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Review Article

Cutting-edge Pharmacological Innovations for Enhanced Post-surgical Wound Healing: Integrating Nanomedicine, Targeted Drug Delivery, and Natural Therapeutics

Journal of Pharmacology and Pharmacotherapeutics
17(3) 321–331, 2026
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DOI: 10.1177/0976500X251367992
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Abstract

Background: Surgical wound healing remains challenging in the clinical setting, bedeviled by infection, inflammation, and dysfunctional tissue regeneration. Present treatments rely on dressings and anti-biotics, whose bioavailability and site-specific delivery limitations necessitate more advanced pharmacological approaches. New trends in nanomedicine, drug targeting, and natural therapeutics are promising to overcome this status by promoting tissue repair and minimizing complications.
Objectives: This review addresses recent advances in pharmacological strategies for facilitating post-surgical wound healing, highlighting the promise of nanotechnology, controlled-release drug delivery, and natural bioactive molecules. Based on recent literature, this review highlights mechanisms, clinical relevance, and potential translational challenges.
Methodology: A comprehensive literature search was conducted on PubMed, Scopus, and Google Scholar from 2013 to 2024. Studies on nanoparticle-based drug delivery, polymeric scaffolds, phytopharmacology, and controlled-release formulations were reviewed. This review integrates preclinical and clinical evidence to present an updated perspective on the efficacy and safety of these interventions.
Results: Nanomedicine-based therapies, including liposomes, hydrogels, and polymeric nanoparticles, improve drug stability, tissue penetration, and controlled release, thereby improving wound closure. Targeted drug delivery by growth factors, cytokines, and gene therapy has been encouraging in preclinical models but awaits clinical validation. Natural bioactive compounds (e.g., curcumin, aloe vera, honey, and flavonoids) exhibit antioxidant, anti-inflammatory, and anti-microbial activities that complement pharmacological treatments. However, drug stability, scalability of formulations, and regulatory compliance limit clinical translation.
Conclusion: Advances in nanomedicine, targeted drug delivery, and natural therapeutics have transformed postoperative wound healing by providing improved efficacy and safety. However, clinical trials and regulatory guidelines are needed to enable clinical translation. Future research should emphasize biocompatibility, long-term safety, and cost-effectiveness to optimize patient benefits.

Keywords

Nanomedicine for post-surgical wound healing, drug targeting, natural therapeutics, controlled release of drugs, pharmacological advances

Received 11 March 2025; **revised** 21 June 2025; **accepted** 09 July 2025

Introduction

Postoperative wound healing remains a significant clinical problem, with millions of patients globally suffering from it. Wound healing is a complex biological process that involves multiple overlapping and dynamic phases, including hemostasis, inflammation, proliferation, and remodeling.[1] The success of the process determines the success of surgical procedures in general, with defective healing responsible for complications such as infection, chronic wounds, excessive scarring, and even a systemic inflammatory response. Despite better surgical techniques and postoperative care, a significant percentage of patients still develop delayed wound healing, particularly those with underlying diseases such as

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diabetes, peripheral vascular disease, or compromised immune status. The increasing incidence of non-healing wounds necessitates the development of novel pharmacological therapies to enhance tissue regeneration, prevent infection, and speed up recovery.[2]

The most critical post-surgical wound healing complication is the development of surgical site infections (SSIs), which contribute to a significant percentage of hospital-acquired infections. SSIs not only add to morbidity and mortality, length of stay, and healthcare costs, but also directly affect healthcare costs.[3] Bacterial colonization, biofilm development, and anti-biotic resistance also complicate infection control, rendering conventional anti-biotic therapy ineffective in most cases. Moreover, compromised vascularization of the wound bed decreases oxygen and nutrient delivery, impairing cellular proliferation and collagen synthesis, which are essential for optimal wound closure. Excessive inflammation, fibrosis, and scarring compromise functional and aesthetic results, requiring novel pharmacologic treatments.[4]

Current treatment protocols for post-surgical wound healing largely depend on conventional wound dressings, topical antiseptics, systemic anti-biotics, and anti-inflammatory drugs. While these treatments provide symptomatic relief, they are riddled with several disadvantages that inhibit maximum healing outcomes.[5] Excessive use of systemic anti-biotics has spawned multidrug-resistant bacterial strains, significantly reducing the efficacy of conventional approaches. Most antibiotics and growth factors also suffer from poor bioavailability, as systemic delivery never achieves therapeutic levels at the wound site.[6] Topical delivery, although effective in some cases, is generally inhibited by poor drug penetration, fast degradation, and short residence time, leading to suboptimal therapeutic outcomes. The slow process of natural tissue repair is also a disadvantage, particularly in patients with chronic wounds, where chronic inflammation and reduced fibroblast activity severely inhibit the proliferative phase.[7]

In recent years, novel pharmacological approaches, such as nanomedicine, targeted drug delivery systems, and bioactive natural therapeutics, have been investigated as potential agents for post-surgical wound healing enhancement. Drug delivery systems based on nanotechnology have revolutionized wound healing strategies by providing controlled and sustained release of drugs, improved bioavailability, and increased cellular uptake.[8] Various nanomaterials, such as liposomes, polymeric nanoparticles, and metallic nanoparticles, have exhibited excellent wound healing efficacy by providing anti-microbial drugs, growth factors, and anti-inflammatory drugs to the wound. Silver nanoparticles, for instance, exhibit enhanced anti-bacterial activity and are used in wound dressings to prevent infection. Similarly, hydrogel-based nanoplatforms with the loading of bioactive compounds create a moist wound microenvironment, enhance tissue regeneration, and facilitate epithelialization.[9]

Targeted drug delivery systems have also been highly well-liked in wound healing research because of the potential to deliver targeted and localized therapeutic action with minimized systemic side effects. Stimuli-responsive drug carriers, such as potential of hydrogen (pH)-sensitive and enzyme-activated nanoparticles, have been designed to deliver drugs based on the specific condition of the wound microenvironment.[10] These systems offer a platform for drug delivery only when and where it is needed, offering maximum therapeutic benefit without side effects. Microneedle patches and biodegradable scaffolds have also been designed for local drug delivery, improving healing by delivering sustained therapeutic action to the wound site.[11]

