Review

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Exploring the Potentials: Therapeutic Uses of Mesenchymal Stem Cells in Treating Corneal Conditions

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Corneal disorders, encompassing injuries, infections, and degenerative diseases, are major contributors to visual impairment globally. Conventional procedures, including corneal transplantation and pharmacological treatments, encounter constraints such as donor shortages, rejection risks, and diminished effectiveness in extreme instances. Mesenchymal stem cells (MSCs) have emerged as viable therapeutic alternatives owing to their regeneration potential, immunomodulatory characteristics, and capacity to differentiate into corneal cell types. This study examines the therapeutic potential of MSCs in addressing various corneal illnesses through the analysis of preclinical studies, clinical trials, and current breakthroughs. MSCs facilitate corneal wound healing, diminish scarring, and reinstate transparency via processes including paracrine signaling, extracellular matrix remodeling, and anti-inflammatory actions. Although early-phase clinical trials indicate the safety and feasibility of MSC-based therapeutics, obstacles persist in optimizing delivery techniques, assuring cell viability, and creating uniform protocols. Additional research is necessary to address these issues and validate MSCs as a feasible clinical alternative. This review aims to summarize the therapeutic applications, challenges, and future prospects of mesenchymal stem cells in corneal treatments, emphasizing their importance as emerging alternatives to traditional therapies.

Keywords: regeneration; immunomodulation; wound healing; clinical trials; paracrine factors

Introduction

The human cornea is a susceptible, delicate, and transparent structure that forms the anterior coat of the eye alongside the sclera. Its exceptionally delicate nature and transparency are maintained by a heavy network of nerve fiber endings, the rapid regenerative ability of the cornea epithelium, its avascularity, and the complex organization of the cornea stroma lamellae. Whereas the inherent properties of the cornea help it maintain its optical function, it also makes it extremely vulnerable [1]. Consequently, minor insults such as superficial corneal injuries, benign lesions, and infections can result in cornea neovascularization, profound scarring, and subsequent vision loss. As a result, it is necessary to manage all ocular conditions affecting the cornea with a sense of clinical urgency. Mesenchymal stem cells (MSCs) are multipotent stem cells that can differentiate into different cell types, and they come in handy [2,3] when managing cornea conditions due to their inherent regenerative [4], anti-angiogenic and immune-modulatory properties [5]. In animal models, MSC therapy has been reported as a promising therapeutic strategy for managing various cornea conditions such as cornea ulcers, keratitis, keratoconjunctivitis sicca [6], and limbal stem cell deficiency (LSCD) [7]. Furthermore, MSCs have also shown remarkable promise as a biological therapeutic agent in human cornea endothelium regeneration and xenotransplantation [8]. MSCs can be obtained from many tissues, such as bone marrow, adipose tissue, and limbal tissue, rendering them adaptable for therapeutic uses.

Table 1. Summary of literature search.

Mesenchymal Stem cells	(“mesenchymal stem cells”[MeSH Terms] OR (“mesenchymal”[All Fields] AND “stem”[All Fields] AND “cells”[All Fields]) OR “mesenchymal stem cells”[All Fields])
Therapeutic	(“therapy”[MeSH Subheading] OR “therapy”[All Fields] OR “treat”[All Fields] OR “treating”[All Fields] OR “treated”[All Fields] OR “treats”[All Fields])
Cornea	(“cornea”[MeSH Terms] OR “cornea”[All Fields] OR “corneal”[All Fields])
Conditions	(“condition”[All Fields] OR “condition s”[All Fields] OR “conditions”[All Fields])

Research has shown that umbilical cord-derived mesenchymal stem cells changed their shape, aligned into organized sheets, and developed endothelial cell-like properties in the human cornea [9]. In addition, human limbus-derived stromal/mesenchymal stem cells (hLMSC) have been suggested as a possible option for managing cornea scars [10]. Although the depth, nature, etiology, associated anterior segment abnormalities, the patient’s systemic co-comorbidities, and availability of cornea surgeons and other supportive health specialists may limit the use of MSC as a complete alternative to cornea transplant in managing cornea-related blindness, it is still a viable and promising option due to its inherent characteristics [11]. This review highlights the potential of MSCs to revolutionize the treatment of corneal diseases and improve patient outcomes.

