Narrative Review Article

Emerging Innovative Cell-Based Wound Dressings for Scarless Wound Healing

Sabrina Kiung

Hillfield Strathallan College, 299 Fennell Ave W, Hamilton, ON L9C 1G3, Canada

ABSTRACT

Effective wound healing is critical for restoring both the function and appearance of damaged skin, yet chronic wounds and visible scars remain a major physical and emotional challenge. Conventional dressings primarily serve as physical barriers that prevent infection and maintain a healing-promoting environment, but do little to stimulate true tissue regeneration. Emerging research in regenerative medicine has led to the development of cell-based wound dressings, combining live cells, such as keratinocytes and stem cells, with engineered support materials. These innovations promote the release of biological signals that reduce inflammation and guide collagen organization (crucial to effective and scarless healing), resulting in more functional and aesthetically improved outcomes. In particular, adipose-derived stem cells (ASCs) and bone marrow-derived stem cells (BMSCs) have demonstrated the ability to accelerate wound closure and minimize fibrosis by producing regenerative signals at the wound site. Dressings arising from the natural regeneration of fetal skin repair provide further direction for designing future therapies that promote complete scarless healing. Although fetal-cell-based treatments display strong potential, ethical and practical challenges remain. This paper reviews current progress in cell-based wound dressings and explores how insights from fetal healing could help achieve faster, more effective, and scarless wound repair in the future.

Keywords: Wound healing; Wound dressing; Cell-based dressing; Scarless healing; Fetal wound; Regenerative medicine

INTRODUCTION

Wound healing is the biological process of restoring the body's damaged protective barrier. Causes of severe wounds can range from traumatic injuries to diabetes and burns. In the U.S. alone, approximately 10.5 million people suffer from chronic wounds a year, and globally, up to 50% of patients admitted to the hospital require wound care (1-2). This prevalence highlights the significant societal impact of wound management worldwide. The wound healing process consists of four main stages: hemostasis, inflammation, proliferation, and maturation (3). Delays or abnormalities during this process can be caused by underlying medical conditions, such as diabetes, poor blood supply, and environmental factors (e.g., inadequate dressings that lack protective ability). There are two primary objectives in wound healing: replacing damaged tissue (closing the wound site) and minimizing scarring. Current advancements in the wound healing field offer a range of approaches that help accelerate healing and minimize infections, such as hydrogel dressing or new classes of antibiotic

Corresponding author: Sabrina Kiung, E-mail: sabrinakiung@gmail.com.

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compounds, etc. (4-6). However, challenges remain in the wound care field, including a high rate of chronic wounds in some patient populations and a high rate of scar tissue formation post-healing. Therefore, the need for a next-generation dressing that can help accelerate healing while eliminating scar formation remains.

Scars can range from fine lines resulting from surgery to potentially painful, raised hypertrophic and keloid scars. Although scar formation allows for rapid closure of a wound, it creates many functional limitations as well. Scars on hands or near joints can cause contracture, leading to restricted motion (7). Scars in the genitalia can affect sexual function and urination (8). Scars on the head and neck are especially dangerous as nerves and vital functions are at risk (8). In addition to the functional impact of scarring, scars can also have an emotional impact. Every year, millions of patients are left with scars either from trauma or surgery, and although many scars are painful or disabling, patients report that clinicians are often unaware of their concerns and commonly do not provide treatment options for their scars (9). A survey by Brown *et al*. (2008) revealed that the majority of their patients were unsatisfied with their scars' appearance due to perceived stigma and psychological factors, which interfered with their social interactions and overall quality of life (10). Moreover, patients with facial scars are especially susceptible to severe anxiety and self-consciousness due to the visibility and difficulty in hiding the scars (10). Singer *et al*. (2000) also surveyed 747 participants on patient priorities of laceration management. Patients from a broad range of demographic groups have similar concerns about scarring, valuing 4 main aspects: normal function (28%), avoiding infection (20%), visual appearance (17%), and reduced pain (17%) (11). Although the visibility of scarring is a prominent issue among patients, it is a natural part of the body's healing process and is unavoidable, particularly with wounds that penetrate the dermis (12). The size and prominence of the scar may differ depending on wound severity, location, genetics, and care; however, even with optimal healing conditions, including rapid hemostasis, controlled inflammation, tissue proliferation, and organized collagen deposition, adult wounds naturally prioritize fast and durable repair over perfect regeneration, which is why scars inevitably form.

