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Review Article

A Progress in Mesenchymal-Stem-Cells and Their Applications: A Comprehensive Review

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Abstract: ***Background***: Multi-potent cells called mesenchymal stem cells (MSCs), are being investigated in clinical settings as a potential new treatments for various immunological disorders. Methods: Indexed publications in Medline Pub-Med, Web of Science, and Google-Scholar databases were used to perform a review. ***Results***: They have recently been demonstrated to affect endogenous tissues, and immune cells, after first being heralded as a therapeutic option for structural tissue repair. Mesenchymal stem cells, can differentiate into non-mesenchymal cells like-neurons, or epithelial cells as well as tissues. Moreover, mesenchymal stem cells have immunosuppressive qualities independent of human leukocyte antigens (HLA). It is especially employed to treat graft versus host disease because of its immunosuppressive qualities. An overview of clinical research on the therapeutic benefits of mesenchymal-stem cells is given in this review. It also emphasizes how MSCs are used in clinical trials to treat cardiovascular disease, and graft versus host disease. MSC biological characteristics are largely responsible for their clinical use; they can be injected intravenously to reach inflammatory sites following tissue damage; they can be differentiated into different cells types, they secrete a variety of biomolecules that can promote the healing of damaged cells, and reduce inflammation; and have immunomodulatory capabilities. ***Conclusions***: These cells can either enhance or improve disease in a pathological milieu. Moreover, mesenchymal-stem-cell therapy, and the course of disease may be positively or negatively impacted by changes to this microenvironment.

Keywords: Exosomes, Mesenchymal Stem Cells, Multipotent, Regenerative Medicine, Therapy, Immunomodulation.

1. INTRODUCTION

Stem cells can generate cells of many lineages, and self-renew. As a result, they serve as a crucial model for cell treatment in many illnesses [1]. Typically, stem cells come in two primary varieties: embryonic, and non-embryonic [2]. The core cell mass of the blastocysts, gives rise to embryonic-stem cells, which can develop into cells from all three germ layers [3]. However, their therapeutic applications, and research are hampered by-ethical issues, and tetratomic production [4]. However, the majority of non-embryonics stem cells are adult stem cells, which are already relatively specialized, and have a restricted capacity for differentiation [5]. They are the most commonly employed stem cells in regenerative medicine, and can be obtained from various tissues [6]. "Mesenchymal stem cells:(MSCs), have a morphological similarity to fibroblasts". Despite not having a particular marker, they display specific surface marker patterns. MSCs have a remarkable capacity for self-renewal, which allows them to cycle repeatedly with minimal alteration to their fundamental characteristics. Numerous cell types, including adipocytes, chondrocytes, osteoblasts, myocytes, and neurons, can be differentiated from MSCs [7, 8]. An overview of current clinical research on mesenchymal stem cells will be given in this review. It will draw attention to how these cells are used in clinical studies to treat cardiovascular disease, and graft-versus-host disease. These cells' characteristics are largely responsible for their therapeutic actions. These characteristics will be covered here, along with the usage-related concerns that need to be resolved when these cell treatments go from clinical trials.

2. MATERIALS AND METHODS

A comprehensive Pub-Med search was conducted to gather research on mesenchymal stem cells that was published between 2020 and 2025. In order to refine the search method, we used specific keywords like

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"Umbilical-cord derived mesenchymal stem cells," "[UC-MSCs] including medication," and (UC-MSCs) and immune problems," along with field tags and Boolean operators. The search was sorted by article kinds, including clinical trials, and restricted to publications released during the given time frame. Applying filters for particular diseases and article accessibility was another refinement step. Excel software 2013 was used to analyze the data.

3. RESULTS AND DISCUSSIONS

After removing duplicates, the literature search yielded 800 publications out of 1.300 published in 2020 and 2025. However, 550 publications were disqualified for a variety of reasons, including insufficient results, full-text not being available, and articles not published in English. After additional evaluation of the complete texts of the remaining 250publications. 104 studies were ultimately included in the results (Fig.1).

