

## EMERGING STRATEGIES IN CHRONIC WOUND CARE: BIOFILM-FOCUSED TREATMENTS, NANOTECHNOLOGY-ENHANCED DRESSINGS, AND THERANOSTIC APPROACHES

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Article Received on 26 Sept. 2025,  
Article Revised on 16 October 2025,  
Article Published on 16 October 2025,  
<https://doi.org/10.5281/zenodo.17472884>

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**How to cite this Article:** Md. Tanvir<sup>1</sup>, Atul Kumar Prasad<sup>2</sup>, Tichakunda Xavier Mharazanye<sup>3</sup>, Maniket<sup>4</sup>, Abu Sufiyan Ansari<sup>5</sup>, Md. Nazir Hussain<sup>6</sup>, Md. Shamim Ahmad<sup>7\*</sup> (2025). EMERGING STRATEGIES IN CHRONIC WOUND CARE: BIOFILM-FOCUSED TREATMENTS, NANOTECHNOLOGY-ENHANCED DRESSINGS, AND THERANOSTIC APPROACHES World Journal of Pharmaceutical Research, 14(20), 252–274.

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### ABSTRACT

**Background**-Chronic wounds cost billions of dollars a year, making them a significant and expanding public health concern. The existence of bacterial biofilms—structured colonies of microorganisms coated in a protective matrix—makes their control considerably more difficult. Due to the high levels of resistance these biofilms impart to host immune responses and antimicrobial drugs, traditional treatments are usually unsuccessful and a state of non-healing is maintained.

**Purpose**-The key role that biofilms play in the pathophysiology of chronic wounds is examined in this review, along with the shortcomings of the anti-biofilm techniques that are currently in use. It also looks at the novel ways that theranostic and nanotechnology-based dressings may be used to address these issues. **Methods**-To clarify the workings of biofilm resistance, the effectiveness of conventional anti-biofilm agents, and the advancement of advanced wound care technologies, such as integrated diagnostic-therapeutic platforms and nanoparticle systems, a thorough review of the literature was carried out.

**Results**-Most chronic wound infections are linked to biofilms, which promote inflammation and hinder the healing process. Despite having antimicrobial qualities, well-known anti-biofilm substances like silver & iodine are limited in their effectiveness by problems including cytotoxicity, resistance to microbial agents, and insufficient penetration. A possible

substitute is provided by dressings based on nanoparticles, which allow for more effective medication administration, improved biofilm matrix penetration, and less adverse effects due to regulated release. Theranostic dressings also mark a paradigm change by enabling focused therapeutic action in conjunction with real-time wound environment monitoring. **Conclusion-** The treatment of chronic wounds linked to biofilms might be completely transformed by advanced wound dressings, especially those that make use of nanotechnology and theranostic properties. To incorporate these creative solutions into routine care procedures, future research must concentrate on removing translational obstacles such as long-term safety assessment, economical production, and validation through extensive clinical trials.

**KEYWORDS:** -Chronic wounds, Biofilms, Nanoparticle-based dressings, Theranostic wound care, Advanced wound management.

## INTRODUCTION

### ANTIBIOFILMBASEDWOUND DRESSINGS

With an anticipated yearly cost to Medicare of over \$30 billion, wounds that persist are an impact on both the economy and public health.<sup>[1]</sup> They provide a challenge to doctors since they are often resistant to standard of care (SOC) therapy.<sup>[2]</sup> Biofilm elimination is a new weapon in the clinician's toolbox in the fight against chronic wounds, since the significance of biofilms in preserving a harmful chronic wound microenvironment is becoming more wellrecognised. Patients with chronic wounds will benefit from treatment strategies that are guided by the amount of evidence supporting antibiofilm agents' capacity to remove biofilm and promote wound healing. Since it is now known that bacteria may form biofilms it has been discovered that biofilms can contribute to the pathogenesis of a number of illnesses, including wounds. Microorganisms naturally exist in two primary states in all environments: the planktonic state, which allows them to live freely, and the attached or sessile condition.<sup>[3]</sup> In vivo, biofilms are made up of several tiny, closely spaced clusters of microorganisms that are separated by host tissue and firmly adhere to one another as well as adjacent surfaces.<sup>[3]</sup> Biofilms are made up of just 5–25% bacteria and 75–95% extracellular polymeric substance (EPS), which can be self-synthesised or modified from host extracellular matrix components.<sup>[4]</sup> Planktonic bacteria, the conventional focus of microbiology study, are free-floating microorganisms in an aquatic environment as opposed to biofilms. Due to biofilms' well-known resistance to medicines and host defences, planktonic bacteria switching to a biofilm lifestyle might be harmful to a host.<sup>[5]</sup> When endogenous, foreign, or widely

