REVIEW ARTICLE

NANO-ENABLED PHYTOACTIVE HYDROGELS AND TRANSFERSOMAL PLATFORMS FOR ADVANCED WOUND THERAPY

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Abstract
Chronic wounds are associated with considerable clinical burden because of the impaired healing processes, which are generally complicated by the presence of persistent inflammation, oxidative stress, microbiologically induced biofilm, and the impairment of angiogenic processes. The standard treatment strategies like dry dressing and topical antiseptics are often inadequate in overcoming the multifactorial barriers associated with such processes. Hence, new treatment methods are required. Hydrogels and transferosomes are innovative delivery systems explored recently in the healing processes as well as skin regeneration. Hydrogels, which are generally created using natural, synthetic, or mixed polymers, support the development of a moist biological environment that ensures the augmentation of cell migration, angiogenic processes, or the deposition of the extracellular matrix. Moreover, the bioactive factors can be delivered using the controlled release feature. Smart gels further increase the healing potential by responding functionally according to specific biological changes associated with the wound sites like pH values, reactive oxygen species, temperature, or enzymatic activities. Transferosomes, which are highly deformable lipid vesicles, support the deep delivery associated with hydrophilic as well as lipophilic drugs. Incorporation of phytoactives like curcumin, Asiaticoside, Epigallocatechin gallate, Quercetin, or Resveratrol has been found effective in the management associated with the deeper interference at the site on the processes mediated by oxidative stress, biofilm formation, or tissue remodeling.

Keywords: Hydrogels, transferosomes, lipophilic drugs, phytoactives, smart gels.

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Introduction

Chronic wounds are among the biggest clinical difficulties because of their healing process is destroyed by variety of pathological conditions. These include persistent inflammation, low oxygen levels, an excess of reactive oxygen species (ROS), insufficient development of blood vessels, and microbial biofilms. All of these components impair the normal healing process. Research reveals that chronic wounds typically get fixed in a prolonged inflammatory phase, partly due to high levels of proteases (such MMPs) and pro-inflammatory cytokines. This leads to the degradation of growth factors and extracellular matrix components that are necessary for tissue regeneration[1-5].

When it comes to healing, biofilm-forming bacteria such as Pseudomonas aeruginosa and Staphylococcus aureus can really throw a wrench into the works. They form antibiotic-resistant colonies that the conventional dressings just cannot eliminate[6]. This addresses reasons why conventional treatments for wounds, including dry dressings, simple gauze, and topical antiseptics, are usually inadequate for chronic wounds.

The major objective of wound treatment is to better the accuracy of diagnosis and prognosis to establish tailored treatment regimens. Over the past decade, there has been a substantial emphasis on studying innovative therapeutic procedures, such as nanotherapeutics, stem cell therapy, and 3D bioprinting[7]. Modern formulations strive to generate a protective layer that is durable, suitable with the skin, and has the active substances. This will boost the therapeutic efficacy of the preparation by accelerating healing in the most effective form and in terms of the absence of indications with an unpleasant effect[8].

Hydrogels and transfersomal systems emerged as two of the most promising next-generation therapeutic platforms in the recent history of wound-healing. Hydrogels offer the optimum moist and bioactive medium for cellular migration, angiogenesis and deposition of extracellular matrix as well as controlled release of in-built bioactives, making them highly efficacious for chronic and acute wound healing[9,10]. Simultaneously, transfersomes (ultra-deformable lipid vesicles) have evolved as brilliant carrier systems capable of squeezing through narrow intercellular paths and reaching deeper layers of the skin, favourably increasing the dermal delivery and retention of hydrophilic and lipophilic bioactive agents[11,12]. Collectively, the incorporation of transfersomes into hydrogel matrices offers a synergistic system for sustained release, enhanced penetration depth, and optimal bioavailability as well as more effective modulation of inflammation, infection and tissue regeneration a leap forward in modern wound-healing technology.

Hydrogels for Advanced wound healing

I. Types of Hydrogel:

1.Natural-polymer hydrogel: They are composed of natural polymers, have a similar surface topology to the skin and extracellular matrix (ECM), exhibit biocompatibility, cell adhesion and are useful for tissue regeneration. Common examples include:

Alginate (sea weed): good exudate absorption, hygroscopic, for high-exudate/chronic wounds [13].

Chitosan/Chitin-derivatives: antimicrobial, biodegradable, promote wound healing and tissue regeneration [14].

Hyaluronic acid (HA), collagen, gelatin, agarose, natural gums and other polysaccharides/proteins: these are for ECM-like architecture, hydration, cell migration and re-epithelialization[15].

Natural hydrogel are particularly beneficial as they provide a biocompatible, bioactive, biodegradable scaffold with inherent cell attachment motifs and have qualities that can expedite wound healing

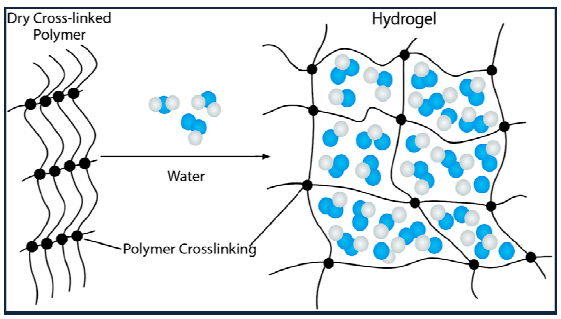

Figure.1: Structure of Hydrogel

2.Synthetic-polymer hydrogel: These hydrogels are based on man-made polymers, and they offer superior mechanical strength, tunable properties, stability, and reproducibility compared to purely natural hydrogels. Examples of such hydrogels include PEG, PVA, PAA, and other methacrylate-based polymers[16]. Synthetic hydrogels are often utilized in wound dressings when enhanced mechanical integrity is required, or specific degradation or drug-release profiles are necessary. Moreover, batch-to-batch consistency is important, such as in clinical applications[17].

3. Hybrid/Composite Hydrogels: To achieve a combination of the advantages of natural and synthetic polymers, including bioactivity, ECM mimicry, and mechanical strength and stability, researchers prepare hybrid hydrogels. They incorporate both natural, such as alginate, chitosan, and gelatin, and synthetic, such as PEG and PVA, components. Nanomaterials, nanoparticles, antimicrobial agents, and growth-factor loaded vehicles can also be incorporated within composite hydrogels to further enhance wound healing by means of infection control, active delivery, structural support, or the stimulation of regeneration[18,19].

II. Smart hydrogel:

Smart hydrogels represent a newer generation of wound dressings, which are capable of actively changing according to the microenvironment of the wound, thus facilitating tissue repair. Smart hydrogel is a controlled drug release based on continuous changing chemical and physical stimuli of the wound. Smart hydrogel changes their water solubility, expansion capability and physical properties depending on external stimuli, which makes it more effective in a wound condition than any other conventional medical dressing[20].

In fact, along with maintaining a moist and oxygen-permeable matrix, they also provide controlled and stimuli-responsive release of antimicrobials and growth factors (pH/ROS/temperature/enzyme triggered) to reduce infection and inflammation and, eventually, to promote angiogenesis and re-epithelialization while matching the mechanical compliance of skin. Smart hydrogels are multifunctional systems that are mostly manufactured from natural polysaccharides (chitosan, hyaluronic acid, alginate) or hybrid polymer-nanoparticle composites (Figure.2). Besides, they also offer on-demand drug delivery and real-time wound monitoring (electrochemical or optical) capabilities, and thus, they are highly potential for chronic and diabetic wounds which require dynamic, localized therapy[21,22].

