

Therapeutic Applications of Quantum Dots in Human Wound Healing: Advances and Future Perspectives

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Abstract

Wound repairing is a highly systematic biological process with significant clinical challenges mostly in chronic, infected and unhealed wounds where traditional treatment often fails to recover tissue integrity. Latest nanotechnology has highlight quantum dots as emerging multifactorial tool with considerable potential in wound recovery due to its unique optical, physicochemical and biological nature. Quantum dots show regulatable fluorescence, high surface to volume ratio, high photostability and nanoscale surface chemistry that make it more feasible towards wound imaging, targeted drug delivery and better therapeutic functions within the wound microenvironment. Emerging studies demonstrate that quantum dots therapy can modulate key process of wound healing pathway through multiple mechanism including activation of fibroblast, antimicrobial effects, regulating inflammatory mediators, stimulating angiogenesis and enabling precise monitoring of healing progression while actively supporting tissue regeneration. Despite all these promising contributions certain concern related to cytotoxicity, long term biocompatibility, biodistribution and regulatory complexity specially for heavy metal-based quantum dots. The designing of carbon based, biodegradable and surface engineered quantum dots have partially addressed this limitation by showing better safety profile and potential biomedical applications. This review critically evaluates the role of quantum dots in human wound healing that mainly focusing on their mechanism of action, material design strategies and current limitations. However, outline future direction emphasizing need to advance quantum dots based wound therapies toward clinical applications.

Keywords: Quantum dots, wound therapy, nanotechnology, antimicrobial, angiogenesis, wound dressing, tissue regeneration

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Introduction

The process of wound healing is very complicated, involving a series of molecular and cellular events, and become particularly notable challenging in instance of non-healing and chronic wounds (Kushwaha et al., 2022). The quality life of the patient is not only decrease by such condition but heavy financial strain are also place on healthcare infrastructure broadly or worldwide, rising about ten billions of

dollars are involving in annual medical expenditure (Chen et al., 2024). The exploration of creative therapeutic strategies is required by this health strain and economic, with the system based on nanotechnology arise as a promising solution due to their ability to modify complicated biological environment and address the limitation of traditional therapies or treatment (Haque et al., 2021). These considerable attention has been

attracted by the quantum dot as modern nanomaterial for their novel spectroscopic characteristics, which contribute to the various application such as bio-recognition, biomedical imaging, and site-specific drug delivery system for improved strategies of wound care (Hussain et al., 2024). Mainly, Adjustable optical and electrical properties are given by quantum dots semiconductor nanocrystal indicating mechanicals characteristics, and are considered important for theragnostic and therapeutic-diagnostic application in skin regeneration (Liu et al., 2023). This review mainly focus on completely explores the recent modern innovation and future possibilities in the use of quantum dots for tissue regeneration or human wound healing, including their mode of action, advantages, challenges and emerging development in wound healing (Bal-Öztürk et al., 2024). Quantum dots are set as highly multifaceted agent for different stages of tissue regeneration from the starting inflammation controlling to tissue reorganization, due to there notable feature of quantum dots such as size-dependent, optical characteristic and electronic characteristics, strong photostabilization and broad absorption spectra (Madaninasab et al., 2025). Their potential to managing the multivariable nature of tissue regeneration by quantum dots and their ability to enhance cellular motility, slow down the microbial growth, and support angiogenesis (Yadav & Bachhuka, 2023). However, even with these advantages, their clinical application encountering difficulties in many challenges related to safety, long-term toxicity, and interconnection with biological system are observed in the quantum dots based therapies for tissue regeneration and which require thorough evaluation of unconventional strategies to reduce adverse effect (Baig et al., 2023). A major technological advancement is represented by incorporating the quantum dot into advanced wound dressing , enabling real-time monitoring of wound condition and sustained release of healing

agent to improve healing outcome. (Liu & Ge, 2025). The key role of quantum dot in antimicrobial activity, inflammation regulation, support angiogenesis, and scar reduction, spotlight their benefit compared to conventional therapies. It also analyse the recent advancement in surface modification technique aimed to increase the biocompatibility and targeting efficiency of quantum dots into the complicated wound microenvironment (Huang & Huang, 2024). QDs are more effective than traditional organic fluorophores for a broad range of biological and biomedical uses by their unique characteristics of quantum dots such as narrow emission spectra, excellent photostability, board fluorescence efficiency (Hussain et al., 2024). Multicolour imaging is support by their size-dependent emission characteristics, enhancing their applicability in modern therapeutic and diagnostic approaches in wound care (Huang & Huang, 2024; Hussain et al., 2022).

Overview of Wound Healing Process

Wound healing involves a complex and dynamic biological process that have four distinct phases : hemostasis, inflammation, proliferation, and remodelling (Paul & Hakkimane, 2025). Although these phases happen naturally and their development can be crucially improved and speed up through appropriate strategies dressing intermediation, including modern nanotechnology based application (Dam et al., 2023). Ideal wound dressing are recently developed by multiple material with enhancing characteristics such as inherent antibacterial factor, more biocompatibility, and environmental sustainability, utilizing natural polymers (Nguyen et al., 2023). Multiple factors are involved for improving tissue regeneration and controlling infection (Moradifar et al., 2024). These modern wound dressing utilize and embody nanomaterial that directly interact at the cellular stage to

overcome hurdles to healing, including persistence infection or prolonged inflammation (Chen et al., 2024; Salimi & Mohammadipanah, 2021). This application become especially important given the limitation of traditional wound dressing which may advance tissue regeneration by elevate bacterial contamination and enough endogenous growth factor (Chen et al., 2024). In contrast, modern multifunctionalities are integrate by quantum dots within these dressing such real-time monitoring of wound condition by movable fluorescence and site-specific delivery of biological activity fragment, eventually increase wound healing properties (Hossain et al., 2023). For example, graphene and carbon quantum dots have the outstanding ability for create free radicals and produce photothermal effects. Additionally, they have shown advance scar-free tissue regeneration and promote antibacterial activity when incorporation into wound disinfection bandage (Yadav & Bachhuka, 2023).

