. (2021) |
| Commercially available phages Sb-1 and PYO | Ciprofloxacin | Dual-species of <i>Staphylococcus aureus/Pseudomonas aeruginosa</i> | Complete eradication of dual-species biofilms | Tkhilashvili et al. (2020) |
| Phage EFLK1 | Vancomycin | Vancomycin-resistant <i>Enterococcus faecalis</i> | Reduction of biomass by 87% | Shlezinger et al. (2019) |
| Phage E79 | Aztreonam lysine | <i>Pseudomonas aeruginosa</i> PA01 | Reduction in biofilm growth over 3-fold | Davis et al. (2021) |
| Phage-encoded endolysin LysP108 | Vancomycin | Methicillin-resistant <i>Staphylococcus aureus</i> XN108 | Inhibition of biofilm | Lu et al. (2021) |
| Bacteriophage (Xcc ϕ 1) - hydroxyapatite complex | Saturated long-chain fatty acids | <i>Xanthomonas campestris</i> in a flow cell system | Removal of biofilm | Papaiani et al. (2020) |
| phage ϕ 44AHJD | Green synthesized nanoparticles | silver <i>Staphylococcus aureus</i> | Rapid dispersion of biofilm | Manoharadas et al. (2021) |
| T7Select phage | Antimicrobial peptide 1018 | <i>Escherichia coli</i> | Eradication of biofilm | Lemon et al. (2019) |
| Phage SA46-CTH2 | Nisin | <i>Staphylococcus aureus</i> | Reduction in biofilm | Duc et al. (2020) |
| Phages PN05 and PN09 | Carvacrol | <i>Pseudomonas syringae</i> pv. actinidiae | Prevention of biofilm regrowth | Ni et al. (2020) |

b. Regulatory and Safety Concerns

The regulatory framework governing the production and application of phage-based products is a crucial aspect that requires special attention. As support for phage therapy as a potential solution to combat antibiotic-resistant bacteria increases, resolving regulatory and safety issues is critical to ensure its successful application in various sectors, including agriculture, food safety, and healthcare. Efforts to streamline regulatory processes and improve public understanding are essential to maximize the effectiveness of phage use in combating bacterial diseases.

The safety of bacteriophages is well-established, as they exhibit high specificity and only infect bacterial hosts within a very limited range, thereby minimizing the risk of secondary infections (Imklin et al., 2024). Bacteriophage therapy does not contribute to antibiotic resistance (Ghani et al., 2024). Bacteriophages can be directly applied to food surfaces, integrated into packaging materials, or used during food processing. Several commercial bacteriophage products have been declared safe for consumption and have been granted Generally Recognized as Safe (GRAS) status by the FDA (Food and Drug Administration) (Dellalibera-Joviliano et al., 2020; Ranveer et al., 2024). Applying bacteriophages as a natural treatment to prevent bacterial growth in fresh produce, dairy, and food products is promising (Imran et al., 2023). Their targeted action and safety profile make them valuable bioadditives for enhancing food safety and quality (Narayanan et al., 2024).

c. Stability and Storage

Bacteriophages face several environmental challenges that can affect their stability as antimicrobial agents. Phages can be sensitive to temperature variations and maintaining an optimal temperature range is crucial for their survival and functionality in antimicrobial applications (Sae-Ueng et al., 2022; Choi et al., 2022). Acidic conditions can damage phages, as they are often less stable in low pH environments, which can reduce antimicrobial activity (Wdowiak et al., 2022; Bagińska et al., 2024). Ensuring a neutral or slightly alkaline pH can

help maintain phage stability and efficacy. Exposure to UV light can damage the nucleic acid components of phages, resulting in a loss of infectivity (Yu et al., 2023). UV irradiation poses a significant challenge for phages, particularly in outdoor or unprotected environments where they may be employed as antimicrobial agents (Vitzilaiou et al., 2022; Liu et al., 2023).

Developing stable formulations and ensuring the long-term storage of phages are crucial for effective phage therapy. Effective phage formulations are needed to protect them from degradation and maintain activity. Encapsulation techniques, such as using excipients like lactose, trehalose, mannitol, PEG, and leucine, have shown promise in protecting phages (Bolsan et al., 2024). These formulations play a vital role in ensuring the survival and effectiveness of phages, especially in combating antibiotic-resistant bacteria. By employing appropriate protection and delivery strategies, phages can be utilized as powerful tools against bacterial infections, addressing the challenges posed by resistance (Choudhary et al., 2023; Flint et al., 2023).

d. Production and Scale-up

Large-scale production of bacteriophages requires specialized facilities and expertise to maintain consistent quality and high phage titers, which are crucial for effectively combating bacteria (Davydov et al., 2023). Additionally, maintaining strict production standards is essential to ensure the purity and safety of phage products for therapy. Enforcing rigorous controls at every stage of production, including phage and bacterial strain identification, fermentation, purification, formulation, quality inspection, and documentation, can assure the purity and safety of phage products (Mutti & Corsini, 2019).

The costs of producing and purifying phages can be high, which may limit the widespread adoption and use of phage therapy (Luong et al., 2020). Efforts to reduce production costs without compromising the quality and effectiveness of phage products are one of the critical challenges. This can be achieved by optimizing growth

conditions for host bacteria and phages, such as temperature, pH, and nutrient supply, to maximize yield and efficiency (Mäkelä et al., 2024). Implementing automated systems to monitor and control the production process can reduce labour costs and improve consistency and quality, leading to cost savings (João et al., 2021).

e. Public Perception

Public perception and acceptance of phage therapy can pose obstacles to the adoption of this technology. A lack of understanding regarding the safety and benefits of phage therapy can lead to doubts among consumers and stakeholders. Therefore, proper and comprehensive education about phage therapy is crucial to enhance its acceptance and adoption in clinical applications and food safety. Despite these challenges, ongoing research and technological advancements play a significant role in overcoming these barriers, ensuring that phage therapy remains a promising tool in improving food safety and addressing antibiotic resistance in the future.

