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Yuvalakshmi E
Postgraduate Research Scholar, GRD College of Pharmacy, Affiliated to The Tamil Nadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

Dhanesh Kumar MR
Assistant Professor, GRD College of Pharmacy, Affiliated to The Tamil Nadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

Dr. Selvaraj D
Professor cum HOD, Department of Pharmaceutics, GRD College of Pharmacy, Affiliated to The Tamil Nadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

Dr. Sathish A
Professor Cum Principal, GRD College of Pharmacy, Affiliated to The Tamil Nadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

Corresponding Author:
Yuvalakshmi E
Postgraduate Research Scholar, GRD College of Pharmacy, Affiliated to The Tamil Nadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

The emerging role of exosomes in skin health and dermatological conditions

Yuvalakshmi E, Dhanesh Kumar MR, Selvaraj D and Sathish A

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Abstract
Exosomes have been used as carrier for vast drug delivering routes but when narrowing them to derma they have been astonishingly helpful. They are secreted by different cells and their nano-size makes them a preferred one. Composition of exosomes can be modified for the desired action like proteins, nucleic acid, bioactive molecules. Exosomes also have been used as diagnostic biomarkers and therapeutic agents. In diseases such as psoriasis, acne, eczema and skin cancer, using exosomes mediated treatment gave better results with reduced side-effects. In this review, we presents, an overview of exosomes, their composition, mechanism of cellular uptakes, clinical approaches of them. Complexity and versatility of the exosomes make them to overcome their drawbacks. Future researches will address the challenges and we can use the exosome based formulations in commercial aspects.

Keywords: Exosomes, dermatology, skin care, psoriasis, chemotherapy

Introduction
The largest organ in our body, the skin, has many functions such as thermoregulation, sensory and protection. The study of intercellular communications provided as, exosomes, a great tool, small, membrane-bound vesicles which is considered as waste removers of our body. Recently, they are portrayed as efficient intercellular communication tool. They have many faces like regulators of tissue repairing, modulating cellular response and contributing in immunogenic responses. Along with this default biological functions, exosomes plays an important role in skin disease managements. Both therapeutics and diagnostics solutions have been found a way of using exosomes [1, 2].

Physiological role of exosomes
Exosomes, small extracellular vesicles having diameter of 30-145 nm, playing a crucial role in biomolecule transportation and cell-to-cell communication [3]. Various cells secretes different exosomes and they have greater roles in health and disease, especially in the derma diseases. Exosome biogenesis is a complex process within the endosomal system of cells that involves endocytosis, maturation into multivesicular bodies (MVBs), cargo incorporation, MVB fates and exosome secretion [4, 5].

Exosomes, enclosed by a lipid bilayer membrane, containing a unique set of proteins needed for exosome biogenesis, cargo sorting and cellular communication. They transport various molecules, including DNA, RNA, lipids, proteins and bioactive molecules. Exosomes engage in interactions with target cells through direct fusion with the target cell's plasma membrane or binding to particular cell surface receptors. Their payload, which includes proteins, genetic material and signaling molecules, is transferred more easily as a result of this contact, affecting recipient cells and altering different biological functions. Exosomes are vital intercellular communication mediators that have a significant impact on immunological responses, wound healing, skin biology and the pathophysiology of dermatological disorders [6, 7].

Composition of exosomes

Tetraspanins are among the proteins found in exosomes, a type of cellular organelle and are essential for exosome production and identification. Heat shock proteins (HSPs), such as HSP70 and HSP90, shield exosome cargo and may affect immunological responses, while other proteins, such as Alix (ALG-2-interacting protein X) and TSG101 (Tumor susceptibility gene 101), help generate intraluminal vesicles. [8] Exosomes are special and have the ability to alter target cell responses because they also carry proteins that are specific to a certain cell. Their varied roles in cellular processes are further enhanced by the presence of different enzymes and signaling molecules [9].

Diverse protein structure of exosomes includes, tetraspanins, major histocompatibility complex-II, Ras-related proteins (Rab), heat shock proteins (Hsp). Cholesterol and sphingomyelin lipids also present in it. Nucleic acid components such as non-coding RNAs, messenger RNA (mRNA) and microRNA (miRNA) are part of the exosomes. [4]

Exosome cellular uptake mechanism

Exosomes are taken up by various mechanisms such as micropinocytosis, phagocytosis, lipid raft-mediated endocytosis, membrane fusion, clathrin-mediated endocytosis, caveolin-mediated endocytosis. [10-12] A schematic representation of the above said mechanisms is given in Figure 1 [13].

