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EGCG–GOLD METAL–PHENOLIC NANOPARTICLES FOR MILD PHOTOTHERMAL ANTIMICROBIAL AND ANTIBIOFILM THERAPY

Saira Bhanu Shaik[*1], Ch. Siva Durga[2], Ch. Janush[3], P. Sai Srinu[4], M. Vamsi Vara Prasad[5], G. Akhila Bhanu Prasanna[6], M. A. V. D. S. Prajna[7], A. Varalakshmi[8]

[1]Assistant Professor, M.Pharm; (Ph.D), Dept. of Pharmaceutical Analysis, Koringa College of Pharmacy, Korangi, Kakinada, Andhra Pradesh, India.

[2-8]B.Pharm Scholar, Department of Pharmacy Practice, Koringa College of Pharmacy, Korangi, Kakinada, Andhra Pradesh, India.

***Corresponding Author: Saira Bhanu Shaik**

Assistant Professor, M.Pharm; (Ph.D), Dept. of Pharmaceutical Analysis, Koringa College of Pharmacy, Korangi, Kakinada, Andhra Pradesh, India. **DOI:** https://doi.org/10.5281/zenodo.23830329

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ABSTRACT

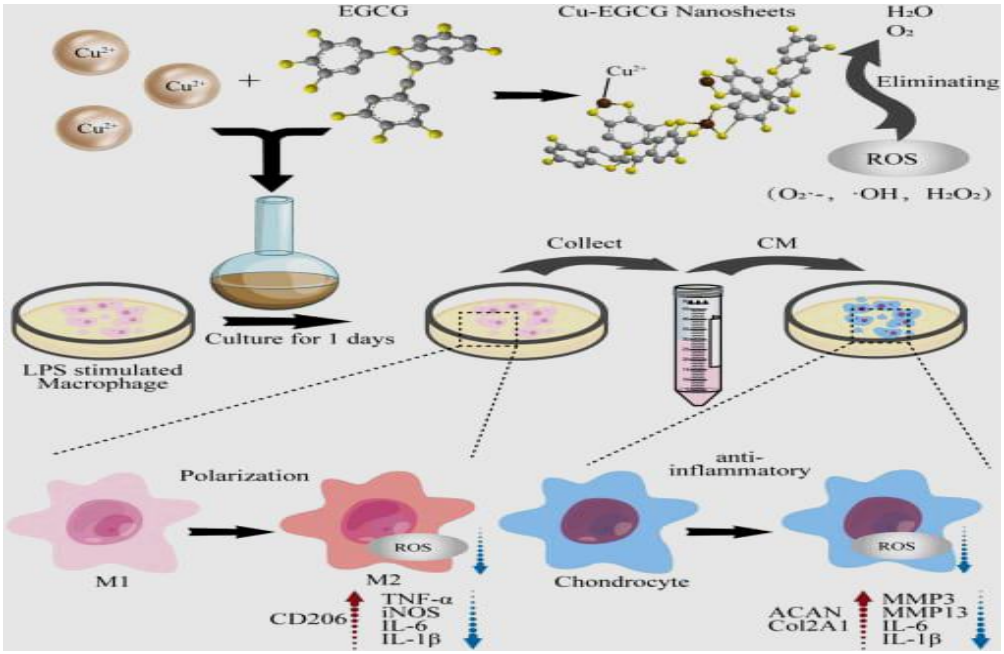
The increasing prevalence of antimicrobial resistance and persistent biofilm-associated infections has created a need for alternative therapeutic strategies that can effectively eliminate microorganisms while minimizing damage to surrounding tissues. Epigallocatechin gallate (EGCG), a major polyphenolic constituent of green tea, possesses well-documented antimicrobial, antioxidant, and anti-biofilm properties; however, its therapeutic application can be limited by poor stability, bioavailability, and rapid degradation. The integration of EGCG with gold nanoparticles (AuNPs) provides a promising nanotechnology-based approach to overcome these limitations and enhance antimicrobial activity. EGCG can contribute to the synthesis and stabilization of gold nanoparticles while also providing inherent biological activity. Upon exposure to near-infrared or suitable light irradiation, gold nanoparticles can generate localized photothermal effects, producing mild heat that may disrupt microbial membranes, enhance oxidative stress, and weaken biofilm architecture. The combined action of EGCG-mediated antimicrobial activity and nanoparticle-assisted photothermal therapy may therefore provide a synergistic approach against both planktonic microorganisms and established biofilms. This strategy has potential applications in the management of difficult-to-treat bacterial infections and the development of localized antimicrobial therapies. Further studies are required to optimize nanoparticle size, EGCG loading, photothermal conditions, antimicrobial efficacy, biocompatibility, and long-term safety before clinical translation.

KEYWORDS: Epigallocatechin gallate (EGCG); Gold nanoparticles; Phenolic compounds; Photothermal therapy; Antimicrobial therapy; Anti-biofilm activity; Nanotechnology; Green tea polyphenols; Bacterial infections; Nanomedicine.

1. INTRODUCTION

Infectious diseases continue to represent a major biomedical problem, and the challenge is amplified by global changes that influence pathogen distribution, antimicrobial use and host–microbe interactions. Drug resistance makes treatment more complicated because microorganisms may withstand medicines that were previously effective. Persistent bacterial populations and biofilm-associated cells add another layer of difficulty by allowing bacteria to survive under conditions that would be unfavorable for freely growing cells.[1,2]

Biofilms are organized microbial communities embedded in a self-produced extracellular matrix. The matrix can restrict penetration of antimicrobial compounds, modify the local chemical environment and create physiological heterogeneity within the bacterial population. Consequently, treatment of a biofilm infection is not equivalent to treatment of planktonic bacteria. The supplied article emphasizes that biofilms can serve as protective barriers and therefore represent an important target for alternative antimicrobial strategies.[4–6,39]



Nanomedicine has emerged as one approach for addressing these limitations. Nanomaterials can interact with microorganisms through physical, chemical and biological mechanisms and can be engineered to combine more than one therapeutic function.

Metal-based nanomaterials are particularly interesting because their optical, catalytic, surface and physicochemical properties can be modified through nanoscale design.[9–12] The E-Au nanoparticle platform described in the supplied PDF combines gold with EGCG, a naturally occurring tea polyphenol. This design places a biologically active molecule within a nanoscale metal–phenolic system and adds the possibility of externally activated photothermal treatment using NIR light.[39]

AIM OF THE REVIEW

The aim of this review is to present a coherent, expanded account of the E-Au nanoparticle strategy, including its rationale, preparation concept, photothermal behavior, antibacterial mechanisms, antibiofilm effects, preclinical applications and safety considerations. The review retains the central findings of the supplied document while using independently written academic language.

