THE EFFICACY OF STEM CELLS IN WOUND HEALING: A SYSTEMATIC REVIEW

Dr. N. Junior Sundresh[1], M.S., FRCS., FACS., Ph.D., A. Farah Tabasum[2], N.S Nithya Shree[3], C. Thanusha[4]

[1]Professor of Surgery, Government Cuddalore Medical College and Hospital, Annamalai Nagar, Chidambaram - 608002.

[2,3,4] Pharm. D, Department of Pharmacy, Annamalai University, Annamalai Nagar, Chidambaram - 608002.

[2]faru8595@gmail.com, [3]nithyashreenarayanan25@gmail.com, [4]thanushaarasu2003@gmail.com

Abstract

This systematic review evaluates the therapeutic efficacy of stem cell–based interventions, particularly mesenchymal stem cells (MSCs), in wound healing across clinical, preclinical, and mechanistic studies. Eight eligible studies were analyzed, including five research articles and three review articles. The findings consistently demonstrated that MSCs enhance wound closure, improve angiogenesis, accelerate epithelialization, and promote collagen remodeling. Stem cells exert their effects through paracrine signaling, immunomodulation, and stimulation of tissue regeneration. Clinical evidence supports their safety and effectiveness in chronic wounds such as diabetic ulcers. Emerging cell-free MSC therapies, including exosomes, show additional promise with reduced risks. Overall, stem cell–based therapy represents a highly effective and evolving strategy for managing complex and chronic wounds.

Keywords*:*

Stem Cells; Wound Healing; Mesenchymal Stem Cells; Chronic Wounds; Diabetic ulcers, Angiogenesis; Paracrine Signal; Immunomodulation; Tissue Regeneration; Epithelialization; Collagen

INTRODUCTION

Wound healing is a complicated and changing process that happens in the body. It involves many steps at the cell, molecule, and chemical levels to fix damaged tissue. Even though there have been improvements in medical care, certain types of long-lasting wounds—like diabetic foot ulcers, leg ulcers from poor blood flow, pressure sores, wounds from radiation treatment, and serious burns—continue to be a big problem around the world. These wounds affect millions of people and can lead to long hospital stays, ongoing pain, loss of movement, and a higher chance of infection or needing an amputation. They also cost healthcare systems a lot of money because the treatments take a long time and often come back.

Because of this, there's a big need for better treatment options that can speed up the healing process, help tissue grow back, and achieve better results, especially for wounds that don't heal on their own or are hard to treat. Older ways of treating wounds, like cleaning the wound, using special bandages, giving antibiotics, using negative pressure therapy, and transplanting skin, may help with symptoms but don't fix the deeper issues that stop healing.

Chronic wounds often have ongoing inflammation, trouble forming new blood vessels, not enough tissue building materials, weak healing cells, and messed-up signals between cells. These problems are caused by

conditions like diabetes, poor nutrition, poor blood flow, infection, and getting older. These overall health issues make it hard for the body to heal naturally, so typical treatments may not work well.

In recent years, using stem cells has become a new and hopeful way to improve wound healing. Stem cells can keep making more cells, turn into different types of cells, and release helpful chemicals that control the immune system and help tissue grow. Mesenchymal stem cells, which come from places like bone marrow, fat, umbilical cord, and placenta, are especially interesting because they are easy to get, don't cause strong immune reactions, and have strong healing abilities. Their healing power comes mainly from releasing chemicals like growth factors, signaling molecules, and tiny pouches of material that help make new blood vessels, build tissue, cover the wound, and control inflammation.

Several review studies have thoroughly explained how stem cells help improve wound healing [1] found that stem cells help at every stage of the wound-healing process by promoting new blood vessel growth, reducing inflammation, and encouraging cell growth [2] noted that mesenchymal stem cells (MSCs) can turn into different types of cells like fibroblasts, keratinocytes, and endothelial cells, and they also help other cells in the body grow and repair damaged areas [3] pointed out that therapies without actual cells, like MSC-derived exosomes, can also help with healing, but they carry fewer risks than using live cells.

Research from original studies backs up the effectiveness of stem cell treatments [4] showed that MSCs greatly improve skin wound healing and tissue regeneration in animal tests. They also looked at new ways to deliver MSCs, such as using hydrogels and scaffolds, which help the cells survive longer and work better at the wound site [5] looked at multiple studies on burn wounds and found that stem cell therapy greatly speeds up healing, helps form new blood vessels, and increases collagen, which suggests it could be very useful for serious skin injuries.