Natural therapeutics have been employed in traditional medicine for centuries to treat wounds, and recent science has established their pharmacological activities. Curcumin, aloe vera, and honey are bioactive plant extracts with high wound-healing potential because of their anti-inflammatory, antimicrobial, and antioxidant activity.[12] Curcumin, a polyphenolic turmeric extract, has been studied extensively for its ability to modulate inflammation, stimulate fibroblast proliferation, and enhance collagen deposition. Aloe vera's cooling and regenerative activity stimulates wound healing by stimulating keratinocyte migration and angiogenesis. Similarly, honey's anti-bacterial and osmotic activity have been added to various wound-care products to prevent infection and stimulate tissue repair.[13] The convergence of these sophisticated pharmacological modalities in wound therapy has the potential to overcome the limitations of traditional treatments, while revolutionizing patient outcomes. With the convergence of nanomedicine with targeted drug delivery and natural therapeutics, researchers are developing multimodal wound healing therapies that target different aspects of the healing process, from infection control and inflammation modulation to tissue regeneration and prevention of scarring. Incorporating biomaterials and bioengineered skin substitutes further augments these therapies, providing structural support and bioactive cues to enhance wound closure.[14]

This review is intended to present a comprehensive overview of the recent pharmacological frontiers of post-surgical wound healing, that is, nanomedicine, targeted drug delivery, and natural therapeutics. Based on a critical assessment of the present drawbacks in wound healing, this review is intended to highlight the role of novel drug delivery systems and bioactive molecules toward tissue repair facilitation, infection rate reduction, and complication minimization. Additionally, it will comment on the translational relevance of these advances, emphasizing the requirement for interdisciplinary collaborative research among pharmacologists, biomedical engineers, and clinicians to take these advances into mainstream medical practice. The results of this review will not only contribute to the existing body of knowledge on wound healing and provide insights into future research and clinical applications.

Review of Literature

Post-surgical healing of wounds is a significant challenge in many clinical specialties, with ophthalmic surgery, surgical interventions, and pharmacotherapy being prominent. Given the importance of targeted drug administration, Yu-Wai-Man and Khaw investigated the opportunity of small-molecule-based novel anti-fibrotic drugs targeting post-surgical wound healing for glaucoma surgery.[15] Bhusal et al. took a closer look at controlled drug release systems delivering drugs in such a way to enhance post-op pharmacotherapy for sustained release with better therapeutic delivery.[16] Askari et al. investigated localized post-surgical drug delivery from stimuli-responsive hydrogels, ensuring drug delivery while avoiding systemic issues.[17] Makvandi et al. carried the drug delivery platform further toward incorporating nanomedicine for promoting tissue regeneration, infection prevention, and cancer,[18] while Eleraky et al. outlined the use of nanomedicine to counter the problem of anti-bacterial resistance during post-surgery infection prevention, which is a critical condition.[19] These efforts emphasize the potential of advanced pharmaceutical interventions in streamlining wound healing, as shown in Table 1.

Methodology

Locating Data

A thorough literature search was conducted across databases such as PubMed, Scopus, Web of Science, and Google Scholar. The search terms to be used were "post-surgical wound healing," "nanomedicine," "targeted drug delivery," and "natural therapeutics."

Data Collection

Relevant review articles, peer-reviewed articles, and clinical trials published over the past two decades were chosen. The inclusion was based on studies that reported on pharmacological advancements for wound healing.

Data Extraction

Information on drug mechanisms, efficacy, safety, and limitations was collected and structured. Nanomedicine research, drug-controlled release, and herbal drugs were accorded greater priority.

Synthesizing Information

The collected data were synthesized and critically examined to highlight current trends, concerns, and future research directions in post-surgical wound healing pharmacotherapy.

The references were purposively selected based on innovation, clinical relevance, and impact, focusing on post-2013 integrative advancements in wound healing pharmacotherapy. High-impact studies introducing novel nanocarriers,[18] anti-fibrotic strategies,[15] and anti-bacterial nanotherapies[19] exemplify the review's translational and preclinical emphasis.

Results

Nanomedicine Breakthroughs in Wound Healing of Postoperative Wounds

Nanomedicine has been a new technique for post-surgical wound healing with controlled release, targeted drug delivery, and enhanced drug bioavailability for therapy. Liposomes,

Table 1. Literature Review—Previous Work on Drug Delivery in Post-surgical Wound Healing.[15–19]

Authors (Year)	Key Finding	Research Focus	Challenges/Limitations	Future Scope
Yu-Wai-Man and Khaw (2015)	Small molecules show promise in modulating fibrosis in post-surgical wound healing.	Anti-fibrotic strategies for glaucoma surgery.	Limited clinical trials and regulatory concerns.	Development of safer, more effective anti-fibrotic agents for ophthalmic applications.
Bhusal et al. (2016)	Controlled-release drug delivery improves postoperative pharmacotherapy.	Sustained drug release for enhanced efficacy.	Drug stability and formulation challenges.	Integration of personalized medicine and biodegradable carriers.
Askari et al. (2020)	Stimuli-responsive hydrogels enable localized drug delivery in post-surgical wounds.	Smart hydrogels for drug-controlled release.	Variable responsiveness and biocompatibility issues.	Optimization of hydrogel formulations for better clinical application.
Makvandi et al. (2021)	Nanomedicine platforms aid in tissue regeneration and infection control.	Nano-based drug delivery for post-surgical healing.	Safety concerns and toxicity profiles.	Clinical translation and large-scale production of nanomedicine formulations.
Eleraky et al. (2020)	Nanomedicine is a promising tool against anti-bacterial resistance.	Nanoparticle-based antimicrobial therapy.	Risk of cytotoxicity and long-term effects.	Advancement of targeted anti-microbial nanoparticles with minimized side effects.

