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# Stem Cell versus Pharmacological Therapies in Rodent Models of Wound Healing: A Comparative Review

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***Abstract*** Wound healing isWound healing is a complex physiological process that restores the structural integrity and function of damaged tissues. Conventional drug-based therapies, the current standard of care, often yield suboptimal outcomes characterized by slow regeneration, particularly in large or chronic wounds. such treatment restrictions have prompted the research of alternative therapies, especially the use of stem cell therapy, as it has a high potential to promote regeneration and more effectively control the healing process. This paper is a review of the new information that has been stated in the rodent model studies that compare therapy performance of the stem cell application to the traditional drug treatment in wound healing and tissue repair. We aimed to critically evaluate the comparative effectiveness, underlying mechanisms, and safety profiles of these approaches. the bone marrow, adipose tissue, and peripheral blood stem cells are beneficial in wound closure, angiogenesis, and skin architecture re-modeling of skin. The comparative analysis has shown that stem cell therapy does not only increase healing rates but also the quality of tissue repair resulting in increased normal restoration of normal functioning and appearance. Improved immunomodulatory capabilities, the ability to produce paracrine factors, and direct involvement in the repair of damaged tissue are some of the qualities that have been attributed to these benefits. Conversely, pharmacological treatments like anti-inflammatory agents and growth factors have fewer effects, and are limited to the effects of controlling inflammation and early tissue regeneration phases, without significantly affecting later tissue regeneration. Recent experimental studies consistently report superior outcomes including accelerated wound closure, enhanced neovascularization, and improved histological architecture in stem cell-treated rodents compared to drug-treated controls. Stem cell therapies are applicable in preclinical studies because of its versatility in that it can be topical, injectable, or scaffold-delivered. To sum up, the current body of evidence places the stem cell-based therapy as a highly promising modality of tissue repair and wound management that has specific benefits over the conventional pharmacological methods in rodent models. Future prospects of stem cell therapy have only gotten better as the source of cells and cell engineering has been developed. This review indicates that in experimental rodent models stem cells are better than drugs to facilitate effective and comprehensive wound healing with further studies being warranted to optimize the use of stem cells in a broader use within clinical settings.

**Keywords:** Stem Cells, Drugs treatment, Rodent, Wound Healing, Tissue Repair



***Introduction*** The process of wound healing and tissue repair is a multifaceted dynamic process whereby the body recovers integrity and functionality of damaged tissues. This occurs through a number of phases (different but overlapping): hemostasis, inflammation, proliferation, and remodeling. As soon as injury is caused, the hemostasis stage is provoked, and blood vessels constrict and platelets aggregate to create a clot that stabilizes the wound and gives cells the opportunity to move. This clot deploys a range of growth factors and cytokines which trigger a new stage of inflammation (1).

The inflammatory stage is marked by neutrophil and macrophage recruitment, which eliminates

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pathogens, clears debris as well as releases mediators that provide and influence subsequent healing processes. Any maltherapy at this point can cause the delayed or impaired healing. This is followed by the proliferative phase which involves the increase in growth and diffusion of the keratinocytes, fibroblasts and endothelial cells after inflammation. It leads to the new extracellular matrix formation, angiogenesis, and the development of granulation tissue, which forms the basis of wound healing and tissue repair (2). At the remodeling stage, collagen fibers can play with each other and cross-link, the granulation tissue is substituted with a scar, and the tissue tensile strength increases gradually. This might take weeks to months and the level of restoration may not reach that of the original tissue which is usually functional and very strong. Wound healing plays a significant role in post-traumatic and post-surgical recovery and failure to heal properly due to infection, underlying illness, or malnutrition may lead to a chronic wound or pathological scarring (3).

The use of rodent models plays a pivotal role in the field of translational research of wound healing and tissue repair because they are genetically, physiologically, and immunologically similar to humans and are reproducible and economical. With the mice and rats, researchers have an opportunity to examine the cellular and molecular processes involved in repair processes in controlled experimental conditions. Rodent models can be used to test the efficacy of new treatment approaches like stem cell therapy. Their brief reproduction cycles, genetic manipulation with ease and laid down procedures of wound induction contribute to the close study of acute and chronic wound conditions. Rat experiments have resulted in the discovery of some of the most important aging, inflammatory, angiogenic and fibrotic mechanisms, which hastened the creation of new medications and treatments that could be applied to patients (4). The existing wound healing drug therapies based on the use of anti-inflammatory agents, antimicrobials, and growth factors have shown an ability to control acute wounds and minimize the possibilities of infections, but they demonstrate serious weaknesses in treating complex or chronic wounds. The used therapies cant repairing of the normal tissue function or regenerating of the tissue structure, that leading into chronic inflammation or incomplete healing. Also, the specificity of many medications leads to a low effectiveness of drugs on the complex cellular and molecular mechanisms needed to produce a strong tissue repair (5).