Wound dressings can create an environment that is apt to minimize the risks of wound tear, infections, patient discomfort, etc., during the healing process. Many criteria must be taken into consideration when developing optimal dressings: 1. Protect the wound site (infection prevention, mechanical strength); 2. Promote optimal wound healing (moisture control, ideal gas transmission, and necrosis reduction); 3. Ensure comfort for the patient (exudate elimination, pain alleviation, and ease of use). Any deficiency in these factors, along with wound type, infection status, and genetics, may cause chronic pain, infection, severely disfiguring scars, and psychological distress. There are many types of conventional wound dressings, including hydrocolloids, alginates, foam dressings, film dressings, and hydrogels (Table 1) (13-15). Each dressing best suits different types of wounds, depending on factors such as the amount of exudate, skin sensitivity, infection, dryness, and overall patient suitability. Considering the ideal features of a wound dressing for effective healing, conventional wound dressings aim to create an environment that protects the body from infection while promoting the natural healing process. Although conventional wound dressings are beneficial in creating the optimal external conditions for wound healing, they may fail to prevent scarring. It is also difficult to manage the wound throughout the healing process and often needs frequent replacement, which increases the risk of infection and discomfort. Moreover, it is challenging to ensure the dressing does not dry out the wound or fail to absorb excess exudate, potentially leading to maceration or slow cell migration. Traditional wound dressings mainly cover and protect wounds, but they cannot actively promote healing, reduce the risk of infection, or minimize scarring as effectively as modern and advanced dressings, such as cell-based dressings (16).

Cell-based dressings are an innovative, emerging wound healing strategy that incorporates living cells within a carrier or biocompatible scaffold (18). Compared to conventional dressings, which primarily provide a protective environment, cell-based dressings directly participate in the healing process. They are typically developed by extracting autologous cells (e.g., keratinocytes, fibroblasts, or mesenchymal stem cells) from the patient's own tissue, including adipose tissue or bone marrow. They are then cultured and seeded or embedded into a supportive matrix (19). Once applied, the embedded cells secrete growth factors and cytokines and guide collagen fibre organization, ultimately reducing the likelihood of irregular healing outcomes. One example of a supportive matrix is electrospun nanofiber meshes (ENMs), which are designed to mimic the natural skin extracellular matrix (ECM). ENMs provide optimal conditions for cell attachment, proliferation, and

Table 1. *Common types of conventional wound dressings and their key characteristics, moisture handling capabilities, suitable wound types, and clinical advantages and limitations.*

Dressing Type	Key Components	Moisture Handling	Suitable Wound Types	Advantages	Limitations
Hydrocolloids	Gel-forming agents (gelatin, pectin) (17)	Maintain moist, autolytic debridement (17)	Low to moderate exudate wounds (17)	Barrier to bacteria, promotes healing (3)	Not for infected or heavily exuding wounds (3)
Alginates	Seaweed-derived polysaccharides (15)	Highly absorbent, forms a gel with exudate (15)	Moderate to heavy exudate wounds (15)	Hemostatic, absorbent (3)	Require secondary dressing; not for dry wounds (3)
Foam dressings	Polyurethane or silicone foam (15)	Absorb moderate to heavy exudate (17)	Pressure ulcers, delicate skin (17)	Moulds and contours to the wound shape (17)	May require frequent dressing change (17)
Film dressings	Thin polyurethane sheets (15)	Permeable to oxygen/ vapour, not exudate (17)	Superficial wounds, low exudate (15)	Transparent, easy monitoring (17)	Do not absorb exudate; risk maceration (17)
Hydrogels	Water/glycerin-based gels (14)	Donate moisture to dry wounds (15)	Dry or necrotic wounds, burns (3)	Soothing, cooling effect (14)	Low absorption; risk of maceration with excess exudate (3)

controlled delivery of growth factors and other bioactive molecules (20).