distributed microorganisms adhere to the wound surface and multiply, wound biofilm development can start.<sup>[6]</sup> The host immune system can combat the development of free-floating or planktonic bacteria in normal conditions.<sup>[6-8]</sup> But when bacterial growth is unchecked or in immunocompromised patients, the bacteria proliferate and form a complex community that is shielded by a matrix of extracellular polymeric substances (EPS) called the biofilm matrix.<sup>[9-11]</sup> The Centres for Disease Control and Prevention (CDC) estimates that biofilms account for more than 65% of all chronic bacterial infections, while the National Institutes of Health (NIH) estimates that biofilms account for about 80% of microbial infections.<sup>[12,13]</sup> Biofilm is medically recognised as a major cause of chronicity. The majority of chronic wounds have widespread polymicrobial biofilms. The EPS-encased mixed-species bacterial communities are naturally resistant to antimicrobials, antiseptics, and antibiotics.<sup>[14-17]</sup> In addition to displaying a variety of defence mechanisms against host immunological responses and external stressors, biofilms also secrete inflammatory mediators that can obstruct the body's normal wound healing cascade while maintaining the biofilm. According to research, the barrier known as EPS, a structurally reinforced complex of interconnected polysaccharide polymers connected with metallic ions and including host and microbial proteins and nucleic acids, must be broken down in order to treat a biofilm.<sup>[18]</sup> There is growing recognition of the part biofilms play in the pathogenesis of chronic wounds. Targeting biofilms is still a sensible strategy to assist clinicians in treating patients with chronic wounds, despite the paucity of data directly proving the advantages of biofilm elimination on wound healing. Numerous products with alleged anti-biofilm properties are on the market. Here, we go over the mechanism of action and clinical importance of the anti-biofilm treatments that are currently on the market, with an emphasis on the degree of evidence supporting their effectiveness in eliminating biofilms and promoting favourable wound healing outcomes.<sup>[19]</sup>

## VARIOUS MARKETED FORMULATIONS

**Table 1: Marketed Anti-Biofilm Wound Dressings: Active Ingredients, Manufacturers.**

Product Name	Active Ingredient	Manufacturer	References
Silvercel	Silver	Smith & Nephew	[20]
Acticoat	Silver Nanoparticles	Kendall	[21]
Biopatch	Gentamicin	Ethicon	[22]
Mepilex	Polyurethane Foam	Mölnlycke Health Care	[20]
Tegasorb	Honey	Medline Industries	[21]
Iodosorb	Iodine	Smith & Nephew	[22]
Aquacel	Hydrofiber	ConvaTec	[20]

Biatain	Hydrocellulose	Coloplast	[21]
Hydrosorb	Hydrocolloid	Hartmann	[22]
DermaTech	Collagen	De Royal Industries	[20]
Prontosan	Betaine/Polyhexanide	B Braun	[23]
Kerlix	Polyhexamethylene Biguanide	Cardinal Health	[24]

## DISADVANTAGES OF ANTIBIOFILM BASED WOUND DRESSINGS

Although advantageous, the use of sophisticated wound dressings has a number of hazards and difficulties. The possibility of infection is one of the main worries since dressings can harbour germs and cause illness if they are not changed on a regular basis.<sup>[25]</sup> Additionally, granulation tissue, which is essential for wound healing, may be lost as a result of repeated dressing changes.<sup>[26]</sup> Caretakers who lack skill may also apply it incorrectly, which might injure the skin around the wound.<sup>[27]</sup> Furthermore, sophisticated dressings may be more costly than conventional alternatives, which would put further strain on finances.<sup>[28]</sup> Because certain patients may be sensitive to the active substances in these dressings, there is also a chance of allergic responses.<sup>[29]</sup> The long-term efficacy of antimicrobial dressings can be diminished by overuse, which can lead to microbial resistance.<sup>[30]</sup> The limited effectiveness of these dressings—not all of them are appropriate for all kinds of wounds—is another problem.<sup>[31]</sup> Certain dressings could not adequately control wound exudate, which might result in maceration and exacerbate the wound's state.<sup>[32]</sup> Since some of the dressings' substances may make the patient uncomfortable or result in negative responses, skin irritation is also a problem.<sup>[33]</sup> Because these dressings might contribute to waste and pollution, it is important to consider the environmental effect of their manufacturing and disposal.<sup>[34]</sup> Another problem is patient compliance; some people could find it difficult to follow the suggested dressing change schedule, which could have an impact on healing.<sup>[35]</sup> Furthermore, many sophisticated dressings require particular storage conditions in order to remain effective, which may not always be possible in all medical environments.<sup>[36]</sup> Additionally, in certain places, the supply of these speciality dressings may be restricted, which might impact their accessibility, patients.<sup>[37]</sup> It may not always be possible for all healthcare practitioners to have the necessary training and expertise to apply these dressings correctly.<sup>[38]</sup> Last but not least, depending too much on sophisticated dressings runs the danger of creating a false feeling of security, which might cause one to overlook other crucial facets of wound care, such as infection control or general wound management.<sup>[38]</sup>