Some recent preclinical and translational studies demonstrate such outcomes as faster closure, less bacterial burden, and better tissue quality in comparison with passive dressings, thus, clinical translation is still in need of standardized safety, scalability, and long-term outcome data[23]

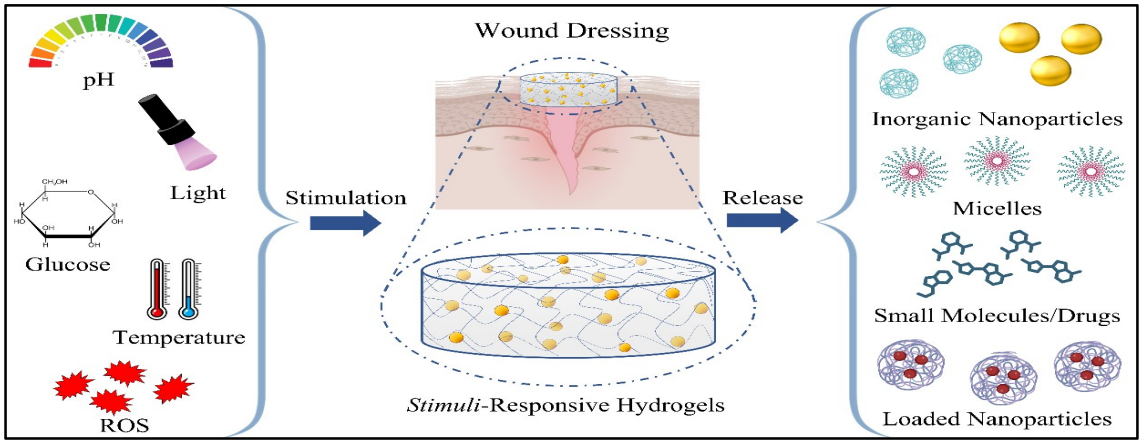

Figure .2 Schematic representation of Hydrogel in wound dressing

Marketed products of Transfersomes

Due to their potential for maintaining a moist wound environment, promoting autolytic debridement, and enhancing tissue regeneration, several hydrogel-based wound dressings are commercially available and widely used in clinical settings. Indications for these marketed hydrogels include acute and chronic wounds, such as pressure ulcers, diabetic foot ulcers, burns, and surgical wounds. Their successful clinical adoption thus far underscores safety, effectiveness, and translational potential in contemporary hydrogel systems for wound management (Table.1).

Table.1 List of marketed Hydrogel

Brand Name	Manufacturer	Ingredients	Uses	References
INTRASITE® GEL	Smith and Nephew	Carboxymethyl cellulose and propylene glycol hydrogel	Chronic wounds, Granulating wounds, abrasions and burns.	[24]
3M™ Tegaderm™ Hydrogel Wound Filler	3M Health care Ltd.	Amorphorus hydrogel	Ulcers, arterial/venous ulcers, diabetic ulcers, surgical wounds	[24]
ActivHeal® Hydrogel	Advanced Medical Solutions Ltd	> 85% water hygrogel	Pressure ulcers, leg ulcer, diabetic foot ulcers and cavity wounds	[25]
Purilon® Gel	Coloplast	Calcium alginate and sodium carboxymethyl cellulose hydrogel	Ulcers, burns and diabetic wounds	[24]
Nu-Gel™	Systagenix	Sodiumalginate hydrogel	Chronic wound, leg ulcers, venous ulcers, diabetic ulcers	[24,25]
Hydrosorb® Gel	Paul Hartmann AG	Amorphorus hydrogel	Pressure or decubitus ulcers and Ulcers,	[25]
Fitostimoline® Idrogel	Damor	Antimicrobial hydrogel	Ulcers, burns and abrasions	[25]
Simpurity™ Hydrogel	Safe n' Simple	Hydrogel sheet	Mild burns, chronic wounds	[10,24]
AquaDerm™	DermaRite Industries	Hydrogel sheet	Pressure ulcers,, Radiation Wounds and minor burns	[10,24]

Note: Table number 1shows selected list of some commercially available hydro-gels that can be applied for the healing of wounds, their compositions, and some details of the manufacturers mentioned according to recent literature.

Transferasomal system for advanced wound healing and skin regeneration

Transfersomes are highly deformable liposomes that can exploit the elasticity of the formulation and the endogenous hydration gradients of the stratum corneum for penetrating the barrier. Composed similarly to conventional liposomes, the formulation contains one or more "edge activators" (typically single-chain surfactants, Span, and/or Tween), that increase the fluidity of the formulation and confer deformability, making it possible for the entire formulation of the transfersome to pass through the tight spaces, thus delivering both hydrophilic and lipophilic substances into the deeper tissues of the skin and the wound site. Transfersomes have been demonstrated to improve the in vitro delivery of therapeutic agents across the skin to a large extent, and they also improve the permeability of the skin to achieve drug concentration similar to those of the subcutaneous route (figure.3).Over the past decade, the concept of transdermal delivery of insulin and/or corticosteroids using transfersome has evolved into the topical delivery of an antimicrobial, growth factors, and phytoactives [26,28].

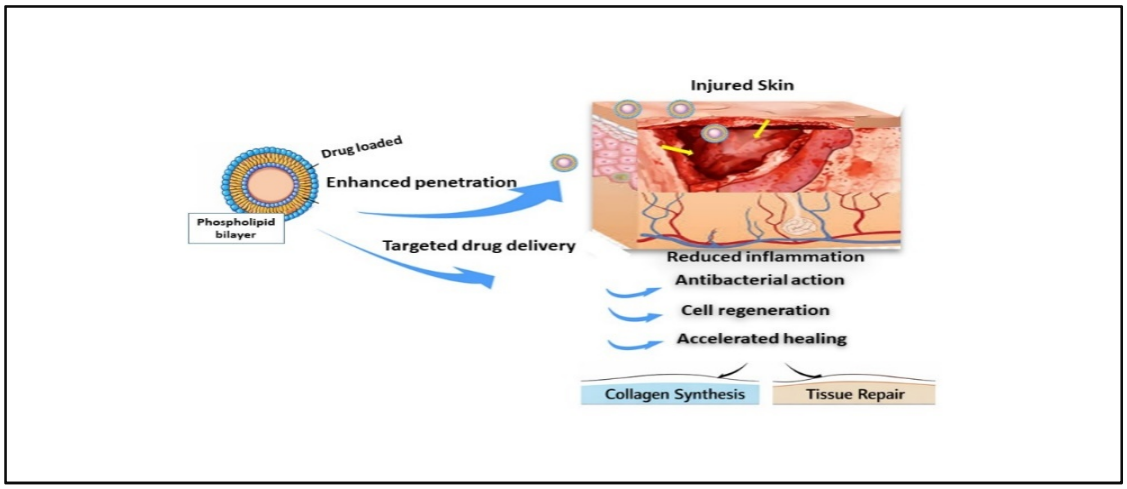

Figure.3 Mechanism of Transfersome-Mediated Delivery in Wound Healing

Note: The figure explaining the mechanism of transfersome-mediated delivery for wound healing. Transfersomes, with their flexible phospholipid bilayers, are capable of encapsulating drugs and increasing their permeation properties in wounded skin. Once applied to wounded skin, transfersomes can help increase the release of bioactive compounds with various properties like decreased inflammation, antimicrobial properties, increased cell growth, increased collagen production, and faster tissue repair, ultimately leading to efficient wound closure.