In real-world medical settings, stem cells have also shown promise [6] did a human study showing that MSC therapy significantly helps heal diabetic foot ulcers, increases the formation of new tissue, and reduces the size of wounds compared to standard treatment. This is especially important because diabetic wounds are a major cause of non-healing ulcers and often lead to amputations. So, effective stem cell treatments could make a big difference in the long-term health of people with diabetes.

More recently, new studies and comparisons have looked at stem cells from different places [7] looked at many stem cell treatments and found that mesenchymal stem cells from fat and umbilical cord work better for healing wounds. This is because they grow more and make more helpful proteins that help the body repair itself [8] did a big study looking at all kinds of stem cells and found that each type has different healing abilities. However, all of them helped wounds heal better than usual treatments. Their work shows it's important to pick the right kind of stem cells and the best way to use them, depending on the type of wound and the patient's condition.

Overall, the research shows that stem cell treatments, especially those using mesenchymal stem cells, have a big chance to change how we treat wounds. These cells help with several problems at the same time, like poor blood flow, ongoing inflammation, and weak tissue repair, which are common in wounds that don't heal. Both lab and real-world studies show that stem cells help wounds close faster, improve the quality of the tissue, make more blood vessels, and reduce scarring. Also, new methods like using cell-free parts, like exosomes, may offer safer and more controlled treatment options without the risks of using live cells.

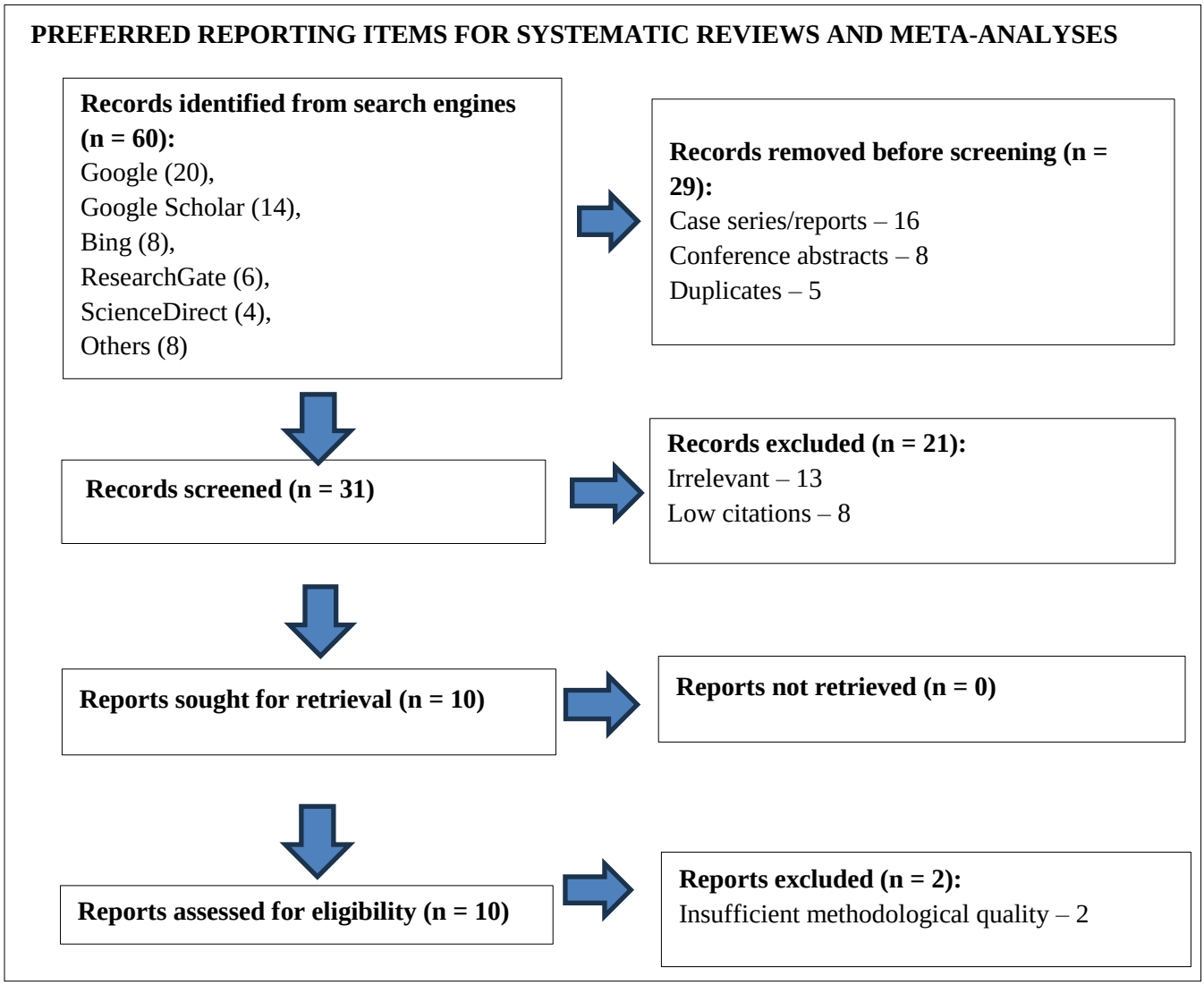
Even though these results are promising, there are still challenges. It's not clear which stem cells are best, how to give them, how much to use, how safe they are long-term, and whether they are cost-effective. More large studies are needed to create standard guidelines. Still, the current findings strongly suggest that stem cells are becoming an important part of regenerative medicine for wound healing.