A comprehensive literature review was conducted using PubMed, focusing on recent advancements in mesenchymal stem cell applications for corneal conditions. Articles were selected based on relevance, recency, and full-text availability. The authors performed a search for related literature on the PubMed database (https://pubmed.ncbi.nlm.nih.gov/) using the keywords “mesenchymal stem cells”, “therapeutic”, “cornea”, and “conditions”. The search summary and algorithm are shown in Table 1.

Preclinical Studies on MSC in Wound Healing

Mesenchymal stem cells have been studied as treatment options in graft versus host disease in the pediatric population in places like Canada and New Zealand [12]. Continuous delivery of Mesenchymal stem cell secretome has been shown to improve cell migration and proliferation in wound healing over the aliquoted delivery pattern of Mesenchymal stem cells [13–15]. Studies show they promote wound healing by migrating to defective sites and secreting anti-inflammatory and growth factors [14–16]. Both preclinical and clinical stage studies have found mesenchymal stem cells very valuable in various ocular surface diseases, like immune-mediated dry eyes, graft versus host disease, and a host of other ocular surface anomalies [17]. The osteogenic differentiation ability of Mesenchymal stem cells has been studied in depth in preclinical settings, but not much has been done in human trials [18]. Under specific conditions, the Mesenchymal stem cells are capable of multi-lineage differentiation, making them suitable too for veterinary regenerative medicine and cell-based therapy [19]. Specifically, the amniotic membrane has been suggested as a good choice for the growth and transplantation of mesenchymal stem cells [20].

MSCs and the amniotic membrane have a wide range of uses in regenerative medicine, specifically Ophthalmology, as they play a role in the management of various forms of corneal erosion, non-healing corneal ulcer, pterygium, corneal epithelial defects and even in glaucoma surgeries [21,22]. Human adipose tissue-derived mesenchymal stem cells can be a viable treatment plan for dry eye syndrome as they help to initiate the transforming growth factor-β (TGF-β) and Janus kinase/signal transducers and activators of transcription (JAK/STAT) signaling pathway, thereby improving corneal barrier function [23–25]. Mesenchymal stem cells are renewable and can become potent forms of other variant cells under specific conditions [26,27]. In a clinical trial carried out to ascertain the viability of limbal mesenchymal stem cells in rabbits with LSCD, as studied through histology, immunochemistry, and confocal microscopy, transferred cells were still viable by day 14, but the newly re-epithelized rabbit corneal did not keep with the presence of viable mesenchymal stem cell within its tissue [28]. Clinical studies have also been carried out to compare the efficacy of mesenchymal stem cells and topical prednisolone in the treatment of chronic superficial keratitis. Although the result showed significant improvement in findings after about 3 months with the mesenchymal stem cells delivered through the subconjunctival route, the improvement was less than those of the conventional group that received topical prednisolone for the same time [29]. Subconjunctival administration of mesenchymal stem cells was therefore recommended as a viable means of introducing it into the eye, as it is minimally invasive and can be used in various treatments delivering high cell doses, especially in conditions caused by deficiency of limbal stem cells [30]. Mesenchymal stem cells derived from the corneo-sclera rim have been found to have a wound healing effect with little or no formation of corneal scar tissue when experimented on mouse cornea using this same route [31]. Table 2 (Ref. [21–24,28–31]) summarizes these findings.

Early-phase and Late-phase Clinical Trials on MSC Use in Treating Eye/Corneal Injury

The transparency and avascular nature of the cornea make it a unique and susceptible target for stem cell ther-

Table 2. Preclinical studies on MSC in corneal wound healing.

Topic	Findings
Uses of MSC & amniotic membrane [21,22]	Used in treating corneal erosion, ulcers, pterygium, epithelial defects, and glaucoma surgeries.
MSC for dry eye syndrome [23,24]	MSCs help initiate TGF-β and JAK/STAT signaling to improve corneal barrier function.
Limbal MSCs in LSCD (rabbit study) [28]	Cells were viable by day 14, but newly re-epithelized corneal tissue lacked MSCs.
MSC vs. prednisolone (chronic keratitis) [29]	MSCs showed improvement after 3 months but were less effective than prednisolone.
Subconjunctival MSCs [30]	Minimal invasive, effective for high-dose cell delivery, especially for LSCD.
MSC from corneo-sclera rim [31]	Found to have wound-healing effects with minimal scar tissue formation in mouse corneas.

