Targeted Treatment of Dermatological Conditions: Utilising Bacteriophage - Enriched Hydrogels for Acne and Skin Conditions

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**Abstract:** Hydrogels enriched with bacteriophages are used as a unique and targeted treatment technique for skin diseases. Staphylococcus aureus is a common pathogen associated with several skin diseases such as impetigo, atopic dermatitis and inflammatory wounds. In addition to disrupting the skin's natural bacteria, traditional treatments such as antibiotics can also increase antibiotic resistance. Viral infections and bacteria-degrading agents such as bacteriophages offer a targeted approach to control bacterial overgrowth without harming beneficial microorganisms. To improve stability and efficacy, this study investigates the creation and use of bacteriophage-enriched hydrogels designed to deliver phages directly to damaged areas of skin. Hydrogels enable controlled and long-term release of phages. Moisturizing properties and biocompatibility of hydrogels support skin healing by reducing inflammation common in diseases caused by Staphylococcus aureus. Previous in vitro and in vivo studies show that phage hydrogel formulations effectively reduce bacterial counts and improve skin health with minimal side effects. These findings suggest that bacteriophage-enriched hydrogels have significant potential as a targeted therapeutic strategy, providing a durable and patient-friendly alternative to traditional antibiotic treatments. The ability of hydrogels to release bacteriophages in a controlled manner ensures a long-lasting antibacterial effect, while their compatibility with the skin promotes healing and reduces inflammatory reactions. Further research and clinical trials are needed to optimise formulations, confirm long-term efficacy and ensure safety. This advance could lead to a major breakthrough in dermatological treatment, addressing both the treatment of S. aureus-induced skin conditions and the broader challenge of antibiotic resistance

**keywords:** treatment of bacterial infections, bacteriophages, environmental samples, dermatological therapy

# INTRODUCTION

Dermatological diseases such as acne and various skin infections often cause serious medical problems because they are associated with bacterial pathogens such as Staphylococcus aureus.[(Enany & Alexander, 2017)](https://paperpile.com/c/KtS0Of/ZOl6) S. aureus is often associated with skin diseases such as impetigo, atopic dermatitis and inflammatory wounds.Due to the excessive use and abuse of antibiotics, more and more resistant bacteria are being isolated from health services and the environment, where the rapid exchange of genetic elements and resistance genes between bacterial classes promotes the spread of antimicrobial resistance (AMR). [(National Academies Of Sciences Engineering et al., 2022)](https://paperpile.com/c/KtS0Of/u9PT)[(Chidambaram et al., 2022)](https://paperpile.com/c/KtS0Of/12jcc).[(Ajay, Sasikala, et al., 2022)](https://paperpile.com/c/KtS0Of/yKMcv).[(Ajay, Rakshagan, et al., 2022)](https://paperpile.com/c/KtS0Of/JUyQE)As many global pharmaceutical players have made strategic financial decisions to end or outsource research programs for new antibiotics, the spread of antibiotic-resistant bacteria calls for the development of alternative treatment options. Bacteriophages, viruses that infect and destroy bacteria, offer a promising alternative to traditional antibiotics. Phage therapy uses the specificity of bacteriophages to target and eliminate bacterial pathogens, reducing the risk of damage to the natural flora of the skin and the development of antibiotic resistance. Previous studies have shown the potential of bacteriophages in the treatment of bacterial infections, including those caused by \*S. aureus\*. [(Suárez & Fernández, 2020)](https://paperpile.com/c/KtS0Of/YOBH)[(Harsha & Subramanian, 2022)](https://paperpile.com/c/KtS0Of/03uma)[(Deepika et al., 2022)](https://paperpile.com/c/KtS0Of/XNVMO)[(Solanki et al., 2022)](https://paperpile.com/c/KtS0Of/5UtwZ)Recent advances have focused on the development of delivery systems that improve the stability and efficacy of bacteriophages. Known for their biocompatibility and ability to release therapeutic agents over a long period of time, hydrogels have become an effective medium for delivering bacteriophages directly to the site of infection. Phages can reduce complications caused by the side effects of conventional antibiotics and ultimately improve treatment efficacy. Physico-chemical properties characteristic of bacteriophages enable bacteriophages to access infection sites where chemical compounds may not reach. Other properties, such as strong bactericidal activity and low toxicity of bacteriophages, make phage therapy a more affordable alternative compared to traditional antibiotics.[(Gorski et al., 2021)](https://paperpile.com/c/KtS0Of/JEbx)[(Ajay, Suma, et al., 2022a)](https://paperpile.com/c/KtS0Of/hQQWW) [(Ajay, Suma, et al., 2022b)](https://paperpile.com/c/KtS0Of/bID4N)[(Katyal et al., 2021)](https://paperpile.com/c/KtS0Of/nKoEa)Due to their moisturising properties, hydrogels enriched with bacteriophages can maintain the viability of phages, ensure a long-lasting antibacterial effect and promote skin healing. [(Pieter & Morteza, 2017)](https://paperpile.com/c/KtS0Of/R8YD) [(Tiwari & Jain, 2023)](https://paperpile.com/c/KtS0Of/ofmXU)[(Graf et al., 2023)](https://paperpile.com/c/KtS0Of/MUnv6). This study investigates the development and use of bacteriophage-enriched hydrogels as a targeted therapy for acne and other skin diseases. By combining the antibacterial properties of bacteriophages with the therapeutic benefits of hydrogels, this approach aims to provide a patient-friendly and sustainable alternative to traditional antibiotic treatments[(Jabin et al., 2021)](https://paperpile.com/c/KtS0Of/Q4P1O)[(Balaji Ganesh S & Sugumar, 2021)](https://paperpile.com/c/KtS0Of/Ec3yb) [(Govindaraj & Dinesh, 2021)](https://paperpile.com/c/KtS0Of/FwAma) . The following sections discuss the composition of bacteriophage-enriched hydrogels, their in vitro and in vivo efficacy, and potential implications for dermatological therapy[(Dharman 2021)](https://paperpile.com/c/KtS0Of/fBBNu)