Challenges in Chronic Wound Management

Despite notable progress in wound healing, major challenges is own by non-healing wound due to their slow healing frequency, high chances of bacterial infection, and complicated pathophysiology (Lu et al., 2025). Underlying systemic condition, including diabetes or vascular disorder may cause these type of wound by affecting the coordinated cellular and molecular processes crucial for victorious wound healing (Ataide et al., 2022; Catanzano et al., 2020). Advanced therapeutic approaches including nanotechnology-based strategies, because of their constant and difficult to treat nature of chronic wound, to control the deficiencies in natural growth factor and control constant inflammation and infection which is helpful in wound healing (Catanzano et al., 2020; Moradifar et al., 2024). The urgent need of advanced wound care solution that moves behind traditional passive dressing toward

the system able to actively monitoring and responding to the wound surrounding is understood by growing global health risk of chronic wound (Kammona et al., 2024; Liu & Ge, 2025). The limitation of conventional therapies reinforcing the essential for more advanced therapeutic intervention is emphasized by the additionally many challenges like bacterial resistance and insufficient endogenous healing properties (Liang et al., 2023). Prolonged inflammation exhibit risk of infection and impaired tissue regeneration characteristic these exhibit chronic, non-healing wound, which contributing to the rising of healthcare cost (Liu & Ge, 2025). This problem is further complicated by the emergence of antibiotic-resistant bacteria and creative strategies behind traditional wound care that provide real-time assessment of wound condition and enable personalize therapies (Cristea et al., 2025).

Quantum Dots (QDs)

Quantum dots are defined as nanoscale semiconductor, commonly measuring between 2 to 10 nm in size, and unique quantum mechanical behaviour are showing by them, these properties provide them adjustable optical and electrical properties. Size-dependent band gap are produced by quantum confinement effect authorise accurate control on their emission and absorption based on different electromagnetic spectrum (Wang et al., 2020). QDs are prepared highly suitable for different biomedical application, including site-specific delivery, biosensing and modern biomedical imaging by this high fluorescence efficiency and outstanding photostability (Dam et al., 2023). In additional, there broad surface area to volume ratio are ease by surface modification, allowing binding of biomolecule for site-specific delivery and improved therapeutic stability into the complicated biological system (Yadav & Bachhuka, 2023). The advantages of quantum dots are very helpful contender for modern approaches of wound healing by

this flexibility, mainly in the expansion of quantum dot advance dressing effective in real-time monitoring and controlled release of drug (Farshidfar et al., 2023). For example, researches reveal that carbon based quantum dot constructively show antibacterial properties due to production of reactive oxidative species which improving the effectiveness in wound care (Farshidfar et al., 2023). In additionally, the optical and electronic characteristic of hydrogel can be outstandingly improved by integration of quantum dots, as a result modern wound care is boosted overall effectively (Omidian & Wilson, 2024).

Rationale for QDs in Wound Healing

The incorporation of physiological properties of quantum dots, including size-dependent photosensitive effect and broad surface-volume ratio make it possible incorporate these nanocrystal into modern wound healing system which allow improving the cellular interconnection and adjustable drug delivery (Baig et al., 2023). This allow the preparation of advanced wound care dressing that can tract the healing progress in real-time and help in the treatment of wound with best therapeutic efficacy, QDs can be combine to a different types of biological active molecules to create more biocompatible and allow site-specific delivery to the wound-related tissues and pathway to be targeted using photoluminescence and electrical characteristic of quantum dots (Kazeminava et al., 2022). Moreover, the photoluminescence and electrical properties of QDs can be leveraged for biosensing applications and providing non-invasive and continuous monitoring of various wound parameters such as pH, temperature, and biomarker concentrations. The exceptional antioxidant and anti-inflammatory properties of certain quantum dots (carbon quantum dots) further contribute to their therapeutic potential by mitigating oxidative stress and modulating the inflammatory response crucial for

optimal wound repair (Moniruzzaman et al., 2022). Additionally, the broad-spectrum antimicrobial activity of various quantum dots (graphene quantum dots and carbon dots) offers a significant advantage in preventing and treating wound infections, a critical factor often impeding successful wound closure (Dong & Wang, 2023; Farshidfar et al., 2023). Moreover, ZnO-QDs, when integrated into hydrogels, demonstrate remarkable antibacterial efficacy against prevalent wound pathogens like *S. aureus* and *E. coli*, attributed to the generation of reactive oxygen species and Zn^{2+} release under acidic conditions (Raha & Ahmaruzzaman, 2022).

Scope of the Review

This review will provide a substantively analyse the multiple uses of quantum dots in human tissue regeneration with a major focus on different factor such as antimicrobial, antioxidant and light matter interaction characteristics that support the therapeutic efficacy of quantum dots. It identifies how the quantum dots nanocrystals use infection management, tissue repairing, inflammation control, it will give its opinion on how it can be used in future diagnostic and site-specific drug delivery system for wound healing. Moreover, this review mentioned the latest progress in incorporation of quantum dots into nanocomposite hydrogel and the different biological material which will discuss how the cross-breed improving the wound management with the help of enhanced cellular binding, multiplication, locomotion and by the controlled release of therapeutic molecules (Alshangiti et al., 2023; Xiong et al., 2024).

