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Review of light activated antibacterial nanomaterials in the second biological window

Suresh Thangudu[1,2*] and Chia-Hao Su[1,3,4*]

Abstract

Bacterial infections continue to pose a major threat to public health, contributing to high mortality rates worldwide. The growing ineffectiveness of conventional antibiotics has created an urgent need for alternative solutions. Nanomaterials (NMs) have emerged as a promising approach to combating bacterial infections due to their unique physicochemical properties, and extensive research has been conducted to address this crisis, yielding notable results. However, challenges such as limited light absorption and inherent cytotoxicity remain significant concerns. Furthermore, the clinical adoption of single-mode phototherapy is often restricted by the shallow tissue penetration of traditional light sources. The second biological window (NIR-II, 950–1450 nm) offers a groundbreaking opportunity for therapeutic and diagnostic applications by enabling deeper tissue penetration. As a result, growing research efforts are dedicated to developing NIR-II activated photosensitizers and nanomaterials to overcome challenges such as poor light absorption, limited tissue penetration, and suboptimal activation. Despite significant advancements, a comprehensive review of antibacterial nanomaterials specifically designed for the NIR-II window is still lacking in literature. This review aims to fill that gap by discussing the latest advancements, challenges, and potential of light-activated antibacterial nanomaterials within the BW-II region. The goal is to enhance understanding and guide the development of more efficient nanomaterials for future biomedical and clinical applications.

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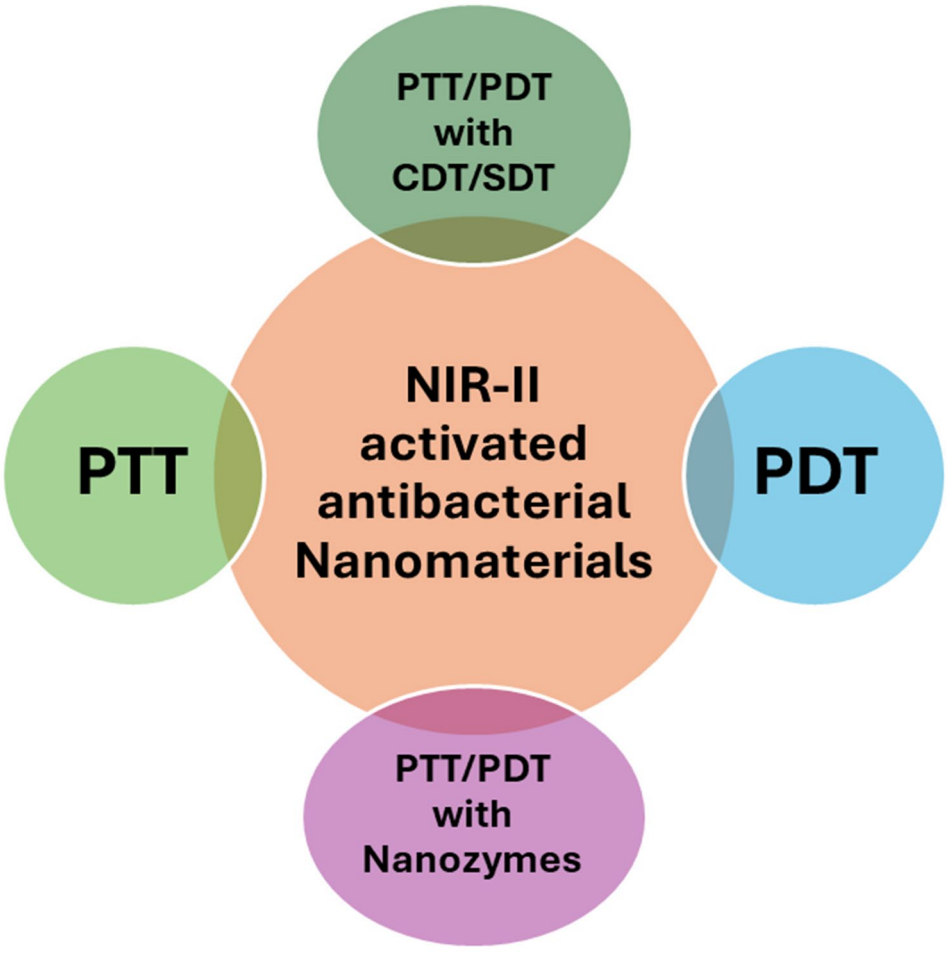
Graphical abstract

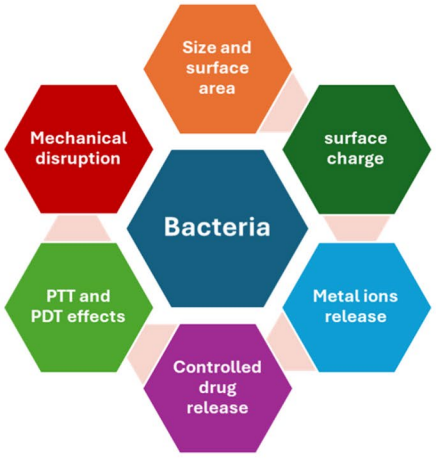


Keywords Nanomaterials, NIR-II biological window, Phototherapy, Combination therapy, Antibacterial activity, Wound healing

Introduction

The invention of antibiotics in the early 20th century revolutionized for the treatment of bacterial infections [1]. However, the overuse of antibiotics later gave rise to antibiotic resistant or drug-resistant bacteria, presenting a grave global public health threat, particularly to hospitalized patients, who are prone to infections. Response measures included the development of antibiotic drugs such as vancomycin and methicillin, but bacterial strains have since emerged that are also resistant to these drugs (VRSA and MRSA) [2, 3]. Conventional clinical therapy for subcutaneous infections generally involves the systemic administration of high dose of antibiotics, which often has detrimental side effects to normal tissues. Indeed, the World Health Organization (WHO) has described antibiotic resistance as "a problem so serious that it threatens the achievements of modern medicine" [4], giving great urgency to the development of new strategies to address drug resistance among bacterial infections. Due to their unique physio-chemical properties, nanomaterials (NMs) have emerged as a potential response [5]. NMs can bind and disrupt bacterial membranes, causing leakage of cytoplasmic components in a process called cell lysis [2]. They can further disrupt intracellular components such as ribosomes, DNA and enzymes, leading to oxidative stress followed by cell death. Nanoparticles (NPs) use multiple mechanisms to kill bacteria, reducing the likelihood of effective adaptation to develop resistance. Figure 1 illustrates key physicochemical properties of nanomaterials that enhance their effectiveness against bacterial infections.

Using the advantages of NMs, several antimicrobial strategies have been developed to combat drug resistance [6–9]. Among all photo-based NMs generate heat



Function	Mechanism of Action
Size and surface area	Smaller nanoparticles can infiltrate bacterial cell membranes, leading to structural disruption NPs high surface area increases their interaction with bacteria, boosting their effectiveness
Surface Charge	Positively charged nanomaterials interact with negatively charged bacterial membranes, and vice versa
Controlled Drug Release	Nanomaterials facilitate the controlled delivery of antibiotics
Metal ions release	Metal NPs releasing toxic ions
PTT/PDT effects	Light-activated nanomaterials kill bacteria by generating heat or reactive oxygen species (ROS)
Mechanical Disruption	Sharp nanomaterials puncture bacterial membranes, causing damage

Fig. 1 An overview of the physicochemical properties of nanomaterials that are effective against bacterial infections

[8, 10] and reactive species such as Reactive Oxygen Species (ROS) [11–15], Reactive Chlorine Species (RCS) [9], and Reactive Nitrogen Species (RNS) [16] under light illumination, have garnered significant attention due to their controllable bactericidal effects. Moreover, their effects extend beyond bacterial eradication, significantly influencing the host immune system and microbiome. Precisely, PTT-induced hyperthermia can trigger an immune response by releasing bacterial and host cell debris, facilitating antigen presentation and activating both innate and adaptive immune pathways [17]. This process may strengthen immune surveillance and offer systemic protection against future infections. However, excessive heat exposure can result in local inflammation and tissue damage, potentially leading to immune suppression or dysregulation. Similarly, PDT generates reactive oxygen species (ROS) to induce bacterial cell death, which also influences immune activity. ROS-mediated stress signals can stimulate cytokine secretion, affecting macrophage polarization and adaptive immune responses [18]. While controlled ROS levels can enhance antibacterial immunity, excessive ROS production may lead to oxidative stress, harming surrounding healthy tissues and potentially causing dysbiosis. Since the discovery of the photocatalytic inactivation of bacteria using TiO_2, numerous semiconductor photocatalysts have been extensively studied for bacterial eradication. However, weak light absorption in the near infrared (NIR) region limits their applications as in vivo NIR light activatable photosensitizers. The clinical use of NMs is also limited by their cytotoxic effects, reduced accumulation at the infected site and non-biocompatibility. The limited tissue penetration of traditional light sources poses a significant challenge to the effectiveness of phototherapy, especially for infections located deep within the body. Conventional light sources, such as visible and ultraviolet (UV) light, primarily penetrate only the superficial layers of the skin and tissues, restricting their ability to reach deeper infections embedded in muscles, organs, or bones [19]. As a result, key therapeutic effects such as reactive oxygen species (ROS) generation for pathogen elimination are significantly reduced in deeper tissues. Additionally, light scattering and absorption further diminish its energy, making it even less effective for treating chronic or deep-seated infections. Besides, owing to the fact that biological tissues exhibit minimal absorption of visible light (> 650 nm), phototherapeutic approaches using NIR excitation in broad biological windows (700–1500 nm: NIR-I, 650–950 nm, and NIR-II, 950–1450 nm) are more appropriate for broad biological applications. While NIR-I therapy (700–950 nm) relies on PTT and PDT effects to generate heat and ROS for bacterial destruction, its effectiveness is often hindered by shallow penetration depth and heat dissipation, which can result in incomplete bacterial elimination and potential tissue damage. In contrast, NIR-II-activated nanomaterials demonstrate significant advantages over their NIR-I counterparts in terms of performance and versatility [20]. The deeper tissue penetration and reduced scattering associated with NIR-II wavelengths allow for enhanced optical clarity and more precise targeting of bacterial infections or cancer tumors, particularly in deeper or more complex tissue environments. Furthermore, NIR-II materials exhibit reduced photothermal damage to surrounding healthy tissues due to their localized heating capability, resulting in improved biocompatibility and safety profiles [21]. NIR-II nanomaterials also often possess superior photothermal conversion efficiency and photodynamic effects, allowing for more effective bacterial eradication at lower energy thresholds [22]. Table 1 presents key comparisons between the antibacterial activity of NIR-I, NIR-II and NIR-III NMs. Overall, NIR-II-activated nanomaterials represent a promising frontier in antibacterial nanotechnology, offering enhanced therapeutic outcomes and

Table 1 Critical comparisons between the antibacterial activity of NIR-I, NIR-II and NIR-III NMs

Property	NIR-I (650–950 nm)	NIR-II (950–1450 nm)	NIR-III (1500–1850 nm)
Penetration Depth in Tissue	Moderate (mm range)	Higher (up to cm range)	Highest (deepest penetration)
Photothermal Efficiency	Moderate	High	Very High
Tissue Absorption	More absorption by hemoglobin and water	Less absorption by water, better tissue penetration	Higher absorption by water (may limit efficiency)
Photothermal Antibacterial Effect	Effective with good nanomaterial design	More effective due to deeper penetration and higher photothermal conversion	Potentially highly effective but limited by high water absorption
ROS Generation	Possible but less efficient	Enhanced ROS production with suitable nanomaterials	Limited ROS generation
Bacterial Killing Efficiency	Good for superficial infections	Superior for deep tissue infections	Effective for deep infections but needs optimized conditions
Thermal Damage to Healthy Tissue	Higher risk due to moderate penetration	Lower risk due to deeper penetration and selective heating	Potential risk due to water absorption

broader applicability in addressing complex bacterial infections compared to NIR-I-based systems. Unfortunately, many nanomaterials cannot effectively absorb NIR-II light, restricting their in vivo applications. Significant advancements in NIR-II-specific materials and technologies are needed to unlock their full potential. This review explores state-of-the-art nanomaterial-based phototherapeutic approaches for bacterial inactivation within the NIR-II range. This in-depth examination of NIR-II-enabled wound healing techniques aims to help researchers better understand current advancements, identify existing challenges, and develop innovative NIR-II-activated antibacterial nanomaterials for future clinical applications.