# MATERIAL AND METHODS

## Isolation of Bacteriophages

Samples were taken from sewage wastewater treatment facilities, and they were transported to the lab in sterile circumstances and with aseptic handling. To identify the different bacteriophages that were in the water, these samples were collected at various times of the day and from diverse locations. Staphylococcus aureus strains associated with skin infections and acne were identified. After that, these bacterial strains were cultivated and kept in ideal growth environments for the phage isolation studies that followed.

## Phage Enrichment

The cultivated host bacteria were combined with the gathered environmental samples in the proper growth media, and the mixture was then incubated in conditions that were favorable to phage replication, such as ideal pH and temperature. The presence of lysis and plaque formation, which are indicators of an active phage infection, was seen in bacterial cultures. The host bacteria were given enough time to replicate the phage, which resulted in bacterial lysis and the release of phage progeny into the culture medium. To maximize phage output while minimising bacterial contamination, optimal incubation periods were determined.

## Phage purification

To separate the host cells and bacterial detritus, the infected bacterial cultures were centrifuged. For additional purification processes, the supernatant containing refined phages was carefully collected. After that, the supernatant containing the phage was passed through sterile filters (e.g., 0.2 µm hole size) to get rid of any remaining bacterial cells, cell debris, and big particles. If more filtrations were required to guarantee a pure phage suspension, they were employed.

## SDS-PAGE Analysis

Proteins can be separated and analyzed according to their molecular weight using SDS-PAGE (Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis). SDS-PAGE ensures the purity and integrity of the proteins in the bacteriophage samples by helping to describe them in this investigation. Proteins are denatured and given a negative charge by reducing agent and SDS in a buffer used to prepare the samples. After that, the samples are passed across a polyacrylamide gel in an electric field, where the smaller proteins migrate more quickly than the larger ones. In order to identify and analyze phage proteins and verify the caliber of the phage preparation in the hydrogels, the gel is dyed to visualize the protein bands.