In addition to their ability to directly promote healing, cell-based wound dressings also address many of the limitations associated with conventional dressings. Traditional wound coverings cannot actively stimulate cellular activity, accelerate angiogenesis, or regulate collagen alignment, thereby often leading to complications such as disfiguring scars. In contrast, cell-based dressings provide both external protection and promote healing by modulating inflammation, reducing infection, and balancing exudate absorption to maintain moisture (21). Due to their autologous composition, cell-based dressings also exhibit low immunogenicity, thereby reducing the risks associated with introducing foreign materials into the body (22). Together, these properties position cell-based dressings as an innovative advancement in healing and redefine the standard of wound care, especially as new therapies are being researched to move healing closer to fetal-like scarless repair. The objective of this paper is to review the current advances in cell-based wound dressings and highlight future directions to move wound healing closer to scarless regeneration.

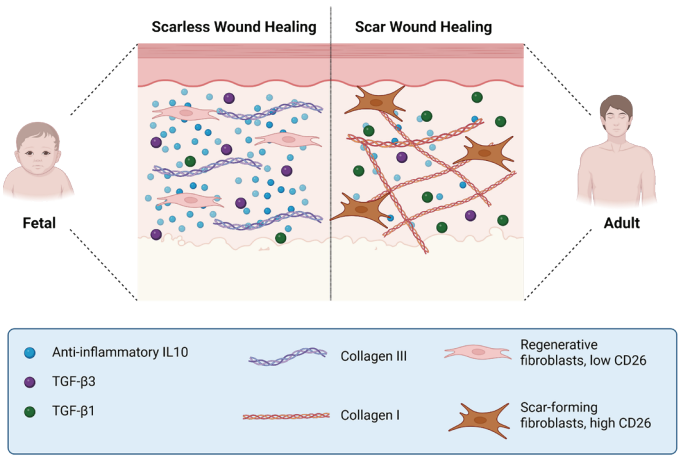

Figure 1. Differences in healing microenvironments between fetal and adult wounds. *Adult wounds display high CD26 expression and high amounts of TGF-β1, leading to scar formation. Fetal wounds exhibit low CD26 expression, high amounts of TGF-β3, and increased anti-inflammatory IL-10 cytokines, promoting scarless regeneration.*

CELL-BASED DRESSINGS UTILIZING DIFFERENTIATED CELL SOURCES

The two primary cell types involved in wound healing are keratinocytes and fibroblasts. The healing process in adults prioritizes rapid wound closure and the re-establishment of the skin's protective barrier, which typically results in fibrotic repair and scar formation. Keratinocytes promote re-epithelialization of the wound surface, while fibroblasts remodel the ECM within the dermis. These two cell types work together during the proliferative stage to restore the skin's integrity, ultimately determining whether healing proceeds effectively or results in excessive fibrosis (23). This makes them key targets for improving wound healing and scarless repair.

Wound healing requires constant communication between keratinocytes and fibroblasts. During the proliferative phase of the healing process, keratinocytes move to the wound site to promote the formation of a new epithelial layer (re-epithelialization) (24-25). This process begins at the wound edge to promote wound closure. This newly formed epithelial layer depends on resident fibroblasts to produce a supportive ECM that ensures their structural integrity. After they migrate to the wound site, keratinocytes release cytokines and growth factors, including epidermal growth factors (EGF), keratinocyte growth factor (KGF), and transforming growth factor-β (TGF-β) (24). These cytokines and growth factors stimulate their own epithelial production and recruit fibroblasts. Coupled with the epithelialization process, fibroblasts beneath the epidermis produce ECM components, such as collagen, fibronectin, and hyaluronic acid, which form the structural foundation for the new tissue (26). These fibroblasts also secrete additional growth factors to accelerate the healing process (positive feedback loop) and differentiate into myofibroblasts that promote wound contraction (26-27). This bidirectional signalling ensures coordination throughout the healing process. However, if this balance is disrupted, such as by prolonged inflammation or excessive TGF-β1 signalling, fibroblasts can become overactivated, leading to excessive collagen deposition and scar formation. Conversely, maintaining a controlled exchange of signals between these two cell types supports organized ECM remodelling and more functional tissue regeneration. Together, keratinocytes and fibroblasts form the cellular foundation of adult wound healing, determining whether repair results in efficient closure or fibrosis (8). Due to their roles in wound dressing, extensive research has been done to incorporate both keratinocytes and fibroblasts into cell-based therapies to promote and regulate healing without the need for local cell migration (28). These biological mechanisms directly inform the design of cell-based dressings: by incorporating keratinocytes and fibroblasts into engineered scaffolds, dressings can recreate this paracrine signalling environment at the wound site, promoting re-epithelialization and controlled ECM remodelling without relying on the patient's endogenous cell migration.