Note: This table summarizes key findings, research areas, issues, and directions for future research on earlier studies on pharmacologic management of surgical wound healing.

polymeric nanoparticles, and metal nanocarriers are a few of the nanoparticles employed for sustained and targeted drug delivery, with reduced systemic toxicity and enhanced therapeutic effects. Stimuli-responsive nanocarriers provide drug-controlled release, with the drug being active for a longer duration at the site of the wound.[20]

The enhanced bioavailability of drugs through nanomedicine is one of the key causes of the enhanced rate of tissue regeneration. Nanoformulations increase drug solubility and stability and enable the deeper penetration of the drug into the wound. In addition, nanoparticles can deliver multiple drug agents, such as anti-biotics, anti-inflammatory agents, and growth factors, in a single drug delivery system, resulting in enhanced wound healing.[21]

Case studies have been used to demonstrate the effectiveness of nanomedicine in wound healing. Silver nanoparticles, for example, have improved anti-microbial activity, decreasing the rate of postoperative infection. Polymeric nanoparticles containing embedded growth factors have been found to enhance tissue healing and collagen synthesis in preclinical models. Lipid nanocarriers have also enhanced hydration and epithelialization and facilitated quick recovery. The findings thus confirm the efficacy of nanomedicine as a new strategy in postoperative wound healing.[22]

Targeted Drug Delivery for Enhanced Wound Healing

Targeted drug delivery has transformed the post-surgical healing of wounds by ensuring site-specific delivery of the drug with decreased systemic toxicity and enhanced drug effectiveness. Relative to traditional drug delivery, which is predisposed to bring about poor bioavailability and off-targeting, targeted delivery can ensure precise targeting of the drug at the site of the wound with maximum therapeutic effect and the least side effects.[23,24]

Intelligent drug delivery systems, like stimuli-responsive hydrogels and microneedle-based systems, have been created with high interest in treating wounds.[25] Stimuli-responsive hydrogels release drugs upon exposure to some physiological stimulants like pH, temperature, or enzymatic activity at the wound site, which in prolonged and sustained drug release. Likewise, microneedle patches offer effective and painless drug delivery in the deeper planes of wound tissues and offer drug permeation without going through systemic circulation, as shown in Table 2.[26,27]

Natural Therapeutics and Phytochemical Interventions in Wound Healing

Phytochemical therapy and natural medicines have gained greater interest because of their potential to contribute to postoperative wound healing as cost-effective, biocompatible, and multipotential therapies. Curcumin, aloe vera, *Centella asiatica*, and honey are some herbs and bioactive molecules that are extensively studied for their wound-healing potential. The phytochemicals enhance angiogenesis, fibroblast proliferation, and collagen deposition, leading to faster tissue formation and better wound closure.[28]

Table 2. Targeted Drug Delivery Systems for Wound Healing.[23–27]

Authors (Year)	Drug Delivery System	Mechanism of Action	Advantages	Targeted Tissue	Therapeutic Effect	Side Effects
Boateng et al. (2008)	Hydrogel-based drug delivery	Provides a moist environment and sustained drug release.	Enhances wound hydration, promotes epithelialization.	Skin and soft tissues	Accelerates tissue regeneration, reduce inflammation.	Potential allergic reactions, risk of infection in chronic wounds.
Toppo and Pawar (2015)	Nanoparticle-loaded scaffolds	Controlled and localized drug release.	High bioavailability, site-specific action.	Deep wound tissues	Enhances antimicrobial efficacy, prevents biofilm formation.	Cytotoxicity at high doses, immune response activation.
Sanjarnia et al. (2024)	Microneedle patch systems	Painless transdermal drug delivery.	Minimally invasive, high patient compliance.	Chronic wound sites	Increases drug penetration, improve vascularization.	Temporary redness and irritation at the application site.
Hoque et al. (2023)	Liposomal drug carriers	Encapsulates drugs to enhance solubility and stability.	Reduces systemic toxicity, prolongs drug release.	Skin ulcers, burn wounds	Enhances the absorption of hydrophobic drugs.	Possible skin irritation, lipid oxidation.
Manzari et al. (2021)	Polymeric nanoparticles	Stimuli-responsive, controlled drug delivery.	Biodegradable, improves targeted action.	Post-surgical wounds	Promotes fibroblast proliferation and collagen deposition.	Potential systemic toxicity, slow clearance.

Note: This table highlights targeted drug delivery systems for wound healing, describing their mechanisms, advantages, applications, therapeutic benefits, and associated side effects.

Anti-inflammatory and anti-microbial properties of phytochemicals are crucial in the prophylactic prevention of post-operative complications. Curcuminoids, flavonoids, and tannins modulate inflammatory processes by inhibiting excessive cytokine production and oxidative stress at the site of trauma.[29] Anti-microbial phytoextracts like neem (*Azadirachta indica*) and tea tree oil (*Melaleuca alternifolia*) possess broad-spectrum anti-bacterial action, successfully controlling wound infections caused by drug-resistant bacteria. These effects make phytochemicals the best option over traditional anti-biotics, as they rectify the problem of anti-biotic resistance and drug side effects.[30]

Various clinical trials have explored the efficacy of plant-based pharmacological treatments in wound healing. Studies on *C. asiatica* preparations revealed improved epithelialization and reduced scar tissue in patients undergoing surgery, and honey dressings were beneficial in reducing bacterial load, pain, and healing time. Integrating natural therapeutics into modern wound healing strategies is an opportunity to develop safer, eco-friendly, and patient-friendly therapies for post-surgical healing.[31]

Comparative Analysis of Conventional Versus Modern Pharmacological Therapies in Wound Healing

Surgical wound healing has relied on conventional therapy using anti-biotics, anti-septics, and wound dressings. Although highly effective in preventing infection, these therapies carry significant disadvantages, like anti-biotic resistance, poor bioavailability, and healing delay. Further, systemic delivery of drugs will most likely provide suboptimal drug concentrations in the wound bed, leading to ineffective therapy, as well as considerable side effects.[32]

On the other hand, sophisticated pharmacological therapies, such as nanomedicine, targeted drug delivery, and bioactive wound dressings, have revolutionized wound management.[33] Nanoparticles, liposomes, and hydrogels deliver controlled release of drugs, allowing drug absorption and retention within the wound site. Targeted therapy minimizes systemic toxicity and maximizes tissue regeneration. Also, natural therapeutics loaded with phytochemicals impart anti-inflammatory, anti-microbial, and antioxidant properties, reducing reliance on synthetic drugs.[34]

A comparison of patient outcomes and safety highlights the benefits of modern interventions. Experiments demonstrate that nanoparticle-based therapies and bioengineered dressings reduce healing time, enhance fibroblast proliferation, and reduce scar formation compared with conventional treatments.[35] Furthermore, biodegradable dressings with embedded growth factors enhance angiogenesis and collagen deposition, resulting in accelerated wound closure. While cost and regulatory concerns remain, modern pharmacological interventions are efficient, patient-friendly substitutes for conventional wound healing processes,[36] as shown in Table 3.