MSC, mesenchymal stem cells; TGF-β, transforming growth factor-β; JAK/STAT, Janus kinase/signal transducers and activators of transcription; LSCD, limbal stem cell deficiency.

apy, particularly MSCs [32]. Initial studies have demonstrated the capacity of MSCs to accelerate wound healing, as evidenced by quicker and more complete epithelial closure observed in preclinical models [33]. Additionally, MSCs exhibit the potential to address immune-mediated ocular diseases. For instance, research has highlighted the success of subconjunctival administered autologous bone marrow-derived MSCs in resolving immune-mediated keratitis without adverse effects [34].

Clinical investigations into MSCs for corneal injuries reveal that human bone marrow stromal cells can migrate to, differentiate within, and regenerate corneal tissue while simultaneously mitigating immune-mediated damage [35]. A significant aspect of this research relies on animal models, which are crucial for developing therapies aimed at human eye injuries. This underscores the necessity of advancing studies on corneal physiology in companion animals, which may improve veterinary and human ophthalmic treatments [36].

Scientists are actively exploring advanced regenerative approaches, utilizing tissue engineering and various stem cell sources, including MSCs, to restore the corneal epithelium. Early clinical trials are focused on assessing the safety and preliminary effectiveness of MSCs in promoting corneal healing. Concurrently, more extensive trials are underway to evaluate their long-term impact and effectiveness, aiming to establish these treatments for broader medical use [37].

MSCs are increasingly demonstrating significant promise in the treatment of corneal and ocular injuries, with promising outcomes observed across both preliminary case studies and advanced clinical trials. Notably, MSCs have shown efficacy in managing chronic dry eye disease (DED), especially cases associated with graft-versus-host disease (GVHD). Early research emphasizes MSCs' dual role in aiding corneal epithelial healing and enhancing tear production. This therapeutic effect is achieved through the modulation of inflammation and tissue repair, as evidenced by animal models and initial human trials [38]. Clinical trials on MSC treatments related to GVHD and Sjögren's syndrome (SS) have reported encouraging findings. In early-phase studies, intravenous bone marrow MSCs provided symptom relief to GVHD patients. Meanwhile, more advanced trials demonstrated durable symptom relief for SS-related DED following a single transconjunctival injection of adipose-derived MSCs without triggering immune-related side effects [39].

Clinical research indicates that injecting adipose-derived stem cells (ASCs) into the lacrimal gland is both safe and effective. Over a 12-month follow-up period, patients experienced improvements in tear production, tear film stability, and a reduction in dry eye symptoms [40]. Unlike traditional treatments, MSC-based therapy provides enhanced anti-inflammatory benefits and a regenerative approach, offering a promising alternative for severe cases of aqueous deficient dry eye disease (ADDE) [41]. Furthermore, a study by El Zarif *et al.* [42] highlighted the potential of ASCs to assist corneal regeneration in keratoconus patients. Utilizing advanced imaging techniques, the study showed that ASCs, when injected into laser-created corneal pockets, increased keratocyte density. These cells may differentiate or stimulate the host's corneal cells, with additional evidence suggesting indirect regenerative effects through the corneal stroma.

Evidence from human clinical trials suggests that MSCs may offer therapeutic benefits for severe eye conditions, such as LSCD [43] and keratoconus. Early-stage trials highlight MSCs' potential in repairing the corneal epithelium and stroma thanks/to their ability to enhance cellular repair, reduce inflammation, and modulate immune responses. Thus far, MSC-based therapies have demonstrated a strong safety profile and have contributed significantly to vision improvement and symptom relief [44], particularly in cases where conventional treatments are either inadequate or associated with a risk of immune rejection. Nonetheless, further late-phase clinical studies are necessary to confirm the long-term efficacy, durability, and optimal application strategies for MSCs in ocular disease management [45].

LSCD is a condition characterized by damage to the limbus of the cornea, which hinders the normal regeneration of the corneal epithelium. Subsequently, later-stage trials focus on refining treatment protocols and evaluating the overall efficacy of MSC-based therapies. The ultimate goal is to advance from traditional corneal grafts to sophisticated cell-engineering techniques. One such method in-

volves the creation of corneal cell sheets from MSCs, which hold the potential to restore clear vision and revolutionize ocular surface reconstruction [46].

Studies have shown that cultivated limbal epithelial transplantation (CLET) significantly enhances corneal epithelial health and is effective in treating LSCD-induced ocular surface failure. This method boasts a 75–80% success rate over three years, particularly in cases unrelated to chemical injuries [47]. A pivotal clinical trial conducted by Calonge *et al*. [48] compared mesenchymal stem cell transplantation (MSCT) to CLET for corneal epithelial damage resulting from LSCD. The trial revealed that MSCT was equally safe and effective as CLET, demonstrating notable epithelial healing without adverse effects and laying the groundwork for further extensive research.