2. Antibiotic Resistance and Persistent Bacterial Infection

Antimicrobial resistance develops when microorganisms acquire or express mechanisms that reduce susceptibility to antimicrobial agents. From a therapeutic perspective, resistance is especially problematic when infections are recurrent, deep-seated or associated with biofilms. Persistent cells may survive treatment without necessarily being genetically resistant in the conventional sense, allowing infection to re-establish when treatment pressure is removed.[1,2]

The supplied article focuses particularly on MRSA, an important resistant Gram-positive pathogen. MRSA is clinically relevant because resistance to beta-lactam antibiotics limits conventional treatment options and because S. aureus can colonize tissues, wounds and implanted or damaged surfaces. A therapeutic platform that acts through multiple mechanisms may therefore provide a complementary strategy to conventional antibiotics.[39] Alternative approaches include phage therapy, antimicrobial nanomaterials, photodynamic therapy, photothermal therapy and combinations of established antimicrobials with materials that improve localization or bacterial damage. Each approach has its own limitations. For example, phage therapy requires appropriate phage–host matching, while nanomaterials require careful evaluation of dose, biodistribution and toxicity.[3,9,11]

2.1 Why Multifunctional Therapy Is Relevant

A single antimicrobial mechanism can be bypassed by bacterial adaptation. Multifunctional systems instead impose several forms of stress. In the E-Au system, the proposed effects include nanoparticle-associated biological activity, ROS-mediated damage, photothermal stress and modification of bacterial proteins and pathogenicity-associated processes. The study therefore illustrates a strategy in which several mechanisms are combined within one treatment platform.[39]

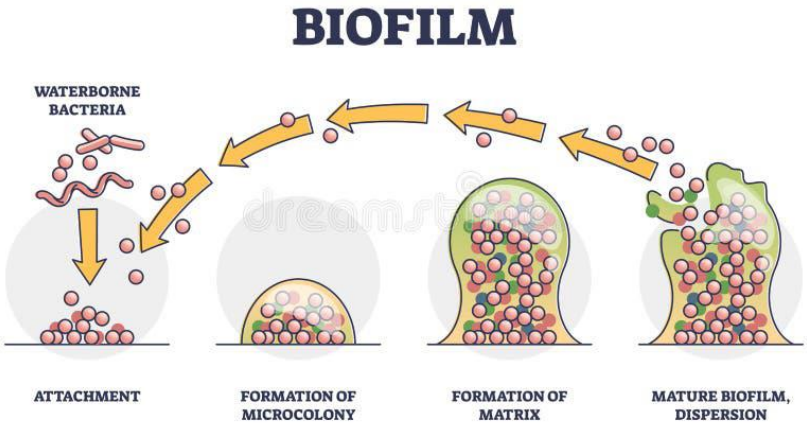
2.2 Clinical Relevance of Biofilm Control

Biofilm disruption is important because the extracellular matrix and altered bacterial physiology can reduce antimicrobial penetration and contribute to treatment tolerance. Strategies that decrease biofilm development or damage established biofilm structures may expose bacterial cells to additional antibacterial effects.[4–6]

3. Bacterial Biofilms and Their Therapeutic Importance

Biofilm formation is a developmental process in which bacteria attach to a surface, produce extracellular polymeric substances and organize into a structured community. The resulting matrix contains polysaccharides, proteins, extracellular DNA and other components. Biofilms can develop on tissues and medical materials and may contribute to chronic or recurrent infections.[5,6]

The E-Au system was evaluated for its ability to interfere with MRSA biofilms. According to the supplied article, E-Au treatment reduced biofilm development and thickness, while NIR irradiation strengthened the effect. The combination is therefore relevant not only for direct bacterial killing but also for structural disruption of a bacterial community.[39]



3.1 Biofilm-Associated Resistance and Tolerance

Resistance and tolerance should be distinguished. Resistance generally involves a heritable reduction in susceptibility, whereas tolerance can describe survival without a corresponding increase in the minimum inhibitory concentration. Biofilms can contain both resistant and tolerant populations.[2,4]

3.2 Biofilm-Targeting Strategies

- ✔ Disrupting matrix components or bacterial adhesion.
- ✔ Increasing penetration or retention of antimicrobial agents.
- ✔ Generating localized oxidative or thermal stress.
- ✔ Using light-activated materials for spatial control.
- ✔ Combining direct antibacterial activity with inhibition of virulence or biofilm-associated pathways.

The E-Au approach incorporates several of these concepts within a single nanoparticle platform.

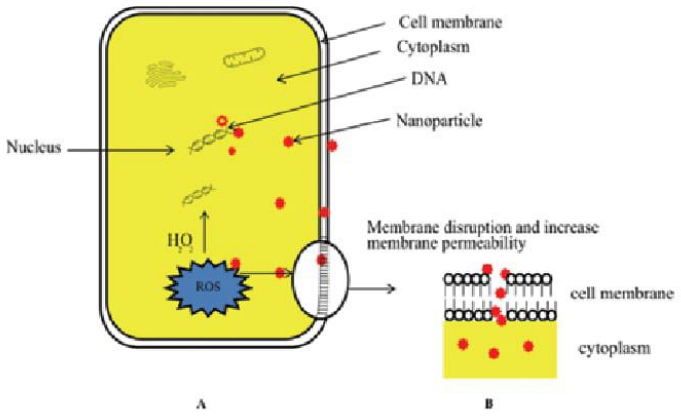
4. Nanotechnology as an Antibacterial Strategy

Nanomaterials provide high surface area and tunable interfaces for interacting with microbial cells. Their antimicrobial activity can arise from membrane interactions, ion release, oxidative stress, catalytic effects, physical disruption or photothermal/photodynamic mechanisms. Their small dimensions also permit formulation strategies that are difficult to achieve with conventional bulk materials.[9–12]

Metal nanoparticles have attracted attention because metals such as gold and silver display distinctive optical and surface properties. Gold is relatively stable and can support strong light–matter interactions, making gold-containing nanosystems useful in photothermal research.

However, the biological response of any nanoparticle depends on its size, shape, surface chemistry, concentration, aggregation state and exposure route.[10,19] Nanomaterial-based antimicrobial therapy can also be designed to reduce dependence on conventional antibiotics.