Fundamentals of Quantum Dots

Synthesis and Types of QDs

The quantum dots have very special characteristics which is based on preparation methods, composition, shape, size and surface properties. These features are accurately regulated by preparation

methods including colloidal synthesis, epitaxial growth and hydrothermal process. Different types of quantum dots like carbon-based (carbon molecular clusters) and graphene quantum dots are nontoxic in nature, highly biocompatible, adjustable optical features and effective in different medical approaches (Dong & Wang, 2023; Kazeminava et al., 2022). Additionally significant classification including noble metal quantum dots (e.g., Au, Ag) and semiconductor quantum dots (e.g. CdSe, ZnS), All types of QDs exhibit different benefits like high light emission, light stability and how to add function to the surface to particular wound care purpose. Each of this material have specific qualities that can be used in wound care and for tissue regeneration. Meaningfully, ZnO, TiO₂ and graphene quantum dots have been identify as photosensitizers and photodynamic therapy treatment (Zhang et al., 2023). Expressly, these have extraordinary ability to improve epithelial cell growth, improving local immunity, reducing the chances of bacterial infection, and inflammation, and speedup recovery time (Bai et al., 2022). Moreover, stimulating the growth of new blood vessels are explain by zinc peroxide nanocrystals which is an advanced technology in tissue regeneration where blood vessel density is need to improve (Alshangiti et al., 2023). The therapeutical efficacy of this nanocrystal is enhanced by their incorporation in system of hydrogel, provide a controlled released system which improved healing and growth factor and accelerate the growth of blood vessel and skin cell (Alshangiti et al., 2023; Ren et al., 2022). The healing process of wound rapidly making the cut have both a structure and functional biological signals into wound dressing (Alshangiti et al., 2023). For instance, the nanostructure material hydrogel have been prepared to by the integration of zinc peroxide and zinc oxide enhanced the tissue restoration and development of blood vessel (Alshangiti et al., 2023). Such combination include

controlled release characteristics through nanoparticle-incorporated hydrogels, thereby enhancing therapeutic efficacy by establishing a sustained and physiologically suitable microenvironment for wound healing (Alshangiti et al., 2023; Dam et al., 2023).

Physicochemical Properties Relevant to Biology

Quantum dots have very large surface area relative to the volume means QDs have nanoscale dimensions, their interlinkage with biosystem is positively affected by the QDs nanocrystal, indicate their cellular absorption and drug disposition and effectiveness. Because of this, researchers can easily attach molecules that authorize well organised surface modification with receptor ligands, medication or molecular imaging agent, enable accurate site-specific delivery to the wound and improved the treatment result. Additionally, the small size of quantum effect the allow the dots to change the way they glow and conduct electricity including photoluminescence. Scientist can be accurately modified these characteristics of quantum dots to for specific medical imaging and diagnostic therapy in complicated serious wound. The adjustable properties enable us to modify quantum dot that have special electronic behaviour that helps them to act as photocatalysts and electrocatalysts which help in antimicrobial treatment, clean wound and accelerate wound healing (Mondal et al., 2024). Besides their innate visual characteristics, quantum dot possesses special electronic behaviour which help them to act as photocatalyst and electrocatalyst. This mechanism of action help in maintain the wound hygiene and also accelerate the tissue regeneration. For example, the properties such as chemical, strength, electrical and heating characteristics can be improved by the integration of biodegradable polymer nanocrystals into hydrogels, this may lead to enhanced interconnection with biosystem and excellent performance as

nanostructure material (Alshangiti et al., 2023). This improved performance is of great importance in wound healing, and how they heal and show effectiveness and their compatibility with the body is directly related to the structure and interaction ability of dressing (Dam et al., 2023). In detail, important strong strength support to the tissue regeneration is impart by the enhanced coefficient of elasticity monitored in hydrogel which is based on nanocrystals, this helps in better closure of the wound and stability (Alshangiti et al., 2023).

Surface Modification and Biocompatibility

The demand and application of quantum dots are increased across different field which increase the strong need to examine the possibility of accumulation and leakage of these nanocrystals into the surrounding. Hence, research on long-term biocompatibility and deterioration mechanism of QDs is also important (Abdelhameed et al., 2024). Thus, knowledge of the subtleties of surface chemistry, especially with related to the ligand exchange and surface of the polymer, become central in the development of QDs with improved *in vivo* stability, less cytotoxicity, and controlled interaction with the cell. It is also possible to explain the high control over the physical and chemical characteristics of the resulting nanocomposite using the sophisticated engineering thus produce biomaterial that directly replicate the extracellular matrix and actively engaged the wound healing (Alshangiti et al., 2023). In particular, rapid standardization of extraction and purification of natural polymer should be implemented to address the limitation in the variation in sources, the possibility of contamination and the inconsistency of mechanical stability characteristics of biological nanocomposite (Bal-Öztürk et al., 2024). Thus, it is possible that more modern method of fabrication such as computational bioprinting, electronic

spinning and the 3D bioprinting are recently studies in order to produce multi-purpose scaffolds with the best long-term safety and uniform physicochemical characteristics and use them in clinical practices (Fadilah et al., 2023).

Mechanisms of QD Interaction in Wound Healing

Antimicrobial Properties

The antimicrobial activity is strongly demonstrated by the quantum dots through different mechanism. These including the production of reactive oxidating species, direct membrane disruption and disruption of metabolic pathway. The quantum dots generate the reactive oxidative species mostly due to light exposure which boost the oxidative stress in the microbial cells that cause lipid peroxidation, damage to the DNA and protein, eventually damaging cellular well-being and longevity. Quantum dots provide a wide range of solution to eliminated a wide range of pathogenic microorganism, including resistant to antibiotic isolate, eliminate the threat of infection in the complicated wounds. Additionally, quantum dots can be interlinked very quickly to the call wall of the bacteria and membrane with the help of their small size and high surface to volume ratio, and cause damage and disruption of cellular portion important for bacterial survival. The heightened permeability of the membrane, release of intracellular content and blockage of vital enzyme due to the direct interaction which together lead to their bacterial or bacteriostatic action. In addition the close microbial activity, quantum dots dependent antimicrobial agents can be controlled released, which increased their effectiveness and thus grant extended protection against infection (Pahlevani et al., 2025). Furthermore, intrinsic antibacterial characteristic as well as UV-shield abilities are design by multiple functional bio-scaffolds, to protect the wound bed both against microbial colonization and light-induced damaged (Fadilah et al., 2023, Han et al., 2025). This

create the attack on pathogen more powerful and focused at low the dosage of antibiotic which counteract the emergence of antibacterial resistance (Stamo et al., 2021). Additionally, the photosensitizers and antibiotic medication within polymer based material exhibit synergistic interaction of quantum dots against both common and multiple drug resistant microorganism such as methicillin-resistant staphylococcus aureus (Hu et al., 2024; Owusu et al., 2020; Stamo et al., 2021). Similarly, ZnO-QDs nanocrystal has exhibited potent antibacterial properties due to their increased specific surface area and high quantum dots nanocrystals (Zala & Patel, 2024) (Table-1; Figure-1).