Conclusion and Future Prospects

In the effort to combat foodborne pathogen biofilms, the use of bacteriophages emerges as a highly promising approach. Bacteriophages, viruses that specifically infect bacteria, have proven effective in targeting and addressing biofilms that are difficult to remove using conventional methods, such as antibiotics and biocides. Research results indicate that bacteriophages can disrupt biofilm matrices and reduce the risk of infection from pathogens like *Listeria monocytogenes*, *Salmonella*, and *Pseudomonas aeruginosa*. Looking to the future, the development of more specific bacteriophages and genetic engineering has the potential to enhance the efficiency of this therapy. Integrating bacteriophages with advanced technologies, such as nanoparticles and enzymes, is expected to improve further effectiveness in combating biofilms. Establishing regulations and safety standards will also be crucial for the widespread application of bacteriophages. With advancements in production technology and a better understanding of bacteriophage mechanisms, the use of bacteriophages in controlling foodborne pathogens holds the promise of being a safer and more environmentally friendly alternative to conventional methods. Broader education and ongoing research support will accelerate the adoption of this technology, making bacteriophages a vital tool in enhancing food safety and addressing the challenges of pathogen biofilms in the future.

Competing Interest: All authors declare no competing interest.

Author's Contributions: Ananda Sekar Kinanti: Visualization, Writing-original Draft. Asep Awaludin Prihanto: Conceptualization, Validation, Writing-original Draft, writing-review and editing. Yoga Dwi Jatmiko: Validation, writing-review and editing. Rovina Kobun: Supervision: Validation, writing-review and editing. Wen Xia Ling Felicia: Writing-original Draft, writing-review and editing.

Acknowledgement: The authors thank Brawijaya University, for Grant on GB-Research Ecosystem, Grant No. 00144.20/UN10.A0501/B/PT.01,03.2/2024.

REFERENCES

- Abdelrahman, F., Rezk, N., Fayez, M.S., Abdelmoteleb, M., Atteya, R., Elhadidy, M., & El-Shibiny, A. (2022). Isolation, characterization, and genomic analysis of three novel *E. coli* bacteriophages that effectively infect *E. coli* O18. *Microorganisms*, 10(3), 589.
- Abdelsattar, A., Dawoud, A., Makky, S., Nofal, R., Aziz, R.K., & El-Shibiny, A. (2022). Bacteriophages: From isolation to application. *Current Pharmaceutical Biotechnology*, 23(3), 337-360.
- Abebe, E., Gugsu, G., & Ahmed, M. (2020). Review on major foodborne zoonotic bacterial pathogens. *Journal of Tropical Medicine*, 1, 4674235.
- Abebe, G.M. (2020). The role of bacterial biofilm in antibiotic resistance and food contamination. *International Journal of Microbiology*, 1, 1705814.
- Abushaheen, M.A., Fatani, A.J., Alosaimi, M., Mansy, W., George, M., Acharya, S., & Jhugroo, P. (2020). Antimicrobial resistance, mechanisms and its clinical significance. *Disease-a-Month*, 66(6), 100971.
- Ahmed, S., Ahmed, M.Z., Rafique, S., Almasoudi, S.E., Shah, M., Jail, N.A.C., & Ojha, S.C. (2023). Recent approaches for downplaying antibiotic resistance: molecular mechanisms. *BioMed Research International*, (1), 5250040.
- Alilesh, A. S., Marwa, E. E., Tasnem, M. A., & Khawla, A. A. (2024). Isolation and characterization of lytic bacteriophage against common pathogenic bacteria. *Al-Mukhtar Journal of Basic Sciences*, 22(1), 30-37.
- Amankwah, S., Abdella, K., & Kassa, T. (2021). Bacterial biofilm destruction: A focused review on the recent use of phage-based strategies with other antibiofilm agents. *Nanotechnology, Science and Applications*, 161-177.
- Araújo, D., Silva, A.R., Fernandes, R., Serra, P., Barros, M.M., Campos, A.M., & Castro, J. (2024). Emerging approaches for mitigating biofilm-formation-associated infections in farm, wild, and companion animals. *Pathogens*, 13(4), 320.
- Argudin, M.Á. (2021). *Staphylococcus aureus* biofilm formation and control. *International Journal of Food Microbiology*, 342, 109035.
- Artawinata, P.C., Lorraine, S., & Waturangi, D.E. (2023). Isolation and characterization of bacteriophages from soil against food spoilage and foodborne pathogenic bacteria. *Scientific Reports*, 13(1), 9282.
- Au, A., Lee, H., Ye, T., Dave, U., & Rahman, A. (2021). Bacteriophages: combating antimicrobial resistance in foodborne bacteria prevalent in agriculture. *Microorganisms*, 10(1), 46.
- Azereido, J., Garcia, P., & Drulis-Kawa, Z. (2021). Targeting biofilms using phages and their enzymes. *Current Opinion in Biotechnology*, 68, 251-261.
- Bagińska, N., Grygiel, I., Orwat, F., Harhala, M.A., Jędrusiak, A., Gębarowska, E., & Jończyk-Matysiak, E. (2024). Stability study in selected conditions and biofilm-reducing activity of phages active against drug-resistant *Acinetobacter baumannii*. *Scientific Reports*, 14(1), 4285.
- Balaura, P.C., & Grumezescu, A.M. (2020). Recent advances in surface nanoengineering for biofilm prevention and control. Part II: active, combined active and passive, and smart bacteria-responsive antibiofilm nanocoatings. *Nanomaterials*, 10(8), 1527.
- Ballén, V., Cepas, V., Ratia, C., Gabasa, Y., & Soto, S.M. (2022). Clinical *Escherichia coli*: from biofilm formation to new antibiofilm strategies. *Microorganisms*, 10(6), 1103.
- Balta, I., Linton, M., Pinkerton, L., Kelly, C., Stef, L., Pet, I., & Corcionivoschi, N. (2021). The effect of natural antimicrobials against *Campylobacter* spp. and its similarities to *Salmonella* spp., *Listeria* spp., *Escherichia coli*, *Vibrio* spp., *Clostridium* spp. and *Staphylococcus* spp. *Food Control*, 121, 107745.
- Bendary, M.M., Abd El-Hamid, M.I., El-Tarabili, R.M., Hefny, A.A., Algendy, R.M., Elzohairy, N.A., & Moustafa, W.H. (2022). *Clostridium perfringens* associated with foodborne infections of animal origins: Insights into prevalence, antimicrobial resistance, toxin genes profiles, and toxinotypes. *Biology*, 11(4), 551.
- Bhadra, S., Chettri, D., & Kumar Verma, A. (2023). Biosurfactants: Secondary metabolites involved in the process of bioremediation and biofilm removal. *Applied Biochemistry and Biotechnology*, 195(9), 5541-5567.
- Bolsan, A.C., Sampaio, G.V., Rodrigues, H.C., De Souza, S.S., Edwiges, T., De Prá, M.C., & Gabiatti, N.C. (2024). Phage formulations and delivery strategies: unleashing the potential against antibiotic-resistant bacteria. *Microbiological Research*, 127662.