Advantages of biological window II

The past 20 years has witnessed the development of numerous nanotheranostic agents with absorption properties tailored to the first biological window (NIR-I, 650–950 nm) for successful use in in vivo theranostic applications [23, 24]. However, persistent challenges are presented by significant photon scattering and absorption caused by biological molecules such as fat, skin, and blood within the NIR-I biowindow, resulting in a low signal-to-noise ratio (SNR) and restricted light penetration depth. As illustrated in Fig. 2**(A)**, light scattering is inversely related to wavelength (λ), meaning longer wavelengths enable deeper penetration with reduced scattering. While 808 nm NIR-I laser light provides a penetration depth of under 1 cm far superior to that of visible light photons it remains insufficient for effectively targeting deep-seated tumors/infections. Compared to the NIR-I biowindow, biological molecules and tissues demonstrate significantly lower absorption of laser light in the second biowindow (NIR-II, 950–1450 nm) [25], as illustrated in Fig. 2**(B)**. This property makes NIR-II light activation a highly advantageous and effective approach for deep cancer theranostics. With reduced scattering and increased penetration depth, NIR-II laser light can

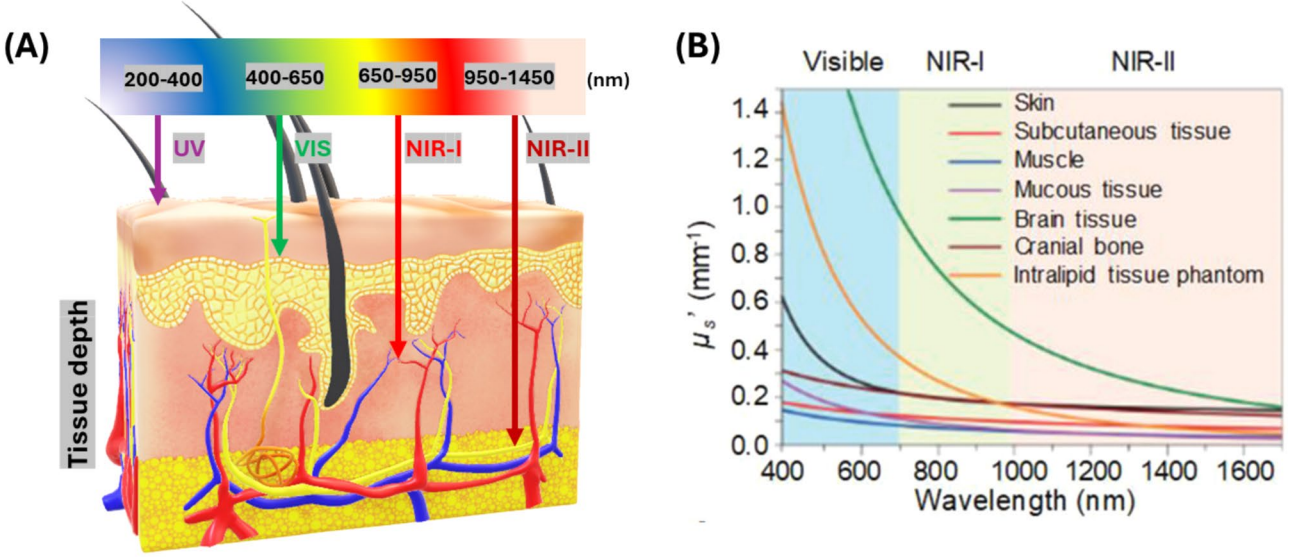


Fig. 2 (**A**) Penetration depth of different wavelengths of light. (**b**) Plot of scattering coefficients (μ's) of various tissues as a function of wavelength from 400 to 1700 nm. Reproduced with permission [25]

Table 2 Key differences in light scattering between NIR-I and NIR-II

Aspect	NIR-I	NIR-II
Scattering coefficient	High (limits depth and resolution)	Low (enhances depth and resolution)
Penetration depth	Moderate (few mm to cm)	High (up to several cm)
Spatial resolution	Lower (blurring at greater depths)	High (sharp and defined images)
Energy distribution	Non-uniform, potential hotspots	Uniform, safer for therapies

Table 3 Percentage of light penetration through 5 mm Thick pork tissue. Reproduced with permission [26]

BW	Laser wavelength (nm)	Light penetration (%)
VIS	660	11.5
NIR-I	808	20
	915	21.6
NIR-II	980	23.1
	1064	24.6
NIR-III	1550	33.4

operate at higher power levels to activate photothermal nanoagents, ensuring optimal therapeutic results while minimizing the risk of skin damage. Some key advantages of NIR-II over NIR-I are listed in Table 2.

In clinical phototherapeutic treatments targeting deep-seated tumors, the ability of excitation light to penetrate diseased tissue is a critical factor influencing treatment effectiveness. To demonstrate this, the tissue penetration capabilities of light in the NIR-I (808 nm), NIR-II (1064 nm), and NIR-III (1550 nm) biological windows were evaluated using a 5 mm thick pork tissue sample [26]. The results clearly show that NIR-III (1550 nm) light achieves the highest transmission rate (33.4%) through the tissue, outperforming NIR-I (808 nm) at 20% and NIR-II (1064 nm) at 24.6% (see Table 3). Moreover, due to the lower photon energy associated with longer wavelengths, such as 1064 nm, the NIR-II window provides better tissue tolerance compared to NIR-I. For instance, the American National Standards Institute (ANSI) permits a maximum permissible exposure (MPE) of 1.0 W/cm² for NIR-II lasers, significantly higher than the 0.33 W/cm² limit for NIR-I lasers [27].

Conventional antibiotics vs. NIR-II activated nanomaterials

Conventional antibiotics face several significant challenges, underscoring the need for alternative approaches such as nanomaterials. One of the most critical issues is

the rapid rise of antibiotic-resistant bacteria, driven by the overuse and misuse of these drugs, which diminishes their effectiveness [28]. Additionally, bacterial biofilms serve as protective barriers, greatly reducing the efficacy of conventional antibiotics and making infections more difficult to eliminate [29]. Many antibiotics also suffer from poor stability, rapid degradation, and limited tissue penetration, resulting in suboptimal therapeutic outcomes. Moreover, prolonged antibiotic use can lead to severe side effects, including organ toxicity and disruptions to the gut microbiome [30]. These limitations highlight the urgent demand for alternative antimicrobial strategies. Nanomaterials present a promising solution by offering improved stability, targeted drug delivery, effective biofilm penetration, and multimodal antibacterial mechanisms, ultimately reducing resistance development and enhancing treatment outcomes.

Specifically, antimicrobial NMs activated by NIR-II offer significant advantages over traditional antibiotics, positioning them as promising candidates for future clinical applications. The key differences between NIR-II activated NMs and conventional antibiotics are outlined in Table 4.

Additionally, compared to other emerging antibacterial strategies like bacteriophage therapy and CRISPR-based antimicrobial interventions, NIR-II nanomaterials offer a rapid, broad-spectrum approach without the need for genetic targeting. While bacteriophage therapy ensures high specificity and minimal off-target effects, its efficacy is often hindered by bacterial resistance and immune clearance [31]. Similarly, CRISPR-based antimicrobials can selectively eliminate antibiotic-resistant bacteria, but challenges such as delivery efficiency and unintended gene edits restrict their clinical application [32]. In contrast, NIR-II nanomaterials provide a non-genetic, externally controlled antibacterial strategy that effectively targets both planktonic and biofilm-associated bacteria, making them a versatile and promising solution for combating multidrug-resistant infections. Building on the benefits of the NIR-II biological window, this review aims to provide a comprehensive overview of the latest advancements in NIR-II activated nanomaterials specifically, metal nanomaterials, nanozymes and synergetic strategies for the treatment of bacterial infections.

Table 4 Key comparison of NIR-II activated antibacterial NMs with conventional antibacterial therapies

Feature	NIR-II Nanomaterials	Conventional Antibacterial Therapies
Mechanism of Action	Photothermal & Photodynamic effects	Antibiotics, antimicrobial peptides, disinfectants
Target Specificity	Highly targeted with minimal collateral damage	Broad-spectrum, potential off-target effects
Resistance Development	Lower likelihood of bacterial resistance	High due to overuse and misuse of antibiotics
Tissue Penetration	Deep penetration due to NIR-II properties	Limited, especially in deep-seated infections
Immune System Modulation	Can enhance immune response via antigen presentation	Some antibiotics may suppress immune function
Microbiome Impact	Less disruption of commensal bacteria with targeted application	Often disrupts gut and skin microbiome, leading to dysbiosis
Scalability and Cost	High cost and scalability challenges	Established production with varying costs
Side Effects	Potential localized heating or oxidative stress	Allergic reactions, gut microbiome imbalance, organ toxicity
Multi-functionality	Can integrate therapy, imaging, and diagnostics	Primarily treatment-focused

Antibacterial nanomaterials in the BW II region

Metal nanomaterials as NIR-II activatable agents

The importance of NIR-II BW has prompted several researchers to investigate various kinds of nanomaterials with extended absorption, to identify efficient methods for treating bacterial infections. For instance, gold nanorods (Au NRs) demonstrate remarkable photostability, biocompatibility, and ease of functionalization with antibodies, producing better results than silver nanoparticles (Ag NPs). Furthermore, altering the shape and size of Au NRs allows them to efficiently absorb near-infrared radiation (NIR), facilitating effective energy transfer to their surroundings. This property significantly enhances their capability to eradicate pathogenic bacteria. *Khan et al.*., confirmed that Au NRs can effectively eliminate pathogenic bacteria, particularly Pseudomonas aeruginosa, using photothermal treatment under Nd-YAG laser (1064 nm) illumination [33]. Their approach successfully targeted wound infections in albino mice, accelerating the healing process. When exposed to laser irradiation, the Au NRs produced significant heat, efficiently eradicating pathogens at the infection sites without damaging adjacent tissue. MALDI-MS analysis further confirmed wound healing, showing no detectable pathogenic bacterial peaks. Combining the plasmonic properties of gold with the widely used biocompatible poly(vinyl alcohol) (PVA) has the potential to create innovative hybrid polymer materials with adjustable photothermal characteristics and diverse applications. To explore this, PVA films embedded with PEGylated gold nanostars (GNSs) were produced and evaluated [34]. The addition of PEGylated GNSs enhanced the mechanical strength of the PVA films, which demonstrated a significant localized photothermal effect when exposed to NIR irradiation (under both NIR I and NIR II laser ranges). This photothermal

effect proved highly effective in eliminating bacteria, paving the way for the development of advanced antibacterial films and protective coatings. *Gao et al.*., designed ultra-small, protein-based nanoparticles (NPs) as novel antibacterial agents with absorption spanning both near-infrared (NIR) I and II windows [35]. These agents use a dual-action antibacterial approach that leverages synergistic photothermal and photodynamic effects. The nanoparticles were engineered by conjugating Ce6 molecules to hydrophilic protein-modified copper sulfide NPs, enabling the conversion of light energy into heat for photothermal therapy and the generation of reactive oxygen species for photodynamic therapy. When exposed to NIR I and II laser irradiation, the nanoparticles demonstrated exceptional antibacterial efficacy against both Gram-positive bacteria (Staphylococcus aureus) and Gram-negative bacteria (Escherichia coli) in vitro, with high safety profiles. In vivo studies in a mouse model confirmed their effective bactericidal activity, as evidenced by the monitoring of photoacoustic signals from blood vessels surrounding the infection site.

Recent years have seen the widespread development and clinical application of silver nanoparticle (Ag NP)-based antibacterial strategies. However, the excessive release of free Ag^+ ions can lead to bacterial resistance and cytotoxicity, potentially causing brain damage and immune system disorders. Thus, there is a pressing need for the development of efficient treatments for MRSA infections that also allow real-time monitoring of therapeutic progress. To address this challenge, *Mei et al.*., proposed an activatable near-infrared II (NIR-II) phototheranostic approach using miniature Au/Ag nanorods (NRs) for synergistic photochemical therapy and in situ monitoring of MRSA infection treatment [36]. These Au/Ag NRs were activated by a ferricyanide solution, enabling the sustained release of Ag^+ ions to eliminate MRSA while enhancing NIR-II photothermal and photoacoustic (PA) performance. The activated NIR-II photothermal effect further accelerated Ag^+ ion release, providing a synergistic effect for eliminating Gram-positive Staphylococcus aureus and promoting wound healing. Post-treatment, this synergistic approach achieved a 20-fold increase in the NIR-II PA signal, with a maximum signal-to-noise ratio of 9.5 observed between the infected site and surrounding normal tissue. This enabled sensitive, real-time monitoring of the Ag^+ ion release process, showcasing the dual therapeutic and diagnostic potential of this strategy. *Gao et al.*., later generated oxygen-deficient black SnO2 – x nanomaterials with significant absorption of NIR (700–1200 nm) light using the NaBH4 reduction method. After modification with hyaluronic acid (HA), the resulting SnO_2–x@SiO_2-HA nanotheranostics demonstrated excellent dispersibility in aqueous solutions and biocompatibility [37]. Upon single NIR-II (1064 nm) light irradiation, SnO_2–x@SiO_2-HA effectively produced both hyperthermia and reactive oxygen species (ROS). This dual action enabled significant tumor inhibition and promoted accelerated wound healing in in vivo experiments under 1064 nm laser exposure. *Zhang et al.*, engineered upconversion element-doped titanium dioxide nanorods (TiO2 NRs) combined with curcumin (Cur), hyaluronic acid (HA), and bone morphogenetic protein-2 (BMP-2) to create a NIR-II-assisted platform (denoted as TiO2:FYH/Cur/BMP-2) for rapid biofilm eradication on bone implants under mild temperature conditions [38]. The synergistic effects of quorum sensing inhibitors, reactive oxygen species (ROS), and the mechanical disruption caused by nanorods effectively eliminated Staphylococcus aureus biofilms on titanium surfaces at a moderate temperature of 45 °C using 1060 nm laser irradiation for just 15 min, both in vitro and in vivo. Furthermore, curcumin reduced immune responses, while BMP-2 enhanced osteogenic differentiation, promoting accelerated new bone formation. *Huang et al.*., developed a hybrid nanosystem, Ag_2S@ZIF-Van NS, through a one-step self-assembly process involving Zn^{2+}, vancomycin (Van), and Ag_2S quantum dots (QDs) [39]. This nanosystem exhibits outstanding second near-infrared transparency window (NIR-II) fluorescence properties, with an emission wavelength of approximately 1200 nm, along with excellent photothermal conversion efficiency and biocompatibility. The system facilitates precise and targeted NIR-II fluorescent imaging of bacterial inflammation in vivo, while simultaneously enhancing antibacterial activity and promoting wound healing.