Anti-inflammatory Effects

Anti-inflammatory activity of the quantum dots is regulating the production of cytokines and activation of immune cells on the wound site. Certain quantum dots have the ability to suppress the expression of pro-inflammatory cytokines, like TNF- α and IL-6, and activate the anti-inflammatory once like IL-10 and restoring immune homeostasis (Hemdan et al., 2023). Additionally, the regulated excretion of therapeutic activity of QD-dressing can maintain anti-inflammatory activity at prolonged stages which exhibit a long-term positive impact on the healing process. This effect is associated with an improved microenvironment of wound healing this neglect the negative consequences of non-healing inflammation which occur due to delay wound healing and fibrosis. Moreover, nanodots are known for outstanding photocatalyst characteristics and biocompatibility that increased the ability to reduce swelling (Yadav & Bachhuka, 2023). Additionally, nanomaterial material such as cerium oxide nanocrystals, has been documented to possess anti-inflammatory and antioxidant action based on its ability to neutralize reactive oxidative species and control cellular signalling pathway like NF- κ B signalling system that ultimately reduce the

swelling, liberation of inflammatory mediators and suppress apoptosis (Yi et al., 2024; Chen et al., 2024; Zhao et al., 2023). The decreased in reactive oxidative species and the mitigation of both *in vivo* and *in vitro* inflammation is depend on anti-inflammatory mechanism (Chen et al., 2024). The ability to scavenging free radicals of cerium oxide nanocrystals determined by their excellent structure give a high oxygen vacancy level and reversible transformation of cerium oxide particles between the Ce³⁺ and Ce⁴⁺ states is the key to neutralize the reactive oxidative species and nitrogen species such as hydrogen peroxide, superoxide radicals and hydroxyls radicals and nitric oxide radicles (Dong & Wang, 2023; Zhao et al., 2023; Chen et al., 2024). Moreover, this nanocrystals act same as natural antioxidant enzymes such as catalase, peroxidase, and superoxide dismutase, the reduced oxidative damage and decreased the synthesis of inflammatory molecules effectively by the cerium oxide nanoparticles, as a result this significantly speedup the tissue regeneration, mainly in high risk condition such as skin injury based on radiation and diabetic ulcer (Hadrick et al., 2025; Yi et al., 2024) (Table-1; Figure-1).

Promotion of Angiogenesis

The blood vessels formation is stimulating with the help of nanocrystal which play unique role to maintain the intracellular oxygen level where the small size of nanocrystals and a wide surface area Ce³⁺/Ce⁴⁺ ratio selectively convince the formation of vascular endothelial cell tube (Chen et al., 2024). Cerium oxide-based nanocrystal is activated through the complex redox reaction and signaling support, they both act as great therapeutic agent for improving the blood vessel formation in injured tissue. Moreover, the transportation of oxygen and nutrient supply is carried by the cerium oxide based nanocrystal, this supply reach to the injured site by the activation of (VEGF) vascular

endothelial growth factor by the Ref-1/APE1 signaling and the HIF-1 alpha pathway (Chen et al., 2024; Zhang et al., 2020). Furthermore, as a result, the vascular endothelial growth factor are increased which leads to improving the blood flow and nutrient supply in the newly formed tissue (Chen et al., 2024). Likewise, the blood vessel formation in injured tissue is increased and prolonged tissue regeneration at the wound site (Figure-1).

Stimulation of Cell Proliferation and Migration

The cellular proliferation and migration are crucially improved by the cerium oxide nanocrystal which is critical in tissue regeneration. The controlled development of cell cycle and cytoskeletal rearrangement is regulated by the different signaling platform where proliferation and movement of fibroblasts and keratinocytes is speedup by the nanoceria, which decreased the destruction of protein and cell membrane (Salimi & Mohammadipanah, 2021). The ability to manage the dynamic balance between Ce^{3+} and Ce^{4+} oxidative stress is a protective mechanism. Thus successfully separate the excess free radical that being affect the cellular function (Yi et al., 2024). The binding of fibroblast, neo-angiogenesis is promoted by the zinc oxide nanocrystals which is play crucial role in overall tissue regeneration due to expression of pro-angiogenic activity such as vascular endothelial growth factor by the production of reactive oxidative species

(Wiesmann et al., 2021). The development of new capillaries from previously present microvessels is characterized by the angiogenesis which is regulated by different factor like VEGF, FGF and angioproteins (Chen et al., 2024; Hassan et al., 2021).

Antioxidant Activity

The synthesis of nitric oxide played beneficial role in blood vessels formation based on the ability of nanocrystals, eNOS or MAPk pathway that accelerated endothelial cell remodelling. (Renuka et al., 2023) (Table-1). Additionally, the reactive oxidative species generation can also be maintained by the quantum dots preparations and it can easily remove microorganism from the infection site and enhanced the wound healing (Chen et al., 2024; Hong & Zhou, 2025). However, some nanocomposite like MoS_2-CeO_2 exhibit the intrinsic superoxide dismutase-mimetic action that empowered the therapeutic effectiveness by reducing the swelling and improving the movement of fibroblast, and promoting the synthesis of collagen and deposition (Dong & Wang, 2023). Similarly, varieties of nanomaterial including metallic and non-metallic nanocrystals play prominent role in wound healing through improving the cell adhesion and mitigation and regulating inflammatory activity, and improved the synthesis of collagen (Dong & Wang, 2023).