This review looks at and brings together evidence from important studies and articles to assess how effective stem cell treatments are for healing wounds, explain how they work, compare different sources of stem cells, and find areas that need more research.

METHODS

The search across several search engines first found 60 records, including articles from Google, Google Scholar, Bing, ResearchGate, ScienceDirect, and other online sources. Then, 29 records were removed before checking them more closely because they didn't meet the basic requirements—16 were case reports or case series, 8 were conference abstracts, and 5 were duplicates. That left 31 articles for checking their titles and abstracts, and 21 of them were excluded because they weren't related to the research topic or didn't have enough citations, showing they didn't contribute much scientifically. Then, 10 full-text articles were looked for, and all of them were found (none were missing). These 10 full-text articles were checked again for eligibility, and 2 were excluded because of poor quality in their methods, like weak study designs or not reporting results clearly enough. In the end, 8 studies met all the criteria. These included 5 original research papers that provided real data on how stem cells work in wound healing and 3 review papers that gave more general ideas and explanations about the topic. These 8 studies became the main source of information for the systematic review.

Figure:1



Studies included in the review (n = 8):
Research articles – 5
Review articles – 3

RESULTS

TABLE 1.1 RESULTS OF REVIEW ARTICLE:

AUTHOR & YEAR	STUDY TYPE	AIM / OBJECTIVE	STEM CELL TYPE / FOCUS	KEY FINDINGS	CONCLUSION
Ayavoo et al., 2021	Narrative Review	To explore the roles, mechanisms, and therapeutic potential of stem cells in cutaneous wound healing.	Mesenchymal stem cells (MSCs) from various sources (bone marrow, adipose tissue, umbilical cord)	• Stem cells accelerate all phases of wound healing—hemostasis, inflammation, proliferation, and remodeling. • Promote angiogenesis via VEGF, PDGF, FGF release. • Reduce inflammation through immunomodulation and cytokine balancing. • Enhance collagen deposition, fibroblast activity, and epithelialization. Paracrine signaling identified as the main mechanism rather than direct differentiation.	MSCs significantly improve wound healing outcomes through multiple cellular pathways. Paracrine effects and immunomodulation are central therapeutic mechanisms. Stem-cell–based therapy holds strong potential for chronic wound management.

Leavitt et al., 2016	Comprehensive Review	To summarize advances in stem cell therapy for chronic wounds and analyze clinical and preclinical evidence.	Adult stem cells, embryonic stem cells, induced pluripotent stem cells (iPSCs); emphasis on MSCs	• Chronic wounds exhibit impaired angiogenesis and persistent inflammation; stem cells counteract these deficits. • MSCs enhance neovascularization and granulation through growth factor secretion. • Stem cell transplantation improves diabetic, ischemic, and radiation-induced wounds in animal models. • Clinical studies show enhanced re-epithelialization, wound closure, and reduced scar tissue.	Strong evidence supports MSCs as a promising therapy for chronic wounds. However, challenges remain regarding delivery efficiency, survival rate, and standardization of protocols.
Ma et al., 2023	Focused Review	To evaluate the therapeutic potential of MSC-derived cell-free therapies (secretome, exosomes) for wound healing.	MSC secretome, exosomes, extracellular vesicles (EVs)	Cell-free therapies mimic the regenerative functions of MSCs without risks of tumorigenicity or immune rejection. • Exosomes promote angiogenesis, fibroblast proliferation, and collagen synthesis. • EV-based therapy reduces inflammation and enhances antioxidant defenses. • More stable, easier to store, and safer than whole-cell therapy.	MSC-based cell-free therapy represents a next-generation wound-healing approach offering superior safety, stability, and efficacy. Further clinical trials are needed for translation.