**Table 2: Risks and Challenges of Advanced Wound Dressings.**

Risk/Challenge	Description	References
<b>Risk of Infection</b>	Dressings can become a source of bacterial growth and infection if not changed regularly.	[25]
<b>Loss of Granulation Tissue</b>	Frequent dressing changes may lead to the loss of granulation tissue, crucial for wound healing.	[26]
<b>Peri wound Damage</b>	Improper application by an inexperienced caregiver can harm the skin surrounding the wound.	[27]
<b>Cost</b>	Advanced dressings can be more expensive compared to traditional options, adding a financial burden.	[28]
<b>Allergic Reactions</b>	Some patients may be sensitive to the active ingredients in these dressings.	[29]
<b>Microbial Resistance</b>	Overuse of antimicrobial dressings can contribute to microbial resistance, reducing their long-term effectiveness.	[30]
<b>Limited Efficacy</b>	Not all dressings are suitable for every type of wound.	[31]
<b>Exudate Management</b>	Some dressings may fail to manage wound exudate properly, leading to maceration.	[32]
<b>Skin Irritation</b>	Certain ingredients in the dressings can cause discomfort or adverse reactions for the patient.	[33]
<b>Environmental Impact</b>	The production and disposal of these dressings can contribute to waste and pollution.	[34]
<b>Patient Compliance</b>	Some individuals may struggle to adhere to their recommended dressing change schedule, potentially affecting healing.	[35]
<b>Storage Requirements</b>	Some advanced dressings have specific storage requirements to maintain their efficacy.	[36]
<b>Limited Availability</b>	The availability of specialized dressings can be limited in certain areas, affecting accessibility.	[37]
<b>Application Technique</b>	Proper application requires adequate training and skill, which may not always be accessible to all health care providers.	[38]
<b>False Sense of Security</b>	Over-reliance on advanced dressings may lead to neglect of other essential aspects of wound care.	[38]

### CHALLENGES IN ANTIBIOFILM BASED WOUND DRESSINGS RESEARCH

There is an unmet need since there aren't enough high-quality research on the advantages of biofilm removal and how it relates to wound healing in individuals with chronic wounds. The reader should be aware that many studies on biofilm used in vitro or animal models, which have inherent limitations in terms of their clinical application and generalisability. Despite the fact that in vitro techniques have been widely employed to investigate. Compared to their in vivo counterparts, biofilms in vitro are distinct.<sup>[39]</sup> Large, single 3-D structures and traditional "mushroom-like" multicellular structures are formed by in vitro biofilms.<sup>[39]</sup> In contrast, in vivo biofilms are much smaller in diameter, do not have mushroom-like structures, and form several tiny aggregates that are separated by host tissue as opposed to a single big structure.<sup>[39]</sup> Furthermore, it is known that biofilm aggregates can grow without