The other significant constraint is the possibility of antibiotic resistance and other systemic undesirable side effects in the course of drug prolongation or repeated drug intake. The treatments applied using growth factors have been hindered by challenges of quick deterioration in the wound bed and the inability to deliver localized high concentrations. Moreover, the specifics of patients, age, comorbidities, and nutritional status may affect the drug efficacy and safety, and the outcomes may not be predictable. At large, the up-to-date drug-based interventions are critical elements of wound care, but these limitations are critical and suggest the introduction of more specific and regenerative treatment approaches (6).

The main objective of this research will be to contrast the therapeutic capability of stem cell-based treatment and conventional medication in rodent models of wound healing. Compare and contrast the effectiveness of stem cell therapy and drug therapy in wound healing, tissue regeneration, angiogenesis and functional repair using controlled rodent experiments. Further, demonstration of the action mechanisms of the stem cells and pharmacological agents which regulate the wound healing. Compare safety profiles and constraints of both treatment methods with emphasis put on possible adverse effects, tumorigenicity and immune responses in preclinical rodent models. Determine translation implications and constraints associated with the wound management as applied to the bench to bedside development of stem cell and drug therapies.

Literature review:

**Wound Healing**:

Wound healing is a complex and highly regulated process that restores the integrity of damaged tissue. It consists of four overlapping phases: hemostasis, inflammation, proliferation, and remodeling (7).

•Hemostasis: Immediately following injury, vasoconstriction and clot formation prevent blood loss.

•Inflammation: In this phase, immune cells are recruited to the site to clear debris and prevent infection.

•Proliferation: This stage involves the proliferation and migration of key cells (fibroblasts, endothelial cells, and keratinocytes) to rebuild the tissue. Critical events include re-epithelialization (covering the wound), angiogenesis (forming new blood vessels), and the deposition of a new extracellular matrix.

•Remodeling: The final phase involves the maturation and reorganization of the newly formed tissue. Collagen fibers are cross-linked and realigned, which gradually increases the wound's tensile strength (number of refrencess).

This synchronized process enables the recovery of tissue structure and functioning although its

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effectiveness may depend on age, nutrition, comorbidities and infection. The pathological outcomes of disruptions at any of the phases can be chronic wounds or hypertrophic scarring. Research progress is still being made to expand knowledge of cellular and molecular processes involved in wound healing, which can be applied to develop new therapeutic modalities (8).

Mechanisms of Wound Healing:

**The healing phases**:

1-Inflammation: The inflammatory response begins shortly after an injury and is manifested by vasodilation, which permits the migration of immune cells (neutrophils and macrophages) to the wound. These cells remove pathogens, cell debris and secrete signaling molecules such as cytokines and growth factors that mediate further healing processes. This stage is characterized clinically by the presence of redness, swelling, heat and pain in the area of the wound. The stage normally takes several days but in chronic wounds, it may run long.

2-Proliferation: In the proliferative stage, there is the formation of new tissues. Fibroblasts travel into the injury and develop external cellular matrix proteins, most specifically, collagen, to create granulation tissue. Angiogenesis occurs in order to recapitulate blood supply and keratinocytes proliferate and migrate to re-epithelialize the wound surface. The stage usually takes a few days to a few weeks depending on the size and condition of the wound. To sustain these processes, the necessary moisture and oxygenation are needed.

3-Remodeling: The remodeling stage which is also known as maturation is a gradual replacement of granulation tissue with a mature scar. The reorganization and cross-linking of collagen are done to enhance tensile strength and elasticity of the repaired tissue. The stage may persist in months to years following injury. It is found that the scar tissue which is formed is usually less elastic and about 20 percent weaker than the one which is formed. Remodeling can lead to dysregulation which could cause hypertrophic scars or keloids. Such stages interact and are interrelated, making sure that the succession towards successful healing is synchronized(9)

-Influences of the efficiency of healing in rodents and clinical translation.

1-Species and Strain Differences: The differences between mouse and rat strain in terms of healing rate and immune response are based on genetic and physiological differences. These differences affect the intensity of inflammation, scarring and angiogenesis.