Due to the rapid recombination of photo-induced electrons and holes, gold nanorods (Au NRs) exhibit excellent photothermal (PT) performance. As plasmonic metal nanostructures, Au NRs are highly efficient at harnessing surface plasmon resonance (SPR) energy to generate hot electrons, particularly at the ends where the LSPR energy is strong. By interacting with surrounding media, including oxygen (O2), these hot electrons can produce reactive oxygen species (ROS), resulting in decreased PT conversion efficiency. Thus, preventing hot electrons from interacting with the environment is vital for improving the efficiency of photothermal therapy (PTT). To address this challenge, *Wang et al.*., developed hybrid plasmonic Au/ZnSe nanodumbbell heterostructures (AZN) for the treatment of bacterial infections through efficient photothermal therapy (PTT) under NIR-II light irradiation [40]. The two ZnSe semiconductor caps, characterized by a higher conduction band (CB), prevent the injection of hot electrons from the Au nanorods (NRs). These ZnSe caps also act as passivation layers, blocking hot electrons from interacting with the surrounding medium, thereby enhancing photothermal conversion efficiency. As a result, AZN generates significantly more heat compared

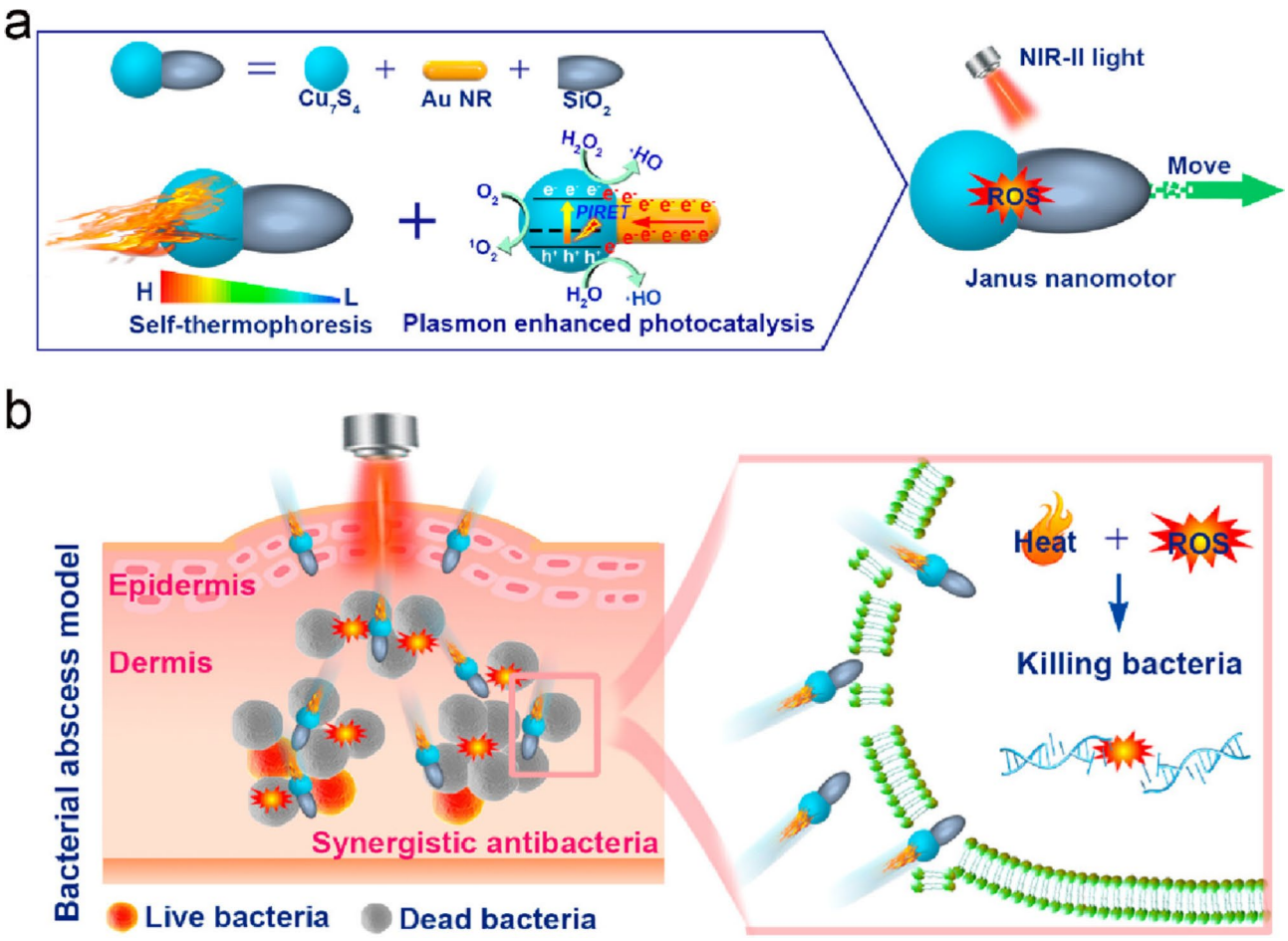


Fig. 3 Design and operation of antimicrobial nanomotors. (**a**) Illustration of the Janus architecture of AuNR-SiO2-Cu7S4 nanomotors, highlighting their plasmon-enhanced photocatalytic activity and self-propulsion driven by thermophoresis under 1064 nm light exposure. (**b**) NIR-II light triggers synchronized autonomous motion, along with combined photothermal and photocatalytic antibacterial actions, improving transdermal penetration and effectively combating infections caused by methicillin-resistant Staphylococcus aureus (MRSA). Reproduced with permission [41]

to Au NRs under identical laser irradiation conditions. The AZN structures demonstrated exceptional antibacterial performance against both Gram-positive and Gram-negative bacteria in both in vitro and in vivo experiments. Infections often remain difficult to treat effectively due to the passive diffusion of antibacterial agents, resulting in weak or nonexistent interactions with bacteria. To address this challenge, *Liu et al..*, developed a Janus dual-plasmonic antimicrobial nanomotor (of) capable of fast, directional motion under NIR-II light [41]. As shown in Fig. 3, this innovation leverages enhanced photothermal and photocatalytic properties of AuNR-SiO2-Cu7S4 for PAI-guided active treatment of deep-seated, drug-resistant bacterial infections. The nanomotors exhibit a remarkable speed of 9.8 μm/s under NIR-II light, significantly improving transdermal penetration and facilitating interactions with bacteria. Their unique configuration also enhances plasmon energy transfer from Au NRs to Cu7S4 nanocrystals, boosting light-to-heat conversion and photocatalytic activity. Consequently, these nanomotors demonstrated exceptional antibacterial performance, achieving 98.3% efficiency against MRSA in vitro and 97.8% efficiency in treating MRSA-infected skin abscesses in vivo. Recently, *Wang et al..*, developed kanamycin-derived carbon nanodots (KCDs) and a nitric oxide donor (BNN6), which were co-loaded into dendritic silica-coated NaYF4:Yb3+/Tm3+@NaYF4 three-layer core–shell upconversion materials (USKB) for enhanced peroxynitrite-mediated anti-infection treatment of diabetic wounds [42]. Upon exposure to NIR-II light, USKB emitted ultraviolet light that activated KCDs and BNN6 to respectively generate superoxide anions and nitric oxide (NO). The interaction between NO and superoxide anions produced highly cytotoxic peroxynitrite (ONOO–), significantly enhancing antibacterial activity. Experimental results demonstrated that USKB activated by NIR-II light not only improved antibacterial efficiency through peroxynitrite-driven biofilm removal in vitro but also accelerated diabetic wound healing in vivo by reducing inflammation and promoting

the recruitment of M2 macrophages. In another study, Cu-containing porous TiO2 coatings were developed on titanium implants to combat implant-associated infections [43]. The use of NIR-II light-activated photothermal therapy amplified the antibacterial effects of Cu ions. This combination of hyperthermia and Cu ions exhibited significantly enhanced antibacterial activity, achieving an efficiency of 99% against Streptococcus mutans in both in vitro and in vivo experiments.

Nevertheless, certain challenges persist regarding these phototherapeutic strategies: (I) directly applying photosensitizers or photothermal agents to the wound site risks excessive concentrations, potentially leading to cytotoxicity and hindering the wound healing process; (II) high-power photothermal treatments can cause adverse effects on healthy tissues surrounding the wound, while reactive oxygen species (ROS) in photodynamic therapy (PDT) have limited lifespans (< 3.5 μs), short diffusion ranges (tens to hundreds of nanometers), and are generally non-selective [30, 31]. Thankfully, hydrogel-based combination therapies have emerged as a promising solution to these issues. Integrating hydrogels with intelligent nanomaterials—such as photothermal nanoagents and photosensitizers—significantly improves precision delivery to the wound site. For instance, *Wang et al.*., designed a nanocomposite comprising a biocompatible poly(vinyl alcohol) (PVA)/polyethylene glycol (PEG) hydrogel, embedded with biodegradable molybdenum oxide (MoOx) nanoparticles and the photosensitizer methylene blue (MB), referred to as MoOx@MB-hy [44]. This innovative hydrogel serves as a photoactivated wound dressing, enabling synergistic photothermal–photodynamic therapy (PTT–PDT) using near-infrared-II 1064 nm and 660 nm lasers. A crucial feature of this system is the controlled heat-induced release of MB from MoOx@MB-hy under 660 nm irradiation, which enhances the production of singlet oxygen (^1O2). Furthermore, MoOx@MB-hy effectively consumes glutathione (GSH) and traps bacteria closer to the reactive oxygen species (ROS) damage threshold, enabling self-migration-enhanced ROS accumulation. This addresses the intrinsic limitations of ROS's short diffusion distance and lifespan. As a result, MoOx@MB-hy demonstrates exceptional antibacterial efficacy, achieving respective eradication rates of 99.28% and 99.16% against ampicillin-resistant E. coli and B. subtilis within just 15 min. The light-activated mechanism also accelerates wound healing, even in cases of infections caused by drug-resistant bacteria. *Huang et al.*., developed GG@PANI(Fe)-borax for the treatment of melanoma and wound healing [45]. This hydrogel was demonstrated to have excellent injectability, rapid self-healing capabilities, and the ability to undergo reversible gel–sol transitions in response to thermal or pH stimuli. By harnessing second near-infrared (NIR-II) photothermal conversion, the hydrogel allows for the enhanced cytotoxic production of hydroxyl radicals (OH) in H2O2-rich tumor microenvironments. Beyond cancer therapy, the hydrogel was also found to be effective against Gram-positive and Gram-negative bacteria (Staphylococcus aureus and Escherichia coli). While PTT shows great promise in treating drug-resistant bacterial infections, its effectiveness is hindered by challenges like poor targeting of infected areas and limited penetration through bacterial cell membranes. Conventional photosensitizers often require coupling with cationic groups or bacterial targeting peptides to enhance bacterial targeting. However, this modification can compromise the original antimicrobial activity of the photosensitizers or negatively affect the natural membrane permeability of free peptides. As a promising alternative, NIR-II photothermal agents with inherent structural bacterial targeting capabilities provide a novel avenue for combating bacterial infections. As shown in Fig. 4, *Zhang et al.*, developed three xanthene derivatives (CNs) with strong light-harvesting capabilities around 1180 nm for effective photothermal and broad-spectrum antibacterial therapy [46]. Their bulky planar structures promote the formation of H-aggregates, which exhibit exceptional photothermal conversion efficiency (39–43%) and excellent photostability within the NIR-II therapeutic bio-window. By modifying the side chains of the CNs, the resulting liposomes acquired surface charges ranging from negative to positive. Notably, intermolecular hydrogen bonding in the CN3 dimer caused the positively charged xanthene skeleton to be exposed on the periphery, conferring natural bacterial targeting properties. As a result, CN3 demonstrated effective NIR-II photothermal activity and broad-spectrum antimicrobial efficacy against both Gram-positive and Gram-negative bacteria, achieving bacterial inactivation rates of 99.4% for S. aureus and 99.2% for E. coli, while significantly enhancing wound healing in bacteria-infected mice with excellent biocompatibility. This structure-inherent bacterial targeting approach highlights a promising and efficient strategy for NIR-II photothermal antibacterial therapy, enabling broad-spectrum bacterial eradication.

Many existing photothermal agents suffer from poor water solubility, restricting their ability to penetrate Gram-negative bacterial cell membranes, resulting in suboptimal antibacterial effects. To address this limitation, *Wang et al.*, used phospholipid polymer conjugates to enhance the surface hydrophilicity of aggregation-induced emission (AIE) nanoparticles (NPs) [47]. This approach not only improved their stability by preventing aggregation but also ensured prolonged circulation in the body. Specifically, biomimetic neutrophil-like AIE nanorobots (CM@AIE NPs) were developed for targeted homing to inflammatory sites and efficient

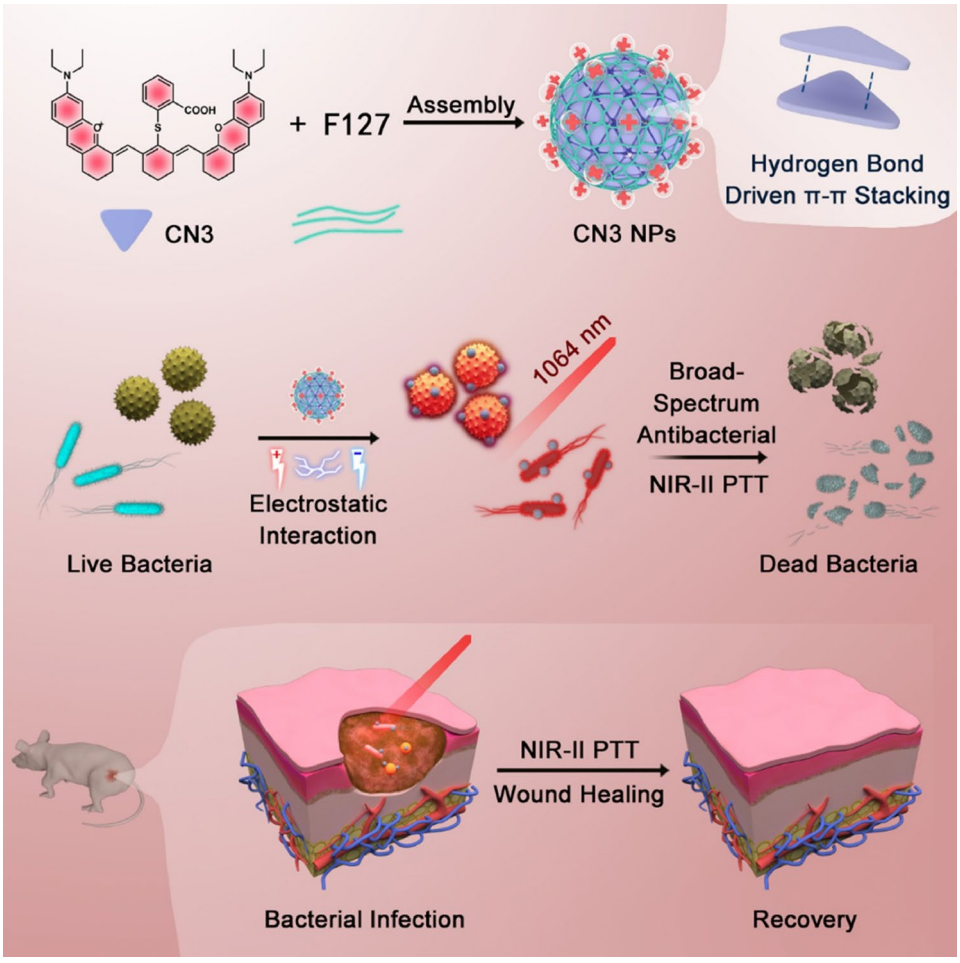


Fig. 4 Schematic illustration of the NIR-II xanthene dye (CN3), designed with an inherently bacterial-targeting structure, enabling effective photothermal therapy and broad-spectrum antibacterial treatment. Reproduced with permission [46]

photothermal therapy (PTT). By incorporating surface-loaded neutrophil membranes, CM@AIE NPs can mimic the functionality of natural neutrophils, interacting with immunomodulatory molecules that would typically target endogenous neutrophils. In addition, their secondary near-infrared absorption and the superior photothermal properties of AIE luminogens (AIEgens) allow for precise localization and treatment of inflammatory sites while minimizing damage to healthy tissues. Similar to metallic nanomaterials, polymers and two-dimensional materials, Polydopamine (PDA) is well-regarded for its photothermal properties and biocompatibility in biomedical applications, but its absorption in the near-infrared (NIR-II) range and antibacterial efficacy are limited. To address these shortcomings, *Fang et al.*., developed Fe-doped molybdenum oxide (MoFeOx)-functionalized PDA composites, which exhibit enhanced NIR absorption, increased reactive oxygen species (ROS) production, and glutathione (GSH) depletion [48]. These properties allow for combined photothermal and chemodynamic antibacterial therapy. Polyethylenimine (PEI) was used as an interlayer to bind MoFeOx to the PDA surface through electrostatic interactions. Compared to pure PDA, the new nanoparticles showed a 145% improvement in photothermal efficiency at the NIR-II wavelength (1064 nm) with just 2.2% MoFeOx incorporation. This enhancement results from electron donor-acceptor interactions within the material, reducing the energy band gap and facilitating better electron migration, as confirmed by ultraviolet photoelectron spectroscopy (UPS). The nanoparticles effectively exhibited synergistic antibacterial effects against E. coli and S. aureus via combined photothermal and chemodynamic therapies. Although metal-based chemical agents have shown encouraging bacteriostatic effects in phototherapy, their limited excitation/emission wavelengths and insufficient phototherapy efficiency hinder their practical use in vivo. To address these challenges, *Xu et al.*., developed a novel Pt(II) metallacycle (Pt1110) that can be activated by a 980 nm laser for photo diagnosis and treatment in deep tissues [49]. Pt1110 demonstrated a significant enhancement in photothermal conversion efficiency (95%