TABLE 1.2 RESULTS OF RESEARCH ARTICLE:

AUTHOR & YEAR	STUDY TYPE	AIM / OBJECTIVE	STEM CELL TYPE / SOURCE	SAMPLE / MODEL	KEY FINDINGS	CONCLUSION
Lee et al., 2016	Experimental research / Preclinical	To evaluate MSC efficacy in cutaneous wound healing and assess novel delivery methods that improve cell survival and therapeutic effect.	Mesenchymal Stem Cells (Bone marrow–derived MSCs)	Animal models (rodents) with induced cutaneous wounds	• MSCs significantly accelerated wound closure and enhanced re-epithelialization. • Advanced delivery systems (hydrogels, scaffolds, nanoparticles) improved MSC retention at the wound site. • Increased collagen production and angiogenesis were observed.	MSCs effectively promote cutaneous wound repair, and novel delivery systems substantially enhance therapeutic outcomes.
Li et al., 2020	Systematic review & meta-analysis (Preclinical)	To evaluate the overall efficacy of stem cell therapy in burn wound healing across preclinical studies.	Various MSC sources (bone marrow, adipose, umbilical cord)	Meta-analysis of animal burn models (n > 20 studies)	• Stem cell therapy significantly improved wound closure time. Enhanced angiogenesis and collagen remodeling. Reduced inflammatory markers and necrosis. Consistent improvement in	Stem cell therapy is highly effective in accelerating the healing of burn wounds in animal models, with strong potential for future clinical translation.

					granulation tissue formation.	
Cao et al., 2017	Clinical trial (Human study)	To analyze the therapeutic effect of MSCs in diabetic foot ulcer healing.	Human Mesenchymal Stem Cells (Bone marrow–derived)	Human participants with diabetic foot ulcers	• MSC-treated wounds showed significantly faster reduction in ulcer size. • Enhanced granulation tissue formation and improved vascularity. • No major adverse effects reported. • Faster epithelialization compared to standard care.	MSC therapy is safe and clinically effective in promoting healing of diabetic foot ulcers, showing strong potential for chronic wound management.
Farabi et al., 2024	Systematic review	To evaluate the effectiveness of stem cells in chronic and acute wound healing based on available human, animal, and in-vitro studies.	Multiple stem cell sources (MSCs, ASCs, UCSCs, EPCs)	Comprehensive review of published studies	• MSCs consistently improved wound closure, angiogenesis, and fibroblast proliferation. • Adipose-derived MSCs showed superior growth factor secretion. • Umbilical cord stem cells offered high proliferative potential. • Noted gaps include poor standardization of dosage and delivery routes.	Evidence strongly supports stem-cell–based therapy as effective for wound healing, though large-scale clinical trials are needed for protocol standardization.
Tong et al., 2025	Meta-analysis	To compare effects of stem cells from different sources on cutaneous wound	Multiple MSC sources (BM-MSCs, AD-MSCs,	Meta-analysis of preclinical and limited clinical studies	• All stem cell types improved wound closure vs. control. • Adipose-derived MSCs showed the highest efficacy in	Different stem cell sources provide variable but consistently positive wound-healing effects. Adipose and umbilical cord MSCs may offer

		healing outcomes.	UC-MSCs)		angiogenesis induction. • Umbilical cord MSCs demonstrated high proliferative and immunomodulatory capacity. • Bone marrow MSCs improved collagen deposition and tissue strength.	superior therapeutic potential.

DISCUSSION

The results from the eight studies together show that using stem cell therapy can really help with wound healing, especially for hard-to-treat and complicated wounds. Both lab tests and studies done on people, backed up by strong evidence, show that mesenchymal stem cells (MSCs) from different places like bone marrow, fat, and umbilical cord have a big impact on healing. These cells work in several ways: they send signals to other cells, help control the immune system, and encourage the growth of new blood vessels. These different actions help fix the main problems that stop wounds from healing, like ongoing inflammation, poor blood supply, and not enough connective tissue forming.