Strategies for design and formulation of transfersomes

The major advantage of transfersomes over conventional liposomes lies in the ability of the former to penetrate the intact deeper levels of the skin after topical administration via paracellular/intercellular routes between the corneocytes. The deformability characteristic of the transfersomes ensures successful transdermal drug delivery as well as drug concentration at the desired site of action in wound healing applications. Phosphatidylcholine with C18 chains, a major constituent of cell membranes, is extensively used in the preparation of transfersomes to ensure excellent skin biocompatibility with minimal irritation to the skin tissue. Transfersomes have already demonstrated the successful incorporation of a broad range of drugs including small molecules, phytoconstituents, as well as macromolecules, marking the versatility of the drug

delivery systems. Optimum lipid concentration, edge activator ratio, and processing conditions are of paramount importance to obtain nanosized vesicles with increased drug loading, mechanical strength, and consistency of the desired effect in the treatment of wound healing [29-32].

Evidence of preclinical studies for Wound healing

Increasing numbers of *in-vivo* studies have revealed that transfersome-loaded gels significantly promote wound healing, histological rearrangement, and biochemical indices of healing compared with non-vesicular systems. Some illustrations are those involving sesamol-loaded transfersomes, which displayed faster contraction in rodent wounds along with improved histological scores, and curcumin and centella transfersomes, which demonstrated increased re-epithelialization and collagen synthesis relative to non-vesicular curcumin. More importantly, surface-modified transfersomes (such as those modified with hyaluronic acid) have been demonstrated to facilitate drug delivery as well as alleviate local irritation, thus revealing versatility in modifying transfersomes with drugs or phytoconstituents [33, 34].

In another *in-vivo* pharmacokinetic studies using rabbits showed that carvedilol-loaded nanotransfersomes significantly improved systemic bioavailability when administered via the intranasal route. The formulation attained an absolute bioavailability of around 63%, which is more favorable compared to other formulations. Results from *ex-vivo* studies validated enhanced permeability and deposition at the nasal mucosa. This study proves that transfersomes are promising as non-invasive drug delivery carriers[35].

In-vivo studies carried out by Mazyed and Abdelaziz showed that acetazolamide-loaded transfersomal gel, also referred to as transfersomes, had good tolerability and lacked ocular irritation effects. *In-vivo* studies showed that intraocular pressure decreased remarkably with transfersomal gel, and a normalized response was achieved within 3 h and was sustained up to 24 h, compared to 6 h with transfersomal dispersion and less than 4 h with the suspension formulation. Inverse kinetics results showed a much enhanced aqueous humor exposure, with elevated values of Cmax and AUC 0-24 with the transfersomes formulation[36].

Marketed products of Transfersomes

One of the earliest transfersome-based clinical products was Diractin(R) (ketoprofen transferesome gel), which was approved by SwissMedic in 2007 for topical analgesic use in the treatment of pain; it showed improved tissue penetration in comparison to traditional gels before being withdrawn from the market, presumably because of the cost of manufacture. This particular example indicates an adaptation of transfersome technology in clinical practice. Although particular examples of transfersome-based wound-healing drugs are yet to appear in clinical practice, IDEA AG and several other companies have already been evaluating transfersome a gel-based formulations for topical use in certain chronic inflammatory skin disorders; several transfersome formulations are already in clinical development stages (Table.2)[37, 38].

Table.2 Marketed transfersomes based products to wound healing

Product Name	Use	Market status	References
Diractin ® (Ketoprofen transfersomal gel)	Topical pain relief with increased tissue penetration	By SwissMedic approval 2007, limited commercial avilability	[39,40]
Sequessome /Flexiseq ® technology	Enhanced dermal/transdermal delivery-antiiflammtory	Commercial technology platform used in clinical products	[41]
Prototype Transfersome gel (Asiatic acid)	Scar management and dermal healing	Emerging translational /prototype	[38]
Sesamol-loaded transfersome gel	Wound healing	Preclinical candidate with strong in vivo efficacy	[42]
Curcumin transfersomal gel	Increased topical delivery of curcumin with wound healing effects	Translational research stage	[43]

Wound Microenvironment-Responsive Delivery: A Paradigm Shift

Wound healing is no longer viewed as a linear biological cascade but rather as a highly dynamic and spatiotemporally regulated microenvironment characterized by fluctuating pH, excessive reactive oxygen species, hypoxia, protease overexpression, and dysregulated immune signaling. Chronic wounds, especially, are stuck in a perpetual state of inflammation dominated by high levels of matrix metalloproteinases, low growth factor availability, and macrophages that fail to transition from their pro-inflammatory M1 to pro-regenerative M2 phenotypes. Traditional wound dressings lack the ability to dynamically respond to such biochemical cues, culminating in delayed or incomplete healing.

Recent studies have focused on hydrogel-transfersome hybrid systems as microenvironment-responsive platforms that can sense and respond to pathological signals at wound sites. Hydrogels might also exhibit sensitivity to stimuli, which, upon proper structural arrangement, would exhibit controlled swelling, degradation, or drug release based on the change in pH, ROS, temperature, or enzymatic action. When combined with transfersomes, it would facilitate the location-specific release of drugs along with their ability to penetrate the wound edge areas more effectively. Such a paradoxical property would help achieve temporal control over anti-inflammatory, anti-bacterial, or regeneration therapies, which would switch from passive protection to active control of the wound sites[41, 23-44].

Immunomodulatory Role of Hydrogel–Transfersome Platforms

The emerging, unexplored frontiers in the area of high-end wound dressings involve: immune system modulation in general, and specifically, modulation of macrophage polarization. Macrophages orchestrate this process, with a Phase transition from proinflammatory phenotype M1 to proliferative phenotype M2 in a healing process. The Phase transition failure represents a hallmark for both chronic and diabetic wounds[45-47]. Hydrogels made from bioactive polymers chitosan, hyaluronic acid, and gelatin displayed inherent immune modulatory properties, favoring M2 macrophage polarization and decreasing exuberant release of proinflammatory cytokines. Along with transfersome-mediated delivery of phytoactives like Curcumin, Quercetin, and Resveratrol, such systems would specifically target NF-κB, STAT3, and TGF-β signaling pathways. Transfersomes are

known to increase drug uptake in macrophages and fibroblasts, and hence can potentiate immune modulatory properties with decreased systemic drug availability. This immunoengineering platform places hydrogel-transfersomes as immune-instructive biomaterials rather than drug-delivery systems[48-53].

Targeting Biofilm-Immune Cell Interactions Using Hybrid platforms

The presence of biofilms in bacteria is an unresolved challenge in wound healing because of its property of antibiotic resistance and maintaining chronic infections. Biofilms in bacteria act as a protective covering for bacteria and show inhibition of both immune response and macrophagic phagocytic function. Biofilms interact with immune components and interfere with its functions. The hydrogel-transfersome system has an outstanding property in modulating and interfering with biofilm and immune system interactions. Hydrogels provide sustained antimicrobial-delivery properties, while transfersomes show penetrating properties in penetrating biofilms and cell membranes in deep tissues. The phyto-compounds (thymol, EGCG, berberine), or metal nanoparticles with antibiofilm activity encapsulated in transfersomes, would act as triple-druga targeting quorum sensing, biofilms, and bio-metabolism in bacteria. Moreover, the immunomodulatory microenvironment provided by hydrogels would enhance facilitating normalization of immune response processes[54-57]. Triple-modal therapy, antimicrobial activity, antibiofilm activity, and immune response normalization is definitely an innovative platform in chronic wound treatment.