Since 1981, keratinocytes have been used to treat wounds. Specifically, autologous keratinocytes were first applied to a burn patient in 1981 by Rheinwald and Green *et al.* (29). Since then, cultured keratinocytes have been used as autografts or allografts to cover many different wound types. In a study by Dong *et al.* (2024), a combination of ECM derived from exogenous fibroblasts and keratinocytes was tested for improved, scar-reduced wound healing. Primary fibroblasts in vitro have a limited lifespan (of varying lengths based on factors like donor age, culture conditions, and temperature) due to replicative senescence, where they stop dividing after a set number of population doublings (30-31). To overcome senescence, they prepared the ECM using reversibly immortalized mouse dermal fibroblasts (imDFs) and primary dermal fibroblasts, resulting in a decellularized matrix that supports keratinocyte proliferation. The results indicate that ECM derived from imDFs combined with keratinocytes promotes re-epithelialization and scarless healing of full-thickness skin wounds. In contrast, ECM from imDFs alone leads to excessive fibrosis (23). In another study by Bayram *et al.* (2005), living allogenic keratinocytes were delivered via microcarriers to treat diabetic foot ulcers. The viability of the keratinocytes was assessed using a trypan blue test (a cell viability assay that uses a dye to distinguish live from dead cells), revealing that an average of 87% of the microcarriers contained viable cells (32). The results indicated that wounds treated with the KMK-2 (Keratinocyte Medium Kit) showed a 92% reduction in wound area within 30 days, compared to a 32% reduction in the control group (28). These findings highlight the importance of cellular interactions between fibroblasts and keratinocytes in scarless wound healing.

Although prior research suggests that using differentiated cells benefits rapid wound healing with minimal scarring, these studies have also revealed limitations. Differentiated cells, such as keratinocytes and fibroblasts, have limited lifespans and replicative potential in vitro due to replicative senescence, a process

linked to telomere shortening (33). This reduces the number of cells that can be expanded for treatment, making it difficult to use for large or multiple wounds (34). Another restriction is delivery and engraftment inefficiencies, as ensuring the cells engraft long-term at the wound site is crucial for their contribution to the healing process. Regarding scarless healing, differentiated cells can make it difficult to control the immune and inflammatory responses, which are essential for healing but are also a major driver of scarring. These cell-type-specific challenges compound broader shared limitations—including poor survival in hostile wound environments and inconsistency in clinical protocols—that are discussed further in the context of stem cell therapies below (35, 36).

CELL-BASED DRESSINGS UTILIZING STEM CELLS

Stem cells are undifferentiated cells with promise for regenerative medicine applications, cell-based wound dressings, and scarless healing, given their ability to self-renew and differentiate into specialized cells (37). Although there are many types of stem cells, mesenchymal stromal cells (MSCs), such as adipose-derived stem cells (ASCs) and bone marrow-derived stem cells (BMSCs), have been most widely studied for their potential to enhance scarless wound healing (38). Researchers have found that MSCs hold strong potential due to their paracrine signalling, including the release of growth factors and cytokines, which promote healing, reduce inflammation, and enhance overall wound repair (39).