Table-1: Therapeutic Applications of Quantum Dots in Human Wound Healing

Mechanism	Key Actions of Quantum Dots	Therapeutic Implications in Wound Healing	References
Antimicrobial Activity	Generation of reactive oxygen species (ROS), membrane disruption, metabolic pathway interference, photoactivated bactericidal effects,	Eliminates a broad spectrum of pathogens and biofilms; reduces infection burden in chronic and complex wounds	Pahlevani et al., 2025; Han et al., 2025; Hu et al., 2024; Zala & Patel, 2024
Anti-inflammatory	Suppression of TNF- α , IL-6, activation of IL-10, ROS	Treat chronic inflammation, prevents	Hemdan et al., 2023; Yi et al., 2024; Zhao et al.,

	scavenging, NF- κ B pathway inhibition	fibrosis, improves wound microenvironment	2023; Dong & Wang, 2023
Angiogenesis	Minimise redox balance (Ce ³⁺ /Ce ⁴⁺), activation of VEGF via HIF-1 α and Ref-1/APE1 pathways, endothelial cell tube formation	Promote angiogenesis, oxygen and nutrient supply, supporting sustained tissue regeneration	Chen et al., 2024; Zhang et al., 2020
Cell Proliferation and Migration	Boost fibroblast and keratinocyte proliferation, cytoskeletal rearrangement, oxidative stress control	Promotes wound closure, re-epithelialization, and granulation tissue formation	Salimi & Mohammadipanah, 2021; Yi et al., 2024; Zhao et al., 2023
Antioxidant Activity	Free radical scavenging, enzyme-mimetic activity (SOD, catalase, peroxidase), collagen synthesis support	Reduces oxidative damage, accelerates tissue repair (diabetic ulcers) and radiation-induced skin injuries	Dong & Wang, 2023; Yi et al., 2024; Renuka et al., 2023; Hong & Zhou, 2025

Therapeutic Applications of QDs in Wound Healing

In Vitro Studies

Quantum dots have antimicrobial properties against wide range of pathogenic bacteria and extend a board field of research in tissue regeneration. For example the breakdown of copper oxide nanocrystals into Cu²⁺ and H₂O₂ under acidic condition are showing strong activity against bacteria (Zhang et al., 2021, Bal-Öztürk et al., 2024; Farshidfar et al., 2023). Similarly, molybdenum disulfide quantum dots were synthesized to kill the microorganism *in vitro* with the help of phototoxicity action (Yadav & Bachhuka, 2023). Additionally, the graphene oxide has been developed into the nanozymes in the form of needle have ability to rupture the cell wall of the bacteria during the production of toxic hydroxyl radicals with the help of peroxide and oxidase mimetic action. This successfully removing the resistant to many drug strains and enhanced tissue regeneration (Maddheshiya & Nara, 2022). The production of modern quantum dots for antimicrobial action provide a rising future for fighting against infection of wound, which is a significant for wound healing

(Dam et al., 2023; Yadav & Bachhuka, 2023). Additionally, different formulations of carbon dots have been produced to improve relocation, growth and fibroblast cell adhesion within scaffolds, this will lead to speed up the tissue repair and reconstruction of the main layer of epithelial tissue with grown-up dermal cells (Farshidfar et al., 2023).

In Vivo Animal Models

Based on these *in vitro* results, animal model which is included in preclinical trials have significant information about the *in vivo* effectiveness and mode of action of quantum dots in improving wound healing. For instance, silver nanocrystals incorporating into the nanodots matrices based on organic cellulose have explain the improved healing of acute wound by increasing the neovascularization, enhanced deposition of collagen, and rapid tissue reconstruction (Yadav & Bachhuka, 2023). Same as pervious, effective prevention of methicillin-resistant *S. aureus* (MRSA) has been shown by the sprayed CuO₂ nanocrystals which decreased swelling, and enhanced blood vessel formation *in vivo*. Thus healing of the wound in improving and reduce the toxicity to the system (Zhang et al., 2021). The infected mouse wound model of MRSA is

confirmed by the quantum dots antibacterial effectiveness where structure and composition like QCS-MoS₂-OFLX showed effective reduction in microorganism growth (Hu et al., 2021). The films based on PVA containing carbon nanocrystals is demonstrated over 90% effectiveness against both *Escherichia coli* and *Staphylococcus aureus* which helped to cover the wound completely within fourteen days after the application as a bandage or patch type dressing (Bal-Öztürk et al., 2024; Mou et al., 2023). Over and above that, the photosensitizer in antimicrobial photodynamic therapy is very effective shown by carbon nanocrystals, where a decrease in population of microorganism *S. aureus* was achieved and full tissue regeneration in mice wound that is contaminated (Romero et al., 2021).

Delivery Strategies for QDs

The quantum dots in tissue regeneration have advanced successful therapeutic approaches which is dependent over the accurate site specific delivery to the wound thus modern approaches are required to ensure the best bioavailability and prolonged release of agents (Kaurav et al., 2023). Sometimes, antibacterial surfactin polypeptide is used for the modification of gold nanocrystals which show excellent antimicrobial action as a nanocrystals bind to the cell wall of bacterial and accelerated their breakdown that promote the rapid tissue regeneration and wound healing in MRSA-infected wound (Yadav & Bachhuka, 2023). Similarly, many researchers preferred quaternized carbon quantum dots (qCQDs) for the treatment of both multiple infection of bacteria with the therapeutic effectiveness due to their consistent morphology (3nm) that show compatible bio-interaction (Zhao et al., 2021). Moreover, quantum dots based on carbon is considered as most important parameter to increase the cell motility and enhance the rate of wound healing process (Partovi et al., 2024). Besides, the mouse model approach is directly used in the

production of ZnO@APTES quantum dots, they enable the specific production of reactive oxidative species to damage the DNA of microorganism and is much more potent as compare to the conventional antibiotic treatment (Du et al., 2025) (Figure-1).

