چهارمین کنگره دانشجویان
4th Congress for Agriculture, Veterinary Medicine, Environment and Natural Resources Students
کشاورزی، دامپزشکی محیط‌زیست و منابع طبیعی
www.ca.cdsts.ir

Role of Liposomal Nanocarriers Containing Medicinal Plant Extracts in Wound Healing

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ABSTRACT

Wound healing is a complex and tightly regulated biological process involving hemostasis, inflammation, proliferation, and tissue remodeling. Disruption of these phases may lead to chronic wounds characterized by persistent inflammation, oxidative stress, impaired angiogenesis, delayed re-epithelialization, and increased susceptibility to infection in both human and veterinary medicine. Chronic wounds represent a major clinical challenge due to their multifactorial pathophysiology, microbial resistance, and poor response to conventional therapies. These limitations have driven the development of novel drug delivery systems, particularly in nanomedicine. Liposomal nanocarriers are phospholipid-based vesicles capable of encapsulating both hydrophilic and lipophilic compounds. These systems enhance the stability, solubility, and bioavailability of bioactive agents while enabling controlled and sustained drug release. Additionally, liposomes improve dermal penetration, increase local drug concentration, and reduce systemic toxicity. Medicinal plants such as Aloe vera, Centella asiatica, Calendula officinalis, and curcumin-rich extracts exhibit strong antioxidant, anti-inflammatory, antimicrobial, and pro-regenerative properties. However, their clinical application is limited by poor stability and low bioavailability. The integration of liposomal nanocarriers with phytochemicals offers a synergistic therapeutic strategy that enhances wound healing through modulation of inflammatory, oxidative, and proliferative pathways.

***KEYWORDS**: Liposomal nanocarriers, wound healing, phytotherapy, drug delivery systems*

1. INTRODUCTION

Wound healing is a highly coordinated biological process that restores the structural and functional integrity of damaged tissues following injury. This process consists of four overlapping phases, including hemostasis, inflammation, proliferation, and remodeling. Successful healing requires precise regulation of cellular responses, growth factors, cytokines, extracellular matrix deposition, and angiogenesis. Under normal physiological conditions, these stages proceed in a sequential manner, resulting in tissue repair and restoration of skin function [1–3]. Despite the remarkable regenerative capacity of the skin, wound healing can be disrupted by several local and systemic factors. Chronic wounds, such as diabetic foot ulcers, venous leg ulcers, pressure ulcers, and infected wounds, fail to progress through the normal healing cascade. Persistent inflammation, excessive oxidative stress, microbial colonization, biofilm formation, and impaired angiogenesis contribute significantly to delayed tissue repair and increased risk of complications [1–3]. The prevalence of chronic wounds has increased worldwide due to aging populations, diabetes mellitus, obesity, vascular disorders, and immunological diseases. These wounds impose a substantial economic burden on healthcare systems and significantly reduce patients' quality of life. Conventional treatment strategies, including antibiotics, antiseptics, wound dressings, and surgical interventions, often demonstrate limited effectiveness because they do not adequately address the complex molecular mechanisms involved in chronic wound pathogenesis[7–12]. Medicinal plants have been extensively utilized in traditional and modern medicine for the treatment of wounds and skin disorders. Numerous plant-derived compounds exhibit antioxidant, anti-inflammatory, antimicrobial, and regenerative activities that can positively influence different stages of wound healing. Herbal extracts obtained from Aloe vera, Centella asiatica, Calendula officinalis, and

Curcuma longa have shown promising therapeutic effects in experimental and clinical studies[7–12]. However, the clinical application of many phytochemicals remains limited because of poor aqueous solubility, chemical instability, rapid degradation, and low bioavailability [9–12]. Recent advances in nanotechnology have provided innovative approaches to overcome these limitations. Liposomal nanocarriers are among the most extensively investigated drug delivery systems due to their excellent biocompatibility, biodegradability, and ability to encapsulate both hydrophilic and lipophilic bioactive compounds. These nanocarriers improve drug stability, enhance skin penetration, prolong retention at the wound site, and enable controlled release of therapeutic agents [4–6]. The combination of liposomal nanocarriers with medicinal plant extracts represents a promising therapeutic strategy for advanced wound care. By integrating the biological activities of phytochemicals with the delivery advantages of nanotechnology, these systems may enhance wound healing outcomes while minimizing systemic adverse effects. Therefore, this review aims to summarize the current evidence regarding liposomal nanocarriers containing medicinal plant extracts and their potential role in promoting wound healing and tissue regeneration[14–18].