adhering to a surface, and because these populations need abiotic surfaces, they are not included in traditional in vitro biofilm models.<sup>[39]</sup> Most significantly, the complex milieu of a human skin wound—that is, the host immune response and metabolic variables that influence the phenotypic and genotypic profiles of the invasive bacteria—is not adequately replicated by in vitro models.<sup>[39]</sup> Although animal models offer a more precise medium for studying biofilms, they are constrained by clear physiologic differences between humans and animals, such as the fact that human and mouse physiology differ in sensitivity to lipopolysaccharide and that contraction is the primary mechanism of wound healing in mice.<sup>[40]</sup> It is nevertheless true that there isn't a single, best in vivo model, and each one may offer solutions to distinct, targeted issues.<sup>[40]</sup> To make it easier for researchers and physicians to compare their findings and inform treatment plans for patients with wounds, standardised biofilm models that more closely mimic the human wound milieu are required.<sup>[40]</sup> Furthermore, there is no gold standard for measuring biofilms; nevertheless, confocal laser scanning microscopy (CLSM) in conjunction with fluorescent in-situ hybridisation (FISH) may be the most effective technique currently in use.<sup>[41]</sup> Although it is also often employed, scanning electron microscopy (SEM) has limitations due to its shallow depth penetration and other issues.<sup>[41]</sup> Numerous research, some of which are covered in this article, do not use imaging to quantify biofilm architecture directly. The plating of recoverable bacteria (PRB) from the surface or wound model is employed as a surrogate sign of antibiofilm activity, although biofilm production is frequently expected but not assessed prior to treatment. High-powered imaging tools should ideally be able to directly see the biofilm architecture both before and after treatment. Two good, recent studies<sup>[41,42]</sup> contain the several biofilm models, measuring methods, and critiques of them. Reducing, eliminating, or avoiding biofilms is still a sensible strategy to aid doctors in the healing of chronic wounds in spite of these important drawbacks. Evidence from in vitro and animal models is useful in screening for antibiofilm efficacy and should be taken into account when selecting therapies, according to recent consensus guidelines for biofilm research.<sup>[43]</sup> Additionally, the selection of such therapies should be based on their evidence of promoting positive wound healing outcomes in the absence of RCT-level data.<sup>[43]</sup> Therefore, the purpose of this study is to examine the mechanism of action and therapeutic relevance of anti-biofilm medicines that are already on the market, with an emphasis on the degree of evidence supporting their effectiveness in rupturing biofilms and enhancing wound healing results.<sup>[19]</sup>



## CHALLENGES IN ANTIBIOFILM-BASED WOUND DRESSINGS

Although they may have advantages, antibiofilm-based wound dressings have drawbacks. One significant problem is biofilm resistance, which can make it difficult to eradicate biofilms entirely and complicate therapy since they can be extremely resistant to antimicrobial treatments.<sup>[44]</sup> Because these treatments are frequently costly, some patients may not be able to use them, particularly those in settings with limited resources.<sup>[45]</sup> Furthermore, applying these dressings calls for specialised knowledge and expertise that isn't always available, which might result in incorrect usage.<sup>[46]</sup> Another issue is patient compliance, which might affect the efficacy of therapy since it can be challenging to ensure adherence to the dressing change schedule.<sup>[47]</sup> The active chemicals in these dressings may also cause allergic responses in certain individuals, which might lead to pain or other health problems.<sup>[34]</sup> Because different types of wounds respond differently to different dressings, antibiofilm dressings may not be as successful as they could be.<sup>[37]</sup> Another issue with these dressings is their potential to contribute to waste and contamination during manufacture and disposal.<sup>[34]</sup> Furthermore, certain dressings could not adequately control wound exudate, which could result in maceration and exacerbate the wound's state.<sup>[48]</sup> Periwound injury, which damages the skin around the wound and makes recovery more difficult, can also result from improper application by unskilled caregivers.<sup>[49]</sup> In order to preserve their effectiveness, these dressings frequently have certain storage needs, which aren't always possible in all medical environments.<sup>[50]</sup> Antimicrobial treatments that are used excessively may eventually lose their efficacy due to microbial resistance.<sup>[51]</sup> Lastly, although though these dressings are intended to aid in wound healing, some patients may find them uncomfortable or irritating, which might make it more difficult for them to accept and utilize them.<sup>[52]</sup> Relying too much on these coverings might also give rise to a false sense of security, which could cause one to overlook other crucial facets of wound care, such infection control and appropriate wound management.<sup>[53]</sup>

## HOW TO OVERCOME CHALLENGES IN ANTIBIOFILM BASED WOUND DRESSINGS

Several tactics must be used in order to overcome the difficulties with antibiofilm-based wound dressings. Using sophisticated drug delivery systems is one efficient strategy that guarantees the efficient and targeted administration of antibiotics, minimizing the possibility of adverse effects.<sup>[54]</sup> By guaranteeing that the dressings are applied correctly, proper training for healthcare professionals is also crucial since it can reduce periwound damage and enhance

overall patient outcomes.<sup>[54,55]</sup> Furthermore, teaching patients the value of following the dressing change schedule can greatly increase patient compliance and boost treatment effectiveness.<sup>[56]</sup> The cost issue may be resolved by creating affordable dressings and looking into insurance coverage alternatives, which would enable a larger group of patients to have access to these cutting-edge dressings.<sup>[56]</sup> Additionally, allergy testing prior to the use of dressings containing possible allergens might assist enhance patient safety and avoid allergic responses.<sup>[54,56]</sup> Combination therapy, which target several facets of wound care and include topical antimicrobials and mechanical debridement, have demonstrated potential in improving treatment effectiveness.<sup>[55]</sup> By creating eco-friendly dressings and encouraging appropriate disposal techniques, environmental issues can be lessened and the total environmental effect of these items can be decreased.<sup>[54]</sup> Frequent monitoring of dressing performance and wound development is essential because it enables prompt treatments and early identification of any problems.<sup>[54,56]</sup> To develop new materials and formulations that are more efficient and less likely to develop resistance, research and development expenditures must be sustained.<sup>[55]</sup> Last but not least, adjusting dressings to each patient's specific requirements according to the kind and extent of their wounds can enhance healing results and provide individualized treatment.<sup>[54]</sup>