- Byun, K.H., & Kim, H.J. (2023). Survival strategies of *Listeria monocytogenes* to environmental hostile stress: biofilm formation and stress responses. *Food Science and Biotechnology*, 32(12), 1631-1651.
- Caldara, M., Belgiovine, C., Secchi, E., & Rusconi, R. (2022). Environmental, microbiological, and immunological features of bacterial biofilms associated with implanted medical devices. *Clinical Microbiology Reviews*, 35(2).
- Cao, Y., Zhang, Y., Lan, W., & Sun, X. (2021). Characterization of vB_VpaP_MGD2, a newly isolated bacteriophage with biocontrol potential against multidrug-resistant *Vibrio parahaemolyticus*. *Archives of Virology*, 166, 413-426.
- Carrascosa, C., Raheem, D., Ramos, F., Saraiva, A., & Raposo, A. (2021). Microbial biofilms in the food industry comprehensive review. *International Journal of Environmental Research and Public Health*, 18(04), 2014.
- Castro, M.S.R., da Silva Fernandes, M., Kabuki, D.Y., & Kuaye, A.Y. (2021). Modelling *Pseudomonas fluorescens* and *Pseudomonas aeruginosa* biofilm formation on stainless steel surfaces and controlling through sanitizers. *International Dairy Journal*, 114, 104945.
- Chaves, R.D., Kumazawa, S.H., Khaneghah, A.M., Alvarenga, V.O., Hungaro, H.M., & Sant'Ana, A.S. (2024). Comparing the susceptibility to sanitizers, biofilm-forming ability, and biofilm resistance to quaternary ammonium and chlorine dioxide of *Salmonella enterica* and *Listeria monocytogenes* strains. *Food Microbiology*, 117, 104380.
- Chegini, Z., Khoshbayan, A., Taati Moghadam, M., Farahani, I., Jazireian, P., & Shariati, A. (2020). Bacteriophage therapy against *Pseudomonas aeruginosa* biofilms: a review. *Annals of Clinical Microbiology and Antimicrobials*, 19, 1-17.
- Chen, X., Thomsen, T.R., Winkler, H., & Xu, Y. (2020). Influence of biofilm growth age, media, antibiotic concentration and exposure time on *Staphylococcus aureus* and *Pseudomonas aeruginosa* biofilm removal in vitro. *BMC Microbiology*, 20, 1-11.
- Chen, Y., Li, X., Wang, S., Guan, L., Li, X., Hu, D., & Qian, P. (2020). A novel tail-associated O91-specific polysaccharide depolymerase from a podophage reveals lytic efficacy of Shiga toxin-producing *Escherichia coli*. *Applied and Environmental Microbiology*, 86(9), e00145-20.
- Chirathanamettu, T.R., & Pawar, P.D. (2020). Quorum sensing-induced phenotypic switching as a regulatory nutritional stress response in a competitive two-species biofilm: An individual-based cellular automata model. *Journal of Biosciences*, 45, 1-16.
- Choi, Y.K., Han, S.M., Lee, S.M., Soh, J.O., Lee, S.K., & Lee, J.H. (2022). Investigation of the relation between temperature and M13 phage production via ATP expenditure. *Processes*, 10(5), 962.
- Choudhary, M., Pereira, J., Davidson, E.B., Colee, J., Santra, S., Jones, J.B., & Paret, M.L. (2023). Improved persistence of bacteriophage formulation with nano n-acetylcysteine-zinc sulfide and tomato bacterial spot disease control. *Plant Disease*, 107(12), 3933-3942.
- Costa, M.J., Pastrana, L.M., Teixeira, J.A., Sillankorva, S.M., & Cerqueira, M.A. (2023). Bacteriophage delivery systems for food applications: Opportunities and perspectives. *Viruses*, 15(6), 1271.
- Danis-Włodarczyk, K.M., Wozniak, D.J., & Abedon, S.T. (2021). Treating bacterial infections with bacteriophage-based enzybiotics: in vitro, in vivo and clinical application. *Antibiotics*, 10(12), 1497.
- Davis, C.M., McCutcheon, J.G., & Dennis, J.J. (2021). Aztreonam lysine increases the activity of phages E79 and phiKZ against *Pseudomonas aeruginosa* PA01. *Microorganisms*, 9 (1):152. doi: 10.3390/microorganisms9010152 106
- Davydov, D.S., Parfenyuk, R.L., Durmanova, Z.V., Merkulov, V.A., & Movsesyants, A.A. (2023). Characteristic aspects of marketing authorization and quality assurance of bacteriophage medicinal products in the Russian Federation. *Biological Products. Prevention, Diagnosis, Treatment*, 23(2), 181-193.
- Dellalibera-Joviliano, R., de Melo, S.A., & Ceni, H.D.M.R. (2020). Alternativas terapêuticas e aplicação de bacteriófagos como estratégia no uso de antibióticos no tratamento de doenças bacterianas. *Revista de Medicina*, 99(1), 88-95.
- Dennehy, J.J., & Abedon, S.T. (2021). Phage infection and lysis. *Bacteriophages: Biology, Technology, Therapy*, 341-383.
- Duc, H.M., Son, H.M., and Ngan, P.H. (2020). Isolation and application of bacteriophages alone or in combination with nisin against planktonic and biofilm cells of *Staphylococcus aureus*. *Applied Microbiology and Biotechnology*, 104(11):5145-5158. doi: 10.1007/s00253-020- 10581-4 116
- Dunne, M., Prokhorov, N.S., Loessner, M.J., & Leiman, P.G. (2021). Reprogramming bacteriophage host range: design principles and strategies for engineering receptor binding proteins. *Current Opinion in Biotechnology*, 68, 272-281.