Translation for Clinical Practice, Manufacturing, and Regulatory considerations

Despite the presence of encouraging data in the preclinical setting, the application of hydrogel transfersomes in clinical applications is a rather complex procedure. This happens because of scalability in the manufacture of vesicles, physicochemical stability, reproducibility of loading, and regulatory classification. In fact, it has been suggested that these types of systems lie between drugs and conventional devices. Increasingly, the quality-by-design paradigm, harmonized characterization procedures, and comprehensive data on biocompatibility over longer periods are considered important by the various regulatory organizations, although advancements in the manufacturing of microfluidics, lyophilization methods, or release testing may be needed to adequately address scalability or storage issues that exist. In addition, harmonization of FDA or ISO combination product procedures would be essential within the clinical setting[58,59]. Early intervention for these translation hurdles would certainly promote bench-to-bedside translation.

Phytoactive compound in wound healing

Pure plant-based remedies have turned out to be a vital part of the treatment of skin conditions and the cure of skin infections, mostly because modern medicines are frequently accompanied by side effects and herbal alternatives are cheaper. Phytochemicals to be very effective agents in both the prevention and the treatment of microbial infections and also in the promotion of wound repair[60,61]. Their antimicrobial, antioxidant, and wound-healing activities enable them to, among other things, stimulate blood clotting, fight pathogens, and energize tissue recovery[62-64]. Medicinal plants loaded with polyphenols have become famous for their potent wound-healing capabilities since phenolic compounds inherently support the repair process due to their astringent nature, antimicrobial effects, and ability to scavenge free radicals[64,65]. This paper aims to provide an updated overview of phytoactive compounds used in wound dressings and other formulations designed to promote wound healing (Table.3).

Table .3 Phytoactive compound in wound healing

Phytoactive constituents	Plant Source	Physico chemical Limitation	Preferred Delivery System	Wound Healing property	References
Curcumin	Curcuma longa	Poor aqueous solubility, chemical instability	Nano emulsion, transfersomes hydrogel	Anti-inflammatory Antioxidant , enhances reepithelialization	[70]
Asiaticoside	Centella asiatica	Low skin Permeability	Transfersomes, nanogels	Stimulates fibroblast proliferation and collagen synthesis	[71,72]
Madecassoside	Centella asiatica	Highly hydrophilic	Hydrogel matrix, nano hydrogels	ECM remodeling and angiogenesis	[71,73]
Quercetin	Onionpeel apple	Poor solubility, light sensitivity	Liposomes, nanogels	Antioxidant, inhibits matrix metalloproteinases	[73-75]
Epigallo catechin gallate (EGCG)	Green tea	pH sensitive, unstable	Hydrogel films, nanocomposite hydrogels	Antimicrobial and anti-inflammatory	[73,75-77]
Allicin	Garlic (Allium sativum)	Volatile and unstable	Encapsulated hydrogels, nanoparticles	Broad spectrum antimicrobial	[71,74,75]
Aloe emodin	Aloe vera	Low aqueous solubility	Hydrogel Dressings	Promotes epithelial cell migration	[71]
Resveratrol	Grapes , berries	Poor solubility, rapid metabolism	Nano emulsion based hydrogels	Antioxidant and pro angiogenic	[73,78]
Thymol	Thyme	Volatile, irritant at high dose	Polymer based hydrogels	Antimicrobial , antibiofilm	[76]
Berberine	Berber is species	Low permeability	Transfersomes,lipid nanoparticles	Antimicrobial and anti-inflammatory	[73]
Chamomile	Celery, chamomile	Poor water solubility	Nanogels, polymeric nanoparticles	Anti-inflammatory suppreses oxidative stress	[73,79,80]
Apigenin	Parsley , chamomile	Lowpermeability through stratum corneum	Transfersomes, lipid based nanocarriers	Promotes fibroblast migration and angiogenesis	[71,74]
Gallic Acid	Tea leaves, berries	Rapid diffusion and clearance	Hydrogel matrices, nano composite gels	Antioxidant; enhances granulation tissue formation	[73,76]
Catechin	Green tea	pH sensitive and unstable	Hydrogel films, nanofiber dressings	Antimicrobial ; reduces oxidative damage	[73,76]

Note: Table number 3 enlists the common phytoactives used in topical applications of wound healing from the point of formulation: The physical and chemical shortcomings of each phytoactive emphasize the need for the use of modern delivery systems such as hydrogels, nano-emulsions, and transfersomes to ensure improved release and diffusion of phytoactives to achieve a dual function of healing of the wound.

Mechanistic mapping of Phytoactive compounds in wound healing

Below is the mechanistic mapping of phytoactive compounds in wound healing. This section outlines the mechanistic roles of five selected phytoactive compounds in wound healing and discusses, in detail, their actions across different phases of the healing cascade. Emphasis has been given to molecular pathways related to inflammation modulation, antioxidant defense, cell proliferation, and tissue remodelling (Figure.4).

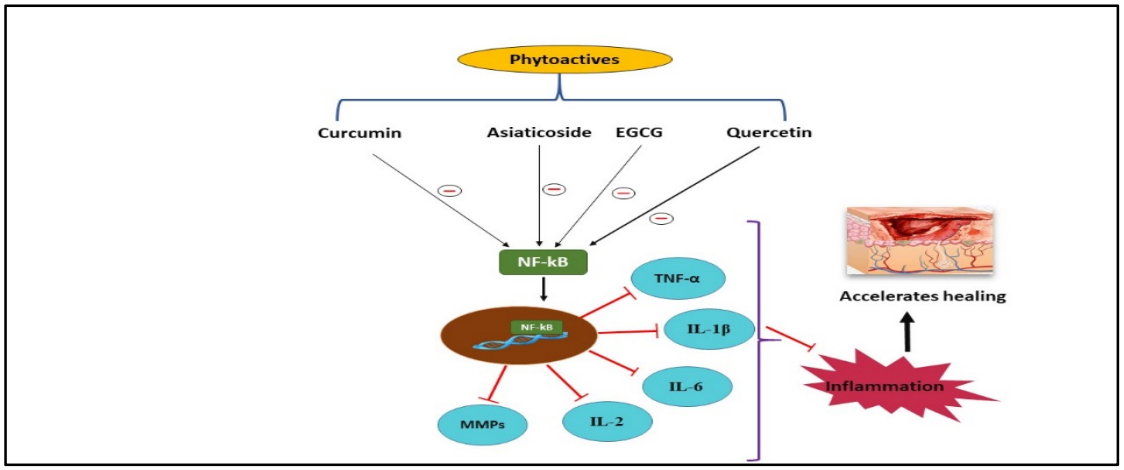

Figure.4 Representing Phytoactives in wound healing

Note: Schematic diagram illustrating the mechanism of phytochemicals in wound healing. Curcumin acts at the wound site by reducing inflammation, exhibiting antimicrobial activity, promoting cell proliferation, and enhancing collagen synthesis. These actions act through the modification of signaling molecules, such as NF-κB, TNF-α, COX-2, ROS, and TGF-β, to accelerate tissue regeneration with enhanced wound closure.

