Authors/Year of Publication	**Level of Evidence (I-VI) ***	**Subject n=**	**Type of Study**	**Proposed Mechanism of Action**	**Outcome**
Hu et al[6] (2019)	N/A**	Mouse (n=18)	Animal study	Exosomes increased procollagen type I and decreased MMP-1 expression via down-regulating TNF-α and up-regulating TGF-β and TIMP-1	Improved skin aging
		HDF (n=N/A)	In-vitro study		
Oh et al[18] (2018)	N/A**	HDF (n=N/A)	In-vitro study	iPSC-exos protected UVB damage to the HDFs by blocking UVB-induced overexpression of MMP1/3. iPSC-exos exerted its anti-aging effects via decreased mRNA expression of MMP1/3 and increased collagen I expression	Improved skin aging
Liang et al[19] (2020)	N/A**	Rat (n=15)	Animal study	ASC-exos exerted its anti-aging properties via increasing collagen I and decreasing collagen III and MMPs expression	Optimized epidermis and dermis thickness, improved skin aging

		Human fibroblasts (n= N/A)	In-vitro study		
Chernoff G[20] (2021)	Level II	Human (n=40)	Double-blinded, randomized controlled study	Microneedling created local inflammation which triggered exosomes to initiate healing properties, including cutaneous stem cells activation and promoting stem cells proliferation and migration to sites of injury. Exosomes aided in healing and reduced post-treatment redness and discomfort via their anti-inflammatory and anti-prostaglandin effects	Applying topical exosomes immediately following microneedling improved skin tone, quality, clarity, and patient satisfaction.
Duncan, Diane Irvine[21] (2020)	Level IV	Human (n=2)	Case series	Exosomes accelerate healing process through delivery of mRNA, cytokines, chemokines, and growth factors; exosomes further induce cellular changes through its paracrine effect	Applying topical exosomes following laser resurfacing improved healing

					time
Cho et al[22] (2020)	Level II	Human (n=21)	Split-face, double-blinded, randomized controlled study	ASC-exos decreased intracellular melanin contents via affecting downstream factors of TYR (TYRP-1, TYRP-2)	Applying topical exosomes reduced dark spots, blemishes, and overall melanin levels
*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-derived exosomes (ASC-exos), tyrosinase (TYR), tyrosinase related protein 1 (TYRP-1), Matrix Metalloproteinase (MMP), polydioxanone (PDO), three-dimensional human dermal fibroblast spheroid-derived exosomes (3D HDF-exos), monolayer culture of human dermal fibroblast (2D HDF-exos), mesenchymal stem cell-derived exosomes (MSC-exos), tissue growth factor beta (TGF-β), tumor necrosis factor alpha (TNF-α), human dermal fibroblast (HDF), tissue inhibitors of MMP 1 (TIMP-1), human induced pluripotent stem cell-derived exosomes (iPSC-exos)					

Table, Supplementary Digital Content 1. A table that summarizes the mechanism of exosomes in skin rejuvenation.