## **TYPES OF NATURAL AND SYNTHETIC ANTIBIOFILM AGENTS AND THEIR USES IN DIFFERENT WOUND DRESSINGS**

Plant phytochemicals such as oil from tea tree, garlic, and aloe vera, microorganisms consisting of *Pseudomonas aeruginosa*, amphibian antimicrobial peptides like magainins, microbe-produced enzymes such as lysozyme along with proteases, as well synthetic antimicrobial peptides made with solid-phase peptide synthesis are examples of natural antibiofilm agents. To prevent biofilm development and encourage wound healing, these substances are added to hydrogel & alginate dressings. Chronic wound dressings employ furanones and their analogues to break down bacterial communication and stop the production of biofilms, whereas alginate lyases are employed to break down alginate in biofilms. Silver along with zinc oxide nanoparticles have strong antibacterial properties, qualities, utilised in hydrogel films and foam dressings to promote wound healing and prevent biofilms.<sup>[57–60]</sup>



**Table 3: Types of Natural and Synthetic Antibiofilm Agents and Their Uses in Different Wound Dressings.**

Type	Agent	Use in Wound Dressings	References
Natural	Phytochemicals (e.g., teatree oil, garlic, aloe vera)	Used in hydrogel films and gauze dressings	[57]
Natural	Biosurfactants (e.g., rhamnolipids)	Applied in textile-based Dressings	[57]
Natural	Antimicrobial Peptides (e.g., magainins, defensins)	Incorporated in hydrogel and Foam dressings	[57]
Natural	Microbial Enzymes (e.g., proteases, glycosidases)	Used in enzymatic debridement Dressings	[58]
Synthetic	Synthetic Antimicrobial Peptides	Used in hydrogel and alginate Dressings	[59]
Synthetic	Macromolecular Agents (e.g., polymers, nanomaterials)	Incorporated in film and foam Dressings	[59]
Synthetic	Chelating Agents (e.g., EDTA)	Used in hydrogel and alginate Dressings	[59]
Synthetic	Quaternary Ammonium Compounds	Applied in gauze and foam Dressings	[59]
Synthetic	Activated Carbon	Used in hydrogel films	[60]
Synthetic	Silver	Incorporated in foam, hydrogel, and alginate dressings	[59]
Synthetic	Honey	Used in honey-impregnated dressings	[59]

### NANOCARRIERS MEDIATED WOUND DRESSINGS

Nanoparticles as therapeutic agent delivery systems for antimicrobial therapy in wound healing. New approaches to enhance the wound-healing process are being made possible by nanotechnology, namely the production of NPs. Numerous studies have demonstrated that wound dressings using biocompatible nanoparticles (NPs) that can deliver therapeutic agents over an extended period of time have become popular platforms and methods for treating skin wounds.<sup>[61]</sup> For instance, NPs enable the delivery and release of antimicrobial medications with relatively low solubility to the site of harm.<sup>[62,63]</sup> Because NPs in dressings for wounds may directly administer lower drug dosages and distribute them into the site of injury with higher effectiveness, this technique reduces the adverse effects of medications. Up till now, a wide variety of NPs containing therapeutic agents—primarily polymeric, liposome, lipid, and inorganic NPs—have been added to wound dressings and demonstrated the capacity to treat infections caused by bacteria and encourage wound healing.<sup>[64]</sup> Table 4 contains a list of recent studies using these NPs.