Several clinical studies have investigated the potential effects of MSCs in the healing process. For instance, adipose-derived stem cells (ASCs) have been frequently explored in research due to their accessibility for collection through liposuction, abundance, and ability to reduce scarring (40). In a clinical study conducted by Yu *et al*. (2018), a cell sheet composed of ASCs was applied to a cutaneous wound on a murine model. By day 28, no ASCs were found in the tissue, indicating reduced long-term side effects, as they are biocompatible, naturally broken down, and are cleared by the body. The ASC sheets formed a neo-skin, which displayed characteristics similar to normal skin, with a similar thickness and organized collagen. The researchers evaluated several paracrine signalling mechanisms that the ASC sheets utilize to improve healing and reduce scar formation. ASCs express a unique protein called C1q/TNF-related protein-3 (CTRP3), an anti-inflammatory protein that inhibits inflammation. This reduction in inflammation ultimately hampers the downstream response from immune cell recruitment to the wound site via cytokines secreted by resident macrophages (CCL2) and other cell types at the wound site (TNF-α and TGF-β1) (41). Furthermore, ASCs release high amounts of hepatocyte growth factor (HGF), which led to the fibroblasts showing fewer scarring traits (with lower expression of TGF-β1 and α-SMA) (42). These results suggest that ASCs can be an effective method for wound treatment and reduce inflammation.

Alongside ASCs, bone marrow-derived mesenchymal stem cells (BMSCs) have also been extensively investigated for their anti-scarring and regenerative potential. They are harvested from bone marrow aspirates, generally from the iliac crest; however, unlike ASCs, the extraction process is typically painful to patients and donors (43). BMSCs are valued for their strong proliferative capacity and ability to differentiate into multiple lineages, including osteoblasts, chondrocytes, and adipocytes. They are beneficial for wound healing due to their paracrine signalling as well (38, 44). BMSCs help modulate the immune response and shift macrophages from a pro-inflammatory (M1) to an anti-inflammatory (M2) phenotype, thereby shortening the entire inflammatory phase of healing (45). Schulman *et al*. (2022) conducted a study on the effects of BMSCs on patients with burn wounds. They used a two-dose escalation protocol: all 10 patients received the initial dose, and 5 received the second dose. The results showed 100% wound closure, minimal fibrosis, improved POSAS (Patient and Observer Scar Assessment Scale) scores, re-pigmentation, and regenerative changes (46). The patients who received only the first dose had a wound closure rate of 3.64 cm^2/day, while those who received the second dose had a rate of 10.47 cm^2/day (46). In addition to their use in isolation, BMSCs have also been explored in conjunction with other biomaterials. For instance, Banu *et al*. (2023) conducted a study on the effects of eggshell membrane (ESM), fibrin glue (FG), and BMSCs on wound healing and reduced scarring (47). They found, through histopathological analysis, that the dressing combination of the three showed the most exceptional healing (47). Overall, BMSCs play a crucial role in promoting reduced-scar healing, highlighting their potential as an important component in advanced cell-based wound dressings.

Based on clinical studies and the effects of MSCs on wound-healing efficiency and reduced scarring (38,

48-49), both ASCs and BMSCs have demonstrated their strong roles in improved healing times and scar appearance. Overall, ASCs generally show advantages over BMSCs, including a 40-fold higher yield and superior ability to induce epithelial regeneration and collagen deposition (50). However, BMSCs secrete more anti-inflammatory cytokines and are effective in treating endotoxic shock (50). It is important to note that ASCs and BMSCs can be used in different circumstances: ASCs are preferred for chronic or diabetic wounds, while BMSCs are better suited for widespread inflammation (51-52). The key difference in pain management is that ASCs eliminate the need for invasive BMSC harvesting, providing a safer, less painful treatment with similar results (53). Thus, ASCs and BMSCs both aid wound healing but do so in different ways, making them preferable in different contexts.

Despite promising results from both preclinical and clinical studies using stem cells, particularly MSCs, there are still limitations regarding scarring. One of the primary concerns is limited survival and engraftment. Many transplanted stem cells do not survive long after application due to the harsh wound microenvironment, which is often hypoxic, inflamed, and enzymatically active (45, 54). This limits the effectiveness of MSCs and might require frequent repeated doses to maintain the therapeutic effects. There is also a lack of consistent protocols for isolating and expanding MSCs across different clinical studies, making it difficult to compare results and determine the optimal combination and variables. For example, protocols for harvesting and isolation, expansion and culture conditions, delivery, and quality control remain inconsistent (55-57). In addition to uniform criteria, more large-scale clinical studies and human trials are needed to demonstrate long-term safety and effectiveness (38, 58). While MSCs show potential through paracrine effects, such as reducing inflammation, they often face challenges with poor retention.