[1] pointed out that MSCs speed up all the steps of healing, especially by releasing growth factors such as vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF). These factors help with making new blood vessels, more fibroblasts, and skin cells growing over the wound. This matches what [4] found in lab studies, where giving MSCs helped wounds close faster and encouraged more collagen and blood vessel development. They also noted that using better ways to deliver the cells, like hydrogels, special materials, and nanoparticles, made the cells last longer and work better in the wound area. This shows that improving how we deliver the cells is important for getting the best results. [2] also said that MSCs fix many issues in long-term wounds, like continued inflammation and poor new blood vessel growth. Their review looked at both animal and human studies, showing that MSCs help with forming new tissue and skin cells growing back. This is similar to the study by [6] , where using MSCs helped heal diabetic foot ulcers faster. In that study, the MSCs improved how quickly the wounds closed, made blood vessels better, and didn't cause serious side effects. This is important because diabetic foot ulcers are a big problem and hard to treat. The ability of MSCs to help with new tissue and blood vessel growth could lower the risk of losing a limb and improve overall health for patients.

In addition, [5] did a detailed review of studies on burns and found solid proof that mesenchymal stem cells (MSCs) work well. Their research showed that stem cell treatments help wounds close faster and lead to better tissue repair. This includes better collagen rebuilding and less inflammation. Burn wounds are tough to treat because they cause a lot of tissue damage and have high levels of inflammation. The good results seen in burn studies show that MSC-based treatments are strong and can work well in different types of wounds. Recent research, like the work by [3], is pointing to new ways using stem cells.

They looked at cell-free treatments like extracellular vesicles and exosomes made from MSCs. These cell-free treatments can do similar healing jobs as living MSCs by sending out microRNAs, proteins, and growth factors. But they don't carry the risks of using live cells. This change to using non-living parts of cells may offer better storage, lower chances of immune reactions, and less risk of cancer.

[7] did a complete review of many studies and found that MSCs from fat tissue (AD-MSCs) and umbilical cord (UC-MSCs) are very powerful. They grow quickly and release a lot of healing proteins. [8] also analyzed many studies and found that all stem cell types help with wound healing. But AD-MSCs are better at forming new blood vessels, while UC-MSCs are strongest at controlling the immune system. Bone marrow MSCs (BM-MSCs) also work well, especially with rebuilding tissue and making it stronger. These findings suggest that choosing the right type of MSC depends on the specific wound and what the treatment goals are.

Even though the evidence for stem cell therapy is strong, there are still some issues. Many of the studies are done in animals, which can give useful information about how things work, but applying these results to people needs careful thought. There aren't enough human trials, like the one by [6], to fully understand how safe and effective these treatments are. More large-scale, controlled studies are needed to figure out the best ways to use stem cells, including how much to give, how to deliver them, and what long-term effects they might have. Also, differences in how stem cells are collected, grown, and given make it hard to compare results between studies. These differences are a big problem in the current research and need to be fixed before stem cell therapy can be used widely in hospitals.

CONCLUSION

A total of 60 records were found from different search engines. Out of these, 29 were taken out before checking because they were duplicates, conference summaries, or case reports. After checking 31 records, 21 were not included because they were not relevant or didn't have enough scientific support. Then, ten full-text articles were looked at closely, but two were left out because their methods were not strong enough. In the end, eight studies met the criteria for inclusion: five research papers and three review articles.

All five research studies showed that stem cell-based treatments had a positive effect on healing wounds. [4] found that bone marrow stem cells helped wounds close faster and improved collagen and blood vessel growth, especially when used with advanced materials. [5] said that stem cell treatment greatly improved healing in burn wounds, helping tissue form and reducing inflammation in lab models. [6] gave clinical proof that stem cells helped heal diabetic foot ulcers without serious side effects. [7] stated that stem cells from fat and umbilical cords had better regenerative power, while [8] found that all types of stem cells helped, with fat-derived cells being the best at making new blood vessels. The three review articles explained how stem cells help wounds heal. They pointed out that stem cells work by sending signals, calming the immune system, and encouraging new blood vessel growth [1,2,3]. They also mentioned that therapies using only stem cell parts, like exosomes, are a good alternative.

In summary, all eight studies show that stem cell-based treatments are effective in helping wounds heal, regardless of the type of wound.

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