1.Curcumin (Curcuma Longa): Curcumin is instrumental in wound healing after it modifies the inflammatory phase of tissue repair. One of its ways to act is to inhibit the activation of the NF-κB signaling pathway, which results in the decreased expression of pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6. At the same time, it reduces oxidative stress by its very potent antioxidant activity. In addition to that, curcumin encourages fibroblast proliferation and collagen deposition during the proliferative phase [67,76].

2.Asiaticoside (Centella asistica): Asiaticoside has been identified as a triterpenoidal saponin that functions as a wound-healing compound by promoting fibroblast proliferation and ECM deposition. It acts by activating TGF-β/Smad signaling and serves in promoting collagen type I, angiogenesis, and granulation tissue formation. The compound has anti-inflammatory properties that facilitate the advancement of the wound from the inflammatory phase into the proliferation phase. Because of its poor permeability through the stratum corneum barrier, delivery can be improved by using formulation in either transfersomes or nanogel hydrogels [48,77,78].

3.Epigallocatechin gallate (EGCG): Several studies validate the medicinal use of highly effective antioxidants in dealing with ongoing problems related to poor healing. Catechins, especially epigallocatechin gallate (EGCG), have been found to have a high scavenging potential for ROS and have been able to speed up the process of healing due to the facilitation of re-epithelialization. EGCG modulates the process of inflammation by decreasing the levels of pro-inflammatory cytokines like IL-1β and TNF- α. Simultaneously, the levels of the anti-inflammatory cytokine IL-10 are increased. Moreover, the antimicrobial properties of EGCG in terms of both bacteriostatic and bactericidal actions have already been well elucidated [79, 80]. Despite its potential in therapy, however, the clinical usefulness of EGCG remains limited by its rapid metabolism and susceptibility to photodegradation, both of which cause high degradation of its bioavailability. In addition, the topical application of EGCG to wound surfaces may lead to localized toxicity due to high concentrations of EGCG being delivered to a target location. This further restricts the therapeutic application of EGCG and makes it necessary to deliver EGCG by employing nanometric systems and EGCG-loaded hydrogels[81].

4.Quercitin (Onion peel and apples): Quercetin is a flavonoid with potent activity in enhancing wound healing by reducing oxidative stress and modulating inflammation. It suppresses the activities of MMPs, thus preventing excessive degradation of ECM components. Quercetin also enhances the migration of keratinocytes, leading to enhanced re-epithelialization. The herbal extract has been able to reduce bacterial load and enhancement of wound contraction. However, with its low water solubility and photo-reactivity, encapsulation in liposomes, nanogels, or transfersomes has been shown to improve its stability, retention capacity in skin, and wound-healing property [82,83].

It exerts an early anti-inflammatory effect, suppressing the expression of cytokines mediated by NF-κB and thus aiding in the transition from the inflammatory stage to the proliferative stage of the wound-healing process. The ratio of collagen III/I denotes the production of elastic fibers of collagen, which plays an important part in remodeling flexible tissue instead of forming scars 84. In addition, it promoted the process of skin wound healing in mice by accelerating the proliferation and migration of fibroblasts, reducing inflammation, and stimulating the expression of growth factors mediated by the Wnt/β-catenin pathway as well as TERT activation[85].

5.Resveratrol: Resveratrol acts as a wound healer due to its antioxidant, anti-inflammatory, and angiogenic properties. It acts as a promoter of fibroblast cells by increasing collagen production and neovascularization, which plays a crucial role in providing oxygen and nutrients to the healing cells. Resveratrol further regulates various inflammation mediators and oxidative stress in the wound area[86,87]. Poorly soluble resveratrol with rapid metabolism restricts its topical application; thus, resveratrol-loaded nanoemulsions and lipid vesicles are used to increase its availability and its localized therapeutic potential[88].

Case studies in wound healing process using Nanotechnology

Nanotechnology has caused radical changes in the treatment of wounds by facilitating the development of highly functional and interactable therapeutics for enhanced tissue repair, infection control, and regulation of inflammation in the wound microenvironment. Unlike conventional dressings, which provide passive protection to the wound, nano-based preparations, such as hydrogels impregnated with nanoparticles, nanofibers, and metal nanocomposites, possess the ability to imitate the extracellular matrix, enable targeted delivery of bioactive molecules, and provide reinforced stimulation of major phases of wound healing, such as cell proliferation, angiogenesis, and extracellular matrix remodelling[89-91].

Antimicrobial, anti-inflammatory, and regenerative effects in the wound

microenvironment have been established by metal and polymeric nano-particles, whereas nanofibers developed by electrospinning and other methods possess the ability to provide strength and favor cell adhesion and migration, much like natural tissues. These nanotechnology-based preparations are known for functions such as sustained drug delivery and inhibition of bacterial accumulation and accelerated epidermal resurfacing, thus marking nanotechnology as an area of radical importance for the future of wound regeneration and repair [90,92,91]. This section will provide a few case studies of the application of nanotechnology in the wound healing process.

One example could thus include the use of hydrogel matrices with metal nanoparticles such as Silver (Ag) and Zinc Oxide (ZnO) having both antimicrobial and scaffold materials for the healing of tissues. In murine models, gold nanoparticles within hydrogel matrices showed around 90 % wound healing on Day 5 compared with controls, with a higher expression of biomarkers for healing, such as CD34 + NANOG, but a lower level of MMP2, thus defining both the antimicrobial and healing roles of nanomaterials[93]. Another study prepared a topical gel with a mixture of nanoparticles of ZnO, Ag, and cerium oxide, and it considerably increased wound closure in aged rat models, with complete healing observed in 14 days. Such findings provide evidence that a combination therapy with nanoparticles could be useful for the treatment of infections by addressing multiple factors like infection, oxidation, and wound healing [94]. Hydrogel patches containing nanoparticles have also demonstrated potential for creating a biomimicking microenvironment conducive to cell adhesion and proliferation, and the delivery of bioactive molecules. The incorporation of nanoparticles into hydrogel patches for wounds has been shown to imitate the microenvironment of the extracellular matrix (ECM), hence improving skin regeneration and infection prevention in animal models[95]. Bioactive small molecules, Baicalin loaded within polymeric nanohydrogels, have additionally been demonstrated to display stronger skin regenerative capabilities with in vivo suppression of essential pro-inflammatory mediators, such as tumour necrosis factor-alpha, and fast fibroblast mobility [96].

In another case, the application of bacterial nanocrystal cellulose/acrylic acid hydrogels induced the adhesion and proliferation of fibroblasts by regulating genes such as IL-6, IL-10, and TGF-β, which play a crucial role in the targeting of tissue injury and have been shown to be involved in many pathophysiological conditions [96].

The significance of these case studies is that they not only focus on the applications of nanotechnology in combating infection and inflammation but also on facilitating and directing the wound-healing axis towards rapid and enhanced wound closure. Recent studies have demonstrated that future applications in wound management would be further expanded with the use of nanomaterials and smart hydrogel technology and growth factors, and this would be one of the pivotal aims for future applications[89] (table.4).