Pharmacokinetics (PK) and Pharmacodynamics (PD) in Wound Healing Therapies

PK and PD are critical to optimize drug effectiveness in wound healing following surgery. Drug absorption, distribution, metabolism, and elimination (ADME) are significant in therapeutic effectiveness, determining how well a drug is delivered and functions at the wound site.[37] Conventional oral and systemic drug delivery is marred by decreased bioavailability and rapid clearance, leading to suboptimal therapeutic effects in tissue repair. To achieve better healing, dosing regimens must be optimized. Controlled and sustained delivery of drugs through formulations such as nanoparticle-based carriers, hydrogels, and liposomes offers localized delivery of drugs, and therapeutic drug concentrations are maintained at the site of the wound.[38] These drug delivery systems reduce the risk of toxicity and increase tissue retention of drugs, and the action is prolonged. Moreover, methods to improve bioavailability, such as lipophilic drug modification, prodrugs, and mucoadhesive carriers, improve drug solubility and penetration into damaged tissues.[39] Targeted delivery through nanocarriers, such as polymeric nanoparticles and lipid vesicles, prevents degradation in the body and offers good drug absorption at the site of injury.[40] PK/PD modeling advances help predict optimal dosing regimens to minimize inflammation and infection risks, and to promote angiogenesis and tissue regeneration. Future research will continue to enhance personalized medicine strategies, tailoring drug delivery based on patient-specific metabolic profiles to achieve optimal wound healing,[41] as shown in Table 4.

Future Directions and Emerging Trends in Wound Healing Pharmacology

Pharmacology in wound healing is evolving very rapidly, supported by new technology and novel treatment technologies. The most promising among these are the application of artificial intelligence (AI) and machine learning (ML) in drug research.[42] These software tools can screen millions of chunks of information, predict drug efficiencies, and seek out new treatment targets for wound healing. AI algorithms also simplify formulations and drug delivery systems of drugs to deliver patient-specific treatment protocols according to a patient's unique profile.[43] Another critical development is the application of novel biomaterials and three-dimensional (3D)-printed drug delivery technologies. Smart hydrogels, bioactive scaffolds, and tissue-engineered constructs are structured to promote drug release in a controlled fashion and regenerate tissue. 3D bioprinting enables controlled deposition of growth factor-loaded, stem cell-loaded, and anti-microbial agent-loaded dressing to enhance the repair efficiency of the wound.[44] In addition, personalized medicine strategies are transforming wound healing therapy by tailoring treatments to each patient's needs. Genomics, proteomics, and metabolomics innovations enable the formation of

Table 3. Comparative Analysis of Conventional Versus Modern Pharmacological Therapies in Wound Healing.[32–36]

Author (Year)	Therapy	Mechanism of Action	Advantages	Disadvantages	Patient Outcomes	Safety Profile
Pereira and Bartolo (2016)	Traditional wound dressings	Provides a physical barrier, absorb exudates.	Cost-effective, readily available.	Limited anti-microbial properties, frequent dressing changes required.	Moderate healing rates, risk of secondary infections.	Generally safe, but may delay wound contraction.
Moses et al. (2023)	Herbal-based therapies	Anti-inflammatory and anti-microbial activity.	Natural, minimal side effects.	Standardization issues, inconsistent bioavailability.	Faster wound closure reduced scarring.	Safe with mild allergic reactions in sensitive patients.
Papageorgiou et al. (2008)	Alkannins and shikonins	Stimulates fibroblast proliferation, enhances angiogenesis.	Potent wound healing activity.	Poor solubility requires delivery enhancement.	Enhanced collagen synthesis, faster epithelialization.	Low systemic toxicity, safe for topical use.
Markiewicz-Gospodarek et al. (2022)	Bioengineered skin substitutes	Provides scaffolding for new tissue formation.	Supports complex wounds, reduces contraction.	High cost, limited availability.	Improved tissue regeneration, reduced healing time.	Safe, but risk of immune rejection in some cases.
Lemo et al. (2022)	Growth factor therapy	Stimulates cellular repair and tissue regeneration.	Directly enhances wound healing.	Expensive, potential for abnormal tissue growth.	Improved wound contraction, enhanced reepithelialization.	Moderate risk of excessive granulation tissue formation.

Note: This table compares conventional and modern pharmacological wound healing therapies based on their mechanisms, advantages, disadvantages, patient outcomes, and safety profiles.

Table 4. Pharmacokinetics (PK) and Pharmacodynamics (PD) in Wound Healing Therapies.[37–41]

Author (Year)	Drug Delivery System	Mechanism of Action	Advantages	Disadvantages	PK/PD Modeling	Personalized Medicine
Levison and Levison (2009)	Anti-bacterial agents	Targeting bacterial infection at the wound site.	Effective against bacterial colonization.	Resistance development, systemic toxicity.	Drug concentration-time curve optimization.	Personalized dosing for patient-specific infection control.
Turnheim (2003)	Systemic pharmacotherapy	Drug absorption, metabolism, and elimination in elderly patients.	Adjusted therapy for geriatric patients.	Altered metabolism leads to drug accumulation.	Age-based PK/PD adjustments.	Dose modification based on patient metabolism.
Avery et al. (2017)	Intravitreal drug delivery	Controlled ocular drug release.	Prolonged drug activity, reduced systemic toxicity.	Limited systemic absorption.	Sustained release PK modeling for an effective therapeutic window.	Optimized intravitreal injections for individualized treatment.
Międzybrodzki et al. (2023)	Bacteriophage therapy	Viral therapy targeting bacterial infections.	Alternative to antibiotics, reducing resistance risk.	PK obstacles, rapid clearance from circulation.	PK optimization for effective phage delivery.	Precision-matched bacteriophages for patient-specific infections.
Stone et al. (2016)	Liposomal drug carriers	Enhanced bioavailability and controlled drug release.	Reduced systemic toxicity, targeted drug action.	High cost, formulation stability issues.	PK models for sustained drug release profiles.	Tailored liposomal formulations for individual patient needs.