Such systems may deliver or activate antibacterial effects at a target site, potentially reducing nonspecific exposure. Nevertheless, translation requires reproducible manufacturing, physicochemical characterization and detailed safety testing.[9,11]



4.1 Metal–Phenolic Nanotechnology

Metal–phenolic systems use the coordination chemistry of phenolic molecules with metal ions to generate nanoscale assemblies or networks. Polyphenols offer multiple binding sites and may simultaneously contribute antioxidant, antimicrobial or anti-inflammatory properties. This combination provides a route to multifunctional materials in which the metal and organic components contribute different properties.[16,33–37]

4.2 Relevance to Pharmaceutical Biotechnology

From a pharmaceutical biotechnology perspective, E-Au nanoparticles illustrate how a naturally derived molecule can be incorporated into an engineered nanosystem. The platform connects natural-product chemistry, nanotechnology, microbiology, phototherapy and tissue repair. Such interdisciplinary design is particularly relevant to drug-resistant infections that require more than conventional antimicrobial exposure.

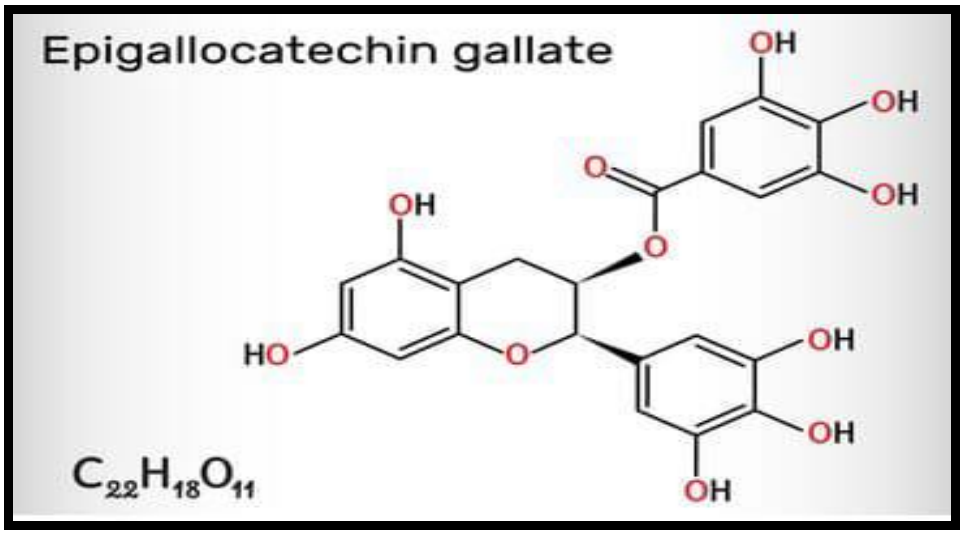
5. Epigallocatechin Gallate: Biological and Chemical Significance

Epigallocatechin gallate (EGCG) is a major tea polyphenol and belongs to a class of plant-derived compounds with multiple phenolic groups. These groups contribute to its chemical reactivity and its ability to interact with biological macromolecules and metal ions. EGCG has been investigated for antibacterial, antioxidant and anti-inflammatory activities, although its biological behavior depends strongly on concentration, formulation, metabolism and exposure conditions.[33,37]

A limitation of many natural polyphenols is that their physicochemical and pharmacokinetic properties can restrict direct therapeutic use. Nanotechnology can provide a means of stabilizing, concentrating or presenting such compounds in a different microenvironment. The E-Au platform uses EGCG not simply as a passive cargo but as a structural component involved in nanoparticle formation.[39]

5.1 EGCG and Metal Coordination

Phenolic groups can coordinate metal ions and participate in supramolecular assembly. In the E-Au system, EGCG interacts with gold ions to produce a metal–phenolic nanoparticle structure through a direct one-step self-assembly approach. This strategy reduces the need for a complex multistep fabrication sequence and integrates the natural molecule with the metal component.[39]



5.2 Functional Contribution of EGCG

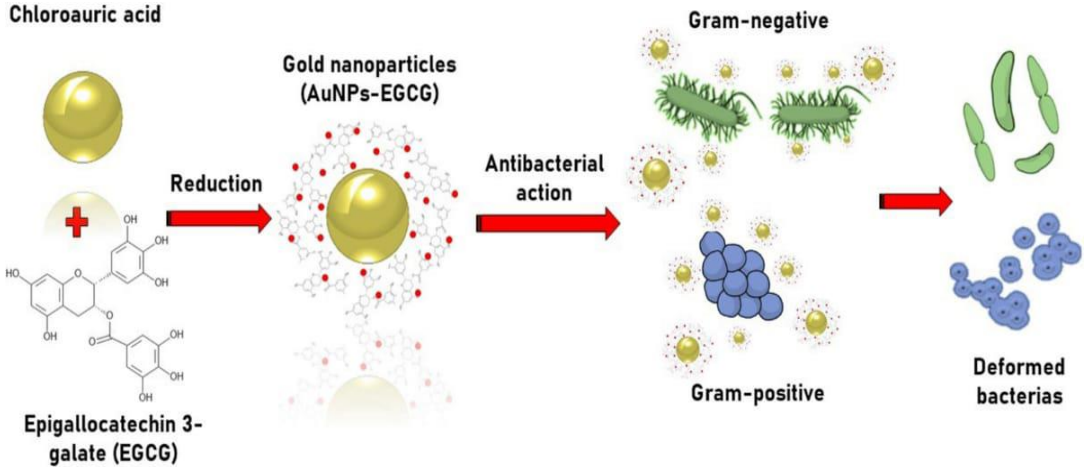
The polyphenol component may contribute biological activity, surface functionality and interactions with bacterial components. The supplied article associates EGCG-containing nanoparticles with protein modification and quinoprotein formation, suggesting that the chemical properties of the polyphenol remain functionally relevant after nanoparticle formation.[39]

6. Preparation and Characteristics of E-Au Nanoparticles

The E-Au nanoparticles described in the supplied article were prepared through a direct one-step self-assembly process involving EGCG and gold ions. In conceptual terms, EGCG provides phenolic coordination sites while gold contributes the metal component and associated nanoscale optical behavior.[39]

A one-step strategy can be advantageous because fewer processing stages may simplify formulation and reduce opportunities for contamination or batch-to-batch variation.

However, simplicity of synthesis does not remove the requirement for rigorous characterization. Particle size distribution, morphology, surface chemistry, optical absorption, aggregation behavior, stability and biological compatibility all influence performance.



6.1 Conceptual Formation Pathway

EGCG phenolic groups
↓
Interaction/chelation with gold ions
↓
Metal–phenolic self-assembly
↓
Formation of E-Au nanoparticles
↓
NIR absorption and photothermal conversion
↓
Combined antibacterial effects.

6.2 Physicochemical Function

The metal component contributes optical and photothermal properties, whereas the polyphenol contributes biological functionality and coordination chemistry. The resulting material can therefore be regarded as a multifunctional nanoplatform rather than a conventional single-mechanism antimicrobial.