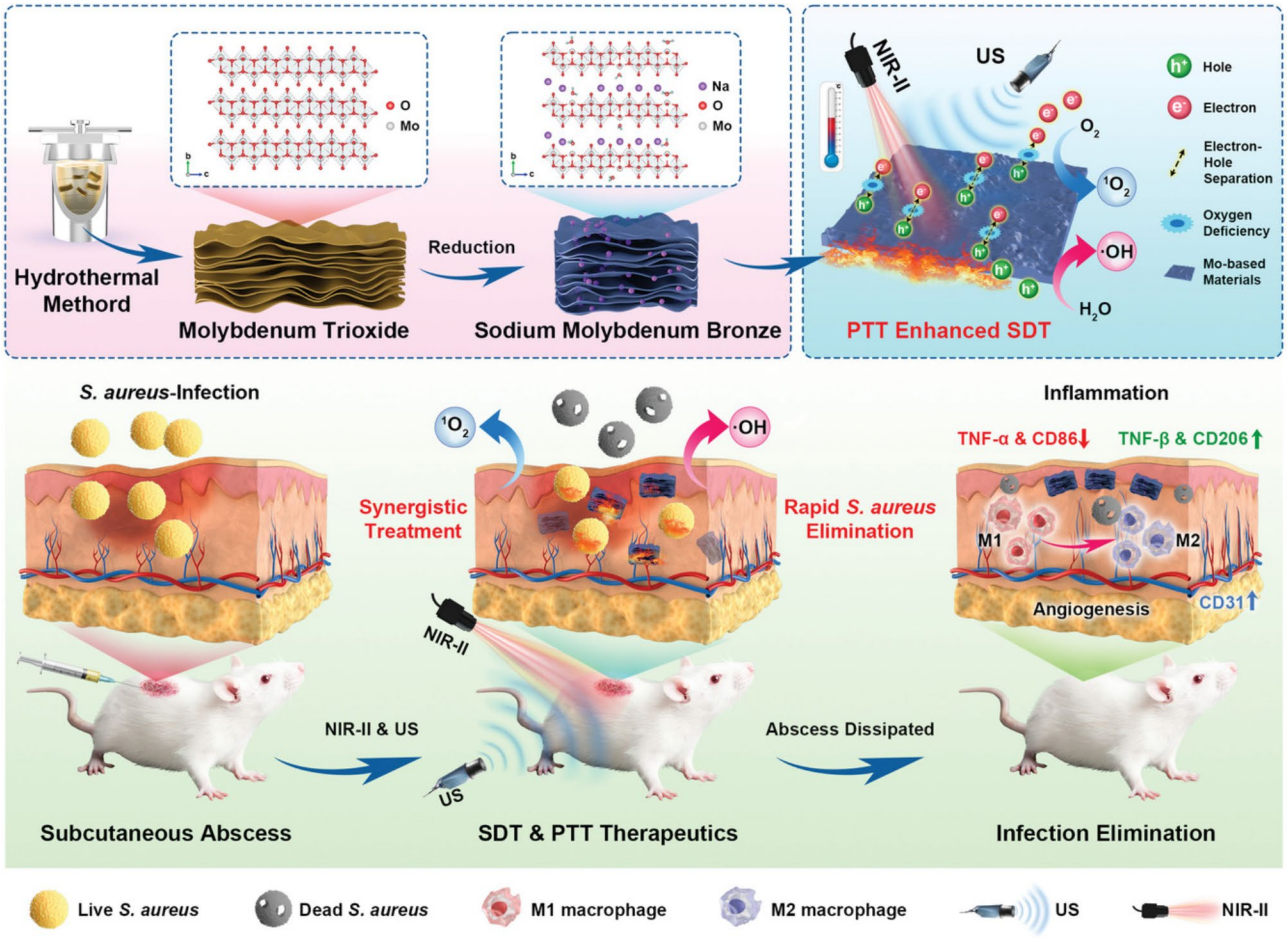


Fig. 5 Schematic illustration detailing the primary synthesis process of an oxygen vacancy-rich sodium molybdenum bronze nanoplatform with a wide interlayer gap, along with its NIR-II-mediated ROS generation mechanism to enhance SDT efficacy against subcutaneous S. aureus infections. Reproduced with permission [50]

improvement) and singlet oxygen (1O 2) generation (ΦΔ increased by 75%) compared to its ligand (1). Moreover, it exhibited effective light-induced sterilization under safe laser irradiation conditions (0.72 W/cm²). When incorporated into liposomes, Pt1110 nanoparticles (NPs) successfully facilitated wound healing in infection and keratitis models following laser irradiation, with precise monitoring enabled by NIR-II fluorescence imaging.

Recent developments in ultrasound (US)-mediated sonodynamic therapy (SDT) offer non-invasive treatments capable of deep tissue penetration. Integrating photothermal therapy (PTT) with SDT can significantly improve therapeutic outcomes through hyperthermia-enhanced bacterial membrane permeability, highlighting the potential value in developing molybdenum-based sonosensitizers for multimodal therapies that combine SDT and PTT. As shown in Fig. 5, *He et al.*, designed sodium molybdenum bronze nanoparticles (SMB NPs) featuring abundant oxygen vacancies to treat subcutaneous Staphylococcus aureus infections [50]. Due to their high oxygen vacancy density and an expanded interlayer gap that narrows the band gap, SMB NPs accelerate the separation of electrons (e^-) and holes (h^+) produced by US, while preventing their recombination under US irradiation. SMB NPs also exhibit a second near-infrared (NIR-II) photothermal effect, further enhancing ROS generation by the sonosensitizer. This innovative system effectively eradicates Staphylococcus aureus and disrupts biofilms, making SMB NPs a promising tool for treating deep-seated bacterial infections through multimodal therapy.

NIR-II activating agents combined with nanozymes

The advancement of nanozymes is anticipated to significantly enhance the field of dual phototherapy. Nanozymes, a unique class of nanomaterials exhibiting enzyme-like catalytic activity, have attracted considerable attention in biomedical research [51–53]. Studies suggest that these enzyme-like properties can be synergistically combined with photodynamic therapy (PDT) and photothermal therapy (PTT) to create a photoresponsive nanocatalytic

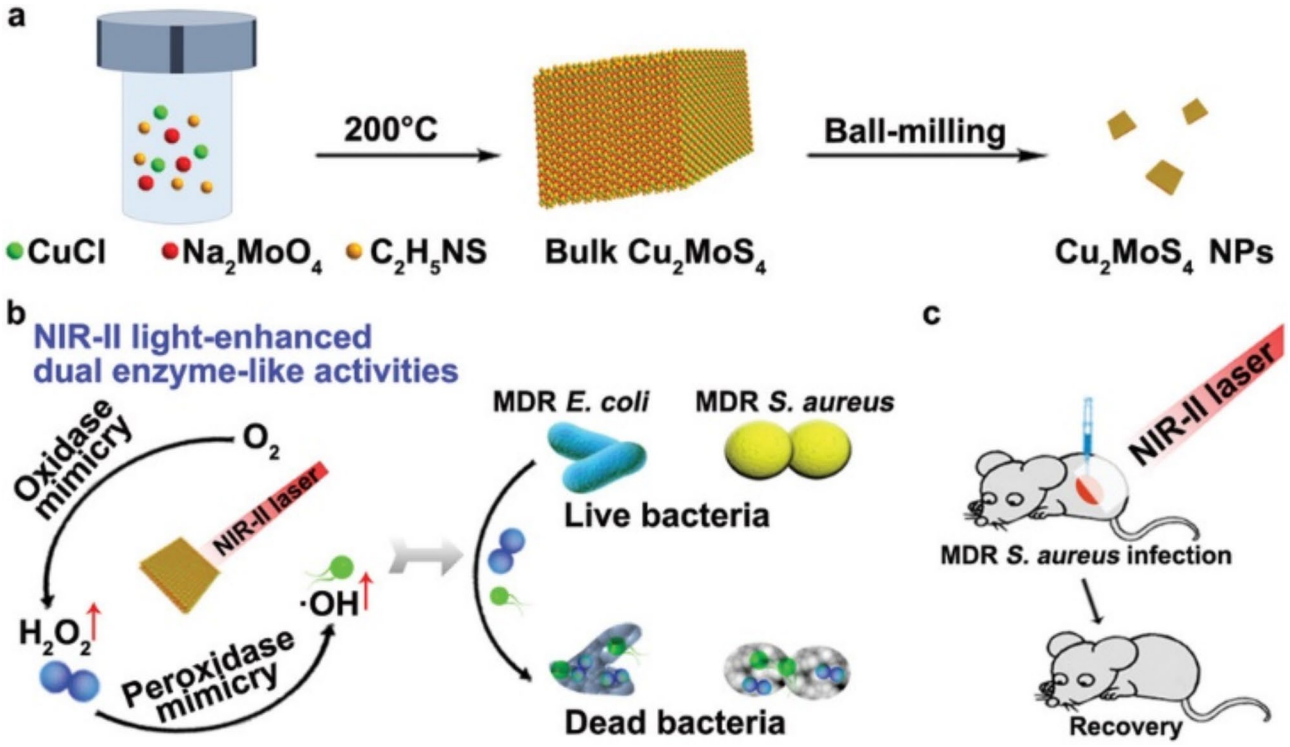


Fig. 6 Schematic illustration of NIR-II light-responsive Cu_2MoS_4 nanoplates for bacterial eradication. (**a**) The preparation process of Cu_2MoS_4 nanoplates (CMS NPs), (**b**) their NIR-II light-enhanced dual enzyme-like catalytic activities for eliminating MDR E. coli and MDR S. aureus in vitro, and (**c**) their application in treating MDR S. aureus infections in vivo. Reproduced with permission [54]

therapeutic platform. This innovative platform integrates photosensitizers, photothermal agents, and nanozymes. Incorporating nanozymes with phototherapeutic agents can effectively address hypoxia, enhance PDT by generating oxygen within endogenous environments, and accelerate the catalytic reaction to produce reactive oxygen species (ROS) under photothermal heat. Their catalytic efficiency is temperature-dependent, as described by the Arrhenius equation, meaning elevated temperatures significantly enhance reaction rates. Using this property, *Shan et al.*., designed Cu_2MoS_4 nanoplates (CMS NPs) as NIR-II light-responsive nanozymes with dual enzyme-like activities to catalytically generate ROS [54]. As shown in Fig. 6, under NIR-II light, CMS NPs showed enhanced oxidase- and peroxidase-like catalytic activities, leading to increased ROS production for effective bacterial elimination. In vitro studies demonstrated that CMS NPs (40 μg/mL) achieved rapid bacterial elimination, reducing 8-log MDR Escherichia coli and 6-log MDR Staphylococcus aureus within just 10 min under NIR-II light (1064 nm, 1 W/cm²). In vivo experiments confirmed their significant therapeutic efficacy against MDR S. aureus infections with negligible toxicity to cells and animals, showcasing their potential as promising antibacterial agents.

To enhance the oxygen-dependent photosensitizing performance of conventional photosensitizers, *Dan et al.*., used gold nanoclusters (BSA@Au) that exhibit second near-infrared (NIR-II, 950–1450 nm) fluorescence and catalase-like activity as innovative alternatives. This BSA@Au-based photodynamic therapy (PDT) strategy demonstrated remarkable effectiveness in treating tumors and combating bacterial infections [55]. *Cao et al.*., synthesized a novel Ag/Bi2MoO6 nanozyme which demonstrated POD activity, NIR-II photodynamic activity, and increased Ag + release with acidity, all of which resulted in ROS generation upon NIR II light irradiation and exceptional antimicrobial properties [56].