NEXT-GENERATION WOUND HEALING: PROMOTION OF FETAL SCARLESS WOUND HEALING

Skin regeneration is equivalent to scarless healing; however, this process typically occurs only during fetal healing. Since the empirical observation that the fetus heals without scars, many researchers have sought to mimic this regenerative phenotype. Fetal wound healing is unique with a distinct growth factor profile, a reduced inflammatory response with an anti-inflammatory cytokine profile, a type III collagen and hyaluronan-rich ECM, and reduced biomechanical stress (59). In contrast, scarring is caused explicitly by excess collagen (mostly type I), prolonged inflammation, and an imbalance in growth factors (too much TGF-β1, not enough TGF-β3) (36, 60-62). Fetuses have increased flexibility during the healing process due to their high amounts of Type III collagen; however, this type of collagen is not as strong as Type I, which is more abundant in adults. Type I collagen prioritizes rapid, mechanically strong healing, leading to the formation of a scar. Fetal and adult wounds also differ in ECM composition and fibroblast phenotype (8). The characteristics are differentiated in Table 2.

Table 2. *Characteristics of fetal and adult wounds. Comparative characteristics highlighting differences in inflammatory response, extracellular matrix composition, growth factor profiles, fibroblast phenotype, and healing outcomes that underpin fetal scarless regeneration versus adult fibrotic repair.*

Fetal wounds (scarless healing)	Adult wounds (scarring)
Minimal inflammation, high IL-10 anti-inflammatory cytokine (8, 63)	Many inflammatory cells, low IL-10 anti-inflammatory cytokine (8, 63)
High Type III collagen (organized, regenerative) (8)	Predominantly Type I collagen (dense, fibrotic) (8)
ECM enriched with hyaluronic acid, fibronectin, and active MMPs (matrix remodelling enzymes) (42)	ECM has lower hyaluronic acid, different/imbalanced MMP activity (42)
Growth factor profile: high TGF-β3, low TGF-β1 (8, 62)	Growth factor profile: low TGF-β3, high TGF-β1 (8, 62)
Fibroblasts: regenerative type, low CD26 expression (64)	Fibroblasts: scar-forming type, high CD26 expression (64)
Healing outcome: complete regeneration (no scar) (63, 65)	Healing outcome: fibrotic scarring (not full regeneration) (63, 65)

Fetal wounds have the remarkable ability to heal without forming scars. This scarless healing is the result of a combination of cellular behaviour, ECM composition, and growth factor signalling (65). Fetal healing provides a blueprint for next-generation wound dressings, and by understanding these mechanisms, researchers aim to not only accelerate healing but also restore skin architecture, potentially shifting healing towards regeneration. Despite vast research into the idea of mimicking fetal healing, it has yet to be fully realized. Current knowledge is that fetal skin develops rapidly in gestation, and its ECM is a loose network that promotes cellular migration. This environment fosters a specific, controlled sequence of events that produces a scarless wound phenotype characterized by abundant hyaluronic acid and a fine, net-like collagen structure (59, 66). Research in cell signalling pathways and transcription factors has shown that fetal wounds exhibit distinct patterns of secondary messenger phosphorylation, chemical modifications that control cells' responses to signals, as well as unique activity of homeobox genes, which guide tissue organization during development (67). These differences allow fetal skin to regenerate rather than form scars.

Studies using fetal cells have proven why scarless healing is possible. In a study by Lorenz *et al*. (1992), small pieces of fetal skin were transplanted onto athymic (nu/nu) mice, which lack a standard immune system and therefore do not reject human tissue. Researchers compared skin healing in both subcutaneous and cutaneous environments. The grafts placed under the surface entirely healed without scars, while those exposed to air developed visible scarring (68).