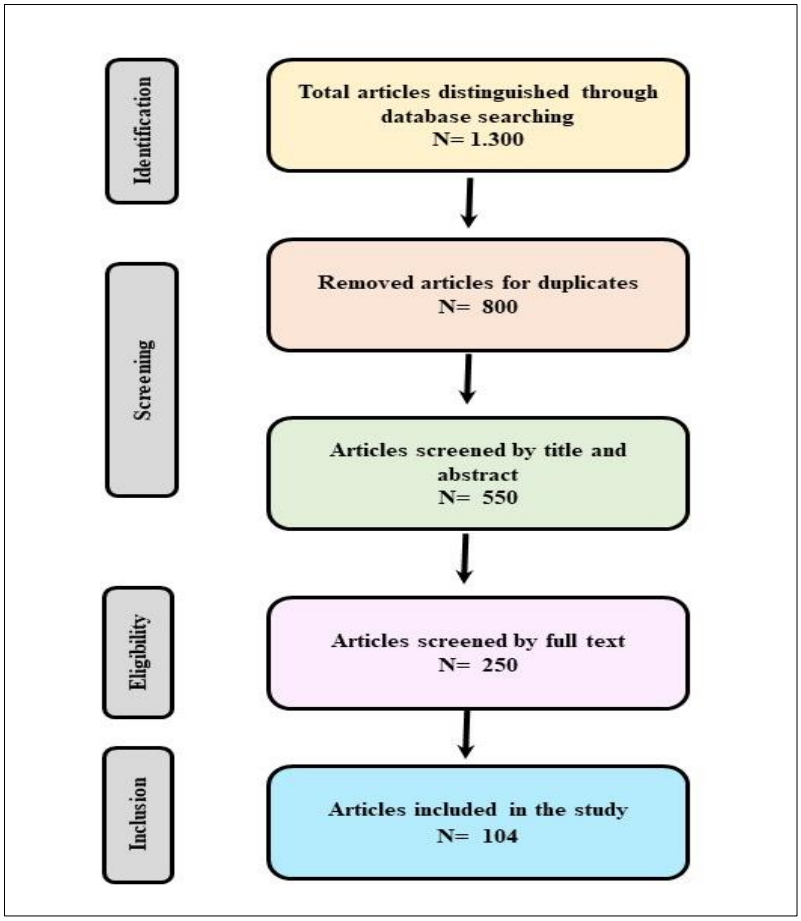

Figure 1: Diagram of included studies

3.1 Biological Characteristics of Mesenchymal Stem Cell

Adult stem-cells, known as mesenchymal-stemcells, can be obtained from different tissues, which are capable of multidirectional differentiation, and self-renewal [9, 10]. It has the ability to chemotactically attract sites of inflammation, and regulate immunity [11, 12]. Mesenchymal stem cells can release a variety of bioactive compounds that can promote the healing of damaged cells, and reduce inflammation [13, 14]. The capacity to carryout immunomodulatory tasks, and the absence of immunogenicity [15]. "MSCs play a significant role through their paracrine activity, angiogenesis stimulation" [16]. Macrophage response, migration, and proliferation of keratinocytes, and dermal fibroblasts, as well as extracellular matrix regulation [17].

3.2 The Immune Boosting Capabilities of MSCs

Mesenchymal stem cells (MSCs) can move to inflammatory regions, and produce soluble substances or interact with lymphocytes on a between cells basis to provide strong immunomodulatory, and anti-inflammatory effects [18]. Thus, there is a lot of promise for future clinical treatment when MSCs are used in a range of disease conditions [19, 20]. MSCs have been used to treating the graft-versus-host disease (GVHD), in phase III clinical studies, and the product has been authorized for use in GVHD in children [21, 22]. "In the early stages of fracture repair, innate immune responses promote bone regeneration, and provide an inflammatory milieu that is conducive to bone regeneration" [23]. Bone remodeling, and regeneration are sustained by adaptive immune responses [24]. Immune cells, and mesenchymal stem cells control one another [25]. MSCs have a potent immunomodulatory ability towards immune cells of all

kinds, and their produced cytokines can control their migration, proliferation, and osteogenic differentiation [26, 27]. MSCs have immunomodulatory qualities that preserve immunological equilibrium when the immune response is either or under activated [28, 29]. "The cytokines, chemokines, signaling molecules, and growth factors secreted by MSCs efficiently aid in the control of inflammatory, and immunological responses" [30, 31]. Direct cell interaction between MSCs, and immune cells, and micro-environmental stimuli, can produce their immunomodulatory effects [32, 33]. Additionally, MSCs that have been pre-engineered or edited can greatly improve their immunomodulatory activities in a range of therapeutic settings [34, 35]. "Future therapeutic approaches for the treatment of immunological illnesses, such as autoimmune, and incurable inflammatory diseases, may employ this" [36]. According to clinical data, mesenchymal stem cells may be very promising for the treating, and prevention of a number of immune-mediated illnesses, like Crohn's disease (CD), multiple-sclerosis (MS), graft_versus_host disease (GVHD), and systemic_lupus erythema-tosus (SLE) [37,38].

3.3 Mesenchymal Stem Cells' Surface Markers

Multipotent mesenchymal stem cells, have the ability to generate hematopoietic supporting stroma, cartilage, or bone. Their criteria include that these cells display surface markers. "Most commonly utilized markers were found to be CD_73, CD_90, and CD_105 for in_vitro research, and STRO_1, CD_29, CD_44, CD_146, CD_166, and CD-271 for bone marrow, and cartilage" [39]. According to other research, MSCs cultivated under-growth circumstances showed an increase in CD-10 expression over-time, indicating MSC differentiation regarding osteoblasts [40]. "The city of Kiel-67 [Ki-67], and (Brd-U) markers were used to measure the MSCs generated from adipose tissue" [41]. More mesenchymal-stem-cell markers are mentioned in Table 1.