2. PATHOPHYSIOLOGY OF CHRONIC WOUNDS

Chronic wounds are characterized by a prolonged inflammatory phase that disrupts the normal healing cascade. In contrast to acute wounds, inflammatory cells remain active for extended periods, resulting in continuous release of pro-inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). Persistent activation of these cytokines contributes to tissue destruction and delayed wound closure [1–3]. Oxidative stress is another key factor involved in impaired wound healing. Excessive production of reactive oxygen species (ROS) causes cellular injury, DNA damage, lipid peroxidation, and protein degradation. Although low levels of ROS are necessary for host defense and cellular signaling, prolonged oxidative stress can inhibit fibroblast activity and reduce tissue regeneration [1–3]. Matrix metalloproteinases (MMPs) are significantly elevated in chronic wounds. These enzymes degrade extracellular matrix proteins and growth factors required for tissue repair. Excessive MMP activity prevents granulation tissue formation and disrupts re-epithelialization, thereby prolonging wound persistence. Impaired angiogenesis also plays a critical role in chronic wound pathology. Reduced expression of vascular endothelial growth factor (VEGF) limits the formation of new blood vessels, leading to poor oxygen and nutrient delivery to the wound site. Furthermore, bacterial colonization and biofilm formation create a protective environment for microorganisms, increasing antimicrobial resistance and maintaining chronic inflammation.

3. LIPOSOMAL NANOCARRIERS IN WOUND HEALING

Liposomes are spherical vesicles composed of one or more phospholipid bilayers surrounding an aqueous core. Their structural similarity to biological membranes provides excellent biocompatibility and makes them highly effective drug delivery systems [4–6]. Depending on their composition and physicochemical properties, liposomes can be classified into conventional liposomes, cationic liposomes, PEGylated liposomes, and deformable liposomes. Each type offers specific advantages in terms of drug loading, stability, tissue penetration, and circulation time. One of the major benefits of liposomal formulations is their ability to encapsulate both hydrophilic and hydrophobic compounds. Hydrophilic agents are entrapped within the aqueous core, whereas lipophilic compounds are incorporated into the phospholipid bilayer. This versatility allows delivery of a wide range of therapeutic agents used in wound management. In wound healing applications, liposomes provide controlled and sustained drug release, enhance dermal penetration, improve retention at the wound site, and reduce systemic toxicity. Moreover, liposomal systems can facilitate cellular uptake through membrane fusion and endocytosis, resulting in improved therapeutic efficacy. Recent advances in nanotechnology have led to the development of stimuli-responsive liposomes capable of releasing their cargo in response to environmental factors such as pH, temperature, or enzymatic activity. These systems may further improve targeted wound therapy and tissue regeneration [13–18].

4. MEDICINAL PLANTS IN WOUND HEALING

Medicinal plants contain a wide variety of bioactive compounds including flavonoids, polyphenols, terpenoids, alkaloids, and polysaccharides. These phytochemicals exert antioxidant, anti-inflammatory, antimicrobial, and regenerative effects that contribute to different stages of wound healing [7–12]. Aloe vera, is one of the most extensively studied medicinal plants in wound care. Its active constituents, including acemannan and glucomannan, stimulate fibroblast proliferation, collagen synthesis, and epithelial regeneration. Additionally, Aloe vera exhibits anti-inflammatory and antimicrobial activities that promote faster wound closure [7,8]. Centella asiatica, contains triterpenoid compounds such as asiaticoside and madecassoside. These compounds stimulate fibroblast proliferation, enhance collagen production, and promote angiogenesis. As a result, Centella asiatica improves wound tensile strength and accelerates tissue remodeling [10,11]. Curcumin, the principal polyphenolic compound of Curcuma longa, possesses potent antioxidant and anti-inflammatory properties. It inhibits activation of the NF-κB signaling pathway, reduces production of inflammatory cytokines, and scavenges reactive oxygen species. These effects contribute to improved wound healing and reduced scar formation [9,12]. Calendula, officinalis contains flavonoids, carotenoids, and triterpenes that enhance granulation tissue formation and epithelialization. Its antioxidant and antimicrobial activities further support tissue regeneration and infection control during the healing process.