Table.4 Nanotechnology-Enabled Wound Healing Case Studies

Sl.no	Study	Nanotechnology Method	Outcomes	Reference
1	Au NP embedded hydrogel (mouse wound model)	Gold nanoparticles in hydrogel matrix	~90% wound closure by day 5; increased fibroblast adhesion, increased NANOG/CD34, decreased MMP-2	[93]
2	Multi-NP gel for aged rat wounds	ZnO + Ag + CeO2 nanoparticles in topical gel	Nearly complete closure by day 14; accelerated healing vs control	[94]
3	NP-incorporated hydrogel patch (animal studies)	Nanoparticle-embedded wound patch	Mimics ECM;improved infection control and regeneration	[95]
4	Baicalin-loaded nanohydrogel (preclinical)	Bioactive nanohydrogel	Enhanced skin restoration; reduced inflammatory markers	[96]
5	Nanocrystal cellulose/acrylic acid hydrogel	Nanofiber hydrogel scaffold	Rapid fibroblast proliferation, modulated gene expression	[96]

Note: Table number 4 shows an overview of the data from the preclinical research that highlights the various nanomaterials such as metal nanoparticles, polymeric nanoparticles, or nanofibers designed to act as scaffolds within the hydrogel/cream formulation to provide efficacy that includes improved antimicrobial action, anti-inflammatory response, angiogenesis, extracellular matrix remodeling, and rates of wound closure compared to the conventional treatment methods.

Conclusion and future directions: The application of phytoactive agents along with hydrogels and transfersomal formulations is a revolutionary strategy for the enhanced healing of wounds and regeneration of the skin. These formulations have shown enhanced penetration and release properties along with reduced infection and inflammation using the bioactive properties of phytoactive agents and enhanced delivery systems. These formulations have shown their efficiency in preclinical research when compared to conventional wound dressings for healing, tissue regeneration, and angiogenesis. The smart hydrogel and transfersomal formulations of phytoactive agents show a responsive and dynamic strategy for chronic wounds. Clinical research and the standardization of the conditions for the formulations need to be performed to apply these strategies effectively in a clinical setup, which can prove to be a revolutionary milestone for the management of chronic wounds.

The future courses of research in wound healing would be toward personalized or intelligent healing systems. One of the future approaches would be the utilization of hydrogel transferesome technology along with biosensors, artificial intelligence for the analysis of the wound by artificial intelligence itself, or by 3D-printing technology. Intelligent wound dressings for online measurement of pH levels, oxygen tension, or the presence of bacteria can enable controlled-release systems for drugs. In addition to that, machine learning algorithms can be utilized for the assistance of the formulation parameters and future treatment pathways of healing based upon patient-specific information. The amalgamation of material sciences, nanotechnology, and digital healthcare is a revolutionary trend for future advancements in the field of wound healing[17-20].

References

1. Eming, S.A., P. Martin, and M. Tomic-Canic, Wound repair and regeneration: mechanisms, signaling, and translation. Sci Transl Med, 2014. 6(265): p. 265sr6.

2. Schultz, G.S. and A. Wysocki, Interactions between extracellular matrix and growth factors in wound healing. Wound Repair Regen, 2009. 17(2): p. 153-62.

3. Sun, J., D-Limonene: safety and clinical applications. Altern Med Rev, 2007. 12(3): p. 259-64.

4. Brem, H. and M. Tomic-Canic, Cellular and molecular basis of wound healing in diabetes. J Clin Invest, 2007. 117(5): p. 1219-22.

5. Bowden, L.G., et al., A morphoelastic model for dermal wound closure. Biomech Model Mechanobiol, 2016. 15(3): p. 663-81.

6. Percival, S.L., et al., A review of the scientific evidence for biofilms in wounds. Wound Repair Regen, 2012. 20(5): p. 647-57.

7. Mamun, A.A., et al., Recent advances in molecular mechanisms of skin wound healing and its treatments. Frontiers in Immunology, 2024. Volume 15 - 2024.

8. Olteanu, G., et al., Advancements in Regenerative Hydrogels in Skin Wound Treatment: A Comprehensive Review. Int J Mol Sci, 2024. 25(7).

9. Gounden, V. and M. Singh, Hydrogels and wound healing: current and future prospects. Gels, 2024. 10(1): p. 43.

10. Solanki, D., P. Vinchhi, and M.M. Patel, Design considerations, formulation approaches, and strategic advances of hydrogel dressings for chronic wound management. ACS omega, 2023. 8(9): p. 8172-8189.

11. Simrah, et al., Transfersome, an ultra-deformable lipid-based drug nanocarrier: an updated review with therapeutic applications. Naunyn-Schmiedeberg's Archives of Pharmacology, 2024. 397(2): p. 639-673.

12. Thakur, A., et al., Transferosomes: An Ultra-Deformable Nanocarriers for Advanced Drug Delivery. 2025.

13. Xu, Y., et al., Advanced polymer hydrogels that promote diabetic ulcer healing: mechanisms, classifications, and medical applications. Biomaterials Research, 2023. 27(1): p. 36.

14. Chelu, M., et al., Natural Regenerative Hydrogels for Wound Healing. Gels, 2024. 10(9): p. 547.

15. Wang, M., et al., Engineering functional natural polymer-based nanocomposite hydrogels for wound healing. Nanoscale Advances, 2023. 5(1): p. 27-45.

16. Yang, X., et al., Multifunctional hydrogels for wound healing. Journal of Polymer Engineering, 2024. 44(3): p. 173-194.

17. Sharma, A.D., E.H. Jarman, and P.M. Fox, Scoping Review of Hydrogel Therapies in the Treatment of Diabetic Chronic Wounds. Plastic and Reconstructive Surgery – Global Open, 2023. 11(5): p. e4984.

18. Wei, L., et al., Chitosan/Alginate Hydrogel Dressing Loaded FGF/VE-Cadherin to Accelerate Full-Thickness Skin Regeneration and More Normal Skin Repairs. International Journal of Molecular Sciences, 2022. 23(3): p. 1249.

19. Choudhary, A., et al., Strategy and Advancement in Hybrid Hydrogel and Their Applications: Recent Progress and Trends. Advanced Engineering Materials, 2024. 26(21): p. 2400944.

20. Jaiswal, R. and A.P. Sherje, Recent advances in biopolymer-based smart hydrogel for wound healing. Journal of Drug Delivery Science and Technology, 2024. 99: p. 105990.

21. Fan, Y., et al., Advances in Smart-Response Hydrogels for Skin Wound Repair. Polymers, 2024. 16(19): p. 2818.

22. Suneetha, M., et al., Fungal Carboxymethyl Chitosan-Impregnated Bacterial Cellulose Hydrogel as Wound-Dressing Agent. Gels, 2023. 9(3): p. 184.

23. Casadidio, C. and R. Censi, Prospects of Hydrogels in Wound Healing: Toward the Next Generation of Smart Biomaterials. Pharmaceutics, 2025. 17(11).

24. Aswathy, S.H., U. Narendrakumar, and I. Manjubala, Commercial hydrogels for biomedical applications. Heliyon, 2020. 6(4): p. e03719.

25. Alberts, A., et al., Advancements in Wound Dressing Materials: Highlighting Recent Progress in Hydrogels, Foams, and Antimicrobial Dressings. Gels, 2025. 11(2): p. 123.

26. Matharoo, N., H. Mohd, and B. Michniak-Kohn, Transferosomes as a transdermal drug delivery system: Dermal kinetics and recent developments. WIREs Nanomedicine and Nanobiotechnology, 2024. 16(1): p. e1918.