Active clinical trials are exploring various MSC-based approaches for treating corneal and ocular surface injuries. These investigations aim to assess the safety and efficacy of different delivery methods, such as eye drops, subconjunctival injections, and intrastromal injections. The targeted conditions include chemical burns, dry eye syndrome, and corneal dystrophies.

Initial clinical trials of MSC-based interventions, including cell transplants and exosome treatments, have underscored the necessity of establishing safety profiles. Promisingly, these trials have demonstrated positive outcomes such as enhanced corneal healing and increased tear production, with only minor side effects reported. Notably, early research into exosome-based eye drops for DED has emerged as a key area of investigation, demonstrating progress with potential cell-free and minimally invasive treatment modalities. These therapies promote the regenerative capabilities of corneal stromal cells, potentially restoring corneal clarity by supporting natural healing processes [49,50].

As research progresses into later stages, the emphasis shifts to evaluating the effectiveness of these treatments in larger cohorts. Advanced trials have reported significant clinical benefits, such as increased tear secretion, alleviation of DED symptoms, and improved vision in conditions like LSCD, corneal scarring, and DED. These studies underscore the potential for MSC-based therapies to revolutionize treatment for complex corneal diseases [49–51].

Exosome therapies represent an innovative advancement, offering a targeted, cell-free, and minimally invasive approach. Exosomes have shown the capability to deliver regenerative signals to corneal stromal cells, thereby enhancing healing while reducing inflammation. Preclinical research is actively addressing key hurdles related to the potency and scalability of these therapies, which are crucial for broader clinical applications in corneal health [50].

Rho (ρ)-associated kinase inhibitors have emerged as a pivotal area of interest for treating corneal endothelial diseases. Two notable surgical techniques—(1) transplanting *in vitro* cultivated corneal endothelial cell sheets on type I collagen and (2) intracameral cell injection therapy—utilize these inhibitors to improve outcomes. These treatments facilitate cell adhesion and minimize apoptosis, contributing to enhanced corneal clarity. However, further trials are needed to confirm their long-term safety and effectiveness [52,53].

MSC therapies continue to be extensively explored for their potential to heal corneal injuries and treat various eye disorders. MSCs can inhibit myofibroblasts, which are responsible for corneal opacity, thereby promoting transparency. Adipose-derived and bone marrow-derived MSCs have shown efficacy in corneal repair [5]. Additionally, alternative sources such as umbilical cord-derived MSCs and dental stem cells provide new possibilities for treating congenital and endothelial-related conditions [54].

One notable study by Liu *et al*. [55] investigated the use of umbilical cord-derived MSCs to treat chronic ocular graft-versus-host disease. They utilized high oxygen-permeable hydrogel lenses, which effectively retained MSCs on the ocular surface, enhancing their anti-inflammatory and immune-modulatory effects. This approach significantly reduced corneal inflammation and immune reactions, showcasing the therapeutic potential of MSCs in ocular disease.

Innovative scaffold-free delivery methods, which bypass the need for biomaterials, have shown promise in treating corneal injuries. These techniques involve the direct application of MSCs and autologous blood products, such as platelet-rich plasma, cell sheets, and amniotic membrane derivatives. By reducing the risk of immune rejection and increasing biocompatibility, these treatments present a viable option for regenerating corneal tissue in conditions like LSCD, corneal ulcers, and DED. Nonetheless, challenges remain in effectively treating more advanced corneal diseases with these techniques [56].

Challenges in MSC Medicine in Cornea Injury Treatment

The therapeutic use of MSC in corneal injury treatment has garnered considerable interest, yet several critical challenges remain to be resolved to optimize its efficacy. These challenges revolve around delivery mechanisms, the survival and stability of the administered cells, and understanding the long-term implications of MSC therapy. These challenges are further discussed below.