Note: This table provides a comparative overview of pharmacokinetic and pharmacodynamic challenges, mechanisms, and advantages of different drug delivery systems in wound healing therapies, emphasizing personalized medicine.

patient-specific drug regimens that optimize healing. New efforts will combine biodegradable nanocarriers, stem cell therapies, and gene editing technologies to maximize therapeutic efficiency and safety in treating wounds.[45]

Discussion

Postoperative wound healing is a complex and multifaceted biological process regulated by many pharmacological, molecular, and physiological parameters. The rising rate of postoperative complications, in the form of delayed tissue regeneration, microbial infection, excessive inflammation, and scarring, has generated the demand for novel pharmacological interventions.[46] Traditional wound healing treatments in systemic anti-biotic therapy and general dressings have revealed several limitations, particularly anti-biotic resistance, poor bioavailability, and variable therapeutic efficacy. The advent of nanomedicine, targeted drug delivery, and natural therapeutics has provided new dimensions in the facilitation of wound healing in the form of sustained drug release, enhanced tissue regeneration, and precision-targeted therapy. This review summarizes existing evidence, highlights pharmacological advances, and underscores the challenges and future directions in treating postoperative wounds.[47]

One of the most significant drawbacks of traditional wound healing therapy is the non-selective release of therapeutic components, leading to inefficient drug concentration at the wound site and systemic toxicity. The advent of nanomedicine-based drug delivery systems has enhanced the drug's solubility, stability, and bioavailability.[48] Nanocarriers, such as liposomes, polymeric nanoparticles, dendrimers, and metal nanoparticles, have been capable of providing enhanced encapsulation efficiency for the drug and controlled release behavior with sustained action.[49] Silver and gold nanoparticles have been investigated more recently for anti-microbial wound dressings, and have been shown to significantly inhibit infection by targeting multidrug-resistant pathogens. Lipid-based nanosystems have also effectively penetrated skin layers, offering maximum drug absorption and epithelialization. Although the future is promising, scalability, cost, and the issue of probable toxicity are areas to be explored further.[50]

Beyond nanotechnology, targeted drug delivery systems have transformed wound healing by reducing off-target drug exposure and site-specific activity. Stimuli-responsive hydrogels have been a cornerstone, with the ability to deliver drugs based on local wound conditions like pH, enzymatic activity, or temperature changes. Such responsiveness enables controlled therapeutic action, avoiding unnecessary drug loss and side effects.[51] To a similar end, microneedle-based drug delivery systems have also emerged as minimally invasive alternatives to traditional administration strategies. Microneedle-mediated delivery of bioactive molecules to the wound bed enables deep tissue penetration and enhanced therapeutic responses. However, clinical translation of these systems is still in its infancy, with patient compliance, regulatory approval, and large-scale manufacture preventing their overall acceptance.[52]

The healing potential of phytochemical and natural therapeutic interventions in wound healing has also received considerable attention. Several medicinal plant bioactive compounds, herbs, and marine animals have shown potent anti-inflammatory, anti-microbial, and regenerative potentials.[53] Curcumin, honey products, aloe vera, and *C. asiatica* have been extensively studied for collagen-stimulating, antioxidant, and angiogenesis-inducing effects. Natural compounds are multifunctional in their activity, stimulating fibroblast proliferation, reepithelialization, and the reduction of oxidative stress.[54] Furthermore, their low toxicity and diminished potential for resistance development make them a desirable choice compared to traditional synthetic drugs. Though promising as therapeutics, batch-to-batch variability, stability, and a lack of adequate clinical trials raise concerns for their complete integration into mainstream medical practice. One of the key determinants of the success of post-surgical wound healing is the PK/PD characteristics of therapeutic drugs.[55] Traditional drug delivery systems are usually poorly absorbed, metabolized rapidly, and cleared from the body, thereby limiting their action at the wound. To overcome this, sustained-release systems have been designed, utilizing biodegradable polymeric carriers, lipid-based vesicles, and bioadhesive matrices to extend the drug residence time.[56]

Furthermore, prodrug manipulations, hydrophilic-lipophilic balance optimization, and enzyme-activated drug release have been investigated to maximize bioavailability and therapeutic longevity.[57] PK/PD modeling is increasingly being utilized to forecast optimal dosing regimens, so that drug levels are maintained within the therapeutic window, with a reduced risk of toxicity. Advances in personalized medicine and pharmacogenomics further simplify drug delivery with therapies optimized based on patient-specific metabolic and genetic information.[58]

Comparative efficacy between conventional and novel pharmacologic approaches also points to the revolutionary potential of newer treatments. Conventional approaches primarily focus on controlling infection and symptom relief, whereas modern strategies include regenerative medicine, biomaterial-based drug delivery, and targeted therapy.[59] Clinical comparisons have shown that nanocarrier-based drug preparations, particularly growth factors and bioactive peptides, have faster rates of wound closure, reduced fibrosis, and improved quality of scars compared with conventional treatments.[60] Moreover, anti-microbial peptides and hydrogel-treated bioengineered innovative dressings showed a superior reduction in inflammatory cytokine levels and bacterial contamination around the wound than conventional treatments. Despite these developments, cost factors, regulatory hurdles, and lack of standardization remain brakes on mass clinic applications.[61]

In the near term, the pharmacological approach to wound healing will be driven by the influence of AI, ML, and regenerative medicine. AI-facilitated drug discovery platforms are accelerating the identification of novel wound-healing drugs, optimizing drug-target interaction, and predicting patient-specific treatment outcomes. Similarly, 3D printing and bioengineered scaffolds are paving the way for designing the next generation of wound dressings to release growth factors, stem cells, and biomolecules in a controlled manner.[62] Gene-editing (clustered regularly interspaced short palindromic repeats-CRISPR associated protein 9 (CRISPR-Cas9)) and ribonucleic acid (RNA)-based therapies are new technologies used to modulate the genetic and molecular processes of abnormal wound healing. Despite these advances, several challenges must be met before novel wound healing therapies can be introduced into clinical practice.[63] Regulatory bodies demand rigorous safety evaluation, large-scale clinical trials, and long-term follow-up studies to determine the efficacy and safety of new treatments. Coordination must also be achieved among biomedical engineers, pharmacologists, and clinical experts to develop patient-specific combined therapeutic approaches. In brief, post-surgical wound healing pharmacology is revolutionizing with the advent of nanomedicine, targeted drug delivery, and natural therapeutics.[64] While conventional therapies remain the cornerstone of wound care, newer technologies offer more therapeutic specificity, fewer side effects, and more significant healing potential. The intersection of AI, personalized medicine, and biomaterial engineering has immense potential to revolutionize wound care. However, more research, clinical trials, and regulatory backing are necessary to translate preclinical advances into clinical reality. With advanced drug delivery technology and interdisciplinary research, the future of post-surgical wound healing is bright, with safer, more efficient, and patient-specific therapeutic candidates on the anvil.[65]

