Authors/Year of Publication	**Level of Evidence (I-VI) ***	**Subject n =**	**Type of Study**	**Proposed Mechanism of Action**	**Outcome**
Wang et al.[4] (2019)	N/A **	HUVECs (n= N/A)	In-vitro study	Promoted wound healing via stimulation of angiogenesis process; FEP gel had components promoting sustained release of ASC-exos, therefore further enhanced exosomes' wound healing effects	Combination use of FEP gel and exosomes had synergistic effect in wound healing; skin appendages formation and less scar tissue
		Mouse (n= 48)	Animal study		
Wu et al.[7] (2021)	N/A **	Human keloid fibroblasts (n= N/A)	In-vitro study	ASC-exos suppressed keloid fibroblast's actions by inhibiting expression of TGF-β1/SMAD pathway	Reduced keloid formation
Yuan et al.[8] (2021)	N/A **	Human hypertrophic scar fibroblasts (n= N/A)	In-vitro study	ASC-exos inhibited fibrosis and scar hyperplasia through its miR-29a-regulated TGF-β2/SMAD 3 pathway	Reduced pathological scar formation
		Mouse (n= 36)	Animal study		

Duan et al.[9] (2020)	N/A **	Human dermal fibroblasts (n= N/A)	In-vitro study	EPSC-exos suppressed myofibroblast differentiation via miR-425-5p- and miR-142-3p-mediated inhibition of TGF-β1 expression	Improved wound healing rate, reduced scar formation during wound healing
		Rat (n= 30)	Animal study		
Kwon et al.[10] (2020)	Level II	Human (n = 25)	Split-face, double-blinded, randomized control trial	ASC-exos induce rapid healing by supplying several anti-inflammatory and regenerative growth factors, as well as optimizing the migration, proliferation, and collagen synthesis of fibroblasts. ADSC-exos also decreased scarring during wound repair via regulating type III: type I collagen, TGFβ3: TGFβ1, and MMP3:TIMP1	Combined use of ASC-exos with resurfacing device provided synergistic effects on the treatment of atrophic acne scar and provided shorter recovery time and fewer side effects
Wang et al.[11] (2017)	N/A **	Human dermal fibroblasts (n= N/A)	In-vitro study	ASC-exos reduced scar formation by increasing collagen III:	Less scar formation

		Mouse (n= N/A)	Animal study	collagen I and prevented differentiation of myofibroblast by increasing TGF-β3: TGF-β1. ASC-exos promoted ECM remodeling by increasing MMP3:TIMP1 in skin dermal fibroblasts via activating ERK/MAPK pathway	
Fang et al.[12] (2016)	N/A **	Myofibroblasts (n= N/A)	In-vitro study	miR-21, -23a, -125b, and -145 suppressed myofibroblast formation by inhibition of TGF-β2/SMAD2 signaling pathway. Collagen I deposition was reduced via inhibiting α-SMA gene expression (UC-exos)	Prevented scar formation during wound healing
		Mouse (n= N/A)	Animal study		
Zhang et al.[26] (2021)	N/A **	Human dermal fibroblasts and epidermal stem cells (n= N/A)	In-vitro study	UC-exos suppressed scar formation by inhibiting myofibroblast differentiation via miR-21-5p- and miR-125b-5p-	Prevented scar formation during wound healing

		Rat (n = 30)	Animal study	mediated TGF-β receptor inhibition	
Hu et al.[27] (2018)	N/A **	Human dermal fibroblasts and endothelial cells (n= N/A)	In-vitro study	UC-exos enhanced wound healing by regulating fibroblasts and angiogenesis via miR-21-3p's effect on PTEN and SPRY1 inhibition	Reduced scar width
		Mouse (n= 20)	Animal study		
Zhou et al.[29] (2021)	N/A **	Mouse (n= N/A)	Animal study	ASC-exos increased the ratios of collagen III to collagen I in the late stage to suppress scar tissue formation	Local smear improved healing time and reduce scar formation; effective combination of IV and topical administration in promoting healing in extensive injuries such as burn and scalds
Hu et al.[30] (2016)	N/A **	Human dermal fibroblasts (n= N/A)	In-vitro study	ASC-exos promoted wound healing in early stages by	Decreased healing time and reduced scar

		Mouse (n= N/A)	Animal study	increasing type I and type III collagen distribution. Whereas in the late stages, ASC-exos inhibited collagen synthesis to reduce scar formation	formation
Zhang et al.[31] (2015)	N/A **	Human dermal fibroblasts and HUVECs (n= N/A)	In-vitro study	Wound healing process was accelerated via hiPSC-MSC-exos stimulation on collagen maturity and neovascularization at wound sites	Promoted granulation tissue formation and angiogenesis, leading to increased healing and reduced scar width
		Rat (n= N/A)	Animal study		
Li et al.[34] (2021)	N/A **	Human hypertrophic scar derived fibroblasts (n= N/A)	In-vitro study	ASC-exos suppressed hypertrophic scar fibrosis via its miR-192-5p-targeted IL-17RA to regulate SMAD pathway	Reduced hypertrophic scar formation
		Mouse (n= 12)	Animal study		
Wang et al.[35] (2019)	N/A **	HUVECs (n= N/A)	In-vitro study	FHE gel had components promoting sustained release of ASC-exos, therefore further enhanced exosomes' wound	Combination of FHE hydrogel and exosomes had synergistic effect in wound healing and skin
		Mouse (n= 48)	Animal study		

				healing effects	regeneration; skin appendages formation and less scar tissue
*Per American Society of Plastic Surgeons Rating Levels of Evidence and Grading Recommendations: Evidence Rating Scale for Therapeutic Studies.[5] **Animal/laboratory studies are considered not ratable in American Society of Plastic Surgeons Rating Levels of Evidence and Grading Recommendations pyramid scheme.					
Abbreviations: adipose-derived stem cell exosomes (ASC-exos), umbilical cord-derived stem cell exosomes (UC-exos), epidermal stem cell-derived exosomes (EPSC-exos), human induced pluripotent stem cell-derived mesenchymal stem cells-derived exosomes (hiPSC-MSC-exos), tissue growth factor beta (TGF-β), interleukin 17 receptor A (IL-17RA), fractional carbon dioxide laser (FCL), matrix metalloproteinase 3 (MMP3), tissue inhibitors of MMPs 1 (TIMP1), Pluronic F127 + oxidative hyaluronic acid + Poly-ε-L-lysine (FHE), Pluronic F127 + PEI + APu (FEP), Sprouty RTK signaling antagonist 1 (SPRY1), extracellular matrix (ECM), alpha-smooth muscle actin (a-SMA), human umbilical vein endothelial cells (HUVECs)					

Table, Supplementary Digital Content 2. A table that summarizes the mechanism of exosomes in scar revision.