- Ehuwa, O., Jaiswal, A.K., & Jaiswal, S. (2021). *Salmonella*, food safety and food handling practices. *Foods*, 10(5), 907.
- El Bayomi, R.M., El Mesalamy, Y., Hafez, A.E., & Ahmed, H.A. (2020). *Clostridium perfringens* in meat and meat products: A mini review on the incidence, public health significance, and the effects of essential oils. *Zagazig Veterinary Journal*, 48(4), 340-353.
- Elois, M.A., Silva, R.D., Pilati, G.V.T., Rodriguez-Lázaro, D., & Fongaro, G. (2023). Bacteriophages as biotechnological tools. *Viruses*, 15(2), 349.
- Farooq, T., Hussain, M.D., Shakeel, M.T., Tariqjaveed, M., Aslam, M.N., Naqvi, S.A.H., & He, Z. (2022). Deploying viruses against phyto-bacteria: Potential use of phage cocktails as a multifaceted approach to combat resistant bacterial plant pathogens. *Viruses*, 14(2), 171.
- Felden, B., & Augagneur, Y. (2021). Diversity and versatility in small RNA-mediated regulation in bacterial pathogens. *Frontiers in Microbiology*, 12, 719977.
- Ferriol-González, C., & Domingo-Calap, P. (2020). Phages for biofilm removal. *Antibiotics*, 9(5), 268.
- Figueiredo, C.M., Malvezzi Karwowski, M.S., da Silva Ramos, R.C.P., de Oliveira, N.S., Peña, L.C., Carneiro, E., & Rosa, E.A.R. (2021). Bacteriophages as tools for biofilm biocontrol in different fields. *Biofouling*, 37(6), 689-709.
- Filik, K., Szermer-Olearnik, B., Oleksy, S., Brykała, J., & Brzozowska, E. (2022). Bacteriophage tail proteins as a tool for bacterial pathogen recognition-a literature review. *Antibiotics*, 11(5), 555.
- Flint, R., Laucirica, D.R., Chan, H. K., Chang, B.J., Stick, S.M., & Kicic, A. (2023). Stability considerations for bacteriophages in liquid formulations designed for nebulization. *Cells*, 12(16), 2057.
- Friedersdorff, J.C., Bright, C., Rooke, D., Creevey, C.J., & Kingston Smith, A.H. (2022). Using the forces of hydrodynamic countercurrent chromatography for the study of bacteriophages. *Access Microbiology*, 4(2), 000310.
- Gallo, M., Ferrara, L., Calogero, A., Montesano, D., & Naviglio, D. (2020). Relationships between food and diseases: What to know to ensure food safety. *Food Research International*, 137, 109414.
- Ghani, S., Ghani, I., & Naureen, S. (2024). Synergizing bacteriophage therapy and computational neuroscience: a ray of hope in the fight against antibiotic resistance. *Asian Journal of Medicine and Health*, 22(7), 140-144.
- Giraffa, G. (2021). *Enterococcus* spp. in food microbiology. *FEMS Microbiology Reviews*, 45(5), 845-858.
- Glonti, T., Goossens, M., Cochez, C., Green, S., Gorivale, S., Wagemans, J., & Pirnay, J.P. (2024). Use of the naturally occurring bacteriophage grouping model for the design of potent therapeutic cocktails. *Antibiotics*, 13(5), 385.
- Gourama, H. (2020). Foodborne pathogens. In *Food safety engineering* (pp. 25-49). Cham: Springer International Publishing.
- Grande, R., Puca, V., & Muraro, R. (2020). Antibiotic resistance and bacterial biofilm. *Expert Opinion on Therapeutic Patents*, 30(12), 897-900.
- Grygorzewicz, B., Wojciuk, B., & Roszak, M. (2021). Environmental phage-based cocktail and antibiotic combination effects on *Acinetobacter baumannii* biofilm in a human urine model. *Microbial Drug Resistance* 27(1):25-35. doi: 10.1089/mdr.2.020.0083 101.
- Guptaa, A.K., & Chaudhary, A. (2022). Food Poisoning: causes, its effects and control. *INWASCON Technology Magazine (i-TECH MAG)*, 4, 42-48.
- Guzmán, C.A., González Hurtado, M.I., Cuesta-Astroz, Y., & Torres, G. (2020). Metagenomic characterization of bacterial biofilm in four food processing plants in Colombia. *Brazilian Journal of Microbiology*, 51, 1259-1267.
- Harrell, J.E., Hahn, M.M., D'Souza, S.J., Vasicek, E.M., Sandala, J.L., Gunn, J.S., & McLachlan, J.B. (2021). *Salmonella* biofilm formation, chronic infection, and immunity within the intestine and hepatobiliary tract. *Frontiers in Cellular and Infection Microbiology*, 10, 624622.
- 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, 6058-6075.
- Huang, L., Jin, Y., Zhou, D., Liu, L., Huang, S., Zhao, Y., & Chen, Y. (2022). A review of the role of extracellular polymeric substances (EPS) in wastewater treatment systems. *International Journal of Environmental Research and Public Health*, 19(19), 12191.
- Huang, Z., Zhang, Z., Tong, J., Malakar, P.K., Chen, L., Liu, H., & Zhao, Y. (2021). Phages and their lysins: Toolkits in the battle against foodborne pathogens in the postantibiotic era. *Comprehensive Reviews in Food Science and Food Safety*, 20(4), 3319-3343.
- Hussain, W., Ullah, M.W., Farooq, U., Aziz, A., & Wang, S. (2021). Bacteriophage-based advanced bacterial detection: Concept,