Conclusion

Wound healing following surgery is a significant problem in clinical medicine, and new pharmacologic interventions are needed to improve recovery, minimize complications, and maximize patient outcomes. Systemic anti-biotics and conventional dressings have not succeeded, with limitations of anti-biotic resistance, poor bioavailability, and delayed healing. New advances in nanomedicine, targeted drug delivery, and natural therapeutics have transformed the field with controlled drug delivery, site specificity, and multifunctional therapeutic activity. Nanoparticles, polymeric carriers, and bioengineered dressings have arrived with great potential in the acceleration of wound repair, with fewer side effects. Natural therapeutics like phytochemicals and bioactive compounds have also arrived with potential in anti-inflammatory, collagen synthesis-stimulating, and infection-preventing activity.

Although these advances are encouraging, some hurdles remain, including regulatory challenges, standardization, and economic constraints. The future of wound healing pharmacology will probably be driven by AI, personalized medicine, and bioengineered drug delivery systems to enable more effective, patient-specific, and minimally invasive regimens. More interdisciplinary investigation and interaction among pharmacologists, bioengineers, and clinicians will be needed to translate these advances to the bedside. With the convergence of new therapeutic paradigms, the future of post-surgical wound healing looks bright with safer, more effective, and targeted therapeutic interventions in preventing complications and optimizing patient quality of life.

Key Takeaways

Postoperative drug therapy for wound healing is increasingly evolving with nanomedicine advancements, targeted drug delivery, and herbal therapeutic intervention. Microneedles, nanoparticles, and hydrogels are revolutionizing drug delivery through controlled and localized drug release at the lesion site, with minimal potential for systemic toxicity. Natural therapeutics are biocompatible and economical, and stimulate wound recovery while inhibiting inflammation and microbial infection. Personalized medicine and AI-enabled drug discovery drive the next generation of precision-based therapies, maximizing treatment efficacy and patient outcomes. Although these technologies promise a lot, hurdles such as regulatory clearances, cost, and standardization must be cleared. Future studies are bound to focus on interdisciplinary strategies, large-scale clinical trials, and translational applications to deliver safer and more efficacious wound healing therapies.

Abbreviations

ADME: Absorption, distribution, metabolism, and elimination; **AI:** Artificial intelligence; **CRISPR-Cas9:** Clustered regularly interspaced short palindromic repeats-CRISPR associated protein 9; **DepoDur™:** Extended-release epidural morphine; **ESG:** Extended-release epidural morphine study group; **EXPAREL:** Liposomal bupivacaine; **IKKβ:** Inhibitor of nuclear factor kappa B kinase subunit beta; **ML:** Machine learning; **PD:** Pharmacodynamics; **pH:** Potential of hydrogen; **PK:** Pharmacokinetics; **RNA:** Ribonucleic acid; **siRNA:** Small interfering RNA; **SPARC:** Secreted protein acidic and rich in cysteine; **SSIs:** Surgical site infections; **3D:** Three-dimensional; **VEGF:** Vascular endothelial growth factor.

Acknowledgments

The authors are thankful to the Department of Shalya Tantra (Surgery), Mahatma Gandhi Ayurved College Hospital and Research Centre, Wardha, for their generosity in providing academic and research sponsorship. The authors appreciate researchers in this field who contributed valuable suggestions, which brought us to this review. Our deepest gratitude is to our mentors, colleagues, and reviewers, whose remarks and suggestions significantly added value to the quality of this manuscript.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval and Informed Consent

This narrative review does not involve direct human or animal studies; hence, ethical clearance was unnecessary. However, all data sources were chosen with caution from credible scientific databases, journals, and peer-reviewed publications to uphold ethical standards. The authors have upheld good academic and research ethics by correctly citing all the materials they used and refraining from plagiarism and data manipulation.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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References