Table 1: Mesenchymal stem cells surface markers from different tissues

Sources	CD markers	References
Bone Marrow:	CD_29, CD_44, CD_45, CD_90, CD_105. CD_49e, CD_56, CD_92, CD_97, CD_156B, CD_156c, CD_220, CD_221, CD_298, CD_315.	[42] [43]
Adipose Tissue:	CD_29, CD_44, CD_90, CD_105. CD_26, CD_81, CD_201, CD_364.	[42] [43]
Amniotic Tissue:	CD_29, CD-44, CD_90, CD_105.	[42]
Hair Follicle:	CD_49a, CD_49b.	[43]
Dental pulp:	CD_9, CD_10, CD_63.	[43]
Umbilical Cord:	CD_44, CD_49f, CD_73, CD_105. CD_90, CD-34. CD_29, Vimentin.	[44, 45] [46] [47]

3.4 Applications of Mesenchymal_Stem Cell

Numerous studies have been performed to determine the viability and effectiveness of MSC treatment for an assortment of therapeutic applications have been made public by the clinical trials database. MSCs seem to be well tolerated it as shown by the effectiveness of MSC infusion for conditions such as heart failure, brain diseases, liver diseases, and GVHD (figure 2).

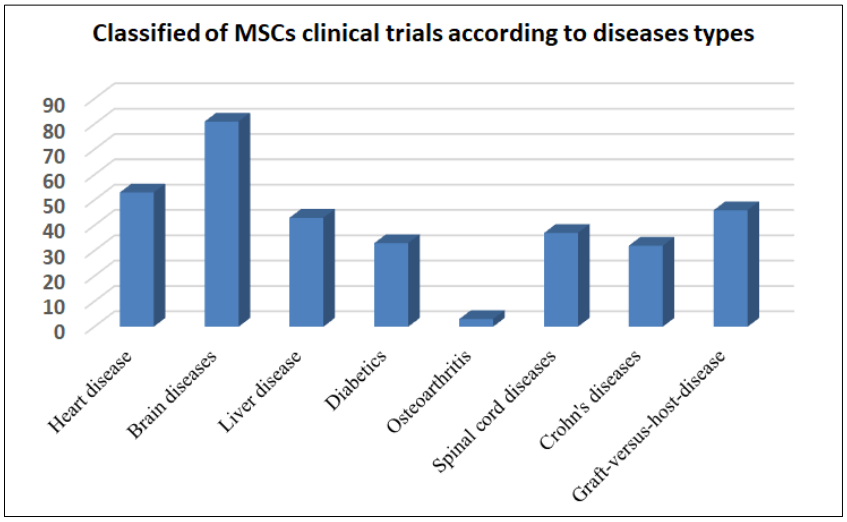

Figure 2: Classified of MSCs clinical trials according to disease types

"Mesenchymal_stem cells, have the ability to migrate to tissue damage sites to generate anti-inflammatory cytokines, aid in immune regulation, and evade the immune system" [48, 49]. Mesenchymal stem cells have anti-inflammatory, anti-aging, regenerative, and wound-healing properties [50]. Aged, and damaged skin may benefit from the therapeutic potential of mesenchymal stem cells [51, 52]. These cells promote the growth of new blood vessels, and cell proliferation during skin regeneration, lowering inflammation in afflicted skin lesions [53, 54]. They aid in the synthesis of collagen, and elastic fibers, suppressing the activity of metalloproteinases, and improving defense against UV–induced aging in skin regeneration [55, 56]. "Because mesenchymal_stem cells can develop into smooth muscle, in response to particular chemical cues, they hold enormous promise for vascular repair, and regenerative medicine" [57].

According to recent research, injecting exosomes produced from mesenchymal stem cells into traumatic brain injury models reduces local inflammatory damage, and encourages neuron regeneration after injury [58]. "Because of their low immunogenicity, ease of preservation, difficulty in reproducing, and tiny size, MSC-derived exosomes are thought to be a promising treatment approach for traumatic brain damage" [59, 60]. Other studies summarize the applications of mesenchymal stem cells (Table 2).