Combination Therapies

The quantum dots and additional therapeutic agent are constantly used in a combination to defect the biofilm formation barrier that is forbidding that often making non-healing wound refractory to traditional antimicrobial treatment (Simonetti et al., 2021). In particular, when the peroxidase like metal sulphides quantum dots is combine with the vancomycin in liposomes make it possible to activate local release the antibiotic on infrared region and increase elimination of bacteria with decrease systemic impact (Zhang et al., 2022). Likewise, antibiotic are combined onto the quantum dots surface make is possible to activate and targeting the different microbial pathway, bacterial resistance system can be easily overcome and that do not affect conventional pharmacological treatment (Llamedo et al., 2025). Likewise, the ability to treat resistant *Enterococcus* infection to vancomycin with the same dose as vancomycin is demonstrated by the nitrogen-doped carbon dots shown the possibility of applying these nanocrystals in the clinical environment as potent, alternative to the resistance-mitigation (Shaw et al., 2021). Additionally, the dual combination application is enable by the development of ZnO QDS@GO-CS hydrogels, in which the photothermal properties of graphene oxide on laser irradiation enhanced the quantum dots antimicrobial activity which shows almost fully elimination of microorganism (Raha & Ahmaruzzaman, 2022). Moreover, research on DFT-C/ZnO topical hydrogel demonstrate that the incorporation of quantum dots with dual-wavelength light irradiation (660 nm and 808 nm) significantly increase reactive oxygen

species production and photothermal energy production, representing an advanced therapeutic strategies for the

treatment of chronic wounds (Weng et al., 2022).

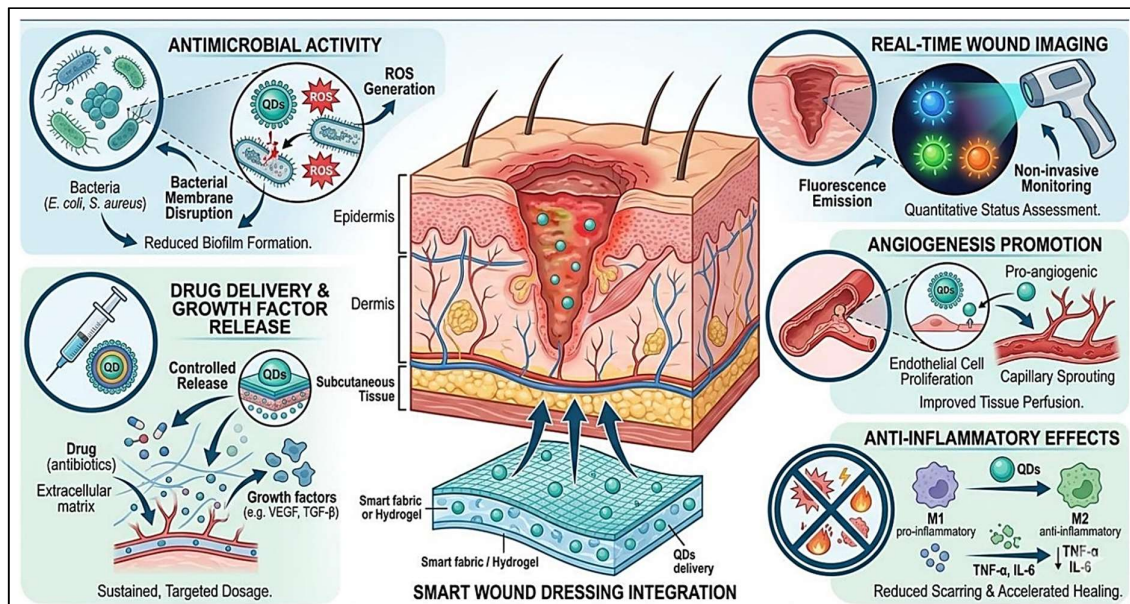


Fig-1: Therapeutic Applications and Mechanism of Quantum Dots in Wound Healing

Safety and Biocompatibility Considerations

Cytotoxicity and Genotoxicity

Although the therapeutic advantages of quantum dots is established already, but there is still anxiety about the toxicity properties of inorganic, semiconductor-based and some carbon derived nanocrystals, which can develop dose dependent side effect in the biological system (Jiang et al., 2023; Seyedjavadi et al., 2026). To counter the such problems, bottom-up design approaches are increasingly followed by the scientist which presuppose giving precedence to enable stimulus activated phytochemistry and the application of natural molecule in which host cell and pathogen are maximise by therapeutic flux (Levy et al., 2019). Furthermore, the surface modification technique is developed with the help of natural polymer such as polyethylene glycol or chitosan that provide outstanding decrease in intracellular gathering and

swelling reaction in healthy fibroblast. Beyond this, the identification of long-term metabolic clearance and the risk of heavy metal deposition persist a censorious of research so that the extensive clinical application of these nanocrystals and the patient safety do not affect. To determine the protocols related to the toxicity studies like systemic bio-distribution study and haemolysis bioassay also included, and it is necessary to determine the safety level required to change these therapeutic and diagnostic medication into the clinical trials on human beings (Gao et al., 2023; Lin et al., 2022). Additionally, green synthesis pathway that use advanced renewable are investigated. These renewable provide an excellent opportunity to decrease the toxicity of the environment and quantum dots biocompatibility is increased in wound care (Yang, 2025). Beyond the physical entrapment, commercial scalability demand stringent control of synthesis parameters including nucleation, crystallization and particle size which

ensure product stability and high quantum yield (Table-2) (Omran et al., 2021).

***In Vivo* Toxicity and Biodistribution**

In vivo safety evaluation are very crucial because the material biodegradation mode of action, systemic deposition in non-specific tissue and organs and effect of immunogenicity are not properly understood (Cai et al., 2025). It is very important that systemic study into the correlation between quantum dots mediated autophagy, oxidative pressure, and inflammatory pathway are important to determine the optimal effects of quantum dots and the effects of host of homeostatic regulation in the long term (Mohkam et al., 2023). Moreover, the development of functionalization and surface modified nanocrystals in future studies should solve the challenges associated with the maintained accumulation, biological persistence and unnecessary organ agglomeration (Bhattacharya et al., 2024). Now there is no recent standard guidelines where standard testing specification have mentioned for different cell margin, international discrepancy across current findings in *in vitro* lab studies and *in vivo* effectiveness in the body (Korah et al., 2020; Nabil & Megahed, 2023). Finally, such transitional challenges can only overcome with the help of interdisciplinary studies to modified surface chemistry (Edwin et al., 2025; Haririan et al., 2025). As well as, to promote the victorious future clinical translation of these nanocrystal that support the metabolic pathway and clearance of the structure to allow the safe integration into the physiological system of humans (Kadian et al., 2025). To address such different issue and show a drastic change towards forming standardized prolonged biocompatibility properties is needed (Table-2) (Li et al., 2025).