27. Rai, S., V. Pandey, and G. Rai, Transfersomes as versatile and flexible nano-vesicular carriers in skin cancer therapy: The state of the art. Nano reviews & experiments, 2017. 8(1): p. 1325708.

28. Bera, P., N. Upamanyu, and J. Jaiswal, Transfersomes and Ethosomes: Nano Carriers and their Clinical Potential in Transdermal Drug Delivery System. International Journal of Pharmaceutical Sciences and Nanotechnology(IJPSN), 2020. 13(2): p. 4793-4807.

29. Prausnitz, M.R. and R. Langer, Transdermal drug delivery. Nature biotechnology, 2008. 26(11): p. 1261-1268.

30. Malakar, J., et al., Formulation, optimization and evaluation of transferosomal gel for transdermal insulin delivery. Saudi pharmaceutical journal, 2012. 20(4): p. 355-363.

31. Karpiński, T.M., Selected medicines used in iontophoresis. Pharmaceutics, 2018. 10(4): p. 204.

32. Ita, K., Perspectives on transdermal electroporation. Pharmaceutics, 2016. 8(1): p. 9.

33. Umam, N., M. Ahmad, and P. Kushwaha, Design and fabrication of Sesamol-loaded transfersomal gel for wound healing: physicochemical characterization and in-vivo evaluation. Drug Development and Industrial Pharmacy, 2023. 49(2): p. 159-167.

34. Lapmanee, S., et al., Transfersomal delivery of Centella asiatica promotes efficient excision wound healing in rats. Drug Deliv, 2025. 32(1): p. 2563649.

35. Aboud, H.M., et al., Nanotransfersomes of carvedilol for intranasal delivery: formulation, characterization and in vivo evaluation. Drug Delivery, 2016. 23(7): p. 2471-2481.

36. Mazyed, E.A. and A.E. Abdelaziz, Fabrication of Transgelosomes for Enhancing the Ocular Delivery of Acetazolamide: Statistical Optimization, In Vitro Characterization, and In Vivo Study. Pharmaceutics, 2020. 12(5): p. 465.

37. Kneer, W., et al., A multiple-dose, open-label, safety, compliance, and usage evaluation study of epicutaneously applied Diractin (ketoprofen in Transfersome) in joint/musculoskeletal pain or soft tissue inflammation. Curr Drug Saf, 2009. 4(1): p. 5-10.

38. Opatha, S.A.T., et al., Asiatic acid-entrapped transfersomes for the treatment of hypertrophic scars: In vitro appraisal, bioactivity evaluation, and clinical study. Int J Pharm, 2024. 651: p. 123738.

39. Binaymotlagh, R., et al., Liposome–Hydrogel Composites for Controlled Drug Delivery Applications. Gels, 2024. 10: p. 284.

40. Rother, M., Efficacy of epicutaneous Diractin® (ketoprofen in Transfersome® gel) for the treatment of pain related to eccentric muscle contractions. Drug Design, Development and Therapy, 2009: p. 143.

41. (2017), N., Flexiseq for osteoarthritis (Medtech innovation briefing MIB80. 2017.

42. Sana, E., et al., Topical delivery of curcumin-loaded transfersomes gel ameliorated rheumatoid arthritis by inhibiting NF-κβ pathway. Nanomedicine (Lond), 2021. 16(10): p. 819-837.

43. Olteanu, G., et al., Unraveling the Microbiome-Human Body Axis: A Comprehensive Examination of Therapeutic Strategies, Interactions and Implications. Int J Mol Sci, 2024. 25(10).

44. Islam, R., et al., Review of Shape-Memory Polymer Nanocomposites and Their Applications. Applied Sciences, 2025. 15(5): p. 2419.

45. Kong, D., H. Cheng, and M. Wang, Novel pyroptosis-immune-related lncRNA signature exhibits a distinct immune cell infiltration landscape in breast cancer. Frontiers in Immunology, 2025. Volume 15 - 2024.

46. Zulkefli, N., et al., Flavonoids as Potential Wound-Healing Molecules: Emphasis on Pathways Perspective. Int J Mol Sci, 2023. 24(5).

47. Liang, J., et al., Long non-coding RNA MEG3 promotes cerebral ischemia-reperfusion injury through increasing pyroptosis by targeting miR-485/AIM2 axis. Exp Neurol, 2020. 325: p. 113139.

48. Diniz, L.R.L., et al., Centella asiatica and Its Metabolite Asiatic Acid: Wound Healing Effects and Therapeutic Potential. Metabolites, 2023. 13(2): p. 276.

49. Hu, Y., et al., Efficacy and safety of two hyaluronic acid fillers with different injection depths for the correction of moderate-to-severe nasolabial folds: A 52-week, prospective, randomized, double-blinded study in a Chinese population. J Cosmet Dermatol, 2022. 21(3): p. 940-948.

50. Sh. Ahmed, A., et al., Pharmacological properties of Centella asiatica hydrogel in accelerating wound healing in rabbits. BMC complementary and alternative medicine, 2019. 19(1): p. 213.

51. Xuan, Y., et al., The activation of the NF-κB-JNK pathway is independent of the PI3K-Rac1-JNK pathway involved in the bFGF-regulated human fibroblast cell migration. J Dermatol Sci, 2016. 82(1): p. 28-37.

52. Yang, H.L., et al., Lucidone Promotes the Cutaneous Wound Healing Process via Activation of the PI(3)K/AKT, Wnt/β-catenin and NF-κB Signaling Pathways. Biochim Biophys Acta Mol Cell Res, 2017. 1864(1): p. 151-168.

53. Zhang, X., et al., IGF-1 inhibits inflammation and accelerates angiogenesis via Ras/PI3K/IKK/NF-κB signaling pathways to promote wound healing. Eur J Pharm Sci, 2024. 200: p. 106847.

54. Zawani, M. and M.B. Fauzi, Injectable Hydrogels for Chronic Skin Wound Management: A Concise Review. Biomedicines, 2021. 9(5): p. 527.

55. Boateng, J.S., et al., Wound Healing Dressings and Drug Delivery Systems: A Review. Journal of Pharmaceutical Sciences, 2008. 97(8): p. 2892-2923.

56. Seth, A.K., et al., Impact of a novel, antimicrobial dressing on in vivo, Pseudomonas aeruginosa wound biofilm: quantitative comparative analysis using a rabbit ear model. Wound Repair Regen, 2014. 22(6): p. 712-9.

57. Trøstrup, H., et al., Pseudomonas aeruginosa biofilm aggravates skin inflammatory response in BALB/c mice in a novel chronic wound model. Wound Repair Regen, 2013. 21(2): p. 292-9.

58. Pintilei, P.S., et al., The Role of Natural Hydrogels in Enhancing Wound Healing: From Biomaterials to Bioactive Therapies. Pharmaceutics, 2025. 17(10).

59. Choudhary, A., P. Teja, and R. Jain, Enhancement of mechanical and microstructural properties of friction stir welded AA2024 by eccentric square tool pin. Materials Chemistry and Physics, 2023. 311: p. 128550.

60. Ayaz, M., et al., Sertraline enhances the activity of antimicrobial agents against pathogens of clinical relevance. Journal of Biological Research-Thessaloniki, 2015. 22(1): p. 4.

61. Ayaz, M., et al., Neuroprotective and anti-aging potentials of essential oils from aromatic and medicinal plants. Frontiers in aging neuroscience, 2017. 9: p. 257193.