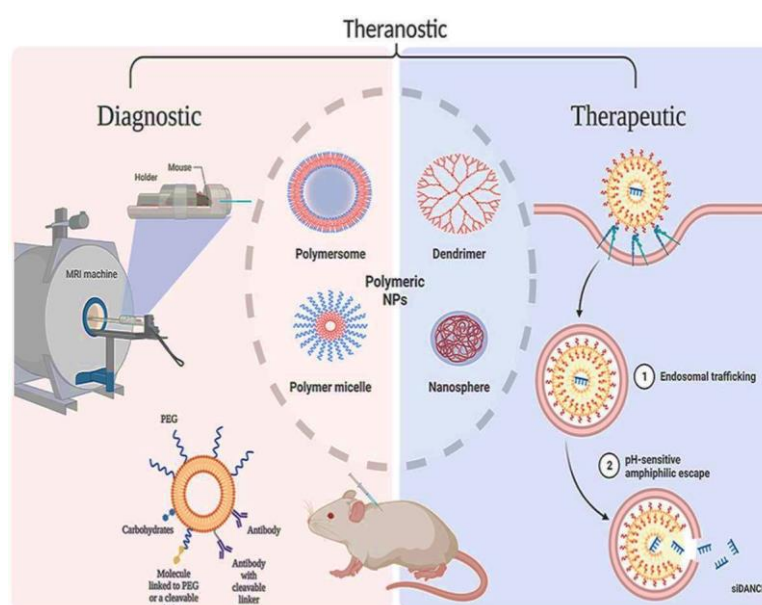
**Table 4: Nanoparticles as delivery of the therapeutic agents for wound healing.**

Type of Carrier	Materials	Drug	Size (nm)	Wound dressing	Bacteria	Animal Models	References
Polymeric nanoparticles	Polycaprolactone nanoparticles	Vancomycin	35.93 ± 3.00	PVA-alginate gel	Saureus	-	[65]
Polymeric nanoparticles	Chitosan	Insulin	-	Electrospun poly (ε-caprolactone) /Collagen	-	Cutaneous wound in rats	[66]
Polymeric nanoparticles	poly (lactic- coglycolic acid)-polyethylenimine nanoparticles	Clindamycin	126 ± 33	-	MRSA	MRSA- infected wounds in mice	[67]
Polymeric nanoparticles	Polymeric nanoparticles	Simvastatin	268.4±2.6	Carbopol ® polymers	-	Full thickness, excisional skin Wounds in rats	[68]
Polymeric nanoparticles	Molecularly imprinted polymer nanoparticles	Gentamicin	-	Polyvinyl alcohol/gelatin nanofiber	-	Wound in rats	[69]
Polymeric nanoparticles	Poly(lactic -coglycolic acid) nanoparticles	Polyethylenimine/ diazeniumdiolate	252 ± 45	-	MRSA biofilm	MRSA biofilm infected wounds in mice	[70]
Polymeric nanoparticles		Vancomycin	~ 150	-	Saureus and MRSA	-	[71]
Polymeric nanoparticles		Azithromycin	165- 217	-	MRSA	-	[72]
Polymeric nanoparticles	Liposomes	Gentamicin	126.2 ± 16.03	Chitosan nanofiber meshes	Saureus, E.coli, Paeruginosa	-	[73]
Polymeric nanoparticles		Collagen mimetic peptide tethered vancomycin	~150	Collagen- based scaffolds	MRSA	MRSA infected wound in mice	[74]
Polymeric nanoparticles	Solid lipid nanoparticles	Silver sulfadiazine	295.5 ± 15.4	Chitosan gel	Paeruginosa PA01	Full thickness burn wounds in rats	[75]
Lipid nanoparticles	Nanostructured lipid carriers	Eucalyptus or rosemary essential oils	50-60		Saureus and Streptococcus pyogenes	burn model in rats	[76]
Lipid nanoparticles	Solid lipid nanoparticles	Antimicrobial peptide and serpin	214.9 ± 2.2/ 214.9 ± 2.2	-	Saureus and E.coli	-	[77]
Inorganic nanoparticles	Silica nanoparticles	Curcumin	36-40	-	Planktonic and bio film forms of Paeruginosa, Saureus	-	[78]
Inorganic nanoparticles	Mesoporous silica nanoparticles	Zn and ciprofloxacin hydrochloride	100 ± 20	Polycaprolactone electrospun fibers.	E.coli	E.coli infected wound in rats	[79]
Inorganic nanoparticles	Silica nanoparticles	Gentamicin and rifamycin	500	Collagen hydrogels	S. aureus and P. aeruginosa	-	[80]
Inorganic nanoparticles	AuNPs	AMP esculetin 1a, Esc (1-21)	14	-	P. aeruginosa and biofilm	-	[81]
Inorganic nanoparticles	AgNPs and AuNPs	Ceftriaxone	10-50, 20-40	-	E.coli	-	[82]