Diabetic wound infections continue to pose significant challenges in clinical settings due to the complex microenvironments of such wounds. Drawing inspiration from glucose metabolism in biological systems, *Shan et al.*., devised an innovative approach to address wound infections by modulating the diabetic wound microenvironment [57]. Specifically, they developed a near-infrared (NIR-II) responsive biocatalytic microneedle patch with glucose oxidase- and catalase-like activities, capable of eradicating bacteria, lowering glucose levels, and generating oxygen. This patch demonstrated highly effective antibacterial properties in vitro and proved to be a promising solution for treating MRSA-infected wounds in diabetic mice. *Meng et al.*., developed a near-infrared-II (NIR-II) light-responsive platform consisting of palladium rough nanoshells on a metal-organic framework (MOF) of UiO-66-NH2 (UiO-66-NH2@Pdshell) for the phototherapeutic treatment of drug-resistant bacterial infections and hypoxia relief in subcutaneous wound

healing [58]. This theranostic platform exhibited excellent photothermal conversion efficiency (44.9%) under NIR-II light irradiation, while maintaining superoxide dismutase (SOD)-like and catalase (CAT)-like activities. Notably, the catalytically driven oxygen generation by UPI effectively mitigated the hypoxic microenvironment, thereby enhancing photodynamic therapy (PDT) efficacy of IR780. The UPI system successfully eradicated MRSA, eliminated pro-inflammatory molecules such as O2•− and H2O2, and downregulated HIF-1α expression. Through synergistic antibacterial therapy combining photothermal therapy (PTT) and PDT, along with sustained oxygen supply, the platform facilitated the polarization of M1 macrophages to M2 macrophages. This shift reduced inflammation, promoted angiogenesis, and supported collagen fibrillogenesis, thus accelerating wound healing. *Wang et al.*., synthesized hexagonal CuS nanosheets (NSs) using a modified one-pot method, leveraging their exceptional photothermal stability and high photothermal conversion efficiency due to their large surface area [59]. These nanosheets exhibit intrinsic peroxidase-like activity and remarkable photothermal properties. Notably, the photothermal effect further enhanced the peroxidase-like activity of the CuS NSs, enabling chemodynamic biocatalytic activity (Km = 1.36 mM) with a significant photothermal conversion efficiency (η = 44.1%). The study revealed that CuS NSs, through photothermally enhanced biocatalysis, successfully eliminated bacteria and destroyed biofilms.

To further enhance bacterial inactivation, *Ren et al.*., developed a MnCNs-incorporated PNMn hydrogel with multienzyme activities and remarkable near-infrared (NIR)-II photothermal properties (Fig. 7) [60]. This hydrogel exhibits

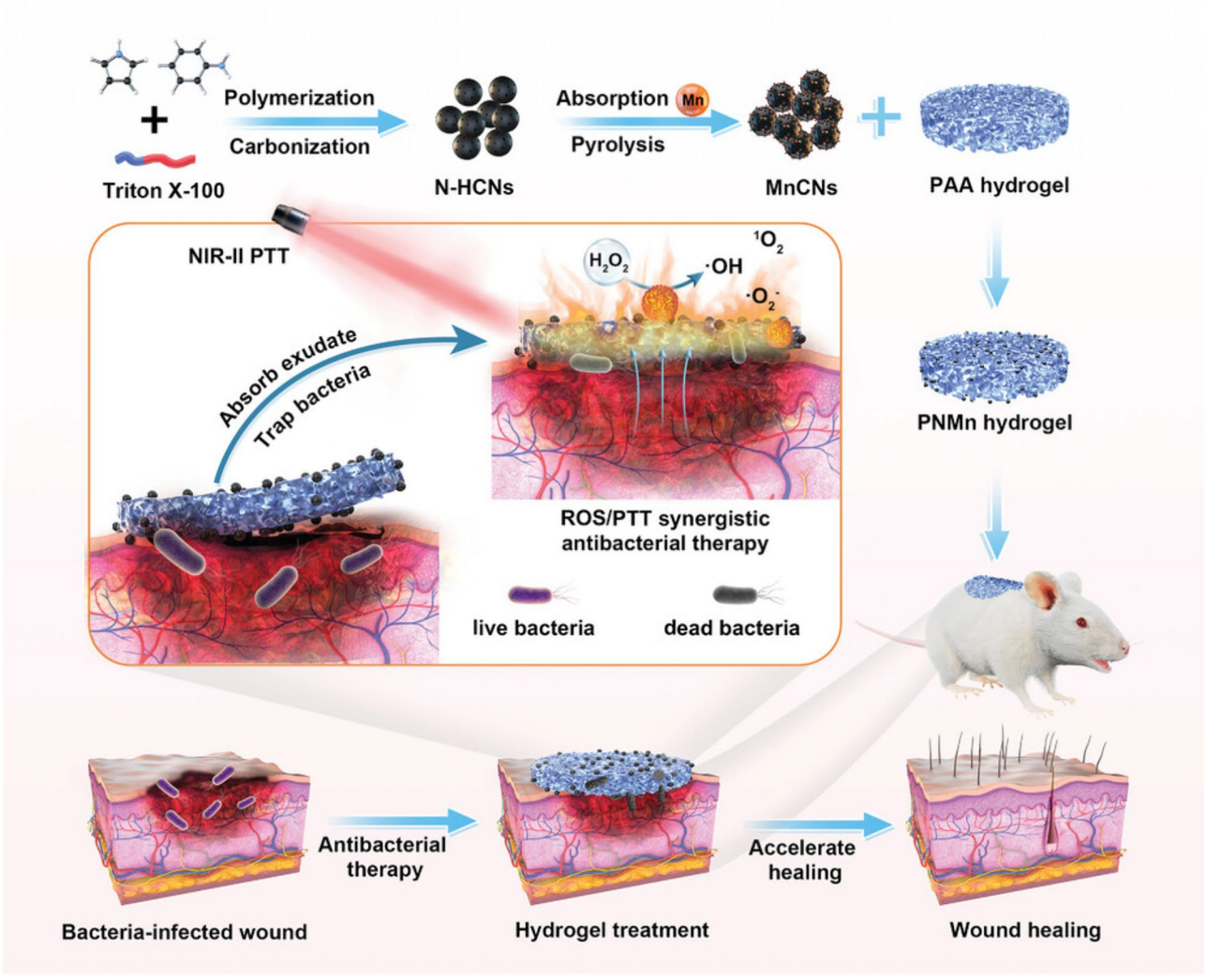


Fig. 7 Illustration showcasing the fabrication and application of the PNMn hydrogel. MnCNs were embedded into a PAA hydrogel matrix to create the PNMn hydrogel, which was applied directly to infected wounds. The hydrogel absorbed exudates, captured bacteria, and leveraged the synergistic effects of ROS and NIR-II PTT to induce potent antibacterial activity by disrupting bacterial cell membranes, thereby facilitating effective wound healing. Reproduced with permission [60]

self-enhanced NIR-II photothermal-catalytic capabilities, effectively eradicating bacteria. It facilitates parallel and cascade reactions to produce •OH, •O2–, and 1O2 radicals from H2O2 and O2 without requiring external energy. In addition, when exposed to a 1064 nm laser (in the NIR-II range) at a safe irradiation power density of 1 W cm − 2, the PNMn hydrogel demonstrates a synergistic antibacterial effect. The hydrogel also boasts strong adhesion, rapid shape adaptability, and exceptional swelling properties, making it ideal for biofluid management and bacterial capture. After treatment, the hydrogel containing dead bacteria and exudate is removed, thus minimizing inflammation and promoting wound healing. In vivo studies confirmed that using PNMn hydrogel as a wound dressing accelerates wound healing by enhancing wound closure, collagen deposition, re-epithelialization, and hair follicle formation. Recently, *Gong et al.*., developed platinum (Pt)- and selenium (Se)-based nanozymes, Pt-Se@Chitosan (PS@CS), showcasing synergistic antitumor and bactericidal effects [61]. PS@CS combines multienzyme activities with photothermal therapy, delivering exceptional antibacterial effects and promoting skin damage repair. This innovative approach provides a comprehensive therapeutic solution for melanoma treatment and wound healing.

Photothermal methods for eradicating bacteria often demand temperatures exceeding 50 °C and extended exposure times (over 10 min), which can irreparably damage adjacent healthy tissues and hinder bone regeneration. Consequently, a critical challenge lies in achieving bacterial eradication under milder thermal conditions. Furthermore, most research on bone infections emphasizes the initial antimicrobial phase, often overlooking the subsequent bone healing process. This oversight is partly due to the rapid metabolic clearance of nanozymes, which restricts their long-term therapeutic impact at the site of infection. Studies indicate that maintaining a localized temperature between 40 and 42 °C enhances osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) and angiogenesis, supporting effective bone reconstruction. To address these limitations, carriers can prolong the half-life and functional duration of nanozymes within the body. Carriers can also act as scaffolds for bone regeneration during the repair process. Hydrogels like GelMA are particularly promising, as they provide a 3D structure that supports cell growth and differentiation, exhibit excellent biocompatibility, and are both biodegradable and injectable. These attributes make GelMA highly suitable for applications in cell carriers and drug delivery systems. As a proof of concept, Cu_2MoS_4 nanoparticles (CMSs) with enzyme-like activity and responsiveness to both pH changes and near-infrared (NIR) light were prepared (Fig. 8) [62]. These CMSs were incorporated into methacrylated gelatin

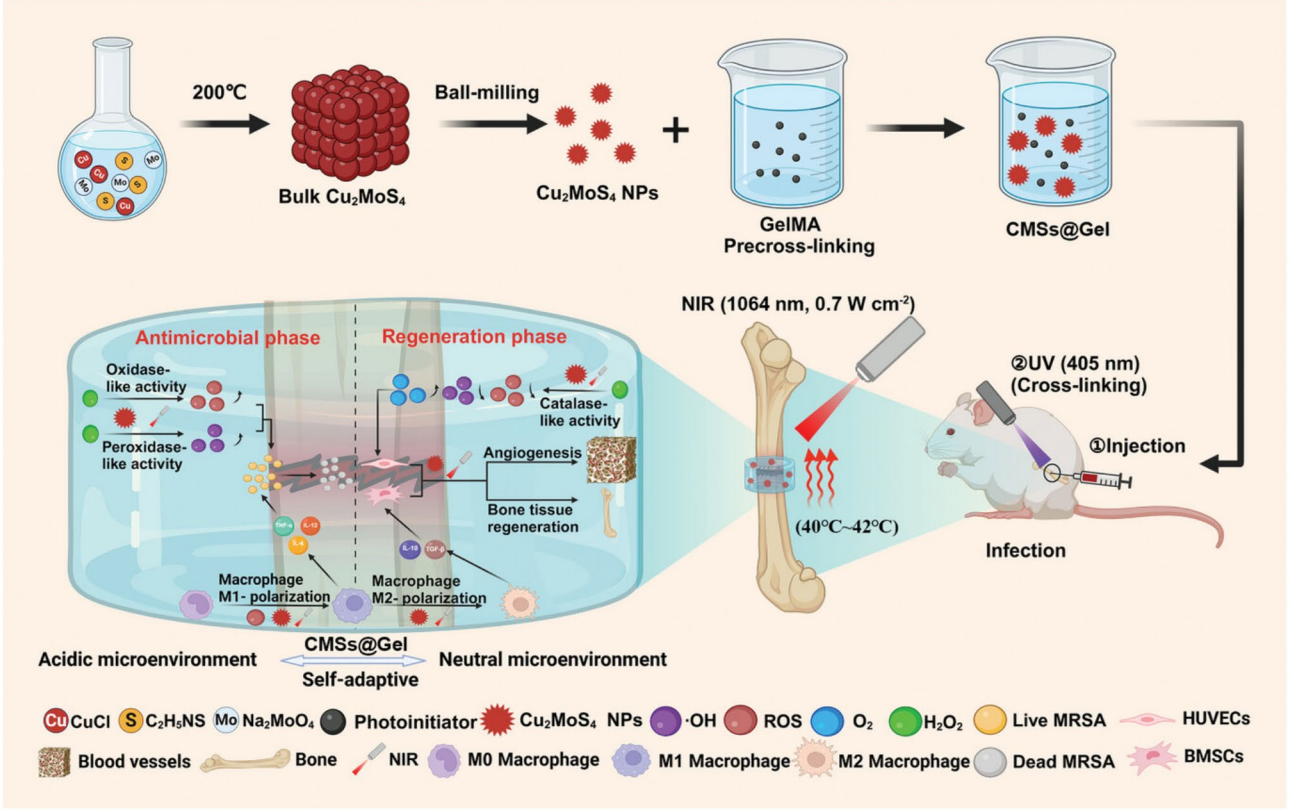


Fig. 8 Schematic illustration depicting the synthesis process of CMSs@Gel and it's in vitro and in vivo mechanism of action. Reproduced with permission [62]

(GelMA) to create CMSs hydrogels (CMSs@Gel), which exhibit antimicrobial properties and promote bone tissue repair. In vitro and in vivo studies confirmed the biocompatibility of CMSs@Gel, along with its peroxidase-like (POD), oxidase-like (OXD), and catalase-like (CAT) activities, exceptional photothermal conversion efficiency, and immunomodulatory potential. Moreover, the hydrogel demonstrated slow degradation, enabling controlled pH-responsive enzyme activity, regulation of reactive oxygen species (ROS) production, and macrophage polarization during treatment. Significantly, these effects were amplified under NIR light. Under NIR irradiation, the CMSs@Gel also maintained a stable fracture environment at a mild temperature range of 40–42 °C, further supporting osteogenesis and angiogenesis.

NIR-II activating agents combined with CDT

Conversely, CDT leverages the elevated levels of hydrogen peroxide (H2O2) naturally present in the lesion microenvironment to produce toxic hydroxyl radicals (·OHs) via a metal-catalyzed Fenton reaction [63, 64]. Compared to other reactive oxygen species (ROS) therapies, CDT requires minimal external stimulation, allowing for deeper treatment penetration and reduced toxicity to surrounding healthy tissues. Notably, synergistic effects emerge when CDT is combined with PTT. Moreover, OH generated by CDT enhances bacterial cell membrane permeability and increases heat sensitivity.