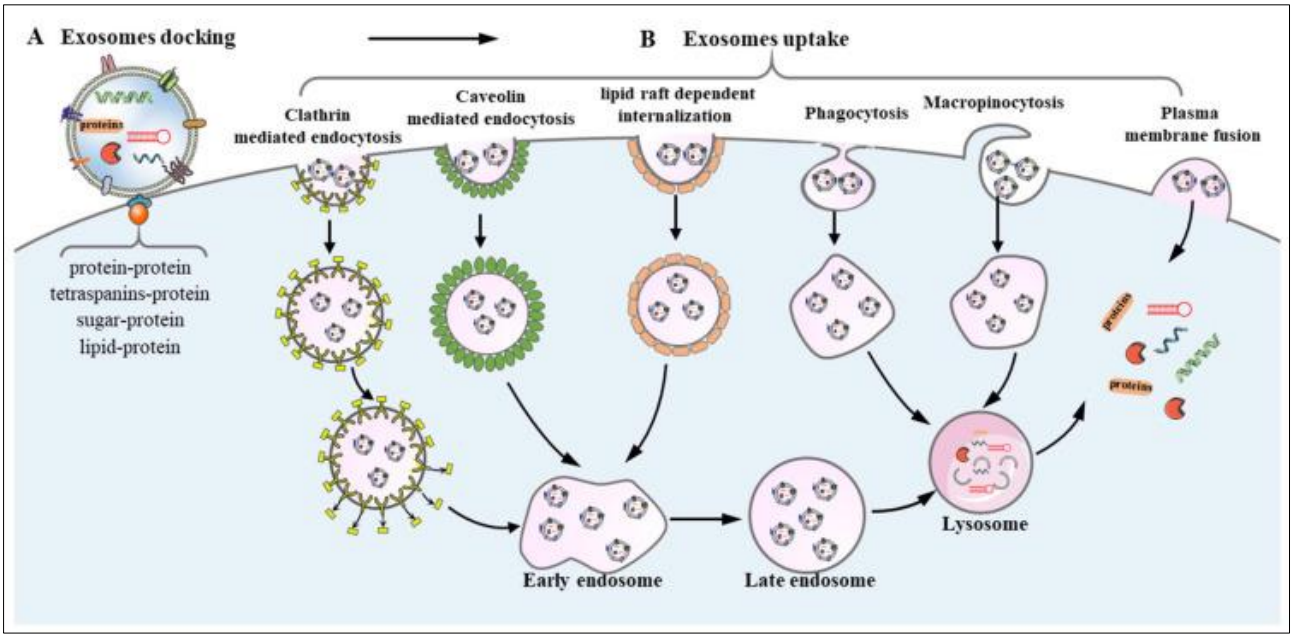

Fig 1: Various Cellular Uptake Mechanism of Exosomes

Dermatological conditions

For healthcare professionals to accurately identify and create effective treatment strategies, they must have a thorough understanding of various dermatological disorders, their causes and clinical manifestations. Furthermore, current dermatology research attempts to increase our understanding of these disorders and enhance treatment strategies.

Table 1: Some common skin conditions, their causes and description

Disease	Description	Causes
Psoriasis [14]	Auto-immune; Rapid skin cell build-up	Immune system dysfunction; Genetic;
Acne Vulgaris [15]	Papules, pustules, nodules and cysts in face, chest and back	Increased sebum production; bacterial infection; inflammation
Vitiligo [16]	Melanocyte loss-depigmentation	Melanocytes destroyed by own immune system
Eczema [17]	Redness, itching and irritation	Immune system dysfunction; Genetic;
Urticaria [18]	Allergic reaction, raised itchy welts	Infections; Allergic foods; Stress
Contact Dermatitis [17]	Skin inflammation-redness and itching	Allergens or irritants
Pruritus [17]	Continuous itchy skin	Kidney dysfunction, liver dysfunction, neuropathic

Exosome Therapy

Mesenchymal stem cell (MSC)-derived exosomes are abundant in cytokines and growth factors that promote tissue regeneration and they may hasten wound healing, reduce scarring and revitalize aged skin. They provide treatment options for inflammatory skin disorders such dermatitis, eczema and psoriasis because of their anti-inflammatory qualities which can alter immune responses. [19, 20] Exosomes are also thought to play a role in controlling the synthesis of melanin, which could help treat pigmentation conditions including vitiligo and hyperpigmentation. They may be helpful for those with alopecia or other hair diseases because of their capacity to stimulate hair follicles and encourage hair growth. Therapeutic chemicals can be transported by engineered exosomes, offering tailored delivery for the treatment of localized dermatological infections and skin cancer [21].