Optimizing Delivery Methods

Delivering MSCs efficiently to the cornea is complex due to the eye's sensitive and protective structure. MSCs have been shown to promote corneal wound healing and reduce inflammation through anti-angiogenic and paracrine activities [5]. Paracrine factors released by MSCs are crucial for facilitating corneal repair. The factors encompass growth factors like hepatocyte growth factor (HGF) and

vascular endothelial growth factor (VEGF), which govern epithelial cell proliferation and angiogenesis. Moreover, the release of anti-inflammatory cytokines, such as interleukin-10 (IL-10) and transforming growth factor-β (TGF-β), inhibits immune responses, fostering an advantageous milieu for tissue regeneration. Recent investigations have shown that MSC-derived extracellular vesicles (EVs) serve as transporters of bioactive compounds, hence augmenting their therapeutic efficiency [5].

Still, challenges like their dual angiogenic roles, potential inflammatory risks from apoptosis, and interspecies differences in models highlight the need for further research into their mechanisms and optimal delivery methods despite encouraging clinical trial results [57].

One delivery strategy involves topical application, which is non-invasive and easy to administer but often suffers from poor cell retention and limited therapeutic impact. According to Wang *et al*. [58] creating an optimal microenvironment that encourages cell adhesion and integration is crucial, as the fragility of cell sheets poses significant obstacles during transplantation efforts.

Hydrogel-based delivery systems present an alternative, offering biocompatibility and controlled release. Innovative hydrogels, as discussed by Visalli *et al*. [59] have been developed to mimic the extracellular matrix and facilitate MSC engraftment. Despite their promise, these systems need to be refined to ensure proper cell differentiation and immune compatibility without affecting corneal transparency [59]. Scaffold-based delivery methods, another area of research, must be carefully engineered to avoid complications, such as inflammation or scarring, which can negate the therapy's benefits. Similarly, a study by Ke *et al*. [60] showed that the combined use of Hardy Orchid-derived polysaccharide hydrogels and MSCs to treat corneal alkali burns significantly improves corneal epithelial regeneration, reduces inflammation and neovascularization, and provides a cost-effective, biocompatible treatment option, despite issues like immune rejection and scalability.

Optimal cell engineering processes employed in stem cell laboratories serve to assure that MSCs are cultured under sterile working conditions, and their viable genotypic and phenotypic characteristics remain intact until delivery [10]. For cell laboratories in geographical locations that grappled with operational issues in controlled storage, cell encapsulation was proffered as an innovative measure to extend MSCs' viable storage time by minimizing heat cell degradation. Carter *et al*.'s [15] association between a three-dimensional mesenchymal stem cell (MSC) culture environment and an increase in MSC secretome expression portended further insight into stem cell engineering techniques. Correlating a measurable scarring index with the therapeutic validity of corneal stromal stem cells as published by Santra *et al*. [61] could provide a new framework to regenerate corneal stroma tissue. Revisiting quality control, stroma (corneal) stem cell cryopreservation media selection bears influence on their therapeutic usability [62]. The expression of conventional corneal endothelial cell physiological/homeostatic properties on human embryonic stem cell-derived (hESC-derived) corneal endothelial-like cells further demonstrated that with proper engineering [63]. In the past decade and a half, both hosts and umbilical MSCs were represented as valuable multipotent keratocyte and corneal endothelial cell progenitors; affirmation that MSCs could differentiate into multiple corneal lamellae [64,65]. These bench and lab studies beamed with optimism for the potential discovery of MSC physiologic properties which could lead gradual transition from excess reliance on donor cornea/allograft tissue to more sustainable MSC therapies [66].

Ensuring Cell Viability and Survival

The efficacy of MSC therapy largely depends on the ability to maintain cell viability during and after transplantation. One major issue is cryopreservation, as freezing and thawing processes can damage cell structures, reducing the therapeutic potential. Soleimani *et al*. [49] emphasize that MSCs can experience a decline in regenerative function if the cryopreservation process is not optimized, leading to inconsistent outcomes.

Although past success of animal trials with MSC conditioned medium indicates the validity of cell-based therapies for dry eye and ocular surface disease; much attention has been paid to determining routes of administration for optimal MSC delivery [23]. Adipose-derived mesenchymal stem cells were previously shown to enhance the *in-vitro* proliferative capacity of corneal stromal cells. Another means via which desirable differentiation of MSCs had been attained was by obtaining progeny cells from native tissue such as the corneal stroma [67]. While combined therapy using biological cell carriers such as the human amniotic membrane demonstrated favorable rates of stem cell migration onto conjunctival-limbal defects; greater success of MSC survival and trans-differentiation into *de novo* limbal and corneal stromal cell populations could advance regenerative therapies in lieu of keratoplasty for LSCD [68]. Unlike living-related conjunctival limbal allograft (lr-CLAL) transplantation for LSCD, MSC-differentiated limbal stem cells bereft of the major histocompatibility complexes are innately immuno-quiescent [28]. Two-fold success attained via grafting limbal epithelial progenitors alongside limbal stromal stem cells *in vivo* in animal studies suggests the critical role of stromal cells in corneal differentiation [69].