## Preparation of Hydrogel (Sample)

Calcium chloride, boric acid, and polyvinyl alcohol (PVA) were prepared for the hydrogel formulation. The PVA was dissolved in distilled water at 90°C while being constantly mixed. Next, calcium chloride and boric acid were added [(Sarvesh et al., 2024)](https://paperpile.com/c/KtS0Of/UGJ5). The hydrogel combination was combined with the isolated phage enzyme(Rafi et al., 2024). The mixture was allowed to dissolve and then incubated for a whole night at 2–8°C. After undergoing many freeze-thaw cycles, the hydrogel was lyophilized in order to facilitate additional examination.

## Characterization and Testing

Plaque assays and spot tests were used in phage typing to measure phage titers and evaluate phage specificity against target bacteria (Tuluwengjiang et al., 2024). To describe the behavior of the phage, the size and shape of the plaques were noted and examined. Samples were produced for electron microscopy in order to ensure purity and integrity while characterizing and seeing the morphology of the phage. To distinguish between several phage morphotypes and evaluate structural differences, micrographs were examined.

## Antibacterial Activity

Nutrient broth was made, infected with Staphylococcus aureus, and incubated at 37°C for two to three hours in order to perform the agar well diffusion assay. To correct for turbidity, the 0.5 McFarland Standard was used. After being prepared aseptically, Mueller Hinton agar was transferred into sterile petri dishes. The bacterial culture was added to the plates, and 10 mm-diameter wells were made. Antibiotic discs served as the positive control and dimethyl sulfoxide (DMSO) as the negative control. The diameter of the inhibitory zones was measured after the plates were incubated for 24 hours at 37°C.

# Results and Discussion

## Antibacterial Assay (Petri Dish Image)

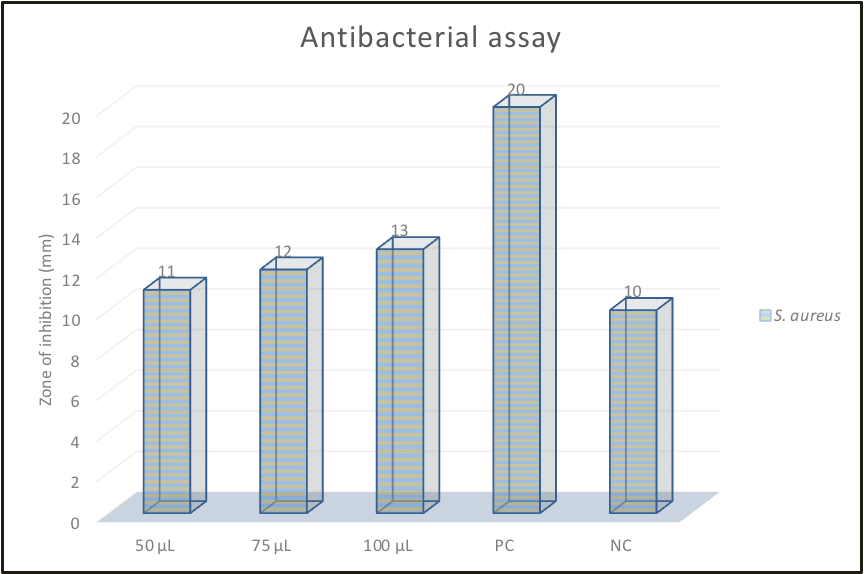
An antibacterial assay is a scientific method used to assess how well a chemical inhibits or eliminates germs. One popular technique is the agar diffusion method, which involves placing disks soaked in the test item on an agar plate that has been infected with bacteria. The clear zone that forms around the disk after this process shows antibacterial activity. An alternative technique is the broth dilution method, which finds the lowest concentration of the test drug that stops observable bacterial growth by cultivating bacteria in a liquid medium containing different quantities of the test substance.



**Fig.1** Physical results of the antibacterial assay on a petri dish. The petri dish is marked with different concentrations of hydrogel samples and control points. Zones of inhibition are visually apparent around the hydrogel samples, clearly indicating areas where bacterial growth is prevented. These zones confirm the antibacterial activity of the hydrogel against Staphylococcus aureus, as higher concentrations of the hydrogel correlate with more significant bacterial inhibition, consistent with the results shown in the antibacterial assay graph.