- mechanisms, and applications. *Biosensors and Bioelectronics*, 177, 112973.
- Imklin, N., Patikae, P., Poomirut, P., Arunvipas, P., Nasanit, R., & Sajapitak, S. (2024). Isolation of bacteriophages specific to bovine mastitis-causing bacteria and characterization of their lytic activity in pasteurized milk. *Veterinary World*, 17(1), 207.
- Imran, A., Shehzadi, U., Islam, F., Afzaal, M., Ali, R., Ali, Y.A., & Rasool, A. (2023). Bacteriophages and food safety: An updated overview. *Food Science & Nutrition*, 11(7), 3621-3630.
- Islam, M., Zhou, Y., Liang, L., Nime, I., Yan, T., Willis, S.P., Mia, M., Bei, W., Connerton, I.F., Fischetti, V.A., & Li, J. (2020). Application of a broad range lytic phage LPST94 for biological control of *Salmonella* in foods. *Microorganisms*, 8(2), p.247.
- Jamal, M., Andleeb, S., Jalil, F., Imran, M., Nawaz, M.A., Hussain, T., Ali, M., Rahman, S., & Das, C.R. (2019). Isolation, characterization and efficacy of phage MJ2 against biofilm forming multi-drug resistant *Enterobacter cloacae*. *Folia Microbiologica*, 64(1), pp.101-111.
- Jelena, J., Vincent, O., Annemieke, M., & Andreja, R. (2021). *Bacillus cereus* food intoxication and toxicoinfection. *Comprehensive Reviews in Food Science and Food Safety*, doi: 10.1111/1541-4337.12785.
- João, J., Lampreia, J., Prazeres, D.M.F., & Azevedo, A.M. (2021). Manufacturing of bacteriophages for therapeutic applications. *Biotechnology Advances*, 49, 107758.
- Karaynir, A., Salih, H., Bozdoğan, B., Güçlü, Ö., & Keskin, D. (2022). Isolation and characterization of Brochothrix phage ADU4. *Virus Research*, 321, 198902.
- Karygianni, L., Ren, Z., Koo, H., & Thurnheer, T. (2020). Biofilm matrixome: extracellular components in structured microbial communities. *Trends in Microbiology*, 28(8), 668-681.
- Kassa, T. (2021). Bacteriophages against pathogenic bacteria and possibilities for future application in Africa. *Infection and Drug Resistance*, 17-31.
- Kim, B.H., Ashrafudoulla, M., Shaila, S., Park, H.J., Sul, J. D., Park, S.H., & Ha, S.D. (2024). Isolation, characterization, and application of bacteriophage on *Vibrio parahaemolyticus* biofilm to control seafood contamination. *International Journal of Antimicrobial Agents*, 64(1), 107194.
- Kumar, J., Sharma, V.K., Parmar, S., Singh, P., & Singh, R.K. (2020). Biofilm: A microbial assemblage on the surface-A boon or bane? In *New and Future Developments in Microbial Biotechnology and Bioengineering: Microbial Biofilms* (pp. 139-150). Elsevier.
- Latka, A., & Drulis-Kawa, Z. (2020). Advantages and limitations of microtiter biofilm assays in the model of antibiofilm activity of Klebsiella phage KP34 and its depolymerase. *Scientific Reports*, 10(1), 20338.
- Lemon, D.J., Kay, M.K., & Titus, J.K. (2019). Construction of a genetically modified T7 select phase system to express the antimicrobial peptide. *Journal of Microbiology*, 57(6):532-538. doi: 10.1007/s12275-019-8686-6 114.
- Lennard, L.B. (2020). Food microbiology and food poisoning. In *Food and Nutrition* (pp. 132-154). Routledge.
- Leprince, A., & Mahillon, J. (2023). Phage adsorption to gram-positive bacteria. *Viruses*, 15(1), 196.
- Letarov, A.V. (2020). History of early bacteriophage research and emergence of key concepts in virology. *Biochemistry (Moscow)*, 85, 1093-1112.
- Lewis, J.M., Williams, J., & Sagona, A.P. (2024). Making the leap from technique to treatment genetic engineering is paving the way for more efficient phage therapy. *Biochemical Society Transactions*, BST20231289.
- Li, Z., Wang, X., Wang, J., Yuan, X., Jiang, X., Wang, Y., & Wang, F. (2022). Bacterial biofilms as platforms engineered for diverse applications. *Biotechnology Advances*, 57, 107932.
- Lila, A.S.A., Rajab, A.A., Abdallah, M.H., Rizvi, S.M.D., Moin, A., Khafagy, E.S., & Hegazy, W.A. (2023). Biofilm lifestyle in recurrent urinary tract infections. *Life*, 13(1), 148.
- Lim, E.S., Baek, S.Y., Oh, T., Koo, M., Lee, J.Y., Kim, H.J., & Kim, J.S. (2021). Strain variation *Bacillus cereus* biofilms and their susceptibility to extracellular matrix-degrading enzymes. *Plos One*, 16(6), e0245708.
- Liu, X., Cao, B., Yang, L., & Gu, J.D. (2022). Biofilm control by interfering with c-di-GMP metabolism and signaling. *Biotechnology Advances*, 56, 107915.
- Liu, C., Hong, Q., Chang, R.Y.K., Kwok, P.C.L., & Chan, H.K. (2022). Phage-Antibiotic therapy as a promising strategy to combat multidrug-resistant infections and to enhance antimicrobial efficiency. *Antibiotics*, 11(5), 570.
- Liu, H., Hu, Z., Li, M., Yang, Y., Lu, S., & Rao, X. (2023). Therapeutic potential of bacteriophage endolysins for infections caused by Gram-positive bacteria. *Journal of Biomedical Science*, 30(1), 29.