## THERANOSTIC WOUND DRESSINGS

Theranostic coverings for wounds: Here, it is suggested that technological advancement can be derived from the accumulated, but frequently disregarded, knowledge of the interactions between biochemical factors, cells, and the surface of biomaterials to create a platform for novel theranostics—that is, devices that, in contrast to conventional dressings, only protect and keep the wound wet will allow it to heal and produce readable cellular and molecular indicators.<sup>[83]</sup> Theranostics combines diagnosis and therapy. Precision medicine and illness management have been transformed by the discovery and development of theranostic

nanoparticles. These materials' nanoscale location makes it possible to monitor the therapeutic effects of clinically utilised nano-formulated medications and make early diagnoses of chronic disorders. These nanoparticles are intended to be multipurpose nanosystems that offer both therapeutic and diagnostic properties at the same time. Compared to other nanosystems, theranostic nanoparticles provide several benefits. Sustained/controlled/sustained release, enhanced pharmacokinetics and biodistribution, targeted drug delivery to the target tissue, imaging, multimodal therapy and therapeutic response prediction, concurrent reporting of disease biochemical and morphological features, minimising systemic toxicity, and lowering the effective dose are the most important functions of theranosticnanosystems.<sup>[84–86]</sup>



**Figure 1: A novel strategy for cancer treatment and diagnostics is the use of theranostic polymeric nanoparticles.**<sup>[92]</sup>

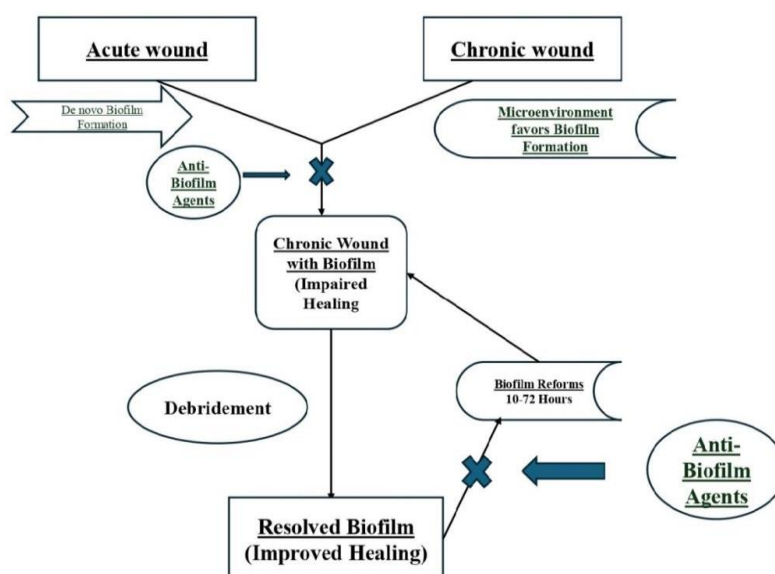
### Classification of the ranosticnano particles

In order to eliminate or resect the lesion, type I is usually employed in conjunction with surgery. They are either equipped with imaging agents like a fluorophore (class II) or have endogenous signalling nature like MRI (class I). An aggregation of nanoparticles is used in the diagnostic function to collect information regarding the kind, location, and boundary of tumours. Surgical resection is part of the therapy. Nonspecific accumulation, poor biological dispersion, and toxicity from inappropriate environmental degradation are the main drawbacks of Type I nanoparticles. Since each modal may be used for a separate procedure's purpose, resection using Type 1 multi-modal nanoparticles is preferred.<sup>[87,88]</sup> Type II is used

to transport chemicals to the intended locations and is less intrusive. Specific delivery of medicinal medicines is made possible by the targeted accumulation of nanoparticles. Type two theranostic nanoparticles include liposomes, micelles, and other drug-carrying vehicles. The particular collection of nanoparticles employed for in vivo assessment of tissue condition allows many pharmacological agents to load into each individual particle. Type III nanoparticles fall into two categories. Class I labelled nanoparticles can release and image simultaneously, and they are employed to deliver therapeutic medicines. One should take into account the difficulty of limited loading capacity and outside functionalization. However, given the variety of deliverable agents and targeting moieties, simultaneous imaging and delivery appear promise.<sup>[89,90]</sup> Stimulus-responsive nanoparticles (Class II of Type III) react to magnetic fields or infrared radiation. Thermal ablative treatment, for instance, uses nanoshells and nanorods that efficiently transform light into heat energy and have absorption maxima in infrared.<sup>[91]</sup>

#### **ROLE OF ANTIBIOFILM AGENTS IN WOUND DRESSINGS**

Because they stop and break up biofilms, which are populations of resistant bacteria, antibiofilm agents are crucial in wound dressings. They stop germs from adhering to the wound surface in the first place, which stops biofilms from forming. Additionally, they degrade pre-existing biofilms, increasing their vulnerability to antimicrobial therapies. Antibiofilm agents increase the penetration of antimicrobial agents by breaking up biofilms, lowering the risk of infection by avoiding infections linked to biofilms. Additionally, they facilitate healing by reducing infection and biofilm development, which improves the environment for wound healing.<sup>[94,95]</sup>