More importantly, nanoparticle morphology plays a pivotal role in cellular uptake and bacterial adhesion [65, 66]. In comparison to nanostructures with smooth surfaces, rough nanostructures have shown superior cellular adhesion and uptake efficiency, making them ideal for applications bacterial capture [67, 68], and wound healing [69], thereby enhancing therapeutic outcomes. Rough nanoparticles have been demonstrated to improve bacterial adhesion and antibacterial efficiency due to the multivalent interactions facilitated by their surface spikes, which effectively engage with the textured bacterial surface [70]. These stronger interactions with bacterial membranes not only result in higher toxicity towards bacteria compared to smoother nanoparticles but also offer the advantage of acting as lysozyme carriers, enriching the local concentration of lysozyme on bacterial surfaces. Recognizing the significance of nanoparticle surface properties in therapeutic applications, *Liu et al.*., designed carbon–iron oxide nanohybrids with rough surfaces (RCF) for synergistic antibacterial therapy activated by NIR-II light [71]. These RCF nanohybrids show outstanding photothermal performance and peroxidase-mimicking activity, enabling a dual-action approach that combines photothermal therapy (PTT) and chemodynamic therapy (CDT) within the NIR-II window. This innovative method leverages deeper tissue penetration and reduced power density for improved therapeutic outcomes. Furthermore, the rough surfaces of RCF promote bacterial adhesion, enhancing interactions with bacteria and boosting the effectiveness of both CDT and PTT. In vivo experiments using a rat wound model infected with MRSA confirmed the robust synergistic antibacterial effects of this strategy. When bacteria invade, the internal environment of the affected area undergoes distinct changes compared to healthy tissue, including an increase in neutrophils, elevated levels of proteolytic enzymes, higher local temperatures, weak acidity, and reduced oxygen concentration. Remarkably, nanoantibacterial reagents leverage these conditions to produce hydroxyl radicals (•OH) from H_2O_2 at the site of infection. These radicals enable synergistic chemodynamic antibacterial therapy (CDAT) and photothermal antibacterial therapy (PTAT) when exposed to laser irradiation. However, the effectiveness of PTAT remains limited due to the similar conditions between infected and healthy tissues. In contrast, infection microenvironment-activated NIR-II PTAT demonstrates selective photothermal conversion in the presence of specific target molecules, allowing for precise pathogen elimination. The overexpression of H_2O_2 and H_2S in the infection microenvironment also significantly enhances the efficiency of both CDAT and PTAT without harming normal tissues. *Yang et al.*., developed infection microenvironment-activated Cu_2O nanoparticles (NPs) for synergistic photothermal antibacterial therapy (PTAT) and chemodynamic antibacterial therapy (CDAT) [72]. These Cu_2O NPs demonstrate high sensitivity to hydrogen sulfide (H_2S) and hydrogen peroxide (H_2O_2) within the bacterial infection microenvironment. Upon in situ injection, the Cu_2O NPs rapidly react with the overexpressed H_2S at the inflammatory site, forming Cu_9S_8 NPs with strong absorbance in the near-infrared-II (NIR-II) region. Under 1060 nm laser excitation, the Cu_9S_8 NPs serve as NIR-II photoacoustic imaging (PAI) agents. The heat generated by Cu_9S_8 NPs induces hyperthermia, which not only produces potent antibacterial activity but also significantly boosts the catalytic efficacy of the Fenton reaction. Both in vitro and in vivo studies confirm the exceptional photothermal-chemodynamic synergistic antibacterial effects of these NPs against multidrug-resistant bacterial infections. By leveraging the unique properties of bacterial infection microenvironments, this responsive multi-modal antibacterial strategy holds promise for advancing intelligent platforms to eradicate pathogens more effectively.

To address drug-resistant bacterial biofilm infections (BBIs), *Wang et al.*., developed a biofilm microenvironment (BME)-responsive nanoplatform, BTFB@Fe@Van, for synergistic NIR-II PTT/CDT/antibiotic therapy [73]. As shown in Fig. 9, this nanoplatform was constructed by self-assembling phenylboronic acid (PBA)-modified

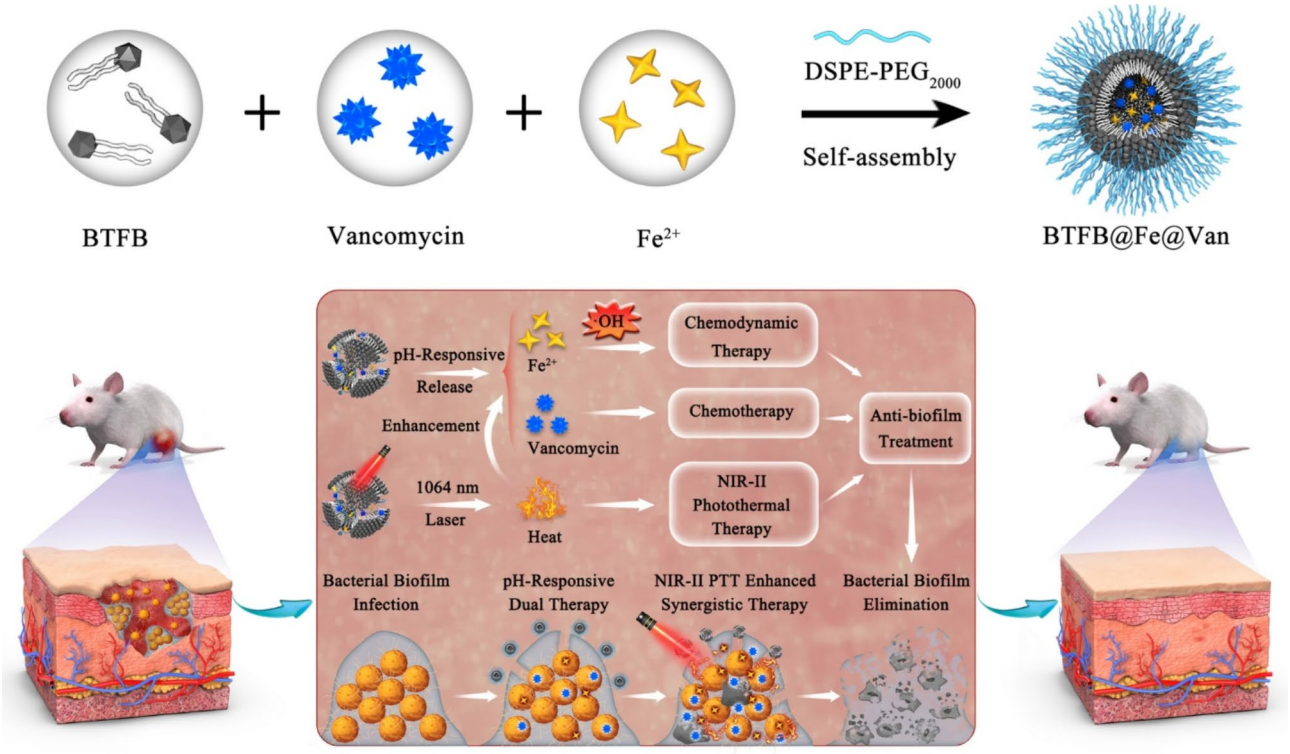


Fig. 9 Schematic illustration of the BME-responsive nanoplatform, BTFB@Fe@Van, designed for synergistic treatment, effectively eradicating drug-resistant bacterial biofilm infections (BBIs). Reproduced with permission [73]

small-molecule BTFB, vancomycin, and Fe^{2+} ions (a CDT catalyst) within DSPE-PEG2000. Vancomycin was linked to BTFB via pH-sensitive PBA-diol interactions, while Fe^{2+} ions were coordinated with the sulfur and nitrogen atoms of BTFB. In the acidic BME, the PBA-diol bonds disintegrated, releasing both vancomycin and Fe^{2+} ions. The Fe^{2+} ions then catalyzed the generation of hydroxyl radicals in the oxidative BME, where H_2O_2 was overexpressed. In addition, upon irradiation with a 1064 nm laser, BTFB@Fe@Van demonstrated excellent hyperthermic performance, enhancing the release of vancomycin and boosting CDT efficacy. Notably, the nanoplatform also enabled precise NIR-II imaging of infected sites. Both in vitro and in vivo studies confirmed that BTFB@Fe@Van effectively combats BBIs through a synergistic NIR-II PTT/CDT/antibiotic mechanism, showcasing its potential as a powerful therapeutic solution.

Thermoresistance, driven by elevated levels of heat-shock proteins (HSPs) and potential secondary damage from local hyperpyrexia remains a significant hurdle for the broader clinical adoption of PTT [74]. Interestingly, numerous studies have shown that heat generated by PTT can accelerate the Fenton reaction, thereby producing more destructive reactive oxygen species (ROS) through CDT. Elevated ROS levels, in turn, suppress HSP expression, effectively addressing PTT's conventional thermoresistance [75]. Overall, the synergy between heat and ·OH generation underscores the promising potential of integrating PTT and CDT for enhanced therapeutic outcomes. To advance this strategy, *Wang et al.*., designed a bacteria-targeting nanozyme based on hollow-structured Cu2MoS4 (PV@HCMS) to perform synergistic NIR-II (1064 nm) PTT and chemodynamic therapy (CDT), shown in Fig. 10. PV@HCMS exhibits excellent photothermal conversion efficiency (64.8%) and peroxidase-like (POD-like) catalytic activity, generating highly cytotoxic ·OH through NIR-II-enhanced Fenton-like reactions [76]. The incorporation of polyethyleneimine-vancomycin (PV) modified copolymers via amide bonds imparts PV@HCMS with robust antibacterial properties through a dual-targeting mechanism, enhancing the synergistic PTT-CDT efficacy. Both in vitro and in vivo studies confirm the nanozyme's impressive bactericidal effects and biocompatibility. Notably, PV@HCMS is further integrated into a thermosensitive poloxamer F127 hydrogel, forming a composite dressing (PHF) with exceptional antimicrobial activity and skin regeneration capabilities, offering a comprehensive solution for treating burn infections. *Lu et al.*., introduced a multifunctional Janus nanostructure consisting of copper peroxide (CP) nanodots attached to a gold nanostar (GNS) and silica nanorod (SiNR), referred to as GNS@CP/SiNR, which exhibited remarkable antibacterial properties [77]. The unique Janus design endowed the

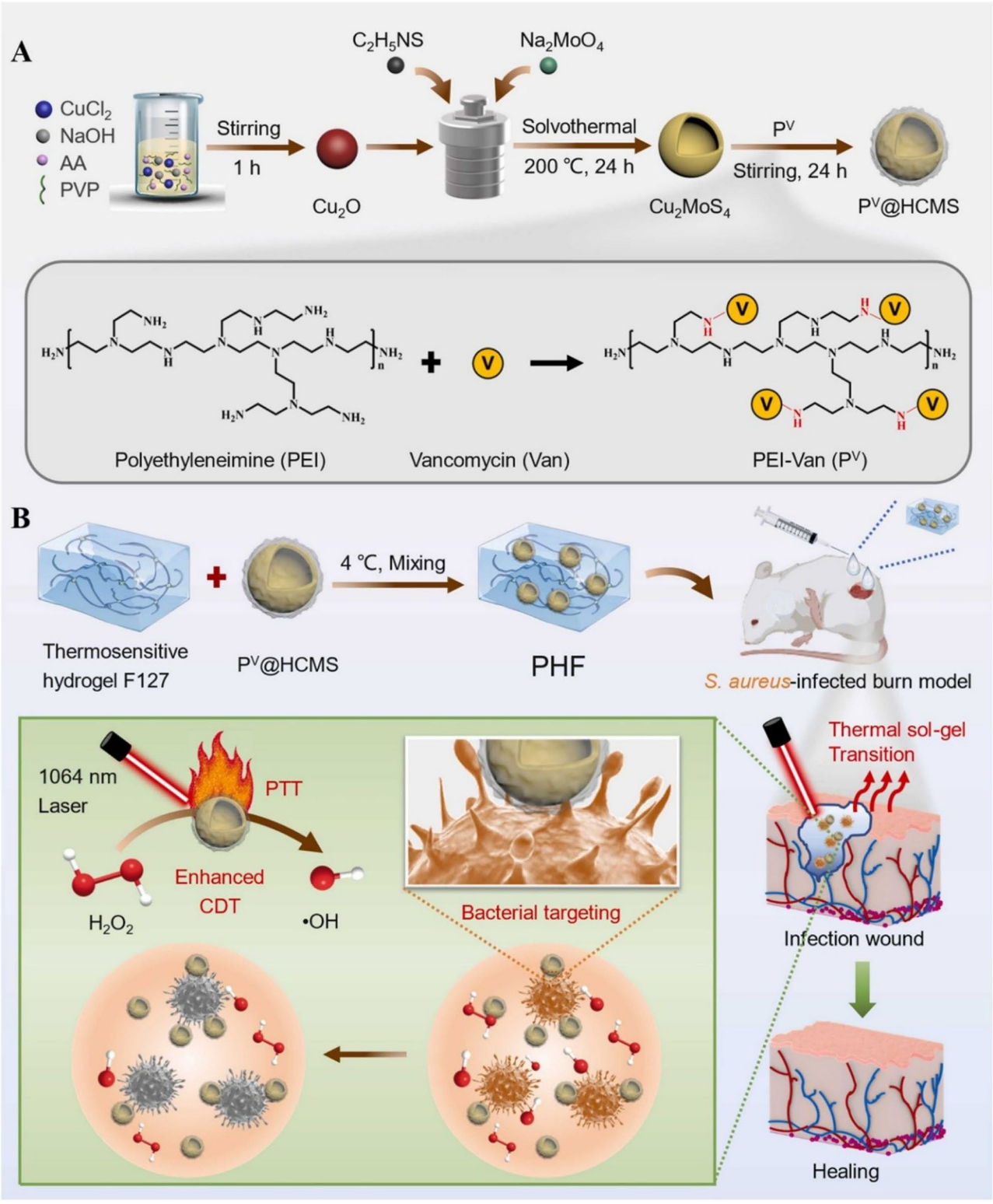


Fig. 10 (**A**) Schematic representation of the synthesis process for the hollow-structured PV@HCMS nanozyme, involving PVP (polyvinylpyrrolidone) and AA (ascorbic acid). (**B**) Fabrication steps for the thermosensitive hydrogel-based composite dressing (PHF) and its use in a burn wound model infected with S. aureus, designed to enhance NIR-II PTT-CDT synergistic anti-infective therapy. Reproduced with permission [76]

structure with strong plasmonic resonance absorption in the near-infrared (NIR)-II region, enabling effective mild photothermal therapy (MPTT). Under acidic conditions, the CP component on the GNS@CP/SiNR rapidly dissociated, releasing Cu^{2+} and H_2O_2, which were subsequently converted into ˙OH radicals through a Fenton-like reaction, facilitating chemodynamic therapy (CDT).