Degradation and Clearance

Enzymatic and hydrolytic degradation mode of action is the main protection approaches of neglecting the systemic

toxicity, significantly with non-biodegradable core shell component that have long residual retention in the spleen and liver (Li et al., 2023). To overcome such deposition problems, the existing approaches are focus on creating redox covering which enable trigger guided degradation to non-toxic molecules on subjection to wound environment (Boopathy et al., 2023). Additional, it is important to keep these nanocrystals using a fast-metabolizing dose that reduce the situation of excessive systemic deposition that complex their application in the clinical today's (Liu et al., 2024). The reduction of structure deficiency and mechanical instability should also be considered into the priority list of International Health Guidelines, as well as the excess amount of generation of nanocrystals of high purity and standardization (Shalaby et al., 2022). Likewise, the shift to mass production in the industrial level instead of laboratory level production is prevented by the substantial fluctuations in the uniformity of batch and the lack of regulatory benchmark which is already established for clinical safety. Besides these regulatory problems, scale level production development should also contemplate how to modify quantum dots during storage and transport so their properties remain constant until the clinical approaches (Zhang et al., 2023). Overall, to solve these complex challenges highlights the need of framework of the issue is needed for the quality assurance and control and regulatory guidelines to make sure the safety, reliability and reproducibility of system based on quantum dots nanocrystals (Table-2) (Barroso et al., 2020; Kurian et al., 2024).

Surface Chemistry and Toxicity Mitigation

The modification of surface ligands is vital to reducing cytotoxicity, the toxic heavy metal ions are released within the internal cell environment (Hussain et al., 2022; Sharma et al., 2025). The bio-inert coating

approaches are used in the water soluble polymer to overcome this problem where steric barrier is generated by the water soluble polymer that maintain leakage of core material and protein (Le & Kim, 2023). In addition, scientist utilize surface passivation and ligand exchange technique by using antibodies, peptides, and DNA that stabilize the core of nanocrystals. With the help of these modification the ADME profile and quantum dots cellular absorption are not precisely enhanced but also enable the development of stimuli-responsive system which support the

continuous tracking of wound parameter (Wagner et al., 2019; Zhu et al., 2019; Huang & Huang, 2024). Additionally, fluorescence signal with wound repair is correlated by the clinician and identifying therapeutic result is provided by the quantitative approaches. As well as, conversion of this approaches into clinical trials is based on strict regulatory framework established by the organization such as the FDA and EFSA, as these organization are require prolonged toxicity data and decomposition (Table-2) (Berdimurodov et al., 2025).

Table-2: Safety aspects, key concern and toxicity mitigation strategies of Quantum dots for wound healing applications

Safety Aspect	Key Concerns	Mitigation Strategies	Key References
Cytotoxicity and Genotoxicity	Dose-dependent toxicity of inorganic and semiconductor QDs; risk of heavy metal ion release and cellular damage	Bottom-up design strategies, phytochemical-assisted synthesis, PEGylation and chitosan coatings to reduce intracellular accumulation and fibroblast toxicity	Jiang et al., 2023; Seyedjavadi et al., 2026; Levy et al., 2019
Surface Modification and Polymer Integration	Intracellular swelling, inflammatory response, and poor biocompatibility	Surface functionalization using natural polymers (PEG, chitosan) and polymeric carriers for physical entrapment of nanocrystals	Gao et al., 2023; Lin et al., 2022; Li et al., 2025
<i>In Vivo</i> Toxicity and Biodistribution	Long-term tissue accumulation, immunogenicity, oxidative stress, and unclear metabolic fate	Advanced surface engineering, biodistribution studies, hemolysis assays, and interdisciplinary toxicity evaluation	Cai et al., 2025; Mohkam et al., 2023; Bhattacharya et al., 2024
Lack of Standardized Toxicity Guidelines	Discrepancies between in vitro and in vivo data; absence of unified regulatory protocols	Development of standardized international testing frameworks and long-term biocompatibility studies	Korah et al., 2020; Nabil & Megahed, 2023
Degradation and Clearance	Retention of non-biodegradable QDs in liver and spleen; delayed clearance	Redox-responsive coatings, enzymatic and hydrolytic degradation pathways, optimized dosing strategies	Li et al., 2023; Boopathy et al., 2023; Liu et al., 2024
Scale-Up and Manufacturing Safety	Batch variability, lack of regulatory benchmarks, instability during storage and transport	Controlled nucleation and crystallization, quality assurance frameworks, industrial standardization	Omran et al., 2021; Shalaby et al., 2022; Zhang et al., 2023
Surface Chemistry and Toxicity Mitigation	Heavy metal leakage due to improper ligand functionalization	Bio-inert coatings, ligand exchange with biomolecules (peptides, antibodies, DNA), surface passivation	Hussain et al., 2022; Wagner et al., 2019; Zhu et al., 2019
Clinical Translation and Regulatory Oversight	Requirement for prolonged toxicity data and degradation profiling	Compliance with regulatory frameworks (FDA, EFSA), long-term ADME and clearance studies	Berdimurodov et al., 2025; Huang & Huang, 2024