6.3 Importance of Formulation Variables

- EGCG-to-metal ratio.
- Particle concentration.
- Aggregation and colloidal stability.
- Surface chemistry and charge.
- Storage conditions.
- NIR wavelength, power density and exposure time.
- Biological medium and protein interactions.

These parameters must be standardized before comparison between laboratories or movement toward clinical studies.

7. Antibacterial Activity of E-Au Nanoparticles

The supplied study evaluated E-Au nanoparticles against bacterial pathogens and placed particular emphasis on MRSA. The overall results showed that the E-Au platform possessed antibacterial activity and that NIR irradiation could strengthen the response. The combination was especially relevant to resistant bacteria and biofilm-associated infection.[39]

The antibacterial response is better understood as a combined effect rather than as the result of one molecular target. Nanoparticle contact can influence the bacterial envelope and intracellular environment; EGCG-associated chemistry can contribute biological interactions; NIR irradiation can activate photothermal behavior; and ROS can impose oxidative stress.

7.1 Activity Against MRSAMRSA

Represents an important target because its resistance limits the usefulness of many beta-lactam antibiotics. A treatment that damages bacteria through physical and chemical mechanisms rather than relying on a single conventional antibiotic target may be useful as a complementary approach. The study reported enhanced

antibacterial activity when E-Au nanoparticles were combined with NIR irradiation.[39]

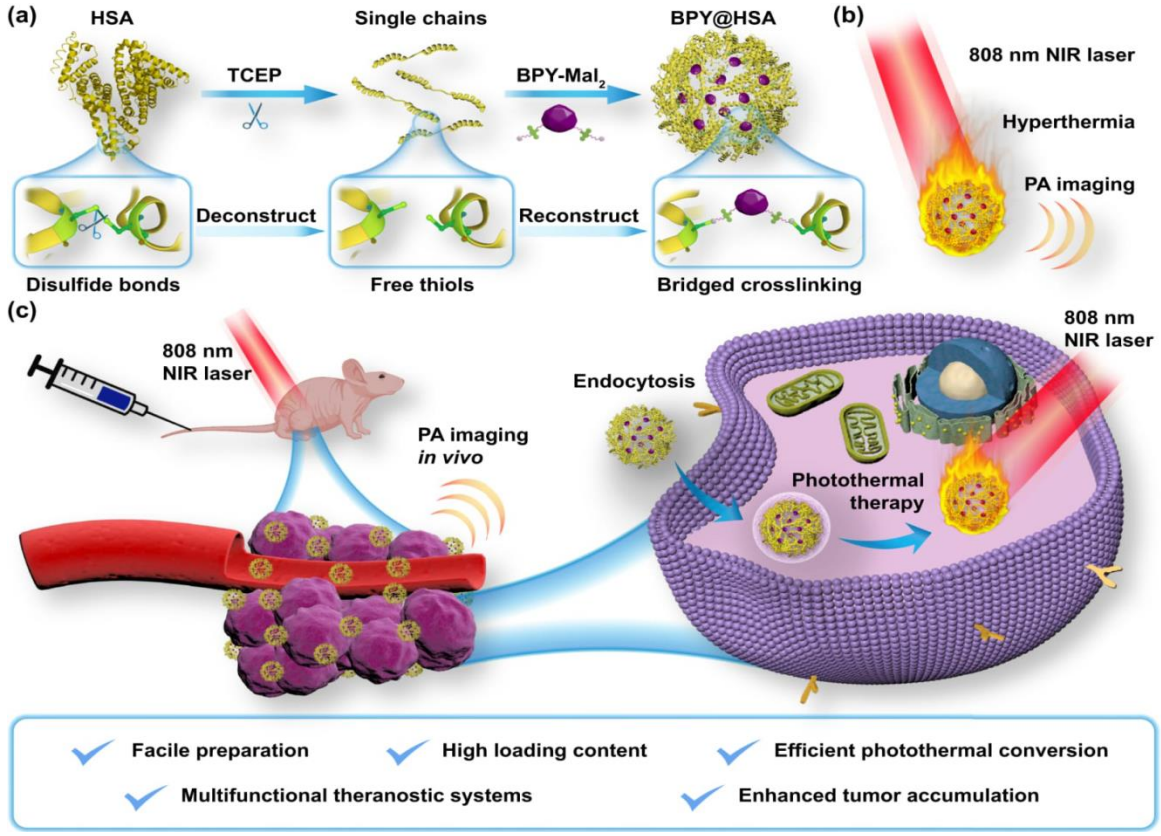
7.2 Activity Against Other Bacteria

The supplied article also reports antibacterial effects against S. aureus and E. coli. These observations indicate that the platform is not restricted to a single bacterial species, although the strongest emphasis in the work is placed on MRSA and biofilm-associated infection.[39]

8. Near-Infrared Photothermal Therapy

Photothermal therapy uses a photothermal agent to absorb optical energy and convert it into heat. In antibacterial applications, localized heating can damage bacterial membranes, proteins and other cellular structures. NIR wavelengths are widely studied because they can activate suitable nanomaterials and provide an externally controlled treatment stimulus.[24,28] The supplied study used an 808-nm NIR laser. E-Au nanoparticles showed a concentration-dependent increase in temperature under irradiation. At a reported power density of 1.0 W/cm², the document reports a temperature increase of approximately 36.0 °C for E-Au nanoparticles compared with approximately 3.3 °C for water under the corresponding conditions.[39]

8.1 Concentration Dependence:- Increasing nanoparticle concentration increased the photothermal temperature change. This relationship demonstrates that the amount of photothermal material is an important treatment variable. Excessive concentration, however, may increase biological exposure and should not automatically be interpreted as desirable.



8.2 Laser Power Dependence: -The photothermal response also increased with NIR power density. This provides another adjustable parameter. A rational treatment window therefore requires simultaneous optimization of nanoparticle concentration, irradiation power and exposure duration.