MXenes, particularly V2C variants, have recently emerged as promising photothermal agents for potential applications in photothermal therapy (PTT), owing to their impressive biocompatibility and exceptional photothermal conversion efficiency. Despite these advantages, V2C MXene's reliance on laser irradiation within the near-infrared region I (NIR-I) limits tissue penetration, posing challenges in achieving comprehensive bacterial eradication with single-effect therapeutic approaches. To overcome this, *He et al..*, engineered an advanced nanoplatform by attaching platinum nanoparticles (Pt NPs) to V2C MXenes, creating Pt@V2C, which leverages NIR-II enhanced nanozyme effects for photothermal and chemodynamic anti-infective therapy [78]. The Pt@V2C platform demonstrates an improved photothermal conversion efficiency (PCE) of 59.6% and benefits from extended irradiation wavelengths (NIR-II) due to the surface plasmon resonance effect of Pt NPs and V2C. Furthermore, Pt@V2C exhibits dual enzyme-like activity, combining chemodynamic therapy (CDT) with enhanced biocatalytic effects under NIR-II irradiation. Density functional theory analysis elucidates the biocatalytic mechanisms underpinning Pt@V2C's effectiveness. In vivo studies highlight Pt@V2C's ability to effectively eliminate methicillin-resistant Staphylococcus aureus from deep-seated tissues, such as subcutaneous abscesses and bacterial keratitis. This leads to accelerated abscess resolution and promotes healing of wounds and corneal tissue via the synergistic actions of PTT and CDT. Transcriptomic analysis further reveals that Pt@V2C targets key inflammatory pathways, providing deeper insights into its therapeutic mechanisms. This research underscores the potential of hyperthermia-enhanced biocatalysis with Pt NPs and MXene nanocomposites as a groundbreaking approach to anti-infective therapy.

MoS_2 nanosheets are widely regarded as reliable and efficient photothermal agents (PTAs) due to their excellent biocompatibility and photothermal performance in the near-infrared I (NIR-I) range (650–900 nm) [79]. However, the majority of MoS_2-based nanomaterials have been limited to NIR-I applications for photothermal therapy (PTT). Unfortunately, these therapies face constraints in clinical applications because of the limited penetration depth of NIR light. Also, most developed 1T-MoS_2 PTT therapies or antimicrobial systems rely on in vivo sterilization at temperatures exceeding 55 °C, posing a significant risk of damaging normal skin tissues [80]. To address this, *Du et al..*, proposed maintaining the experimental temperature of nanomaterials around 50 °C to enhance peroxidase-like activity while minimizing harm to healthy skin [81]. As a proof of concept, their team developed a $MoWS_2$ composite, a novel antibacterial strategy that combines photothermal and enzyme catalysis, leveraging overheating to enhance nanozyme activity (Fig. 11). By doping tungsten ions into 2 H-MoS_2, the material's defect regulation improved its near-infrared II (NIR-II) absorption and enzyme catalytic performance. Consequently, the $MoWS_2$ composite demonstrated an impressive photothermal efficiency of 36.9% in the NIR-II window along with superior peroxidase-like activity. This synergistic approach of PTT and chemodynamic therapy (CDT) resulted in enhanced bactericidal effects while avoiding heat-induced tissue damage, making $MoWS_2$ composites highly advantageous for antimicrobial applications.

Periodontitis is a prevalent global health issue characterized by inflammation and uneven alveolar bone loss caused by periodontal pathogens [82]. Effective treatment necessitates a combination of antibacterial therapy and strategies for bone regeneration. Drug delivery systems responsive to reactive oxygen species (ROS) hold significant promise for targeted and controlled therapeutic release. However, their rapid response to ROS and sustained delivery of antibacterial agents are limited by the complex microenvironment of periodontitis. A promising strategy to address these challenges involves combining ROS-responsive systems with photocatalytic technologies. In this context, *Liang et al..*, designed a pillararene-embedded covalent organic framework (PCOF) loaded with the antibacterial prodrug thioacetal (TA) for the treatment of periodontitis [83]. This TA-loaded PCOF nanoplatform uses self-amplifying ROS generation to boost therapeutic effectiveness. PCOFs exhibit remarkable photosensitivity and ROS production capabilities as drug carriers. Upon interaction with ROS, the TA within the nanoplatform is activated and cleaved to cinnamaldehyde (CA), a highly effective antibacterial agent. By harnessing visible light for precise infection targeting, TA-loaded PCOF provides an effective solution for managing periodontitis, representing a significant advancement in antibacterial drug delivery technology. However, periodontitis treatments have traditionally focused on eliminating bacteria, often overlooking the critical role of bacterial co-aggregation in disease progression. A novel approach combining chemodynamic therapy (CDT) and photothermal therapy (PTT) has shown potential as an effective treatment for periodontitis. However, the limited availability of endogenous H2O2 hampers the efficiency of CDT. To overcome these limitations, *Lin et al..*, developed an innovative single-material system, Cu3P@PAH@Lox, which integrates dual functionalities

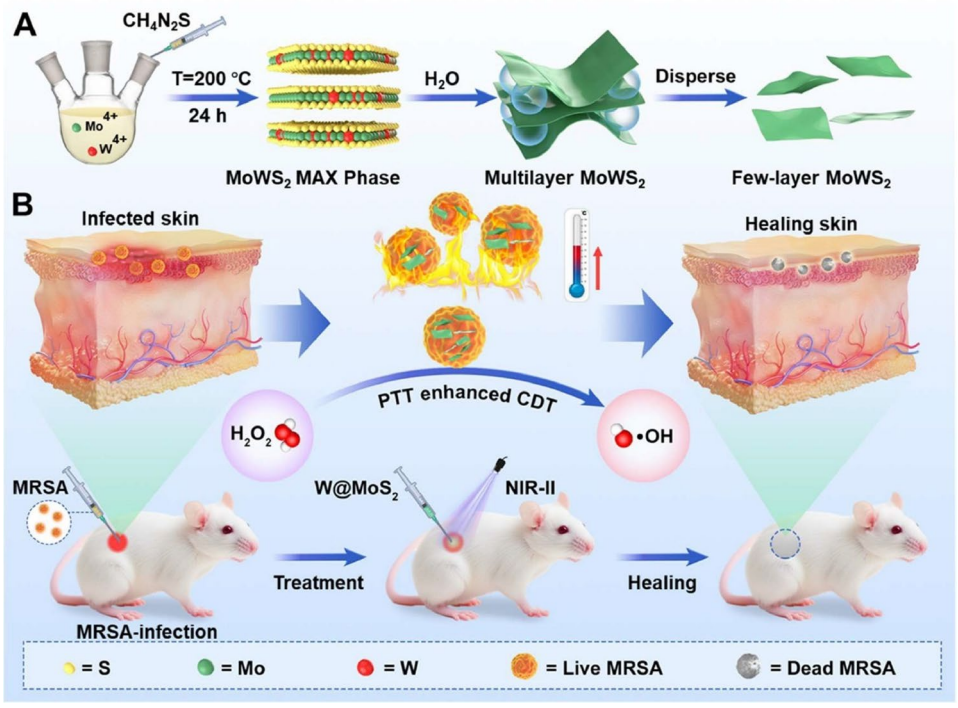


Fig. 11 Schematic illustration of the fabrication of few-layer MoWS2 and its activation using 1064 nm laser irradiation to heal Staphylococcus aureus-infected abscesses in vivo. Reproduced with permission [81]

to enhance antimicrobial effects and significantly reduce pathogen co-aggregation [84]. This system uses NIR-II PTT to elevate local temperatures, promoting •OH generation in CDT while suppressing heat shock proteins to improve PTT effectiveness, creating a self-sustaining feedback mechanism. Lactate oxidase is also used to convert lactate from periodontal biofilms into hydrogen peroxide, further enhancing CDT efficacy.

Leveraging the advantageous properties of the BW-II region, researchers expanded their focus to the BW-III and BW-IV regions. However, progress was initially hindered by a lack of nanomaterials capable of absorbing long-wavelength near-infrared (NIR) light, particularly within the NIR-III (1500–1850 nm) and NIR-IV (2100–2300 nm) ranges. Recently, *Thangudu et al..*, addressed this limitation by developing plasmonic copper-doped Bi_2O_3 (CBO) transition metal oxides, which exhibit robust and tunable NIR light absorption [85]. Their study demonstrated the effectiveness of CBO bMPs in treating multidrug-resistant Staphylococcus aureus (MDRSA) skin infections using an in vivo mice model (Fig. 12). This was achieved through a synergistic dual-modal therapeutic approach combining NIR photodynamic therapy (PDT) and photothermal therapy (PTT) across the NIR-I, -II, and -III biological windows. CBO bMPs, with their high molar extinction coefficients, effectively absorb and convert long-wavelength NIR light (980 and 1550 nm) into thermal energy, while also generating cytotoxic reactive oxygen species (ROS) and mimicking enzymatic activity. These characteristics make them highly effective for in vivo treatment of drug-resistant bacterial infections. Notably, this research represents the first reported use of a long NIR-III light-activatable CBO bMP photocatalyst for bacterial eradication in vivo. Beyond demonstrating the multifunctional capabilities of CBO bMPs as a potent agent against bacterial infections across a broad biological window, the study also provides a valuable framework for designing advanced bimetallic nanoplatforms to tackle drug-resistant bacterial infections in the extended BW regions. Some of the reported NIR-II activated antibacterial nanomaterials are presented in Table 5.

Although some promising results have been seen with NIR-II activated NMs for bacterial infections, many key gaps remain in the literature. Some are as follows,

i) Limited Variety of NIR-II Responsive Photosensitizers: Most studies have focused on a narrow range of NIR-II activated nanomaterials, such as rare-earth-doped nanoparticles, conjugated polymers, and a few small-molecule dyes. It is necessary to expand the library of NIR-II absorbing photosensitizers with higher photothermal conversion efficiency and enhanced ROS generation.
ii) Incomplete Understanding of Antibacterial Mechanisms: Despite the fact that some NIR-II nanomaterials have promising antibacterial activity, a deeper understanding of the mechanisms is needed,

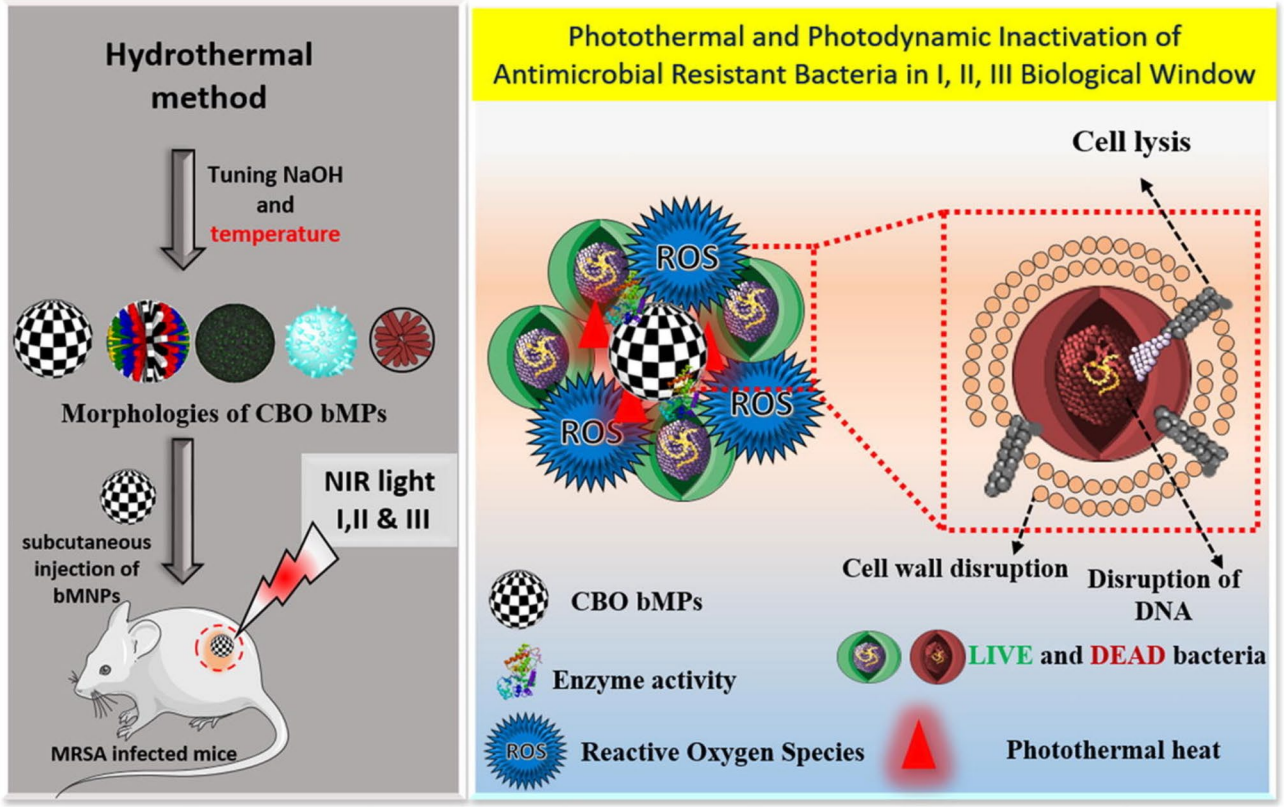


Fig. 12 Schematic depiction of an NIR-III activated dual-modal PTT/PDT strategy, leveraging the enzyme-mimetic properties of $CuBi_2O_4$ bMPs to eliminate multidrug-resistant Staphylococcus aureus (MDRSA) infections *in vivo*. Reproduced with permission [85]

particularly the role played by PDT rather than PTT effects, oxidative stress, and disruption of the bacterial membrane.

iii) In Vivo Validation and Long-Term Studies: Most research is still in the in vitro stage, with limited in vivo validation. The long-term effects, immune response, biodistribution, and clearance mechanisms of NIR-II nanomaterials in bacterial infection models remain largely unexplored.

iv) Selectivity and Biocompatibility Concerns: Many reported NIR-II nanomaterials lack specific bacterial targeting, increasing the risk of toxicity to mammalian cells. Developing biocompatible, bacteria-specific targeting strategies, such as ligand-functionalized NMs, remains a significant challenge.

v) Scalability and Clinical Translation: The synthesis of NIR-II activated nanomaterials is often complex and costly, restricting large-scale production. Overcoming challenges related to reproducibility, stability, and regulatory approval is crucial for successful clinical translation.

vi) Synergistic Strategies and Combination Therapies: Although some studies have explored integrating NIR-II nanomaterials with antibiotics or immune modulators, comprehensive research on synergistic antibacterial mechanisms and resistance mitigation is still lacking.