**Figure 2: Antibiofilm agents' function in a wound care paradigm.** In order to improve wound healing, antibiofilm agents can be used to stop biofilm development or to stop reformation following debridement. It is crucial to remember that addressing biofilm alone might not be enough to address poor wound healing; additional variables, such as malnutrition or chronic venous insufficiency, may need to be addressed.<sup>[93]</sup>

## FUTURE PROSPECTIVES

Significant progress in the treatment of chronic wounds is anticipated as a result of new materials, improved therapeutic strategies, and developing technology. Improved wound care results are anticipated from developments in host-defense peptides (HDPs), antibiofilm agents, and novel nanoparticle-based wound dressings. These substances seek to enhance the effectiveness of antibiotics by upsetting the stability of biofilms. Therapy will be precise and regulated thanks to stimuli-responsive nanoparticles, which release medications in response to certain triggers. Environmental issues will be lessened by biodegradable nanoparticles like polylactic acid and plant-derived polymers. Point-of-care diagnostic dressings, AI-integrated theranostics, non-invasive imaging methods, patient-centered and personalized wound care, smart dressings, patient education platforms, sustainable materials, cost-effective manufacturing, standardized biofilm models, and combination therapy integration are some of the theranostic applications that are being revolutionized. With the support of multidisciplinary cooperation and technology innovation, these developments have the potential to make the treatment of chronic wounds more individualized, effective, and sustainable, which would enhance patient outcomes and quality of life.

## CONCLUSION

The combination of biofilm-targeted treatments, dressings based on nanoparticles, and theranostic advancements is set to revolutionise the treatment of chronic wounds. Nanoparticle-based dressings have potential for improved healing, tailored medication administration, and fewer side effects, whereas conventional antimicrobial dressings confront issues such as resistance development, patient discomfort, and low cost-effectiveness. Real-time wound monitoring and individualised treatment plans are possible using theranostic dressings, which combine therapeutic and diagnostic properties. Nonetheless, there are still significant obstacles to overcome in order to maximise affordability, environmental sustainability, and medicinal uses. Chronic wound care will be revolutionised by the creation of eco-friendly, biodegradable materials, sophisticated AI integration, and non-invasive diagnostic techniques.

In addition to improving treatment results, patient-centered, intelligent wound care solutions that make use of AI, point-of-care diagnostics, and controlled medication delivery systems will also increase the accessibility, affordability, and sustainability of wound care. To overcome these obstacles and fully realise the promise of these advances in improving patient outcomes, interdisciplinary collaboration is crucial. The need for sophisticated wound care technology is anticipated to increase significantly in the near future due to the ageing population, the growth in chronic illnesses, and the development of antibiotic resistance.

## ACKNOWLEDGEMENTS

The authors would like to express their sincere gratitude to the School of Pharmaceutical Science, RIMT University, for providing the necessary resources, infrastructure, and supportive environment that were essential for the completion of this comprehensive review. Special thanks are extended to our colleagues for their insightful discussions and constructive feedback throughout the research process. We also acknowledge the scholars whose valuable work, cited in this article, formed the foundation of our analysis and discussion.

## Authorship Contribution

MdTanvir-Conceived the review idea, designed the manuscript structure, conducted the primary literature analysis, data curation, and wrote the original draft.

Atul Kumar Prasad-Assisted in data collection, literature review, and contributed to the drafting of specific sections, particularly on biofilms and marketed formulations.



Tichakunda Xavier Mharazanye-Participated in data organization, literature synthesis, and provided critical intellectual input during the editing and finalization of the content.

Maniket-Contributed to the writing and critical revision of the manuscript, with a focus on challenges and limitations in wound dressing research.

Abu Sufiyan Ansari-Assisted in data collection and the preliminary literature review, particularly on natural and synthetic agents.

Md Nazir Hussain-Contributed to the compilation of references and formatting of tables and data.

Md Shamim Ahmad-Supervised the project, provided overall guidance, and performed the final review and approval of the manuscript for publication.

All authors have read and approved the final version of the manuscript submitted for publication.

### **Funding**

This research was conducted without any specific financial support from funding agencies in the public, commercial, or not-for-profit sectors. All work was carried out as part of the authors' institutional roles and academic pursuits.

### **Conflicts of Interest**

The authors hereby declare that there are no conflicts of interest regarding the publication of this article. No financial or personal relationships with other people or organizations have inappropriately influenced the work reported in this manuscript.

### **Declaration**

This manuscript is an original work and has not been published previously, nor is it currently under consideration for publication in any other journal. All authors have approved the manuscript and agree with its submission.

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