8.3 Mild Photothermal Therapy

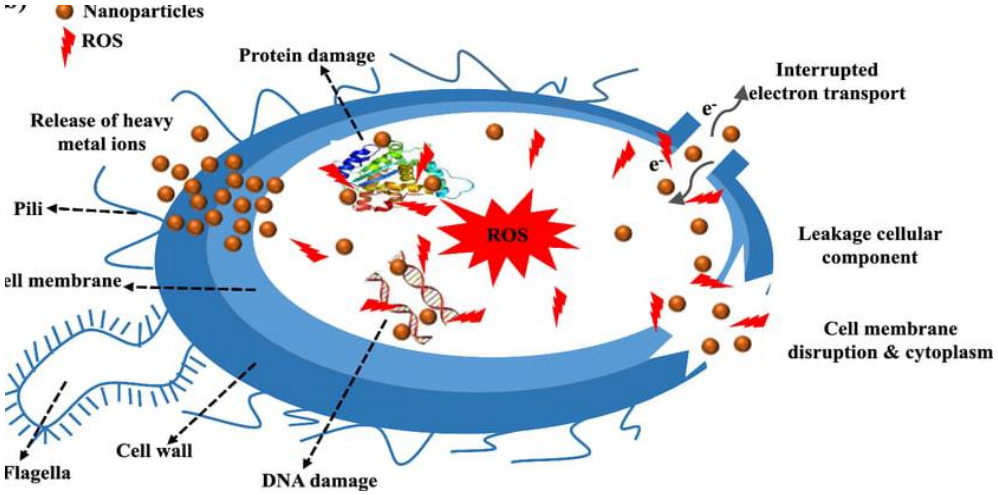
The study emphasizes mild-temperature photothermal therapy rather than relying solely on severe hyperthermia. Moderate heating can be combined with ROS and nanoparticle-associated antibacterial mechanisms, potentially reducing the need for extreme thermal exposure to host tissues.[39]

9. Mechanisms of Antibacterial Action

The E-Au system illustrates a multifunctional antibacterial mechanism. The major mechanisms described in the supplied PDF are mild photothermal activity, ROS generation, protein modification and quinoprotein formation, regulation of pathogenicity-associated processes, and disruption of biofilm structures.[39]

9.1 Photothermal Stress

NIR absorption by the nanoparticle produces localized heat. Thermal stress can disturb bacterial proteins, membranes and metabolic processes. Because the heating is externally controlled, the treatment can be activated only during irradiation.



9.2 Oxidative Stress

ROS can damage proteins, lipids, nucleic acids and other cellular components when their formation exceeds bacterial antioxidant defenses. In the reported system, reduction of antibacterial activity following ROS scavenging supported the contribution of ROS to the overall effect.[39]

9.3 Protein Modification

The study associates E-Au nanoparticles with protein-related damage and quinoprotein formation in MRSA. Modification of proteins can interfere with enzymes and structural components required for bacterial survival.

9.4 Pathogenicity Regulation

The reported treatment altered expression of genes associated with bacterial pathogenicity. This suggests that the platform may affect infection-associated functions in addition to directly reducing viability.

9.5 Combined Action

The significance of the platform lies in the convergence of several stress pathways. A bacterium exposed simultaneously to thermal, oxidative, structural and regulatory disturbances may have fewer opportunities to compensate through a single adaptive mechanism.

10. Reactive Oxygen Species and Oxidative Stress

Reactive oxygen species are chemically reactive molecules capable of modifying cellular macromolecules. Bacteria normally maintain redox balance through enzymatic and non-enzymatic defenses. When ROS production increases beyond the capacity of these defenses, oxidative stress can impair cell function.

The E-Au study examined the contribution of ROS by using a ROS scavenger. When ROS were scavenged, antibacterial activity was reduced, supporting the conclusion that oxidative processes contribute to the nanoparticle response.[39]

10.1 Relationship Between ROS and Photothermal Therapy

NIR irradiation does not simply provide heat as an isolated event. In the E-Au platform, irradiation strengthens the overall antibacterial response and occurs alongside oxidative effects. This creates a combined physical and chemical stress environment.

10.2 ROS-Mediated Cellular Damage

- Protein oxidation or modification.
- Membrane and lipid damage.
- Disturbance of enzyme activity.
- Damage to intracellular structures.
- Loss of redox homeostasis.
- Contribution to bacterial death.

10.3 ROS and Biofilms

Biofilm cells can experience strong protection from conventional antimicrobial agents. Oxidative stress may damage matrix components or exposed bacterial cells and may therefore contribute to biofilm disruption. In the E-Au system, ROS-mediated activity forms one component of the broader antibiofilm mechanism.

11. Protein Damage and Quinoprotein Formation

Protein function depends on correct structure, folding and chemical modification. Bacterial enzymes, transport proteins and structural proteins are essential for growth and survival. A treatment that chemically modifies proteins can therefore affect multiple pathways simultaneously.

The supplied study reports quinoprotein formation associated with E-Au nanoparticle treatment of MRSA. Quinoproteins are proteins containing quinone-derived modifications, and their formation can alter protein

function. The observation provides evidence for a biochemical contribution beyond simple heating.[39]

The EGCG component is important because polyphenol chemistry can participate in oxidation and protein interactions. In the E-Au system, the polyphenol-containing interface may therefore facilitate chemical modification of bacterial proteins.

ROS production and protein modification are not mutually exclusive mechanisms. Oxidative conditions can promote chemical changes in proteins, while modified proteins can further disturb cellular redox and metabolic balance.

Mechanisms that do not depend on inhibition of one antibiotic target may be valuable against resistant organisms. However, the possibility of bacterial adaptation to nanomaterial-induced stress remains an important research question and requires long-term experimental evaluation.

12. Regulation of Pathogenicity-Associated Processes

Pathogenicity is determined by a network of bacterial functions, including adhesion, colonization, biofilm formation, stress response and production of virulence-associated factors. Altering the expression of genes involved in these functions can reduce the ability of a bacterium to establish or maintain infection.

The supplied article reports that E-Au nanoparticle treatment altered the expression of pathogenicity-related genes in MRSA. This finding expands the concept of antibacterial action from direct cell killing to modulation of infection-associated biology.[39]

Biofilm development requires coordinated changes in bacterial physiology. If nanoparticle treatment interferes with pathways needed for adhesion, matrix production or persistence, biofilm development may be weakened.

Gene regulation occurs in the context of other stresses produced by E-Au nanoparticles. Photothermal exposure, ROS generation and protein modification can all alter bacterial physiology and may contribute indirectly to changes in gene expression.

The gene-regulation finding is important but should not be interpreted as proof of a single causal molecular pathway. Additional transcriptomic, proteomic and mechanistic studies are needed to identify primary targets and distinguish direct effects from downstream stress responses.