2-Type and Location of 2 Wound Model: The dynamics of healing depend on the presence of an excisional or incisional wound or a burn wound, and the location. The skin of rodents is loose and under vascularization than in humans, and occasioned contraction may occur instead of regeneration.

3-Age and Health Status: Aging or systemic (e.g., diabetes, etc.) animals have a delayed healing process, which is considered chronic wounds in humans(10).

4- More Clinically Relevant Animal Models: Using aged, diabetic, or obese animals with complex wounds.

1.Focusing on the Mechanism of Action: Understanding how the therapy works (e.g., via paracrine signaling) allows for the development of cell-free alternatives (exosomes, conditioned media) that are easier to manufacture and regulate.

2.Robust Biomarker Identification: Finding measurable biomarkers that can predict a patient's response to therapy.

3.Advanced Delivery Systems: Developing "smart" biomaterials that enhance cell survival and control their release of therapeutic factors.

Influencing Factors of Clinical Translation.

1-Skin Structure Differences: Human skin is characterized by a thicker epidermis and dermis and has tighter attachments accompanied by different cellular composition. This is an anatomical difference that restricts the extrapolation of rodent studies directly.

2-Immune System Variability: Varying immune cell subsets and responses can have an influence on the inflammation and resolution phases across species.

3-Environmental and Lifestyle Influences: Patient nutrition, comorbidities, drugs, and mechanical forces are environmental and lifestyle factors that cannot be thoroughly simulated in laboratory experiments (12) (13).

**Stem Cells in Wound Healing**

- Stem Cell Source: (BM-MSCs, ADSCs, EPCs)

A few kinds of stem cells have shown therapeutic promise in wound healing studies and this is largely attributed to their self-renewal and differentiation capabilities as well as their capacity to modulate the healing microenvironment. The primary ones that are used are:

1-Bone Marrow-Derived Mesenchymal Stem Cells (BM-MSCs): The multipotent adult stem cell is capable of differentiating to provide skin cell types (fibroblasts and keratinocytes) in the direct pathway to tissue regeneration. BM-MSCs release a wide variety of growth factors and cytokines to stimulate angiogenesis, extracellular matrix remodeling and immunomodulation. They have been shown to be

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effective in wound healing and enhancement of dermal thickness in multiple preclinical and clinical studies.

2-Adipose-Derived Stem Cells (ADSCs): ADSCs are obtained by adipose tissue hence they are abundant and easy to harvest which makes them a viable option of stem cell therapy. These cells have a high growth potential and high secretion activity of proangiogenic factors, which improve vascularization and promote the formation of granulation tissues. ADSCs have demonstrated effectiveness in diabetic ulcers, venous ulcers and other chronic wound models.

3-Endothelial Progenitor Cells (EPCs): EPCs play a major role in neovascularization by converting into endothelial cells which cover the inner wall of the newly created blood vessels. They play a vital role in restoration of blood supply to tissues in the healing process, particularly ischemic wounds, through oxygenation and delivery of nutrients. These stem cells do not simply differentiate, but additionally mediate their effects via paracrine, where they release extracellular vesicles and soluble factors that mediate the effects of inflammation, endogenous cell recruitment, and regenerative processes. The application of hydrogels or scaffolds in the process of combinatorial delivery further increases their therapeutic value (14, 15, 16).

**Stem cell mechanisms**:

Stem cells contribute to wound healing in various ways that all work together to improve the repair and regeneration of the tissue. These are paracrine, direct differentiation and immunomodulation.

1-Paracrine Effects: This is one of the main mechanisms that help stem cells to heal by releasing a plethora of bioactive molecules including growth factors, cytokines and extracellular vesicles. They include activating angiogenesis and recruiting endogenous progenitor cells and adjusting the inflammatory microenvironment to facilitate tissue healing. Among the most important paracrine mediators, there are vascular endothelial growth factor (VEGF), transforming growth factor-b (TGF-b), interleukins, which trigger fibroblast proliferation, remodeling of the extracellular matrix, and neovascularization (17).

2-Differentiation: Stem cells also differentiate in other specialized cell types that are of use in skin repair like keratinocytes, fibroblasts and endothelial cells. This direct cellular replacement helps in the re-formation of the epithelial barrier, development of new connective tissue, and development of new blood vessels. This capability is important in the process of restoring the structural and functional integrity of the damaged skin (18).