In addition, due to the challenges of graft rejection and prolonged immunosuppression, and despite progress in limbal epithelial stem cell (LESC) therapies and alternative stem cell approaches, key obstacles remain in evaluating therapy effectiveness and achieving consistent results, necessitating ongoing research and novel methods in corneal

Table 3. Therapeutic effects of mesenchymal stem cell therapy.

Therapeutic effect	Mechanism	Outcome	Limitations
Anti-inflammatory [16]	Secretion of cytokines and growth factors	Reduced inflammation and immune response	Variability in cytokine production
Promotion of wound healing [13,14]	Cell migration and differentiation	Accelerated epithelial regeneration	Short-term retention in corneal tissue
Prevention of scarring [61]	Extra cellular matrix (ECM) remodeling	Maintained corneal transparency	Limited long-term data
Immunomodulation [73]	Suppression of pro-inflammatory pathways	Enhanced graft survival	Risks of prolonged immunosuppression

tissue engineering [70]. Other considerable challenges include cellular heterogeneity from varied sources, inconsistent results from diverse harvesting and culture techniques, donor-dependent variations affecting MSC quality, potential immune reactions, complexities in preparing concentrated cell solutions, and risks like tumor formation, necessitating careful clinical consideration [71].

Recent developments in delivery technologies, including hydrogel-based systems and scaffold-free cell sheets, have enhanced MSC retention and survival rates. These techniques replicate the ocular milieu, promoting cell adhesion and sustained activity [72]. Nonetheless, challenges like as inconsistency in cell quality and scalability persist as constraints.

Long-term Effects of MSC Therapy

MSCs hold promise for enhancing corneal healing and regeneration by mitigating inflammation and modulating immune responses, yet their therapeutic effectiveness is hindered by challenges such as inflammation, neovascularization, limited donor supply, and immune rejection risks, with outcomes highly dependent on variables like MSC origin, administration timing, and dosage, warranting further research to refine their use and elucidate underlying mechanisms [73]. The immunomodulatory properties of MSCs, which are beneficial in the short term, could potentially cause issues over extended periods. Persistent immunosuppression may leave the cornea vulnerable to infections or impact natural regeneration, a risk that continues to be evaluated through long-term monitoring [30,74]. The therapeutic effects of MSC therapy are summarized in Table 3 (Ref. [13,14,16,61,73]).

Conclusions

Although animal models have yielded essential insights into the mechanisms and prospective therapeutic benefits of mesenchymal stem cell (MSC) therapy, considerable discrepancies exist between these models and human clinical trials. Interspecies variations in corneal physiology, immunological response, and wound-healing mechanisms influence the translation of preclinical results to clinical applications. Rabbit models have shown fast corneal healing following MSC treatment; nevertheless, the long-term retention and activity of these cells in humans remain ambiguous.

Contemporary standard therapies, including corneal transplantation, provide dependable vision restoration but encounter obstacles such as donor shortages and immunological rejection. Conversely, MSC-based therapies offer an immunomodulatory and regenerative option; nevertheless, issues related to their delivery techniques, survival rates, and scalability remain unresolved. The capacity of MSCs to regulate inflammation and facilitate repair independently of donor tissues establishes them as a groundbreaking, albeit emerging, alternative.

MSC-based therapies hold significant potential for corneal wound healing and ocular regeneration, offering a promising alternative to traditional treatments. However, further research is needed to optimize delivery methods, improve cell survival, and assess the long-term effects of establishing MSC therapies as a routine clinical practice for ocular diseases.

Author Contributions

MZ, CG, and MM designed the research study. MZ, CG, MM, FDE, AL, DT, BIB, AS and EC performed the research. FDE, AL, and DT provided guidance on review content. MZ, MM, and CG analyzed the data. All authors were involved in the drafting and critical revision of the manuscript. All authors have read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

AS and MM work at the Department of Ophthalmology, Africa Eye Laser Center Ltd. EC and MM work at the Department of Ophthalmology, Center for Sight Africa Ltd. Other authors declare no conflict of interest.

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