62. Mehta, P., et al., Pharmacokinetic profile of phytoconstituent (s) isolated from medicinal plants—a comprehensive review. Journal of traditional and complementary medicine, 2015. 5(4): p. 207-227.

63. Ovais, M., et al., Wound healing applications of biogenic colloidal silver and gold nanoparticles: recent trends and future prospects. Applied microbiology and biotechnology, 2018. 102(10): p. 4305-4318.

64. Deshmukh, P.T., et al., Wound healing activity of Calotropis gigantea root bark in rats. Journal of ethnopharmacology, 2009. 125(1): p. 178-181.

65. Lopes, G.C., et al., Influence of extracts of Stryphnodendron polyphyllum Mart. and Stryphnodendron obovatum Benth. on the cicatrisation of cutaneous wounds in rats. Journal of Ethnopharmacology, 2005. 99(2): p. 265-272.

66. Agrawal, D., M.P. Singh, and G.K. Sharma, Pharmacodynamic approaches of phytoconstitutents in wound healing mechanisms. Pharmacological Research - Natural Products, 2024. 5: p. 100119.

67. Gupta, S.C., S. Patchva, and B.B. Aggarwal, Therapeutic roles of curcumin: lessons learned from clinical trials. Aaps j, 2013. 15(1): p. 195-218.

68. Shedoeva, A., et al., Wound Healing and the Use of Medicinal Plants. Evid Based Complement Alternat Med, 2019. 2019: p. 2684108.

69. Trinh, X.T., et al., A Comprehensive Review of Natural Compounds for Wound Healing: Targeting Bioactivity Perspective. Int J Mol Sci, 2022. 23(17).

70. Nguyen, T.L.A. and D. Bhattacharya, Antimicrobial Activity of Quercetin: An Approach to Its Mechanistic Principle. Molecules, 2022. 27(8).

71. Anand David, A.V., R. Arulmoli, and S. Parasuraman, Overviews of Biological Importance of Quercetin: A Bioactive Flavonoid. Pharmacogn Rev, 2016. 10(20): p. 84-89.

72. Zawani, M. and M.B. Fauzi, Epigallocatechin Gallate: The Emerging Wound Healing Potential of Multifunctional Biomaterials for Future Precision Medicine Treatment Strategies. Polymers, 2021. 13(21): p. 3656.

73. Szulc-Musioł, B. and B. Sarecka-Hujar, The Use of Micro- and Nanocarriers for Resveratrol Delivery into and across the Skin in Different Skin Diseases-A Literature Review. Pharmaceutics, 2021. 13(4).

74. Valmy, J., et al., Anti-inflammatory effect of chamomile from randomized clinical trials: a systematic review and meta-analyses. Pharm Biol, 2025. 63(1): p. 490-502.

75. Chen, G., et al., Essential Oil of Matricaria chamomilla Alleviate Psoriatic-Like Skin Inflammation by Inhibiting PI3K/Akt/mTOR and p38MAPK Signaling Pathway. Clin Cosmet Investig Dermatol, 2024. 17: p. 59-77.

76. Zhang, Z., et al., Localized delivery of curcumin by thermosensitive hydrogels for promoting wound healing. Journal of Cosmetic Dermatology, 2022. 21(10): p. 5081-5091.

77. Gohil, K.J., J.A. Patel, and A.K. Gajjar, Pharmacological Review on Centella asiatica: A Potential Herbal Cure-all. Indian J Pharm Sci, 2010. 72(5): p. 546-56.

78. Shukla, A., et al., In vitro and in vivo wound healing activity of asiaticoside isolated from Centella asiatica. Journal of Ethnopharmacology, 1999. 65(1): p. 1-11.

79. Kar, A.K., et al., Polymer-Assisted In Situ Synthesis of Silver Nanoparticles with Epigallocatechin Gallate (EGCG) Impregnated

Wound Patch Potentiate Controlled Inflammatory Responses for Brisk Wound Healing. Int J Nanomedicine, 2019. 14: p. 9837-9854.

80. Se, A.M., L. Li, and M. Yu, Poloxamer-based hydrogel with EGCG and rhEGF for diabetic foot ulcer treatment. Journal of Materials Science: Materials in Medicine, 2025. 36(1): p. 65.

81. Ding, P., et al., Hydroxyproline-Modified Chitosan-Based Hydrogel Dressing Incorporated with Epigallocatechin-3-Gallate Promotes Wound Healing Through Immunomodulation. Gels, 2025. 11(9): p. 732.

82. Zulkefli, N., et al., Flavonoids as Potential Wound-Healing Molecules: Emphasis on Pathways Perspective. International Journal of Molecular Sciences, 2023. 24(5): p. 4607.

83. Yadav, E., et al., Cutaneous Wound Healing Activity of Quercetin Functionalized Bimetallic Nanoparticles. Chemistry & biodiversity, 2024. 22: p. e202401551.

84. Wu, D., M. Jiang, and J. Zhang, Dual Role of Quercetin in Promoting Early Wound Healing via Inhibiting Inflammatory Factors and Attenuating Scar Formation by Suppressing Myofibroblast Differentiation. Front Biosci (Landmark Ed), 2025. 30(7): p. 40077.

85. Mi, Y., et al., Quercetin promotes cutaneous wound healing in mice through Wnt/β-catenin signaling pathway. Journal of Ethnopharmacology, 2022. 290: p. 115066.

86. Zhou, X., et al., Resveratrol accelerates wound healing by attenuating oxidative stress-induced impairment of cell proliferation and migration. Burns, 2021. 47(1): p. 133-139.

87. Jia, Y., et al., Emerging Effects of Resveratrol on Wound Healing: A Comprehensive Review. Molecules, 2022. 27(19): p. 6736.

88. Li, X., et al., Microneedles based on hyaluronic acid-polyvinyl alcohol with antibacterial, anti-inflammatory, and antioxidant effects promote diabetic wound healing. International Journal of Biological Macromolecules, 2024. 282: p. 137185.

89. Aliyev, A., et al., Nanotechnology in Wound Healing: A New Frontier in Regenerative Medicine. Micro, 2025. 5(4): p. 60.

90. Paul, P. and S.S. Hakkimane, Nanoparticle-based approaches for wound healing: a comprehensive review of nanomaterials enhancing tissue regeneration. Discov Nano, 2025. 20(1): p. 201.

91. Guo, S. and L.A. DiPietro, Factors Affecting Wound Healing. Journal of Dental Research, 2010. 89(3): p. 219-229.

92. Chouhan, D., et al., Emerging and innovative approaches for wound healing and skin regeneration: Current status and advances. Biomaterials, 2019. 216: p. 119267.

93. Batool, Z., et al., Hydrogel assisted synthesis of gold nanoparticles with enhanced microbicidal and in vivo wound healing potential. Scientific Reports, 2022. 12(1): p. 6575.

94. Yousaf, I., A. Anwar, and A. Umer, Formulation and Therapeutic Assessment of a Zinc Oxide, Silver, and Cerium Oxide Enriched Ointment for Accelerated Wound Healing in Aged Models. arXiv preprint arXiv:2510.10717, 2025.

95. Dam, P., et al., Wound healing strategies based on nanoparticles incorporated in hydrogel wound patches. RSC Advances, 2023. 13(31): p. 21345-21364.

96. Wang, W., et al., Nano-drug delivery systems in wound treatment and skin regeneration. Journal of Nanobiotechnology, 2019. 17(1): p. 82.