1. DasGupta R, Yap A, Yaqing EY, et al. Evolution of precision oncology-guided treatment paradigms. *WIREs Mech Dis* 2023; 15: e1585. doi: 10.1002/wsbm.1585
2. Xu C, Zhang S, Zhang Y, et al. Evolving landscape and academic attitudes toward the controversies of global immuno-oncology trials. *Int J Cancer* 2021; 149: 108–118. doi: 10.1002/ijc.33503
3. Dare AJ, Anderson BO, Sullivan R, et al. Surgical services for cancer care. In: Gelband H, Jha P, Sankaranarayanan R, et al. (eds) *Cancer: disease control priorities*. 3rd ed. Washington D.C.: The International Bank for Reconstruction and Development/The World Bank; 2015. doi: 10.1596/978-1-4648-0349-9
4. Quigley HA and Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006; 90: 262–267.
5. Addicks EM, Quigley HA, Green WR, et al. Histologic characteristics of filtering blebs in glaucomatous eyes. *Arch Ophthalmol* 1983; 101(5): 795–798.
6. Battegay EJ, Raines EW, Seifert RA, et al. Transforming growth factor beta induces bimodal proliferation of connective tissue cells via complex control of an autocrine platelet-derived growth factor loop. *Cell* 1990; 63: 515–524.
7. Roberts AB, Sporn MB, Assoian RK, et al. Transforming growth factor type B: rapid induction of fibrosis and angiogenesis *in vivo* and stimulation of collagen formation *in vitro*. *Proc Natl Acad Sci U S A* 1986; 83: 4167–4171.
8. Tomasek JJ, McRae J, Owens GK, et al. Regulation of alpha-smooth muscle actin expression in granulation tissue myofibroblasts is dependent on the intronic CArG element and the transforming growth factor-beta1 control element. *Am J Pathol* 2005; 166(5): 1343–1351.
9. Bainbridge D, Martin J, Arango M, et al. Evidence-based perioperative clinical outcomes research. Perioperative and anaesthetic-related mortality in developed and developing countries: a systematic review and meta-analysis. *Lancet* 2012; 380: 1075–1081.
10. O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Am J Infect Control* 2011; 39: S1–S34.
11. Mehuys E and Vervaet C. Oral controlled release dosage forms. *J Pharm Belg* 2010; 65(2): 34–38.
12. Portenoy RK, Sciberras A, Eliot L, et al. Steady-state pharmacokinetic comparison of a new, extended-release, once-daily morphine formulation, Avinza™, and a twice-daily controlled-release morphine formulation in patients with chronic moderate-to-severe pain. *J Pain Symptom Manag* 2002; 23: 292–300.
13. Hoffman AS. The origins and evolution of controlled drug delivery systems. *J Control Release* 2008; 132: 153–163.
14. Yasin MN, Svirskis D, Seyfoddin A, et al. Implants for drug delivery to the posterior segment of the eye: a focus on stimuli-responsive and tunable release systems. *J Control Release* 2014; 196: 208–221.
15. Yu-Wai-Man C and Khaw PT. Developing novel anti-fibrotic therapeutics to modulate post-surgical wound healing in glaucoma: enormous potential for small molecules. *Expert Rev Ophthalmol* 2015; 10(1): 65–76.
16. Bhusal P, Harrison J, Sharma M, et al. Controlled-release drug delivery systems to improve postoperative pharmacotherapy. *Drug Deliv Transl Res* 2016; 6(5): 441–451.
17. Askari E, Seyfoori A, Amereh M, et al. Stimuli-responsive hydrogels for local post-surgical drug delivery. *Gels* 2020; 6(2): 14.
18. Makvandi P, Josic U, Delfi M, et al. Drug delivery (nano) platforms for oral and dental applications: tissue regeneration, infection control, and cancer management. *Adv Sci* 2021; 8(8): 2004014.
19. Eleraky NE, Allam A, Hassan SB, et al. Nanomedicine fight against antibacterial resistance: an overview of the recent pharmaceutical innovations. *Pharmaceutics* 2020; 12(2): 142.
20. Al-Jamal KT, Al-Jamal WT, Wang JT, et al. Cationic poly-L-lysine dendrimer complexes doxorubicin and delays tumor growth *in vitro* and *in vivo*. *ACS Nano* 2013; 7(3): 1905–1917. doi: 10.1021/nn305860k
21. Alkhorayef M, Mahmoud MZ, Alzimami KS, et al. High-intensity focused ultrasound (HIFU) in localized prostate cancer treatment. *Pol J Radiol* 2015; 80: 131–141. doi: 10.12659/PJR.892341
22. Bazak R, Houri M, El Achy S, et al. Cancer active targeting by nanoparticles: a comprehensive review of literature. *J Cancer Res Clin Oncol* 2015; 141(5): 769–784. doi: 10.1007/s00432-014-1767-3
23. Boateng JS, Matthews KH, Stevens HN, et al. Wound healing dressings and drug delivery systems: a review. *J Pharm Sci* 2008; 97(8): 2892–2923.
24. Toppo FA and Pawar RS. Novel drug delivery strategies and approaches for wound healing managements. *J Crit Rev* 2015; 2(2): 12–20.
25. Sanjarnia P, Picchio ML, Solis AN, et al. Bringing innovative wound care polymer materials to the market: challenges, developments, and new trends. *Adv Drug Deliv Rev* 2024; 27: 115217.
26. Hoque M, Hossain MS, Akram T, et al. Advancing healthcare: exploring recent innovations in drug delivery systems. *Int J Multidiscip Res Growth Eval* 2023; 4(5): 50–55.
27. Manzari MT, Shamay Y, Kiguchi H, et al. Targeted drug delivery strategies for precision medicines. *Nat Rev Mater* 2021; 6(4): 351–370.