- Liu, S., Quek, S.Y., & Huang, K. (2023). Advanced strategies to overcome the challenges of bacteriophage-based antimicrobial treatments in food and agricultural systems. *Critical Reviews in Food Science and Nutrition*, 1-25.
- Liu, X., Yao, H., Zhao, X., & Ge, C. (2023). Biofilm formation and control of foodborne pathogenic bacteria. *Molecules*, 28(6), 2432.
- Lu, Y., Wang, Y., & Wang, J. (2021). Phage endolysin lysp108 showed promising antibacterial potential against methicillin-resistant *Staphylococcus aureus*. *Frontiers in Cellular and Infection Microbiology*, 11:668430. doi: 10.3389/fcimb.2021.668430 107.
- Lukman, C., Yonathan, C., Magdalena, S., & Waturangi, D.E. (2020). Isolation and characterization of pathogenic *Escherichia coli* bacteriophages from chicken and beef offal. *BMC Research Notes*, 13, 1-7.
- Luong, T., Salabarría, A.C., Edwards, R.A., & Roach, D.R. (2020). Standardized bacteriophage purification for personalized phage therapy. *Nature Protocols*, 15(9), 2867-2890.
- Łusiak-Szelachowska, M., Weber-Dąbrowska, B., & Górski, A. (2020). Bacteriophages and lysins in biofilm control. *Virologica Sinica*, 35(2), 125-133.
- Mäkelä, K., Laanto, E., & Sundberg, L.R. (2024). Determinants in the phage life cycle: The dynamic nature of ssDNA phage FLiP and host interactions under varying environmental conditions and growth phases. *Environmental Microbiology*, 26(7), e16670.
- Manaa, O., Asma, M., Mahran, Ali, Ahmed, I.M., Helal, & Heba, S. (2022). Rapid assessment of spoilage and food poisoning microbes in common meat products. *Suez Canal Veterinary Medical Journal* doi: 10.21608/scvmj.2022.152870.1091
- Manoharadas, S., Altaf, M., Alrefaei, A.F., Devasia, R.M., Badjah Hadj, A.Y.M., & Abuhasil M.S.A. (2021). Concerted dispersion of *Staphylococcus aureus* biofilm by bacteriophage and green synthesized silver nanoparticles. *RSC Advances*, 11(3):1420-1429. doi: 10.1039/D0RA09725J 112
- Martins, P.V.G., Dos Santos Nascimento, J., Da Silva Martins, F.M., & Ceotto, V.H. (2021). Vibriosis and its impact on microbiological food safety. *Food Science and Technology*, 42.
- Maszewska, A., Moryl, M., Wu, J., Liu, B., Feng, L., & Rozalski, A. (2021). Amikacin and bacteriophage treatment modulates outer membrane proteins composition in *Proteus mirabilis* biofilm. *Scientific Report*, 11(1):1522. doi: 10.1038/s41598-020-8 9907-9 102.
- Matamp, N., & Bhat, S.G. (2019). Phage endolysins as potential antimicrobials against multidrug resistant *Vibrio alginolyticus* and *Vibrio parahaemolyticus*: current status of research and challenges ahead. *Microorganisms*, 7(3). doi: 10.3390/microorganisms7030084
- Matamp, N., & Bhat, S.G. (2020). Genome characterization of novel lytic Myoviridae bacteriophage φVP-1 enhances its applicability against MDR-biofilm-forming *Vibrio parahaemolyticus*. *Archives of Virology*, 165, 387-396.
- Mazaheri, T., Cervantes-Huamán, B.R., Bermúdez-Capdevila, M., Ripolles-Avila, C., & Rodríguez-Jerez, J.J. (2021). *Listeria monocytogenes* biofilms in the food industry: is the current hygiene program sufficient to combat the persistence of the pathogen?. *Microorganisms*, 9(1), 181.
- McClane, B.A. (2023). *Clostridium perfringens* and foodborne illness. *Toxins*, 15(1), 47.
- Mendez, E., Walker, D.K., Vipham, J., & Trinetta, V. (2020). The use of a CDC biofilm reactor to grow multi-strain *Listeria monocytogenes* biofilm. *Food Microbiology*, 92, 103592.
- Mutti, M., & Corsini, L. (2019). Robust approaches for the production of active ingredient and drug product for human phage therapy. *Frontiers in Microbiology*, 10, 2289.
- Naaz, T., Kumar, A., Vempaty, A., Singhal, N., Pandit, S., Gautam, P., & Jung, S.P. (2023). Recent advances in biological approaches towards anode biofilm engineering for improvement of extracellular electron transfer in microbial fuel cells. *Environmental Engineering Research*, 28(5).
- Nafarrate, I., Mateo, E., Amárita, F., de Marañón, I.M., & Lasagabaster, A. (2020). Efficient isolation of *Campylobacter* bacteriophages from chicken skin, analysis of several isolation protocols. *Food Microbiology*, 90, 103486.
- Nahar, S., Ha, A. J.W., Byun, K.H., Hossain, M.I., Mizan, M.F.R., & Ha, S.D. (2021). Efficacy of flavourzyme against *Salmonella Typhimurium*, *Escherichia coli*, and *Pseudomonas aeruginosa* biofilms on food-contact surfaces. *International Journal of Food Microbiology*, 336, 108897.
- Nandhini, P., Kumar, P., Mickymaray, S., Alothaim, A.S., Somasundaram, J., & Rajan, M. (2022). Recent developments in methicillin-resistant *Staphylococcus aureus* (MRSA) treatment: A review. *Antibiotics*, 11(5), 606.