Fibroblast and keratinocyte exosomes have the potential to cure scars and stretch marks because they affect extracellular matrix components that are essential for skin

elasticity and structure. They have demonstrated efficacy in improving wound healing, lowering oxidative stress and encouraging collagen formation. Clinical studies have demonstrated its potential in anti-aging treatments with skincare products containing exosomes showing notable improvements in skin moisture and suppleness. [22-24] Because skin problems vary widely, personalized exosome-based therapies allow for customisation in dermatological treatments. In addition, these therapies are generally safe and have less side effects than conventional treatments, which makes them desirable for long-term usage in the treatment of dermatological disorders [25].

Commerically available exsomes based products

Size-exclusion chromatography, polymer-based precipitation, and ultracentrifugation are methods for isolating exosomes. Table 2 offers a thorough overview of important exosome-based products together with their therapeutic uses. [26-29]

Table 2: Commercially available exosome-based products

Product (Manufacturer)	Type of Exosome	Application
ELEVAI enfinity (ELEVAI Skincare)	Not Mentioned	Normal skin treatment at home
Cellese Exosome Products (Cellese)	Not Mentioned	Skin rejuvenation
CICA Exosome Replenishing Treatment Orbs (Snow Fox Skincare)	*Centella asiatica*	Post-treatment skin recovery, hydration
Renewosome™ Exosome Serums ((plated)™ Skin Science)	Platelet-derived exosomes	Skin and hair rejuvenation
Licorice Exosome Brightening Treatment Orbs (Snow Fox Skincare)	Licorice root	Hyperpigmentation, skin brightening

Patents on exosome-based products

A list of few patents available on exosome-based products is provided in Table 3.

Table 3: Patent list on Exosome-based Products

Patent Title	Patent Number	Inventor
Methods for Enhancing Wound Healing [30]	US11324768B2	RoosterBio Inc.
Exosome-Based Drug Delivery System [31]	US10576136B2	Codiak Biosciences Inc.
Method for Large-Scale Exosome Production [32]	WO2019229865A1	Exopharm Ltd.
Nanovesicle Composition for Skin Rejuvenation [33]	JP2020035462A	ExoCoBio Inc.
Compositions and Methods for Treating Skin Aging [34]	US20200331271A1	Kimera Labs Inc.

Future Directions

To guarantee constant quality and safety for clinical applications, standardized procedures for the separation and characterisation of exosomes must be established. More specialized treatments are possible by optimizing exosome cargo loading with therapeutic substances like proteins or nucleic acids. Additionally, there is great potential for tailoring exosome-based treatments to each patient's unique profile, taking into account variables like genetic variants and particular dermatological diseases [35, 36]. Effectiveness may be increased by examining the potential synergistic effects of exosome therapies in conjunction with other dermatological treatments like laser therapy or conventional medications. Comprehend the effects of repeated therapies on skin health, especially for chronic illnesses, thorough long-term safety studies are also essential.

Need to create precise criteria and approval procedures that put patient safety and treatment effectiveness first for that researchers, doctors, and regulatory agencies must work together. As these treatments develop, patient education is essential to ensuring that people are aware of the risks as well as the advantages. Furthermore, for exosome medicines to be widely available, their affordability and accessibility must be addressed through cost-effective production techniques and insurance coverage. The ethical implications of exosome sourcing, especially from stem cells, necessitate ongoing investigation and the development of strong ethical guidelines. Last but not least, advancing innovation and comprehensive knowledge in the field of exosome-based therapeutics requires a multidisciplinary approach including dermatologists, cell biologists, material scientists, and bioengineers.

Conclusion

Small extracellular vesicles called exosomes, which are released by different cell types, have become effective intercellular communication mediators with great promise for the dermatological profession. They are attractive prospects for novel dermatological treatments because of their critical functions in tissue regeneration, immunomodulation, wound healing and skin homeostasis. In the end, exosome-based dermatology has a bright future as long as cooperation, research and creativity remain at the forefront. The dermatological community may anticipate a time when exosomes will be crucial in improving the health, beauty and general well-being of skin by embracing these new advancements.

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