Table 2: Clinical Applications of Mesenchymal_Stem Cells

Tissue, sources	Applications	Mechanisms	References
Bone-Marrow	Aging frailty	Regeneration and anti-inflammation.	[61]
	Idiopathic Pulmonary Fibrosis	Immune regulation by interaction with T, B cells, dendritic cells, and natural killer cell, serves as anti-apoptotic.	[62],
	Osteoarthritis	Production of collagen type II and prevention apoptosis by IL-1β inhibition.	[63]
	Obesity, and Osteoporosis	Micro-RNA regulation.	[64]
	Ferro-ptosis	Inhibited by miR124-3p in exosomes MSCs.	[65]
	Alzheimer disease	Activation of glial cells and prevention of neuro-inflammation.	[66]
	Wound healing of diabetic ulcers	Epidermal growth factor activation lead to cells proliferation, differentiation and angiogenesis.	[67]
	Heart failure	MicroRNA-30e overexpression.	[68]
	Liver fibrosis	Regulation of nuclear-factor kappa-B and mitogen-activated protein kinase.	[69]
	Re-myelination of neuro-inflammation in the CNS	Regulation of cytokines and microglia, production of myelin basic protein, and decrease density of amyloid-β-precursor protein.	[70]
	Type 1 Diabetes mellitus	β-cells regulation and glycemic control.	[71,72]
Umbilical-cord	Ischemic heart disease	Angiogenesis by cytokines activation, and anti-inflammatory regulation.	[73]
	Anti-inflammatory for patients with COVID-19	Regulate the pro-inflammatory (Th1) and anti-inflammatory (Th2).	[74]
	Rheumatoid arthritis	Regulation of cytokines expression.	[75]
	Type 2 Diabetes mellitus	Activation of phosphatidylinositol-3- kinase/protein kinaseB (PI3K/Akt) pathway.	[76-77]

Tissue, sources	Applications	Mechanisms	References
	Hematological disorders	Synthesis of granulocyte colony-stimulation factor (G-CSF) and stimulate the hematopoietic stem cells production.	[78]
	Inflammatory bowel disease	Secretion of tumor necrosis factor-α stimulated gene 6 (TSG6) for immune regulation and tissue repair.	[79]
	Premature Ovarian Failure	Activation of follicle-stimulating hormone receptor, increase of ovarian markers, and Estradiol levels.	[80]
	Myocardial infarction,	Decreasing monocyte chemoattractant protein1(Mcp1), and increasing chemokine receptor (Cx3cr1) macrophage.	[81]
	Recessive dystrophic epidermolysis bullosa	Polarization of macrophages and reduced-infiltration of mast-cells.	[82]
	Psoriasis,	Inhibited the phyto-hemagglutinin (PHA), type 1, 17-T helper cells, and secretion of inflammatory cytokines.	[83]
Adipose-tissue	Acute Ischemic stroke	Decrease interleukins secretion, regulate the inflammatory conditions, and promote angiogenesis.	[84]
	Wound healing, and tissue regeneration	Promote fibroblast proliferation, collagen production, vascularization, and re-epithelialization.	[85]
	Skeletal muscle regeneration	Increased-expression and proliferation of the myocyte-related genes.	[86]
	Facial skin aging	Promote fibroblast proliferation, collagen production.	[87]
	Diabetic Osteoporosis	Inhibited the IL-1β, 18, TNF-α, and inactivated the inflammation.	[88]

3.5 Sources of Mesenchymal Stem Cells Tissue

Although "mesenchymal stem cells" observed in a several tissues, bone marrow_MSCs have been the focus of this research and are the subject of the defining criteria because they are the first to be described in "bone-marrow". More than 20 years ago, mesenchymal stem cells were found in dental procedures [89]. The paracrine and immune-modulatory qualities of MSCs have drawn a lot of interest in recent years. It is becoming more-well acknowledged that mesenchymal stem cells obtained from the umbilical cord have more therapeutic potential [90]. As a novel therapeutic strategy to encourage skin wound healing, MSCs obtained from adipose tissue have been viewed as promising therapeutic instruments for tissue regeneration [91]. MSCs generate from bone marrow, are a diverse mass of cells have the ability to proliferate on their own. With the right microenvironment or mechanical control, can develop in several directions and become "chondrocytes, osteoblasts, osteocytes, and adipocytes" [92].

4. CONCLUSION

Mesenchymal stem cells are extremely versatile, and the ability to differentiate into several distinct cells types. Subsets of unique or partially interconnected markers or combinations have been found by researchers. In a variety of physiological or pathological circumstances, single-cell sequencing investigations reveal both their traditional, and recently identified roles, and connections. Skeletal stem-cells, and adipocyte precursor cells are two examples of pluripotent stem cell types with clinically useful characteristics. Mesenchymal-stem-cells have a variety of effects on their milieu, including promoting hematopoiesis, tissue regeneration, and immune modulation. Additionally, this microenvironment controls mesenchymal-stem-cell development, proliferation, and function. These cells have the ability to either enhance or improve disease in a pathological milieu. Moreover, mesenchymal-stem-cell therapy, and the course of disease may be positively or negatively impacted by changes to this microenvironment.

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