- Narayanan, K.B., Bhaskar, R., & Han, S.S. (2024). Bacteriophages: Natural antimicrobial bioadditives for food preservation in active packaging. *International Journal of Biological Macromolecules*, 133945.
- Naureen, Z., Dautaj, A., Anpilogov, K., Camilleri, G., Dhuli, K., Tanzi, B., & Bertelli, M. (2020). Bacteriophages presence in nature and their role in the natural selection of bacterial populations. *Acta Biomedica Atenei Parmensis*, 91.
- Ni, P., Wang, L., Deng, B., Jiu, S., Ma, C., Zhang, C., & Wang, S. (2020). Combined application of bacteriophages and carvacrol in the control of *Pseudomonas syringae* pv. actinidiae planktonic and biofilm forms. *Microorganisms*, 8(6), 837.
- Nikolaev, Y., Yushina, Y., Mardanov, A., Gruzdev, E., Tikhonova, E., El-Registan, G., & Polishchuk, E. (2022). Microbial biofilms at meat-processing plant as possible places of bacteria survival. *Microorganisms*, 10(8), 1583.
- Odo, S.E., Uchechukwu, C.F., & Ezemadu, U.R. (2021). Foodborne diseases and intoxication in Nigeria: Prevalence of *Escherichia coli* 0157: H7, *Salmonella*, *Shigella* and *Staphylococcus aureus*. *Journal of Advances in Microbiology*, 20(12), 84-94.
- Pal, M., Ketchakmadze, D., Durglishvili, N., & Ketchakmadze, K. (2022). *Staphylococcus aureus*: A major pathogen of food poisoning: A rare research report. *Nutrition Food Process*, 5(1), 1-3.
- Papaiani, M., Ricciardelli, A., & Casillo, A. (2020). The union is strength: the synergic action of long fatty acids and a bacteriophage against *Xanthomonas campestris* biofilm. *Microorganisms*, 9(1):60. doi: 10.3390/microorganisms9010060, 108
- Pinto, R. M., Soares, F. A., Reis, S., Nunes, C., & Van Dijk, P. (2020). Innovative strategies toward the disassembly of the EPS matrix in bacterial biofilms. *Frontiers in Microbiology*, 11, 952.
- Pradhan, J., Mallick, S., Mishra, N., Patel, S., Pradhan, J., & Negi, V.D. (2023). *Salmonella* biofilm and its importance in the pathogenesis. In *Understanding Microbial Biofilms* (pp. 447-459). Academic Press.
- Priyadarshane, M., & Das, S. (2023). Bacterial extracellular polymeric substances: biosynthesis and interaction with environmental pollutants. *Chemosphere*, 332, 138876.
- Quendera, A.P., Seixas, A.F., Dos Santos, R.F., Santos, I., Silva, J.P., Arraiano, C.M., & Andrade, J.M. (2020). RNA-binding proteins driving the regulatory activity of small non-coding RNAs in bacteria. *Frontiers in Molecular Biosciences*, 7, 78.
- Ranveer, S.A., Dasriya, V., Ahmad, M.F., Dhillon, H.S., Samtiya, M., Shama, E., & Puniya, A.K. (2024). Positive and negative aspects of bacteriophages and their immense role in the food chain. *NPJ Science of Food*, 8(1), 1.
- Roshankhah, R., Jackson, K., Nguyen, T.T.N., Pelton, R., Hosseinidoust, Z., & Ghosh, R. (2023). Purification of phage for therapeutic applications using high throughput anion exchange membrane chromatography. *Journal of Chromatography*, 1229, 123867.
- Roy, S., Chowdhury, G., Mukhopadhyay, A.K., Dutta, S., & Basu, S. (2022). Convergence of biofilm formation and antibiotic resistance in *Acinetobacter baumannii* infection. *Frontiers in Medicine*, 9, 793615.
- Sae-Ueng, U., Bhunchoth, A., Phironrit, N., Treetong, A., Sapcharoenkun, C., Chatchawankanphanich, O., & Chitnamsub, P. (2022). Thermoresponsive C22 phage stiffness modulates the phage infectivity. *Scientific Reports*, 12(1), 13001.
- Schilcher, K., & Horswill, A.R. (2020). *Staphylococcal* biofilm development: structure, regulation, and treatment strategies. *Microbiology and Molecular Biology Reviews*, 84(3), 10-1128.
- Sehgal, S., Aggarwal, S., Khakha, H.P., & Kaushik, P. (2024). Biofilms on food contact surfaces: current interventions and emerging technologies. *Microbial Biotechnology in the Food Industry: Advances, Challenges, and Potential Solutions*, 167-185.
- Sharma, G., Sharma, S., Sharma, P., Chandola, D., Dang, S., Gupta, S., & Gabrani, R. (2016). *Escherichia coli* biofilm: development and therapeutic strategies. *Journal of Applied Microbiology*, 121(2), pp.309-319.
- Sheng, L., & Wang, L. (2021). The microbial safety of fish and fish products: Recent advances in understanding its significance, contamination sources, and control strategies. *Comprehensive Reviews in Food Science and Food Safety*, 20(1), 738-786.
- Shlezinger, M., Copenhagen-Glazer, S., Gelman, D., Beyth, N., & Hazan, R. (2019). Eradication of vancomycin-resistant *Enterococci* by combining phage and vancomycin. *Viruses*, 11(10):954. doi: 10.3390/v11100954 104.
- Šilha, D., Sirotková, S., Švarcová, K., Hofmeisterová, L., Koryčanová, K., & Šilhová, L. (2021). Biofilm formation ability of *Arcobacter*-like and *Campylobacter* strains under different conditions and on food processing materials. *Microorganisms*, 9(10), 2017.
- Singh, A., Padmesh, S., Dwivedi, M., & Kostova, I. (2022). How good are bacteriophages as an alternative therapy to mitigate biofilms of nosocomial infections. *Infection and Drug Resistance*, 503-532.
- Sionov, R.V., & Steinberg, D. (2022). Targeting the holy triangle of quorum sensing, biofilm formation, and antibiotic resistance in pathogenic bacteria. *Microorganisms*, 10(6), 1239.