3-Immunomodulation: Stem cells have strong immunomodulatory effects, which aid in the regulation of the inflammatory process. They may inhibit overinflammation by the activation and proliferation of immune cells e.g. T cells and macrophages and stimulate inflammatory phenotypes to antiinflammatory phenotypes. This modulation decreases tissue damage due to chronic inflammation and provides the environment in which healing is beneficial (19,20).

**Drug-Based Wound Healing**

There are many drugs that are currently being used in wound healing to address various facets of the healing process such as inflammation, tissue regeneration, and prevention of infections. Their action is designed to respond to targeted stages or problems of wound care.

**1- Anti-Inflammatories:** The main objective of the drugs is to cut down on excessive inflammation which may slow down healing and result in chronic wounds. NSAIDs, which include ibuprofen, diclofenac, are inhibitors of cyclooxygenase (COX) enzymes, lowering the rate of prostaglandin production, thus lowering pain, swelling, and inflammation. Inflammation is also suppressed by corticosteroids which inhibit various inflammatory mediators and immune responses but are applied carefully because they may suppress tissue regeneration provided they are overused (21).

**2-Growth Factors:** These biologic factors facilitate healing by enhancing cellular proliferation, migration and differentiation. Key growth factors include:

**A- Vascular Endothelial Growth Factor (VEGF):** This growth factor triggers angiogenesis which enhances the circulation of blood vessels.

**B-Transforming Growth Factor-b (TGF-b):** Modulates the action of fibroblasts, the production of collagen, and the ECM deposition.

**C-Platelet-Derived Growth Factor (PDGF):** Promotes the migration of different cells including fibroblasts and smooth muscle cells to the injured area.

These agents are used either topically or biomaterial-delivered to increase tissue healing, particularly in chronic, non-healing wounds (22).

**3-Antimicrobials:** The prevention of wounds is very essential in wound healing. Topical agents used as antimicrobials are antibiotics (e.g., mupirocin, neomycin), antiseptics (e.g., povidone-iodine, chlorhexidine), and systemic antibiotics when required. Their action entails suppressing the growth of bacteria or killing of bacteria, directly by interfering with cell wall production, protein production, or metabolic pathways, increasing microbial load and

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wound infection leading to a slower healing process. These medications tend to be applied with a combination therapy (depending on the needs of the wound) the purpose of which is to manage the infection, mediate an inflammatory response, and promote tissue regeneration (23).

**Direct Comparative Evidence in Rodent Models:**

The results of rodent models of stem cell therapy versus drug therapy of wound healing show that a number of key points are important to consider with regard to efficacy, wound closure, histological and molecular outcomes.

**1-Efficacy and Wound Closure Rate:** In any case, stem cell therapies always have proven to be extremely faster in wound closure than traditional drug-based treatment. Various researches have indicated that rodents that received mesenchymal stem cells (MSCs) or adipose-derived stem cells (ADSCs) exhibit much quicker wound healing and absolute healing. This is explained by the improvement of cellular proliferation, angiogenesis, and migration of skin cells towards the wound site (24).

**2-Histological Improvements:** The histological analysis of wounds in stem cell therapy demonstrates the enhanced grating tissue formation, greater collagen deposition with a better structure, and more intense neovascularization. Recently developed tissue is more similar to normal skin architecture, with greater numbers of fibroblasts and less inflammatory infiltrates, than is the case with drug-only treatment. Such alterations are related to better tensile strength and functional integrity of healed wounds (25).

**3-Molecular Outcomes:** Stem cell therapy increases the molecular and signal pathway activities associated with healing, including the angiogenic signal that is mediated by VEGF, the fibroblast-activating signal of TGF-b, and the anti-inflammatory cytokines. It enhances the moderate inflammatory response, reducing the pro-inflammatory cytokines, such as TNF-a and IL-6, and increasing the anti-inflammatory one. On the other hand, drug therapies tend to regulate a smaller range of pathways and have no multipronged regenerative activity as with stem cells. The identified results confirm the regenerative efficiency of stem cell therapies in the wound healing experimental models, which has a mechanistic basis on the subsequent development and clinical translation (26), as shown in table (1).

This comparison highlights the superior efficacy and complexity of stem cell therapies in enhancing wound healing, tissue regeneration, and functional recovery versus the more limited effects of conventional drug treatments. The data reflect findings from experimental rodent models and suggest valuable directions for clinical application development.