## Antibacterial Assay

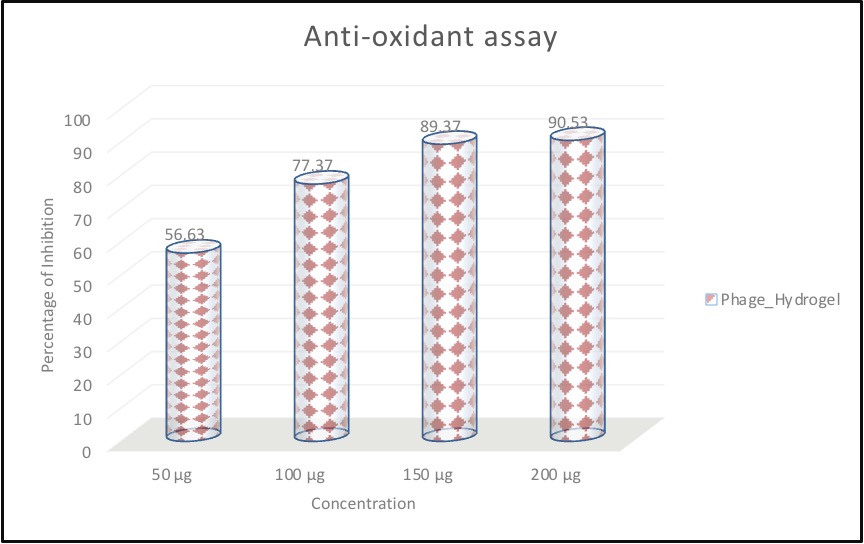
**Fig.2** The bar graph illustrates the antibacterial activity of different hydrogel samples against S. aureus. Hydrogel samples were tested at concentrations of 50 µL, 75 µL, and 100 µL. The positive control (PC) shows a maximum zone of inhibition of 20 mm, indicating strong antibacterial activity. In contrast, the negative control (NC) exhibits no antibacterial activity. The results indicated significant antibacterial properties, with the hydrogel-infused with phages showing the highest inhibition of bacterial growth.



## Antioxidant Assay

A laboratory test called an antioxidant assay gauges a substance's capacity to scavenge free radicals or stop oxidative damage. Antioxidants shield cells from oxidative stress, which is connected to a number of chronic diseases like cancer, cardiovascular disease, and neurological problems. This is why these tests are crucial. Researchers can gain a better understanding of the potential health advantages and ways in which foods, supplements, and other substances can help prevent disease by assessing their antioxidant capability.

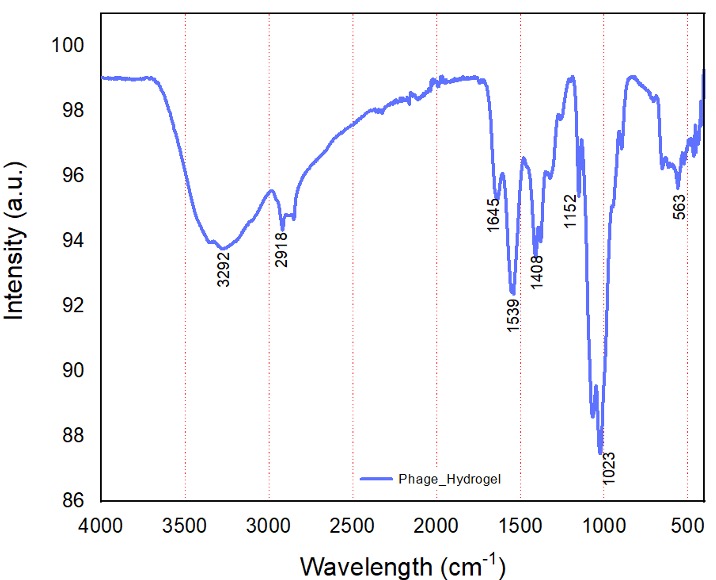
**Fig.3** The bar graph displays the percentage of inhibition at different concentrations (50 µg, 100 µg, 150 µg, 200 µg) of the hydrogel. The percentage of inhibition increases with concentration, starting at 56.63% for 50 µg and reaching 90.53% for 200 µg. This data demonstrates that the hydrogel has significant antioxidant properties, which improve with increasing concentration.