- Stefani, E., Obradović, A., Gašić, K., Altin, I., Nagy, I.K., & Kovács, T. (2021). Bacteriophage-mediated control of phytopathogenic xanthomonads: A promising green solution for the future. *Microorganisms*, 9(5), 1056.
- Su, Y.C. (2022). *Vibrio* control in seafood. *Comprehensive Reviews in Food Science and Food Safety*, 21(2), 1203-1220.
- Tan, W.S., Law, J.W.F., Law, L.N.S., Letchumanan, V., & Chan, K.G. (2020). Insights into quorum sensing (QS): QS-regulated biofilm and inhibitors. *Progress in Microbes and Molecular Biology*, 3(1), a0000141.
- Tan, C.W., Rukayadi, Y., Hasan, H., Abdul-Mutalib, N.A., Jambari, N.N., Hara, H., & Radu, S. (2021). Isolation and characterization of six *Vibrio parahaemolyticus* lytic bacteriophages from seafood samples. *Frontiers in Microbiology*, 12, 616548.
- Teklemariam, A.D., Al-Hindi, R.R., Qadri, I., Alharbi, M.G., Ramadan, W.S., Ayubu, J., & Harakeh, S. (2023). The battle between bacteria and bacteriophages: a conundrum to their immune system. *Antibiotics*, 12(2), 381.
- Telegdi, J., Shaban, A., & Trif, L. (2020). Review on the microbiologically influenced corrosion and the function of biofilms. *International Journal of Corrosion and Scale Inhibition*, 9(1), 1-33.
- Teschler, J.K., Nadell, C.D., Drescher, K., & Yildiz, F.H. (2022). Mechanisms underlying *Vibrio cholerae* biofilm formation and dispersion. *Annual Review of Microbiology*, 76(1), 503-532.
- Tian, F., Li, J., Nazir, A., & Tong, Y. (2021). Bacteriophage—a promising alternative measure for bacterial biofilm control. *Infection and Drug Resistance*, 205-217.
- Tkhilaishvili, T., Wang, L., Perka, C., Trampuz, A., & Gonzalez Moreno, M. (2020). Using bacteriophages as a Trojan Horse to the killing of dual-species biofilm formed by *Pseudomonas aeruginosa* and methicillin resistant *Staphylococcus aureus*. *Frontiers in Microbiology*, 11:695. doi: 10.3389/fmicb.2020.00695 103.
- Toushik, S.H., Roy, A., Alam, M., Rahman, U.H., Nath, N.K., Nahar, S., & Roy, P.K. (2022). Pernicious attitude of microbial biofilms in agri-farm industries: Acquisitions and challenges of existing antibiofilm approaches. *Microorganisms*, 10(12), 2348.
- Treccani, L. (2023). Interactions between surface material and bacteria: from biofilm formation to suppression. *Surface-Functionalized Ceramics: For Biotechnological and Environmental Applications*, 283-335.
- Tuon, F.F., Dantas, L.R., Suss, P.H., & Tasca Ribeiro, V.S. (2022). Pathogenesis of the *Pseudomonas aeruginosa* biofilm: a review. *Pathogens*, 11(3), 300.
- Urganci, N.N., Yilmaz, N., Alaşalvar, G.K., & Yıldırım, Z. (2022). *Pseudomonas aeruginosa* and its pathogenicity. *Turkish Journal of Agriculture-Food Science and Technology*, 10(4), 726-738.
- Valenti, M., Ranganathan, N., Moore, L.S., & Hughes, S. (2021). *Listeria monocytogenes* infections: presentation, diagnosis and treatment. *British Journal of Hospital Medicine*, 82(10), 1-6.
- Vestby, L.K., Grønseth, T., Simm, R., & Nesse, L.L. (2020). Bacterial biofilm and its role in the pathogenesis of disease. *Antibiotics*, 9(2), 59.
- Vitzilaiou, E., Liang, Y., Castro-Mejia, J.L., Franz, C.M., Neve, H., Vogensen, F.K., & Knöchel, S. (2022). UV tolerance of *Lactococcus lactis* 936-type phages: Impact of wavelength, matrix, and pH. *International Journal of Food Microbiology*, 378, 109824.
- Wang, Z., & Zhao, X. (2022). The application and research progress of bacteriophages in food safety. *Journal of Applied Microbiology*, 133(4), 2137-2147.
- Wang, K., Yuan, X., Wang, J., Huang, Z., Yu, S., Jin, H., & Ding, Y. (2024). Isolation and characterization of a novel *Bacillus cereus* bacteriophage vBce-DP7. *Microbial Pathogenesis*, 194, 106792.
- Wdowiak, M., Paczesny, J., & Raza, S. (2022). Enhancing the stability of bacteriophages using physical, chemical, and nano-based approaches: A review. *Pharmaceutics*, 14(9), 1936.
- Węgrzyn, G. (2022). Should bacteriophages be classified as parasites or predators? *Polish Journal of Microbiology*, 71(1), 3-9.
- Wintachai, P., & Voravuthikunchai, S.P. (2022). Characterization of novel lytic Myoviridae phage infecting multidrug-resistant *Acinetobacter baumannii* and synergistic antimicrobial efficacy between phage and Sacha Inchi oil. *Pharmaceutics*, 15(3), 291.
- Wu, R. A., Feng, J., Yue, M., Liu, D., & Ding, T. (2024). Overuse of food-grade disinfectants threatens a global spread of antimicrobial-resistant bacteria. *Critical Reviews in Food Science and Nutrition*, 64(19), 6870-6879.

- Yu, M., Gao, R., Lv, X., Sui, M., & Li, T. (2023). Inactivation of phage phiX174 by UV254 and free chlorine: Structure impairment and function loss. *Journal of Environmental Management*, 340, 117962.
- Yuan, L., Hansen, M.F., Røder, H.L., Wang, N., Burmølle, M., & He, G. (2020). Mixed-species biofilms in the food industry: current knowledge and novel control strategies. *Critical Reviews in Food Science and Nutrition*, 60(13), 2277-2293.
- Zinke, M., Schröder, G.F., & Lange, A. (2022). Major tail proteins of bacteriophages of the order Caudovirales. *Journal of Biological Chemistry*, 298(1).
- Zurabov, F., & Zhilenkov, E. (2021). Characterization of four virulent *Klebsiella pneumoniae* bacteriophages, and evaluation of their potential use in complex phage preparation. *Virology Journal*, 18, 1-20.

Int J Agri Biosci