13. Antibiofilm Activity

The ability to interfere with biofilm formation is one of the most important features of the E-Au system. The supplied study reports reduction of MRSA biofilm development and thickness, with a stronger effect when E-Au nanoparticles were combined with NIR irradiation.[39]

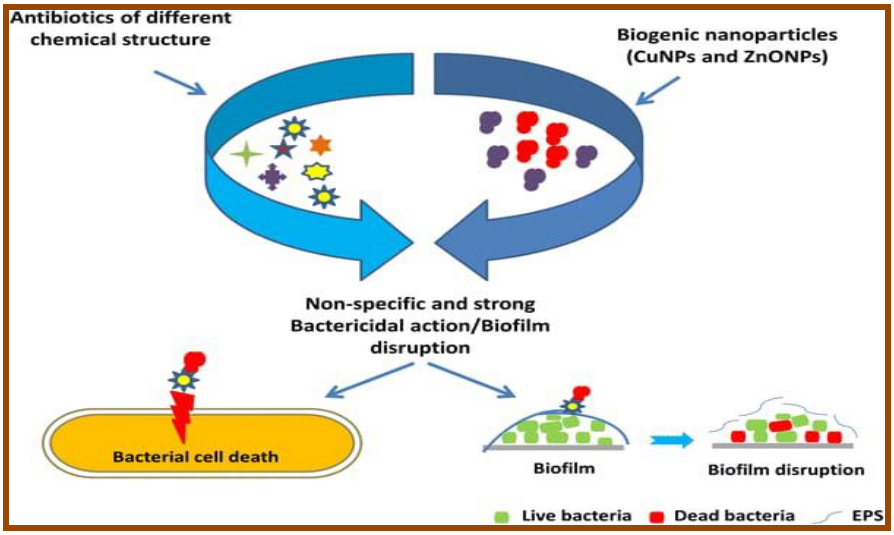
A biofilm can be viewed as a structured microbial ecosystem rather than a simple collection of cells. Therefore, effective antibiofilm treatment may require simultaneous disruption of the matrix, impairment of cell viability and interference with the biological processes supporting community maintenance.

13.1 Biofilm Disruption

E-Au nanoparticles provide multiple mechanisms capable of contributing to structural damage. Nanoparticle interaction, oxidative stress and mild thermal effects can act on both bacterial cells and the surrounding biofilm environment.

13.2 Advantages of Combined NIR Treatment

NIR provides an external trigger that can amplify nanoparticle activity at the treatment site. The supplied work indicates that E-Au plus NIR was more effective than the corresponding individual treatments in reducing MRSA biofilm structures.



13.3 Relevance to Superficial Infections

Superficial wound infections and corneal infections are attractive targets for light-controlled systems because the treatment site is accessible to external irradiation. The approach may therefore be more immediately compatible with localized disease than infections located deep within the body.

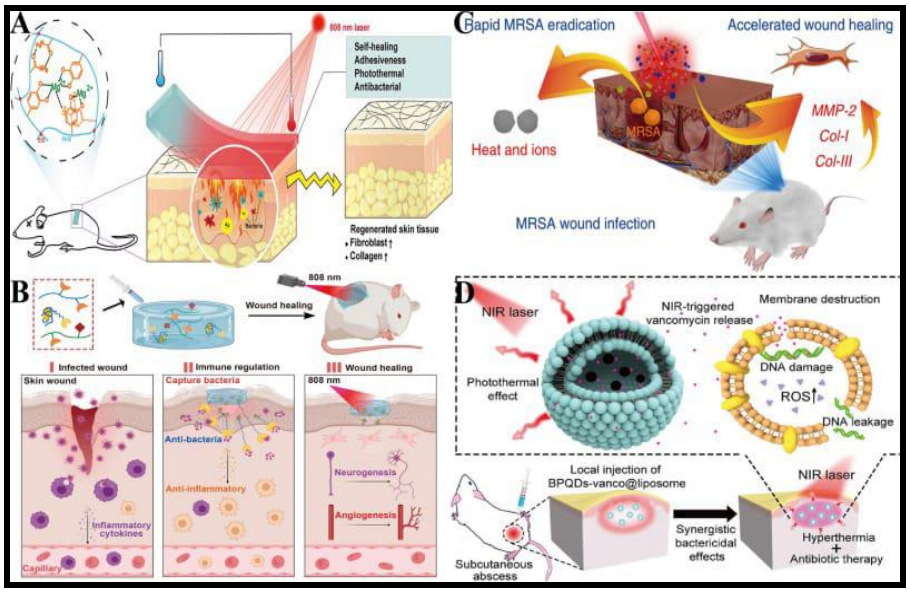
14. Application in MRSA-Infected Skin Wounds

The study evaluated E-Au nanoparticles in a murine model of MRSA-infected skin wounds. The model involved creation of a full-thickness circular wound followed by MRSA inoculation. Treatments included PBS, EGCG, EGCG with laser, E-Au nanoparticles and E-Au nanoparticles with NIR irradiation.[39]

The reported findings showed that E-Au treatment reduced bacterial burden and that NIR irradiation enhanced the therapeutic response. Wound tissues treated with E-Au plus NIR showed improved healing-related outcomes, including a shorter epithelial gap. Histological and inflammatory assessments were also consistent with improved tissue recovery.[39]

14.1 Antibacterial Effect

Quantification of viable bacteria demonstrated lower MRSA levels after E-Au treatment, with the combined E-Au/NIR condition showing a particularly strong effect. This supports the concept that photothermal activation can strengthen antibacterial performance in vivo.



14.2 Wound Healing

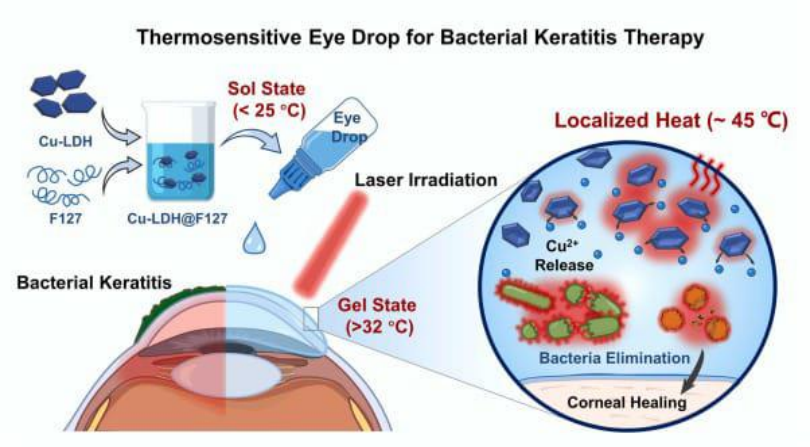
Successful infection treatment requires more than bacterial killing. Excessive inflammation can delay tissue repair. The study reported reduced inflammatory responses and improved wound-healing parameters following E-Au treatment.

The wound model provides an important proof-of-concept because it tests the nanoparticle system in a biological environment rather than in bacteria-only experiments. Nevertheless, mouse wound models do not establish human clinical efficacy.