Molecular Pathways and Mechanisms Hundreds of important molecular pathways such as PI3K/Akt, Notch, SDF-1/CXCR4, cytokines, and chemokines are involved in mediation of wound healing processes and are regulated by stem cell therapy as well as drug treatment.

**1- Phosphoinositide 3-Kinase (PI3K)/Akt Pathway:** The phosphoinositide 3- kinase (PI3K)/Akt signal pathway is basic in facilitating cell survival, proliferation, migration, and angiogenesis during wound repair. This pathway increases migration of keratinocytes and growth of fibroblasts to promote tissue healing. PI3K/Akt is stimulated by both stem cells and by some drugs to have a faster healing process (27).

**2-Notch Signaling**: Notch signaling controls the processes of cell differentiation, proliferation, and apoptosis in skin repair. It regulates the epidermal cell fate choice and has an impact on inflammation. Stem cells regulate the Notch pathway to scale between regeneration and scarring whereas certain pharmacological agents indirectly regulate the Notch signaling to stimulate tissue repair (28).

**3-SDF-1/CXCR4**: Axis Stromal cell-derived factor-1 (SDF-1) and its receptor CXCR4 mediate recruitment of the stem/progenitor cells to the wound bed. This axis is essential in guiding the endogenous and transplanted stem cells to the damaged tissue to promote neovascularization and repairing. A number of treatments aim to inhibit the SDF-1/CXCR4 axis to enhance the results of cell homing and healing (29).

**4-Cytokines and Chemokines:** Pro- and anti-inflammatory (e.g., TNF-a, IL-6, IL-10) cytokines and chemokines coordinate the immune cells recruitment, the elimination of inflammation, and the regeneration of tissues. Stem cells normally facilitate a switch towards anti-inflammatory cytokines, which offer a regenerative environment, but some drugs are meant to adjust the cytokine signaling so that undue inflammation is inhibited. Collectively, these pathways comprise a sophisticated network in which the stem cell and drug therapies have their effects on wound healing at the molecular and cellular levels (30, 31).

**Safety, Limitations, and Adverse Outcomes:** Safety is an important issue in the assessment of both stem cell and drug therapy of wound healing, especially prior to clinical translation. Rodent experiments are useful in revealing the possible risks of tumorigenicity, immune response, or other undesirable outcomes.

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**1-Tumor Formation:** As much as the regenerative potential of stem cells is promising, there has been concern over the possibility of their ability to form tumors particularly in the case of the use of pluripotent stem cells or in the occurrence of genetic anomalies due to cell propagation regimens. Preclinical rodent models have in some cases reported the development of teratma with embryonic stem cells or induced pluripotent stem cells. Nevertheless, the adult stem cells, such as mesenchymal stem cells (MSCs), show a significantly reduced risk, but long-term safety follow-ups are necessary (32).

**2-Immune Response:** Autologous stem cell transplant as well as allogeneic transplant can result in immune reaction. Allogenic MSCs in rodent models have exhibited a low immunogenicity and are capable of regulating host immune responses, however, rejection and inflammatory reactions still can take place, especially with repeated injections or non-mesenchymal cells. These challenges are being addressed by immune suppression strategies or cell engineering. Stem cell therapies have an immune reaction that is different in terms of cell source and host compatibility. The autologous stem cells are also known to produce few immune responses, whereas allogeneic stem cells can produce immune rejection or inflammation, particularly in the case of repeated injections. MSCs possess a well-known immunomodulatory effect, which typically suppresses harmful immune effects, yet such action is prone to different rodent models and should be considered in detail (33).

**3-Adverse Effects:** Other adverse effects in rodents include undesired differentiation, fibrosis, and embolism with regards to delivery method and cell dose. Drug treatment is not without its own risks namely, systemic toxicity, allergic reactions and resistance to antibiotics. The two methods need optimized dosing, as well as exhaustive testing of toxicity in preclinical models. Other side effects other than tumorigenicity and immune response are inappropriate differentiation, fibrosis and side effects of delivery methods like microvascular embolism. Although drug therapies are well-studied in terms of safety, they are not devoid of potential risks (including systemic toxicity, allergic reactions, development of antimicrobial resistance, etc.). Maximizing dosing schedules and continuous monitoring of the toxicity in rodents are critical to reduce these risks on both of these treatment modalities. The rodent safety data would indicate that stem cell therapies in most cases have an acceptable safety profile though require a stringent examination of tumor risk and immunogenicity. In comparison, drugs are well-characterized in terms of safety, but there are issues that are associated with toxicity and resistance. These facts give relevance to the need to have further preclinical evaluation so that therapeutic utilization will continue to be safe. The rodent safety evidence highlights that besides promising potential, stem cell therapies should undergo careful clinical translation to ensure that they are examined in terms of tumor risk, immune compatibility, and off-target activity and that existing concerns in pharmaceutical safety are taken into account (34).