Current Challenges and Future Perspectives

Standardisation of QD Synthesis

The conversion of laboratory based nanocrystals into clinical trial approaches affected by the absence of systematized synthesis method as well as batch to batch difference create difficulties to establish dependent safety standard (Mohkam et al., 2023). To address these challenges, green synthesis approaches using intermediate based on plant are offers excellent pathway to improving the biocompatibility of material during manage the high cost and environmental problems related to the conventional material synthesis (Hussain et al., 2024). Furthermore, the microfluidic related production platform could significantly improve the particle size controlled and structural uniformity which reduce the regulatory approval and therapeutic standard. Moreover, nanocrystal based on protein modification are developed as site specific drug delivery system, with the help of this targeted and individual treatment for complicated wound can be stimulate (Sharda et al., 2023). Thinking about the future, method like real time monitoring including humidity, sensor for pH and inflammatory response will surely incorporate into the clinical trials to dynamically adjust therapeutic interventions based on the evolving physiological state of the wound (Hamed et al., 2023). In the final analysis of accurate clinical result, standard preclinical model are required to construct for the prolonged assessment of reaction between these multiple functional nanocrystals and human wound (Li et al., 2023). Further research must fill the gap between preclinical outcome and clinical application by the development of advanced translational framework that work for the physiological heterogeneity of human wound (Fadilah et al., 2023).

Long-term Biocompatibility and Clinical Translation

The effective clinical adaptation depends on establishing ideal preclinical models that reflect the complexity of chronic and non-healing wound to fill the gap between initial discovery and human therapeutic trials (Li et al., 2023). With this aim, future research must shift towards the development of personalized, multifunctional bio-scaffolds that account for the inherent biological heterogeneity of diverse patient pathologies. Furthermore, the adaptation of large animal skin models is essential to better replicate human wound healing kinetics and ensure a more accurate assessment of degradation and integration (Wang et al., 2022). In addition to this framework, fostering interdisciplinary collaborations between material scientist, toxicologist and clinicians will be paramount to addressing the translational hurdles of long-time systemic biocompatibility and regulatory compliance (Lo et al., 2023). These efforts should be complemented by the integration of smart delivery system like stimuli-responsive hydrogels which offer superior control over the spatial and temporal release of therapeutic agents to optimize healing trajectories (Abdelhakim & Ogawa, 2025).

Regulatory Landscape

Navigating the recent regulatory aspects necessitates the development of comprehensive assessment framework that directly address the different toxicological profiles of semiconductor-based versus carbon-based quantum dots. This needs a bifurcated safety testing protocol that account for the potential bioaccumulation of heavy metal cores in the earlier process, for the establishment of degradation kinetics and clearance pathway of the system (Bielska & Miłowska, 2025). This types of regulatory system must also prioritize the establishment of rigorous, standardized toxicological assays to ensure that the long-term biological performance of these nanomaterials remain consistent

across diverse clinical and environmental contexts (Farokhi et al., 2022). Furthermore, the monitoring of post market surveillance nanomaterial integrated wound dressing is likely made simple the development of dedicated registry and the collection of long-term information, ultimately bridging the translational gap between laboratory innovation and standard of care clinical practices (Wang et al., 2024). Likewise, the incorporation of responsive drug delivery modules like those sensitive to protease activity or oxygenation could facilitate a transition towards truly adaptive wound management strategies

Integration with Smart Wound Dressings

The integration of quantum dots with advanced wound dressing enables the transformation of passive protective barriers into active effective diagnostic interfaces capable of continuous physiological monitoring. By the addition of these biosensor within various types of dressing the biological alternation in the real time allowing for the precise, stimuli-responsive release of therapeutic agent to mitigate infection and accelerate tissue regeneration (Marjanović et al., 2025; Nasra et al., 2024). Additionally, utilizing carbon-based nanocomposite hydrogel which address superior stability in such aqueous conditions, offers a robust framework for embedding these responsive interfaces. Such advanced systems further enable the creation of remote intervention strategies where mobile terminals allow clinicians to adjust drug delivery parameters dynamically based on the processed microenvironmental data (Zhang et al., 2021).

Personalized Wound Care

The shift toward precision dermatology is driving the development of personalized, self-adaptive wound care platform tailored to the unique metabolic and inflammatory

profiles of individual wound (Zhao et al., 2025). Multiplexed biosensors employ in real-time monitoring of key biomarkers, supporting autonomous and environmental-specific therapeutic delivery (Khumngern & Jeerapan, 2024; Liu & Ge, 2025). Combination of these data with AI allows continuous biomarker tracking, predictive modeling and proactive optimization of treatment while reducing manual interventions (Lu et al., 2022; Meng et al., 2024). Integration with wearable biosensing and modular microneedle systems. These platforms facilitate holistic wound assessment and precise, localized delivery of therapeutics and connecting advanced diagnostics with targeted clinical management (Palani et al., 2025; Tao et al., 2025).

Conclusion

The integration of quantum dots nanocrystals into the wound healing architectures is acknowledged as the most unique transformative shift toward advancement, autonomous and patient-centric therapeutic treatment. By synthesizing high-resolution diagnostic sensing with targeted nanotherapeutic delivery, these systems address the inherent limitation of conventional wound management through real-time feedback loops and optimized tissue regeneration strategies (Li et al., 2023; Prakashan et al., 2024). As these innovation transition from laboratory to clinical environment the successful standardisation of biocompatibility protocol and the refinement of manufacturing precision will be essential to ensure scalable, safe and effective patient outcomes. In a long term, the synergy between AI-driven predictive analysis and nanotechnology will faster the development of precision-engineered dressing capable of decreasing healthcare load and improving long-term recovery rates throughout diverse clinical populations (Guan et al., 2025). The researcher futuristic efforts must now focus on filling the gap between theoretical

laboratory efficacy and rigorous demand of regulatory compliance to facilitate widespread clinical translation. Moreover, establishing standardized longitudinal studies is imperative to evaluate the long-term systemic impact and environmental compatibility of quantum dot-based materials (Wang et al., 2024). Additional of AI into these diagnostic workflow will again streamline the assessment of complex biomarker data and personalized therapeutic implementation (Vo & Trinh, 2025). Furthermore, the application of computational biology and machine-learning framework remains critical to elucidating the complex interactions between these nanomaterials and cellular environments. Thus, ensuring the development of inherently non-toxic, tailor-made therapeutic (Renuka et al., 2023).

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