15. Application in MRSA Keratitis

Keratitis is a corneal infection in which bacterial growth and inflammation can rapidly affect tissue transparency and ocular function. Local treatment must balance antimicrobial efficacy with preservation of delicate corneal structures. The supplied article therefore evaluates E-Au nanoparticles in a murine MRSA keratitis model.[39]

The reported treatment produced improvements in clinical and pathological parameters, including reduced inflammation, improved corneal epithelial recovery and better tear-related outcomes. The combined E-Au/NIR treatment was associated with enhanced therapeutic effects.



15.1 Ocular Advantages of Local Photothermal Activation

The cornea is accessible to external light, creating a practical rationale for externally activated nanoparticle therapy. Controlled irradiation may permit treatment to be concentrated at the infected surface while limiting exposure elsewhere.

15.2 Ocular Safety Considerations

Because the eye is highly sensitive to thermal and chemical injury, safety assessment is essential. The study examined corneal epithelial viability, retinal morphology and intraocular pressure, together with systemic indicators. Nanocarriers and biofilm-targeting systems are being investigated for ocular delivery and keratitis. The E-Au strategy adds an externally triggered photothermal component to this broader field.[13,38]

16. Biosafety and Biocompatibility

Antibacterial potency alone is insufficient for development of a therapeutic nanoparticle. The material must also be compatible with host tissues at the intended dose and exposure conditions. The supplied study therefore assessed local ocular effects, cellular viability, systemic biochemical parameters and major-organ histology.[39] In human corneal epithelial cells, the reported viability remained relatively high under the tested conditions. The supplied document reports approximately 81.57% viability at 400 μg/mL without laser irradiation and approximately 87.58% with laser irradiation. These are experimental observations from the reported conditions and should not be generalized to all doses or clinical settings.

16.1 Systemic Safety

Routine blood and biochemical measurements did not show major abnormalities in the reported experimental groups. Histological examination of major organs likewise did not reveal considerable pathological changes under the tested conditions.[39]

16.2 Importance of Dose Optimization

Nanoparticle concentration and laser energy must be optimized together. Increasing either parameter may improve antibacterial effects but can also increase the possibility of unwanted tissue stress. A therapeutic window therefore needs to be established experimentally.

16.3 Long-Term Safety

Short-term safety findings do not establish long-term toxicological safety. Future studies should address biodistribution, clearance, repeated dosing, immune responses, chronic exposure and potential accumulation of gold-containing materials.

17. Comparative Perspective With Other Photothermal Nanomaterials

Photothermal antibacterial nanotechnology includes gold nanoparticles, gold nanorods, carbon-based materials, metal oxides and metal–phenolic systems. The choice of material influences absorption wavelength, photothermal efficiency, stability and biological compatibility.[24,28]

The supplied study compares E-Au nanoparticles with EGCG–silver nanoparticles and reports a substantially stronger photothermal temperature change for the gold-containing system under the tested irradiation conditions. The reported comparison illustrates that metal identity can significantly influence photothermal behavior.

17.1 EGCG-Modified Gold Systems

Other EGCG-containing gold nanostructures have also been explored for antibacterial and photothermal applications. Published work on EGCG-modified gold nanorods and selenium composites demonstrates the broader feasibility of combining EGCG with gold-based photothermal materials for bacterial infection treatment.[40]

17.2 EGCG–Iron Systems

EGCG–ferric complex nanoparticles have also been reported as green photothermal antibacterial materials with biofilm and wound-healing activity, showing that the metal–polyphenol concept is not restricted to gold.[41]

These studies support the broader design principle that polyphenols can serve as functional components of metal-containing nanomaterials. They do not, however, establish equivalence between different formulations; each system requires independent evaluation.

18. Therapeutic Advantages of E-Au Nanoparticles

- The E-Au platform has several experimentally supported characteristics that make it scientifically interesting. First, the material integrates a natural polyphenol with a metal-based nanostructure. Second, the system can be activated with NIR irradiation. Third, antibacterial activity involves several mechanisms. Fourth, the platform has demonstrated activity in animal models of superficial infection.[39]
- Multifunctional antibacterial action.
- Activity against MRSA.
- Antibiofilm effects.
- Externally triggered NIR activation.
- Mild photothermal approach.
- Potential anti-inflammatory benefit.
- Demonstrated activity in wound and keratitis models.
- One-step self-assembly concept.

 # Potential Pharmaceutical Applications

Potential applications include topical treatment of resistant skin infections, infected wounds, localized biofilm infections and selected ocular infections. The platform could also be considered as a component of advanced wound dressings or localized photothermal formulations, although such applications require formulation and clinical development.

 # Potential Biotechnology Applications

From a biotechnology viewpoint, the system provides a model for integrating natural-product chemistry with nanoscale materials engineering. It also demonstrates how microbiological endpoints such as viable counts, biofilm thickness and pathogenicity-associated gene expression can be combined with physicochemical measurements.

19. Limitations and Challenges

Despite promising preclinical findings, several barriers remain before clinical translation. Nanoparticle systems can be sensitive to synthesis conditions, and differences in particle size, surface chemistry or aggregation may change biological activity. Standardized manufacturing and characterization are therefore essential.

The therapeutic response also depends on NIR irradiation conditions. Power density, wavelength, exposure duration and tissue geometry influence temperature and penetration. A treatment optimized in mice cannot automatically be transferred to humans.

- **Biological Limitations**
  - Animal models cannot fully reproduce human infection.
  - Long-term toxicity remains incompletely defined.
  - The effect of repeated dosing requires investigation.
  - Biodistribution and clearance require detailed study.
  - Host immune responses may vary between individuals.
- **Manufacturing Limitations**
  - Batch-to-batch reproducibility.
  - Control of particle size and aggregation.
  - Stability during storage.
  - Sterility and microbial control.
  - Scale-up of one-step self-assembly.
  - Regulatory characterization of the final product.
- **Clinical Limitations**

The evidence described in the supplied PDF is preclinical. Clinical trials are required to establish human safety, appropriate dosing, irradiation parameters, treatment frequency and therapeutic efficacy. The system should therefore be described as a promising experimental platform rather than an established clinical treatment.

20. Future Perspectives

Future research should focus on improving reproducibility, understanding molecular mechanisms and defining a safe therapeutic window. Advanced omics approaches could clarify how E-Au treatment changes bacterial transcription, protein composition and metabolic state. Such studies may identify which effects are primary and which are downstream consequences of photothermal or oxidative stress.

Material optimization may involve controlling EGCG-to-gold ratios, particle dimensions, surface chemistry and NIR absorption. Formulation into hydrogels, films, sprays or ocular preparations could improve retention at localized infection sites.

- **Combination Therapy**

E-Au nanoparticles could be investigated in combination with conventional antibiotics, antimicrobial peptides, phage-derived approaches or other nanotherapeutics. Such combinations should be tested carefully to determine whether interactions are additive, synergistic or antagonistic.