## FTIR (Fourier-Transform Infrared Spectroscopy) Analysis

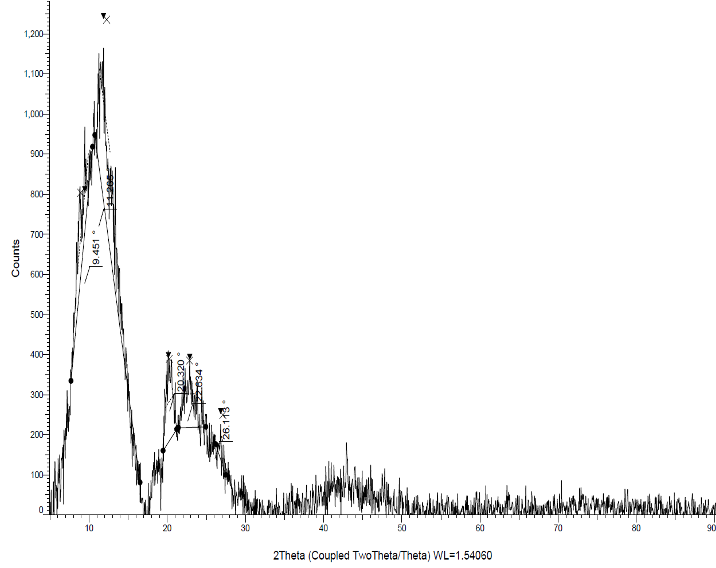
Fourier Transform Infrared (FTIR) spectroscopy is an analytical technique for identifying organic, polymeric, and inorganic compounds by analyzing their infrared spectra. By exposing a sample to infrared light, this technique detects the vibrations of chemical bonds inside the sample, creating a distinct spectral fingerprint that may be used to identify and examine the material's composition and structure. For quality control, material verification, and molecular interaction research, FTIR is useful in a variety of sectors, including chemistry, materials science, pharmaceuticals, and environmental science. Its quick, non-destructive, and extremely specific analysis makes it an invaluable tool.

**Fig.4** The graph illustrates the FTIR spectrum of the hydrogel infused with bacteriophages, highlighting the characteristic peaks.Peaks at specific wavelengths, such as 3222 cm⁻¹, 2918 cm⁻¹, 1645 cm⁻¹, 1406 cm⁻¹, 1152 cm⁻¹, 1023 cm⁻¹, and 589 cm⁻¹, indicate the presence of various functional groups. The shifts in these peaks suggest interactions between the hydrogel and bacteriophages.



## XRD (X-Ray Diffraction) Analysis

A method for examining the composition, physical characteristics, and crystallographic structure of materials is X-ray diffraction (XRD) examination. Depending on the arrangement of atoms within the crystal, X-rays are diffracted in different directions when they strike crystalline materials. Researchers can identify unfamiliar materials, ascertain the crystal structure, and learn more about the phase composition, strain, and size of the crystallites by analyzing the angles and intensities of these diffracted beams.An XRD pattern indicating a primarily amorphous material would have a broad, diffuse peak in the lower 2θ area and no distinct peaks at higher angles. At higher 2θ values, distinct and sharp peaks signify a crystalline structure. According to the transition you describe, a material may have changed from amorphous to crystalline properties in the sample if it first exhibits amorphous characteristics (wide peak) and subsequently exhibits crystalline features (sharp peaks) at higher angles [(Dilipan et al., 2023; Selvamani et al., 2025)](https://paperpile.com/c/KtS0Of/MxDY+MaZn). The peaks in the XRD pattern confirm the successful integration of bacteriophages into the hydrogel matrix, supporting the structural characterization of the material.



**Fig.5** The graph displays the XRD pattern of the hydrogel, showing the amorphous nature of the material and the incorporation of crystalline components from the bacteriophages. The position and sharpness of peaks in X-ray diffraction (XRD) can be used to determine the characteristic pattern of crystalline and amorphous materials [(Dilipan et al., 2023)](https://paperpile.com/c/KtS0Of/MxDY).