**Translational Potential**

1-Prospects and Challenges: The translational potential of stem cell therapies and drug treatments in wound healing is a highly promising approach to wound healing that has numerous challenges to be overcome before it can be broadly used in clinical practice. These difficulties are crucial to the knowledge of the future of regenerative medicine beyond the rodent preclinical work to effective human uses.

2-Barriers to Clinical Translation:- It is difficult to produce high-quality, phenotype, and potency stem cells in large quantities that can be used in clinics. Cell source, isolation and culture variations influence cell efficacy and safety of therapy.

3-Regulatory Hurdles: The stem cell therapies will have to undertake the rigid regulations such as Good Manufacturing Practice (GMP), safety profiling, and long-term monitoring. Regulatory regimes are changing yet are complicated and unequal throughout the world.

4-Immunogenicity and Safety Concerns: According to the discussion above, immune rejection, tumorigenicity, and off-target effects risks are immunogenicity risks that can be only effectively studied in relation to all cell types and delivery methods before clinical application.

5-Delivery and Integration: An advantageous delivery, retention and functional integration of stem cell in wound tissue, is a persistent challenge. The use of biomaterial scaffolds and controlled release systems has potential and could use further optimization (35) .

**Future Research Directions**

1-Increasing the Stem Cell Potency: The genetic modification, preconditioning, and exosomes or secretomes of the stem cells seek to increase the therapeutic potential by reducing the risks.

2-State of the Art Biomaterials: Hydrogels, scaffolds, and nano-platforms to enhance cell delivery and survival and regulated factor release is a pressing field of study.-

3-Approaches to Personalized Medicine: The customization of therapies according to patient-related

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variables, e.g. genetics, comorbidities, the type of wound may improve the outcomes and safety profiles.

3-Large Animal Models and Clinical Trials: An intensive testing of efficacy and safety in large animal models and well-designed clinical trials will play a significant role in validating the mode of action (36, 37).

**Conclusion**

Stem cell therapies present a revolutionary method for wound healing and tissue restoration, surpassing traditional pharmacological treatments. These therapies utilize complex functional systems such as paracrine signaling, direct differentiation, and immunomodulation to promote faster healing and improved tissue quality, which pharmacological agents alone cannot achieve. Studies in preclinical mouse models indicate that stem cells significantly enhance angiogenesis, granulation tissue formation, and inflammatory response balance. Unlike conventional pharmacotherapy, which may have side effects and inadequate tissue regeneration, stem cell approaches can be optimized through delivery systems and biomaterials to improve cell survival and effectiveness. Personalized stem cell and pharmacological treatments stand to enhance overall efficacy and safety. The integration of stem cell science with medication and biomaterial development is poised to transform healing practices and enhance patients' quality of life.

**Conflict of interest**

There is no conflict of interest in this study as stated by the authors.

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Table (1): show summarizing the typical findings comparing stem cell therapy and conventional drug therapy for wound healing (summarizing by the authors

| Parameter | Stem Cell Therapy | Conventional Drug Therapy |
|---|---|---|
| Wound Closure Speed | Significantly faster, with reduced time to partial and full closure | Slower healing, often shows no significant improvement over controls in chronic wounds |
| Blood Vessel Formation | Promotes strong, mature, and well-organized angiogenesis within healing tissue | Induces only modest and short-lived angiogenic effects |
| Collagen Deposition & Structure | Produces higher collagen density and better organization, with early maturation to type I collagen | Collagen is often disorganized and remains immature longer (type III collagen) |
| Scar Quality and Strength | Results in scars more closely resembling healthy skin, achieving higher tensile strength | Scar quality is generally inferior, with less functional strength |
| Inflammatory Response | Regulates immune response, accelerating resolution of inflammation by promoting healing-supportive immune cells | Broad immune suppression or lack of targeted immunomodulation; antibiotics lack direct immune effects |
| Mechanism of Action | Multifaceted and dynamic, impacting multiple phases of healing simultaneously through signaling and direct cell participation | Limited to single or few targets, typically focusing on one aspect such as reducing inflammation or infection |