vii) Nanoparticle aggregation, immune response, and clearance rates: Despite their promise, NIR-II activated nanomaterials face several challenges, including nanoparticle aggregation, immune response, and clearance rates, all of which can impact their antibacterial effectiveness and biocompatibility. In physiological environments, nanoparticle aggregation can compromise stability and alter optical properties, diminishing both photothermal and photodynamic efficiency. This aggregation is often driven by protein corona formation or fluctuations in ionic strength, making surface modifications such as PEGylation or biomimetic coatings—essential for maintaining colloidal stability. Moreover, the immune system may detect and clear these nanomaterials before they reach bacterial infection sites, limiting their therapeutic potential. While surface engineering can help evade immune recognition, excessive modifications may inadvertently alter their bioactivity. Clearance rates present another challenge, as larger nanomaterials tend to accumulate in organs like the liver and spleen, raising toxicity concerns, whereas

Table 5 Literature reports on NIR-II activated antibacterial nanomaterials

S.No.	Nanomaterial	Function	Laser and power	Application	Ref
1	Cu2-xS on GO (GO-Cu2-Xs)	PTT and CDT	1064 nm (1.0 W/cm^2)	Antibacterial coatings	[86]
2	Photothermal polymer	PTT	1064 nm (1.0 W/cm^2)	Wound healing	[87]
3	D–A–D-type NIR-II small molecule	PTT (η = 44.3%)	980 nm, (1.2 W/cm^2)	Diabetic wound healing	[88]
4	PNIR-II	ROS, NO, and RNS	1064 nm (1.0 W/cm^2)		[89]
5	TMH@Gel,	PTT and CDT	1064 nm (0.64 W/cm^2)	Wound healing	[90]
6	Gel(AIPH/POM)	PTT (η = 62.4%) and thermodynamic synergistic therapy	1060 nm (1.0 W/cm^2)	Wound healing	[91]
7	ILGA@Gel	PTT (η = 44.2%)	1064 nm (1 W/cm^2)	Wound healing	[92]
8	CuS@CaO2@Dex	PTT (η = 16.8%) and CDT	1064 nm (0.75 W cm− 2)	Wound healing	[93]
9	Au/CdSexSy with precise Ag doping (ACA)	PDT	1064 nm (1.0 W/cm^2)	In vivo antibiofilm	[94]
10	PEG-b-PArg-modified Lu-Bi2Te3@ Fe3O4	PTT (η = 34.14%) and thermocatalytic effects	1064 nm (0.33 W/cm^2)	Periodontitis treatment	[95]
11	Au-MnOx	PTT (η = 40.78%) and CDT	1064 nm (1.0 W/cm^2)	Wound healing	[96]
12	CuHDB@CaP Nanospheres	PTT (η = 37.80%) and glutathione oxidase (GSHOx)-like and peroxidase (POD)-like enzyme activities	1064 nm (1.0 W/cm^2)	Wound healing	[97]
13	Fe SACs	PTT and CDT	1064 nm (2.0 W/cm^2)	Wound healing	[98]
14	CuNx-CNS	POD- and OXD-like or cascaded CAT- and OXD-like reaction	1064 nm (1.0 W/cm^2)	Superficial skin wound and deep implant-related biofilm infections	[99]
15	SFT-B Gel	PTT (η = 38.13%)	1064 nm (1.0 W/cm^2)	Wound healing	[100]
16	fluorine (F)-doped TiO2 nano-platforms	PTT and SDT	1060 nm (0.6 W/cm^2)	In vitro bacterial infection elimination	[101]
17	Au nanorods@selenium composites	PTT	1064 nm (1.0 W/cm^2)	Wounds healing	[102]
18	Ag-doped Mo2C-derived polyoxometalate (AgPOM) nanoparticles	PTT (η = 45.91%) and CDT	1060 nm (1.0 W/cm^2)	Wound healing	[103]
19	PDA/Gel/GOAu nanocomposite	PTT (η = 54.62 and 59.57%)	1064 nm (0.75 W/cm^2)	In vitro antibacterial activities	[104]
20	CuFe 2 S 3 @LOD AC-BioHJzyme	NIR-II activated enzymatic activity	1064 nm, (0–2 W)	Wound regeneration	[105]
21	vanadium nitride MXene (V2N)	PTT (η = 31.67%), oxidase-like and peroxidase-like activities	1060 nm (1.0 W/cm^2)	Anti-infective therapy	[106]
22	Cu/Mn-DSAzymes	PTT (η = 38.7%), CAT-like and OXD-like enzyme	1064 nm (1 W/cm^2)	Wound healing	[107]
23	HSA–R820@OA@ZIF-8 (HIROZ)	Zinc ion and PTT (η = 42.4%)	1064 nm (1.0 W/cm^2)	Implant-associated biofilm infection	[108]

smaller ones may be excreted too quickly to exert meaningful antibacterial effects. Striking a balance between stability, immune evasion, and optimal clearance remains a key hurdle in the clinical application of NIR-II antibacterial nanomaterials, necessitating further research into size optimization, biodegradable formulations, and targeted delivery approaches.

Future perspectives on NIR-II activated antibacterial nanomaterials

The development of antibacterial nanomaterials activated by second near-infrared (NIR-II, 950–1450 nm) light is a rapidly advancing field with significant potential to address the global challenge of bacterial infections and antibiotic resistance. Below we summarize several future perspectives on the advancement of NIR-II activated antibacterial nanomaterials to be considered in future designs.

i). Optimized Nanomaterials: Innovative nanomaterials with higher absorption in the broad biological window region (NIR-II to NIR-IV), improved photothermal conversion efficiency, and superior reactive oxygen species (ROS) generation will eliminate deep seated bacterial infections. For instance, *Thangudu et al..*, developed an NIR-III activated nanomaterial [85] and *Hwang et al..*, developed an NIR-IV activated nanomaterial for bacterial inactivation [109]. One effective method is engineering NMs with improved NIR-II absorption by doping or alloying them with elements that enhance their plasmonic or photonic properties. Additionally, surface functionalization with organic dyes or conjugation with molecules that boost photothermal conversion can significantly enhance light absorption and energy transfer.

Optimizing the size, shape, and composition of NMs is another crucial strategy, as it maximizes their absorption cross-section while minimizing energy dissipation.

ii). Hybrid Systems: Combining NIR-II irradiation with complementary therapeutic modalities, such as antibiotics or enzyme-mimicking nanozymes or with CDT, can also enhance treatment efficacy while reducing unwanted thermal damage, making these approaches highly promising for clinical translation. Therefore, more research should be focused on developing multifunctional nanomaterials for bacterial inactivation.

iii). Minimizing Cytotoxicity and Improving Biocompatibility: The synthesis, stability, and potential toxicity of NIR-II activated nanomaterials are critical factors in determining their effectiveness and safety in biological environments. Various fabrication techniques, including hydrothermal, solvothermal, and chemical vapor deposition methods, are utilized to develop NIR-II responsive nanomaterials such as rare-earth-doped nanoparticles, semiconducting polymers, and two-dimensional (2D) materials, etc. To improve stability and biocompatibility while preventing aggregation under physiological conditions, surface modifications like polyethylene glycol (PEG), etc., functionalization and biomimetic coatings are commonly applied. However, maintaining the long-term stability of these nanomaterials in complex biological environments remains challenging, as factors such as pH fluctuations, enzymatic degradation, and protein corona formation can alter their physicochemical properties. Moreover, their potential toxicity is a significant concern, as prolonged exposure and organ accumulation may induce oxidative stress, inflammation, and cytotoxic effects. While certain NIR-II nanomaterials, such as carbon-based and biodegradable polymer nanoparticles, demonstrate minimal toxicity and efficient renal clearance, others particularly heavy metal-based quantum dots pose risks due to ion release and bioaccumulation. Therefore, ongoing research is essential to optimize the design of NIR-II nanomaterials, ensuring high stability, controlled degradation, and minimal toxicity for safe and effective biomedical applications. The development of biocompatible nanomaterials by incorporation of natural polymers or biomimetic surface modifications or FDA approved polymers can enhance biocompatibility and reduce immune system activation.

iv). Targeted Antibacterial Strategies: Nanomaterial interaction with bacteria plays a key role in therapeutic efficacy. To this end, functionalizing nanomaterials with targeting ligands (e.g., antibodies, peptides, or aptamers) can improve specificity toward pathogenic bacteria while sparing healthy microbiota. Developing stimuli-responsive nanomaterials (e.g., with pH, thermal, ROS responsive or enzyme activity) that release antibacterial agents upon bacterial detection will enhance precision and reduce off-target effects.

v). Integration with Imaging and Diagnosis: Combining NIR-II activated nanomaterials with imaging modalities like fluorescence or photoacoustic imaging can enable real-time infection localization, monitoring, and therapy. Developing NIR-II activated materials that can detect bacterial infections through spectroscopic shifts or signal amplification can facilitate early diagnosis and tailored treatments.

vi). Translation to Clinical Applications: Most of the reported work is still sourced from clinical settings. Therefore, conducting thorough preclinical studies using infection models that mimic clinical conditions will be critical for assessing efficacy and safety. Addressing regulatory hurdles by demonstrating consistent, reproducible, and scalable synthesis of nanomaterials with clear safety profiles will facilitate clinical translation.

vii). Eco-Friendly Synthesis and scalability: Despite the promising antibacterial potential of NIR-II activated nanomaterials, their scalability and cost-effectiveness present major obstacles to real-world applications. The synthesis of these materials often requires complex processes, including high-temperature reactions, intricate doping techniques, and precise surface modifications, making production both time-consuming and expensive. The dependence on rare-earth elements, noble metals, and sophisticated semiconducting polymers further escalate costs and limits large-scale manufacturing. Additionally, maintaining batch-to-batch consistency while ensuring high photothermal conversion efficiency, biocompatibility, and stability remains a challenge, particularly when transitioning from laboratory-scale synthesis to industrial production. Moreover, stringent purification and functionalization steps necessary for optimizing biological performance add to the overall expense. Regulatory challenges related to the long-term safety and environmental impact of these nanomaterials may further delay their clinical adoption. To overcome these barriers, researchers must prioritize cost-effective synthesis strategies, such as green chemistry approaches, scalable bottom-up fabrication methods, and the use of earth-abundant materials, to facilitate the widespread integration of NIR-II antibacterial nanomaterials into healthcare applications.

viii). Point-of-Care Systems: Incorporating NIR-II responsive systems into portable or wearable devices could revolutionize infection management, especially in resource-limited settings.

ix). Combatting Resistance Development: In addition to developing innovative nanomaterials, continuous research on mechanisms to prevent bacteria from developing resistance to nanomaterial-based therapies is crucial for long-term efficacy.

x). Long term cytotoxicity evaluation: Most reported NMs assess cytotoxicity through the following methods: (a) In vitro: Cytotoxicity assays conducted on normal cells or fibroblasts. (b) In vivo: Histological analysis using H&E staining of major organs, along with liver and kidney function assays. However, for the successful clinical translation of NIR-II activated NMs, a comprehensive evaluation of their long-term cytotoxicity, biodistribution, and stability in vivo models is essential.

xi). Safety considerations should be taken into account when developing and deploying NIR-II activated antibacterial NMs: The toxicity of nanomaterials, including their composition, surface chemistry, and degradation byproducts, must first be comprehensively assessed through in vitro and in vivo studies. It is essential to ensure that these materials do not trigger cytotoxicity, immunogenic responses, or long-term accumulation in vital organs. Additionally, their photothermal conversion efficiency should be optimized to enable antibacterial effects at safe power densities, thereby preventing overheating and potential damage to surrounding healthy tissues. Evaluating their biodistribution, clearance pathways, and environmental impact is also necessary to mitigate the risk of unintended bioaccumulation. Furthermore, compliance with safety regulations established by organizations like the FDA or EMA is critical for successful clinical translation. Lastly, strict sterilization and handling procedures must be enforced to preserve efficacy and prevent contamination during deployment.

xii). Precise surface engineering of NIR II NMs: Many conventional NIR-absorbing materials perform well in the NIR-I region but struggle to maintain efficiency in the NIR-II range due to fundamental electronic and optical limitations. While bandgap engineering, doping, and defect modulation can enhance absorption, these approaches often introduce instability and increase synthetic complexity. Additionally, low quantum yield and inefficient photothermal conversion remain significant challenges, frequently necessitating hybrid material designs or plasmonic enhancements. For optimal optical performance, stability, and biocompatibility particularly in biomedical applications the size, morphology, and surface chemistry of nanomaterials must be meticulously controlled. Promising materials like rare-earth-doped nanoparticles and organic dyes often experience aggregation-induced quenching (AIQ) or face scalability challenges due to intricate synthesis processes. Overcoming these obstacles requires innovative nanostructure design, precise surface engineering, and scalable fabrication strategies to develop highly efficient, stable, and biocompatible NIR-II-active nanomaterials.

Conclusion

Light-activated antibacterial nanomaterials operating within the second biological window (NIR-II, 950–1450 nm) represent a significant innovation in addressing multidrug-resistant bacterial infections. These materials offer deep tissue penetration with minimal photodamage and scattering, alongside precise spatiotemporal control of antibacterial activity, making them particularly beneficial for clinical use. We reviewed the state-of-the-art advancements in NIR-II activated nanomaterials for antibacterial wound healing applications. Advances in nanomaterial design such as photothermal and photodynamic agents, nanozyme-integrated phototherapy, and chemodynamic therapy (CDT) have achieved remarkable antibacterial effects with minimal side effects. However, challenges remain, including optimizing nanomaterials for efficient NIR-II light absorption, ensuring biocompatibility and biodegradability, and mitigating potential long-term toxicity. Future research should emphasize the development of multifunctional platforms that integrate imaging and therapeutic capabilities, as well as advancing scalable, cost-effective production methods. In vivo studies and clinical trials are critical to confirming the physiological safety and efficacy of these materials. An increasing number of detailed studies are anticipated, emphasizing the importance of interdisciplinary collaboration among material science, microbiology, and clinical medicine. Such collaboration is crucial for fostering innovation and developing safer, more effective, and widely accessible antibacterial solutions to tackle global health challenges. In summary, we believe that the insights summarized here will benefit researchers in material science, nanomedicine, and clinical medicine to better understand the latest advances, challenges and future prospects of NIR-II activated antibacterial nanomaterials, facilitating the design of innovative strategies for future clinical applications.

Supplementary Information

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Supplementary Material 1

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Author contributions

S.T. performed conceptualization and wrote the original draft and reviewed and edited the final manuscript. C-H.S. acquired funding acquisition, performed supervision, reviewed and edited the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

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Not applicable.

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Competing interests
The authors declare no competing interests.

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