This shows that fetal skin naturally can repair itself without scarring, even outside the womb; however, when placed in an adult environment, the same tissue tends to heal with fibrosis, or scar tissue. Another study by Wilgus *et al*. (2004) focused on the role of inflammation in this difference, particularly involving the enzyme cyclooxygenase-2 (COX-2), which is known to trigger inflammatory responses by producing prostaglandins. Researchers examined COX-2 expression in fetal mouse wounds and found that scarless healing during early gestation has minimal COX-2 activity, while higher COX-2 levels were linked to fibrotic repair. When prostaglandin E2, a product of COX-2, was added to early fetal wounds, healing slowed and scars formed, showing that inflammation directly contributes to fibrotic healing (69). Building on this knowledge, scientists have begun developing treatments that use fetal-derived cells to create this effect. In one study by Biniazan *et al*. (2022), placenta-derived human amniotic epithelial cells (hAECs) were applied to cutaneous wounds in a mouse model. The wounds treated with hAECs healed faster than the control, with reduced fibrosis and scar formation and lower expression of inflammatory and fibrotic markers, including TGF-β1 (70). Together, these results demonstrate that fetal-derived cells can influence adult wound healing by regulating inflammation and promoting tissue regeneration, supporting their potential use in future scarless dressings and therapies.

Despite their strong potential, using fetal cells for scarless wound healing poses several challenges and limitations. One primary concern is ethical and regulatory issues, as sourcing fetal tissue involves strict protocols and criteria governed by institutional review boards and national regulatory frameworks, which significantly limit access to tissue and slow clinical translation. There are also practical challenges when harvesting cells, especially for large-scale clinical use, and in keeping them viable and functional outside the body (71). There is a risk of immune rejection, especially if the cells are not perfectly matched to the patient (72). In addition, fetal cells can behave differently depending on their environment, and there are limitations in creating effective dressings that incorporate living fetal cells while maintaining sterility and ease of application (68). Importantly, these challenges have spurred interest in fetal-mimicking alternatives that do not require fetal tissue — such as the exogenous delivery of TGF-β3, manipulation of the IL-10/TGF-β1 signalling axis, and the engineering of hyaluronic acid-rich scaffolds that replicate the fetal ECM. These approaches represent promising translational strategies that may achieve scarless healing without the ethical and logistical barriers of fetal-derived therapies. These challenges imply that, although fetal-cell-based dressings are a promising advancement for reducing scarring, significant research and development remain needed before they can become a standardized clinical therapy.

CONCLUSION

Wound healing remains one of the most intricate and vital biological processes, and achieving scarless healing remains a crucial goal in regenerative medicine. Conventional wound dressings, while essential for protection and moisture balance, are limited in their ability to promote cellular regeneration or minimize fibrosis actively. In contrast, cell-based dressings, especially those incorporating differentiated cells, such as keratinocytes and fibroblasts, or stem cells like ASCs

and BMSCs, represent a significant advancement by involving key players that modulate the healing process. By secreting growth factors, cytokines, and extracellular matrix components, cells in these dressings not only accelerate tissue repair but also reduce inflammation and abnormal collagen deposition, two key contributors to scarring. It is important to note, however, that most stem-cell-based dressings remain at the preclinical or early clinical trial stage; only a handful of keratinocyte-based products (such as cultured epidermal autografts) have achieved widespread clinical use, and MSC-based therapies are still being evaluated for long-term safety and efficacy. Fetal wound healing provides an ideal model for these next-generation therapies, revealing how anti-inflammatory signalling, type III collagen dominance, and unique fibroblast phenotypes enable complete tissue regeneration without scar formation. Although fetal-cell-based approaches show promise, they face ethical, logistical, and immunological challenges that currently limit their clinical use. Future research must focus on translating the mechanisms of fetal healing into safe, accessible, and standardized cell-based dressings. Ultimately, integrating insights from fetal biology with the engineering of biocompatible scaffolds and stem cell technology may enable a new generation of wound therapies capable of not only closing wounds efficiently but restoring the skin's natural network, bringing medicine closer than ever to true scarless healing.

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CONFLICT OF INTEREST

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