- **Advanced Photothermal Control**

Future systems may incorporate temperature monitoring, feedback-controlled irradiation or targeting ligands. These technologies could help maintain antibacterial temperatures while reducing unnecessary host exposure.

- **Translation**

Clinical development will require standardized manufacturing, pharmacokinetic and toxicological studies, device compatibility for NIR delivery, and controlled clinical trials. Regulatory assessment will need to consider both the nanoparticle formulation and the light-activation procedure.

21. Integrated Mechanistic Model

The E-Au system can be summarized as a sequence of interconnected events. EGCG interacts with gold ions to form the metal–phenolic nanoparticle. The resulting nanosystem interacts with bacterial cells and can exert

intrinsic antibacterial effects. When NIR irradiation is applied, the nanoparticles convert absorbed optical energy into localized heat. This photothermal response occurs together with oxidative and chemical effects.

The combined stress can increase ROS generation, modify bacterial proteins and promote quinoprotein formation. Changes in bacterial physiology are also associated with altered expression of pathogenicity-related genes. At the community level, these effects can interfere with biofilm development and reduce biofilm thickness.[39]

Mechanistic Flow

EGCG + Au ions
↓
Metal–phenolic self-assembly
↓
E-Au nanoparticles
↓
Bacterial interaction
↓
NIR activation
↓
Photothermal heating + ROS generation + protein modification
↓
Pathogenicity-related changes
↓
Bacterial damage and biofilm disruption
↓
Reduced infection burden
↓
Improved tissue repair.

Host-Level Outcome

In the reported wound and keratitis models, reduction of bacterial burden was accompanied by lower inflammatory responses and improved tissue repair. The therapeutic concept therefore extends beyond direct antibacterial activity to restoration of the infected tissue environment. Overall Interpretation.

The central scientific value of the E-Au platform lies in integrating several complementary functions in a single material. This multifunctionality is experimentally supported in the reported preclinical models, while the long-term translational potential remains to be established

22. Tables and Summary of Experimental Findings

Parameter	Reported finding	Interpretation
Nanoparticle formation	One-step EGCG–gold self-assembly	Simple metal–phenolic fabrication concept [39]
NIR wavelength	808 nm	External photothermal activation [39]
Photothermal response	Concentration and power dependent	Treatment can be tuned through formulation and irradiation [39]
ROS	Scavenger reduced antibacterial activity	Supports ROS contribution [39]
Biofilm	Reduced MRSA biofilm thickness	Antibiofilm potential [39]
Wound model	Reduced MRSA burden and improved healing	Preclinical topical efficacy [39]
Keratitis model	Reduced inflammation and improved corneal outcomes	Preclinical ocular potential [39]
Safety	No major systemic or organ abnormalities under tested conditions	Supports further safety studies [39]

22.1 Key Advantages and Research Needs

The evidence supports a balanced interpretation. The system demonstrates multifunctional antibacterial activity and promising local therapeutic effects, but the evidence remains preclinical. The next research stage should therefore emphasize reproducibility, mechanism,

long-term safety and clinically relevant models rather than assuming that laboratory efficacy will directly translate into patient benefit.

22.2 Relevance to Pharmaceutical Research

The platform is relevant to pharmaceutical research because it links formulation science, natural products, nanotechnology, microbiology and controlled physical therapy. It can serve as a model for designing drug-free or antibiotic-sparing antimicrobial systems.

23. DISCUSSION

The development of E-Au nanoparticles reflects a broader shift in antimicrobial research from single-target drug design toward multifunctional therapeutic platforms. Conventional antibiotics remain essential, but resistance and biofilm-associated tolerance create situations in which additional mechanisms are desirable. Nanomaterials can provide physical and chemical mechanisms that complement antimicrobial drugs.[9–12]

The E-Au system is particularly interesting because EGCG is integrated into the nanoparticle architecture rather than simply mixed with gold. This creates a combined material in which the polyphenol and metal components influence the overall biological and photothermal response. The use of NIR adds another layer of control by allowing external activation.

The study's use of MRSA-infected wound and keratitis models is important because these conditions are localized and accessible to topical treatment. The observed reductions in bacterial burden, inflammatory response and tissue damage provide evidence that the system can function in a living organism.[39] However, the results should be interpreted within their experimental context. Mouse models are useful for proof-of-concept but cannot reproduce the full diversity of human wounds, ocular infections, immune responsesand pharmacokinetics. In addition, the long-term fate of gold-containing nanoparticles requires further investigation.

❖ Scientific Significance

The study contributes to the growing field of metal–phenolic nanomedicine by demonstrating that a natural polyphenol can be combined with gold to produce a photothermally active antibacterial material. It also connects photothermal treatment with ROS generation, protein modification, gene regulation and biofilm disruption.

❖ Translational Significance

The most realistic near-term translational direction is likely to involve localized superficial infections where the nanoparticle can be applied directly and NIR irradiation can be controlled. Deeper or systemic infections would require substantially more evidence regarding distribution, targeting and light penetration.

24. CONCLUSION

Antibiotic-resistant bacteria and biofilm-associated infections require therapeutic strategies that can address bacterial survival through multiple mechanisms. The EGCG–gold nanoparticle system described in the supplied PDF represents one such multifunctional approach. EGCG provides a natural polyphenolic component capable of interacting with gold ions and contributing biological activity, while the gold-based nanostructure provides photothermal functionality under NIR irradiation.[39]

The reported E-Au nanoparticles showed antibacterial activity against relevant bacterial pathogens, with particular emphasis on MRSA. Their activity was enhanced by NIR irradiation, and the mechanism involved mild photothermal stress, ROS generation, protein modification and quinoprotein formation, together with changes in pathogenicity-associated processes. The nanoparticles also interfered with MRSA biofilm structures.[39]

Preclinical studies in MRSA-infected skin wounds and keratitis models further demonstrated reductions in bacterial burden and inflammation and improvements in tissue repair. Safety investigations reported relatively high corneal epithelial viability under tested conditions, no major systemic biochemical abnormalities and no major histological abnormalities in examined organs.[39]

Taken together, the E-Au platform provides a useful proof-of-concept for combining natural polyphenols, metal nanotechnology and externally controlled photothermal therapy. Nevertheless, these findings should not be interpreted as evidence of established clinical efficacy. Long-term toxicology, pharmacokinetics, manufacturing reproducibility, irradiation optimization and controlled clinical studies remain necessary. The continued development of such multifunctional systems may contribute to future antibiotic-sparing strategies for localized resistant infections and biofilm-associated disease.

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