5. LIPOSOME–HERBAL SYNERGY

The combination of liposomal nanocarriers with medicinal plant extracts represents an advanced and multifunctional strategy in wound healing therapy. This approach integrates the biological activity of phytochemicals with the physicochemical advantages of nanocarrier systems, resulting in improved therapeutic efficiency compared to conventional herbal formulations. A major limitation of phytochemicals is their poor aqueous solubility, rapid degradation under physiological conditions, and low bioavailability. Compounds such as curcumin and flavonoids are highly unstable when exposed to light, oxygen, and enzymatic environments, which significantly reduces their clinical efficacy. Liposomal encapsulation addresses these limitations by protecting active compounds within phospholipid bilayers, thereby enhancing chemical stability and prolonging systemic and local retention [4–6,9,12]. At the wound site, liposomal–herbal systems act through multiple synergistic mechanisms. During the inflammatory phase, they suppress excessive production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, thereby reducing prolonged inflammation. In the proliferative phase, they enhance fibroblast migration, keratinocyte proliferation, and collagen synthesis, contributing to faster re-epithelialization. During the remodeling phase, they support extracellular matrix reorganization and improve tissue tensile strength [1–3,7–12]. Furthermore, liposomes enhance dermal penetration through interaction with lipid-rich skin barriers and facilitate intracellular drug delivery via fusion and endocytosis mechanisms. This leads to higher local drug concentration at the wound site while minimizing systemic exposure and potential toxicity [4–6,13–15]. Recent studies have also highlighted the antimicrobial and anti-biofilm activity of liposomal herbal formulations. This is particularly important in chronic infected wounds, where bacterial resistance and biofilm formation are major barriers to healing [5,15–18]. Overall, liposome–herbal synergy offers a promising multi-targeted approach that simultaneously addresses inflammation, oxidative stress, infection, and impaired tissue regeneration in chronic wounds

6. ADVANTAGES AND LIMITATIONS

Liposomal nanocarrier–based herbal systems provide a multifunctional platform for wound healing by targeting multiple biological pathways simultaneously. Their main advantages include improved drug solubility, enhanced stability, controlled and sustained release, and increased bioavailability of phytochemicals [4–6,13–15]. In addition, these systems enable targeted delivery to the wound site, reducing systemic distribution and associated side effects. Their biocompatibility and biodegradability further support their suitability for clinical applications [4–6].

Liposomal formulations can also be incorporated into various dosage forms such as gels, creams, sprays, and wound dressings, increasing their practical usability in both human and veterinary medicine [13–18]. Limitations, Despite their promising potential, several challenges limit the widespread clinical translation of liposomal herbal systems. One of the main limitations is the high cost of production and scale-up difficulties associated with maintaining liposomal stability during manufacturing and storage [4–6]. Physicochemical instability, including leakage of encapsulated compounds and lipid oxidation, can affect long-term efficacy [5,6]. Furthermore, the absence of standardized regulatory guidelines for nanophytomedicine formulations remains a significant barrier [13–15]. Another important limitation is the lack of large-scale, randomized clinical trials confirming their efficacy and safety in human subjects [1–3]. Addressing these limitations through improved formulation techniques, large-scale clinical studies, and regulatory standardization is essential for future clinical translation

7. CONCLUSION

Liposomal nanocarriers combined with medicinal plant extracts represent a promising and innovative strategy for the management of acute and chronic wounds. This approach integrates the advantages of nanotechnology with the therapeutic potential of phytochemicals, resulting in a multi-targeted system capable of addressing the complex pathophysiology of impaired wound healing. simultaneously modulating inflammatory responses, reducing oxidative stress, enhancing angiogenesis, and promoting extracellular matrix remodeling, liposomal herbal systems significantly improve wound healing outcomes [1–3,7–12]. Their ability to enhance drug stability, bioavailability, and targeted delivery further strengthens their therapeutic potential [4–6,13–15]. However, despite encouraging preclinical and experimental results, further research is required to overcome current limitations, including formulation instability, high production costs, and limited clinical evidence [4–6,13–18]. Large-scale clinical trials and standardized regulatory frameworks are essential to validate their safety and efficacy. In conclusion, liposomal nanocarriers incorporating medicinal plant extracts represent a next-generation therapeutic platform with strong potential for future application in advanced wound care and regenerative medicine.

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