A unique and focused method of treating dermatological diseases, especially those brought on by bacterial infections like Staphylococcus aureus, is the application of bacteriophage-enriched hydrogels. [(Abedon et al., 2017)](https://paperpile.com/c/KtS0Of/Rwdr)[(Sabaratnam & Madhu Laxmi, 2021)](https://paperpile.com/c/KtS0Of/Fl4uJ)[(Sushanthi et al., 2021)](https://paperpile.com/c/KtS0Of/JSORr)[(Harsha et al., 2022)](https://paperpile.com/c/KtS0Of/1En1p). This technique combines hydrogels—gel-like substances that can carry these phages directly to the skin—with bacteriophages—viruses that particularly infect and lyse bacterial cells. The skin's natural microbiota is preserved because the hydrogels deliver a controlled release of bacteriophages that target and eradicate harmful bacteria without endangering helpful species. This method presents a viable substitute for conventional antibiotic therapies, which frequently result in resistance to antibiotics and disturb the beneficial bacteria on the skin. The creation of bacteriophage therapeutics has received more attention in recent years as a solution to the rising issue of antibiotic resistance. Bacteriophages are capable of killing particular forms of bacteria, including those resistant to antibiotics, according to studies. It has been investigated if bacteriophages and hydrogels can work together to improve phage stability and transport to infection sites. Phage-enriched hydrogels have been shown in vitro and in vivo to effectively lower bacterial numbers and enhance skin health with little adverse effects. This creative method supports ongoing research for long-term, viable substitutes for traditional antibiotics in the treatment of bacterial illnesses. Hydrogels loaded with bacteriophages have many benefits. First off, only pathogenic bacteria are harmed by the targeted activity of bacteriophages, protecting the good bacteria that are essential for maintaining healthy skin. Second, a prolonged antibacterial impact is made possible by the controlled release characteristics of hydrogels, which lowers application frequency and increases patient compliance. Atopic dermatitis, impetigo, and inflammatory wounds can all benefit from the hydrating and biocompatible qualities of hydrogels, which also promote skin healing and reduce inflammation. Additionally, this method reduces the possibility of developing antibiotic resistance, which is a major issue with conventional therapies.This technique has some limitations, however. Because bacteriophages are species-specific, a phage designed to target one type of bacteria might not work against another, necessitating a detailed knowledge of the bacterial strains present in each condition. [(Brüssow, 2019)](https://paperpile.com/c/KtS0Of/QtKf)[(Neha et al., 2021)](https://paperpile.com/c/KtS0Of/U8zSC)[(Maliael et al., 2021)](https://paperpile.com/c/KtS0Of/8z8Ay)[(Lakshmi, 2021)](https://paperpile.com/c/KtS0Of/r2naR). Bacteriophage manufacturing and purification can also be difficult and expensive processes. Further difficulties include the necessity for lengthy clinical trials and regulatory barriers to guarantee the efficacy and safety of phage therapy. Further investigation is necessary to comprehend the enduring impacts of applying hydrogels enriched with bacteriophages on the skin microbiome.In light of this, the goal of this topic is to create and enhance bacteriophage-enriched hydrogels as a focused treatment for acne and other Staphylococcus aureus-related skin conditions. The goal of the research is to develop formulations that offer a controlled release and long-lasting effect by fusing the medicinal advantages of hydrogels with the antibacterial capabilities of bacteriophages. The ultimate objective is to offer a durable, patient-friendly substitute for conventional antibiotic therapies that addresses the more general problem of antibiotic resistance in addition to the pressing requirement for efficient bacterial control. In order to improve these formulations, validate their effectiveness, and guarantee their safety for broad usage in dermatological applications, more investigation and clinical testing will be necessary.

# CONCLUSION

Hydrogels supplemented with bacterial bacteriophages show promise in the treatment of dermatological diseases brought on by pathogenic bacteria such as Staphylococcus aureus. This method overcomes the drawbacks of conventional antibiotic treatments by fusing the advantageous qualities of hydrogels with the specificity of bacteriophages. Studies have demonstrated effectiveness in lowering bacterial counts and improving skin health while having few adverse effects. To guarantee safety, validate long-term efficacy, and improve formulations, more research and clinical trials are necessary. The creation of hydrogels enhanced with bacteriophages has the potential to transform dermatological treatment and tackle antibiotic resistance in a focused and approachable way for patients.

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