28. Antonelli M, De Pascale G, Ranieri VM, et al. Comparison of triple-lumen central venous catheters impregnated with silver nanoparticles (AgTive®) vs conventional catheters in intensive care unit patients. *J Hosp Infect* 2012; 82: 101–107.
29. Chen Y-M, Dai A-P, Shi Y, et al. Effectiveness of silver-impregnated central venous catheters for preventing catheter-related bloodstream infections: a meta-analysis. *Int J Infect Dis* 2014; 29: 279–286.
30. Benoit MA, Mousset B, Delloye C, et al. Antibiotic-loaded plaster of Paris implants coated with polylactide-co-glycolide as a controlled release delivery system for the treatment of bone infections. *Int Orthop* 1998; 21: 403–408.
31. Price JS, Tencer AF, Arm DM, et al. Controlled release of antibiotics from coated orthopedic implants. *J Biomed Mater Res* 1996; 30: 281–286.
32. Pereira RF and Bartolo PJ. Traditional therapies for skin wound healing. *Adv Wound Care (New Rochelle)* 2016; 5(5): 208–229.
33. Moses RL, Prescott TA, Mas-Claret E, et al. Evidence for natural products as alternative wound-healing therapies. *Biomolecules* 2023; 13(3): 444.
34. Papageorgiou VP, Assimopoulou AN, and Ballis AC. Alkannins and shikonins: a new class of wound healing agents. *Curr Med Chem* 2008; 15(30): 3248–3267.
35. Markiewicz-Gospodarek A, Kozioł M, Tobiasz M, et al. Burn wound healing: clinical complications, medical care, treatment, and dressing types: the current state of knowledge for clinical practice. *Int J Environ Res Public Health* 2022; 19(3): 1338.
36. Lemo N, Marignac G, Reyes-Gomez E, et al. Cutaneous reepithelialization and wound contraction after skin biopsies in rabbits: a mathematical model for healing and remodeling index. *J Clin Dermatol Ther* 2022; 7(2): 167–180.
37. Levison ME and Levison JH. Pharmacokinetics and pharmacodynamics of antibacterial agents. *Infect Dis Clin North Am* 2009; 23(4): 791–815.
38. Turnheim K. When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. *Exp Gerontol* 2003; 38(8): 843–853.
39. Avery RL, Castellarin AA, Steinle NC, et al. Systemic pharmacokinetics and pharmacodynamics of intravitreal aflibercept, bevacizumab, and ranibizumab. *Retina* 2017; 37(10): 1847–1858.
40. Międzybrodzki R, Kasprzak H, Letkiewicz S, et al. Pharmacokinetic and pharmacodynamic obstacles for phage therapy from the perspective of clinical practice. *Clin Infect Dis* 2023; 77(Suppl. 5): S395–S400.
41. Stone NR, Bicanic T, Salim R, et al. Liposomal amphotericin B (AmBisome®): a review of the pharmacokinetics, pharmacodynamics, clinical experience and future directions. *Drugs* 2016; 76: 485–500.
42. Curcio M, Cirillo G, Saletta F, et al. Carbon nanohorns as effective nanotherapeutics in cancer therapy. *J Carbon Res* 2021; 7(1): 3. doi: 10.3390/c7010003
43. Devi S, Kumar M, Tiwari A, et al. Quantum dots: an emerging approach for cancer therapy. *Front Mater* 2022; 8: 798440. doi: 10.3389/fmats.2021.798440
44. Dos Reis SB, de Oliveira Silva J, Garcia-Fossa F, et al. Mechanistic insights into the intracellular release of doxorubicin from pH-sensitive liposomes. *Biomed Pharmacother* 2021; 134: 110952. doi: 10.1016/j.biopha.2020.110952
45. Han B, Yang Y, Chen J, et al. Preparation, characterization, and pharmacokinetic study of a novel long-acting targeted paclitaxel liposome with antitumor activity. *Int J Nanomed* 2020; 15: 553–571. doi: 10.2147/IJN.S228715
46. Kamba T and McDonald DM. Mechanisms of adverse effects of anti-VEGF therapy for cancer. *Br J Cancer* 2007; 96(12): 1788–1795. doi: 10.1038/sj.bjc.6603813
47. Karve S, Werner ME, Sukumar R, et al. Revival of the abandoned therapeutic wortmannin by nanoparticle drug delivery. *Proc Natl Acad Sci U S A* 2012; 109(21): 8230–8235. doi: 10.1073/pnas.1120508109
48. Carmeliet P, Moons L, Luttun A, et al. Synergism between vascular endothelial growth factor and placental growth factor contributes to angiogenesis and plasma extravasation in pathological conditions. *Nat Med* 2001; 7(5): 575–583. doi: 10.1038/87992
49. Rodríguez C, Rodríguez-Sinovas A, and Martínez-González J. Lysyl oxidase as a potential therapeutic target. *Drug News Perspect* 2008; 21(4): 218–224. doi: 10.1358/dnp.2008.21.4.1184042
50. Schwartz MA, Schaller MD, and Ginsberg MH. Integrins: emerging paradigms of signal transduction. *Annu Rev Cell Dev Biol* 1995; 11: 549–599. doi: 10.1146/annurev.cb.11.110195.003001
51. Duan Y, Guan X, Ge J, et al. Cationic nano-copolymers mediated IKKb targeting siRNA inhibit the proliferation of human Tenon's capsule fibroblasts *in vitro*. *Mol Vis* 2008; 14: 2616–2628. https://pubmed.ncbi.nlm.nih.gov/19137066/
52. Nakamura H, Siddiqui SS, Shen X, et al. RNA interference targeting transforming growth factor-beta type II receptor suppresses ocular inflammation and fibrosis. *Mol Vis* 2004; 10: 703–711. https://pubmed.ncbi.nlm.nih.gov/15467516/
53. Wang F, Qi LX, Su Y, et al. Inhibition of cell proliferation of Tenon's capsule fibroblast by S-phase kinase-interacting protein 2 targeting SiRNA through increasing p27 protein level. *Invest Ophthalmol Vis Sci* 2010; 51(3): 1475–1482. doi: 10.1167/iovs.09-4498
54. Seet LF, Su R, Toh LZ, et al. *In vitro* analyses of the anti-fibrotic effect of SPARC silencing in human Tenon's fibroblasts: comparisons with mitomycin C. *J Cell Mol Med* 2012; 16(6): 1245–1259. doi: 10.1111/j.1582-4934.2011.01398.x
55. Rose JS, Neal JM, and Kopacz DJ. Extended-duration analgesia: update on microspheres and liposomes. *Reg Anesth Pain Med* 2005; 30: 275–285.
56. Hartrick CT and Hartrick KA. Extended-release epidural morphine (DepoDur™): review and safety analysis. *Expert Rev Neurother* 2008; 8: 1641–1648.
57. Alam M and Hartrick CT. Extended-release epidural morphine (DepoDur™): an old drug with a new profile. *Pain Pract* 2005; 5: 349–353.
58. Pasero C and McCaffery M. Extended-release epidural morphine (DepoDur™). *J Perianesth Nurs* 2005; 20: 345–350.
59. Viscusi ER, Kopacz D, Hartrick C, et al. Single-dose extended-release epidural morphine for pain following hip arthroplasty. *Am J Ther* 2006; 13: 423–431.
60. Gambling D, Hughes T, Martin G, et al. A comparison of DepoDur™, a novel, single-dose extended-release epidural morphine, with standard epidural morphine for pain relief after lower abdominal surgery. *Anesth Analg* 2005; 100: 1065–1074.

61. Carvalho B, Roland LM, Chu LF, et al. Single-dose, extended-release epidural morphine (DepoDur™) compared to conventional epidural morphine for post-cesarean pain. *Anesth Analg* 2007; 105: 176–183.
62. Onel E, Miller H, Patou G, et al. (eds). EXPAREL, a liposomal bupivacaine local analgesic, extends pain relief and decreases opioid use. *Annual meeting of American Society of Anesthesiologists*. San Diego, California, 16–20 October 2010. Medscape.
63. White PF, Ardeleanu M, Schooley G, et al. (eds). Pharmacokinetics of depobupivacaine following infiltration in patients undergoing two types of surgery and in normal volunteers. *Annual meeting of the International Anesthesia Research Society*, San Diego, California, 14–17 March 2009. Lippincott.
64. Bagsby DT, Ireland PH, and Meneghini RM. Liposomal bupivacaine versus traditional periarticular injection for pain control after total knee arthroplasty. *J Arthroplasty* 2014; 29: 1687–1690.
65. McAlvin JB, Reznor G, Shankarappa SA, et al. Local toxicity from local anesthetic polymeric microparticles. *Anesth Analg* 2013; 116: 794.