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Review Article

Exosomes And Their Therapeutic Promise in Modern Medicine

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ABSTRACT

Exosomes are nanosized extracellular vesicles secreted by diverse cell types, playing pivotal roles in intercellular communication, disease progression, and therapeutic innovation. Their unique biogenesis, heterogeneous composition, and ability to transport proteins, lipids, and nucleic acids make them highly versatile mediators of physiological and pathological processes. This review provides a comprehensive overview of exosome biology, including their formation, maturation, isolation techniques, and protein composition. The functional significance of exosomes in health and disease pathogenesis—ranging from cancer and neurodegenerative disorders to fibrosis and immune modulation—is highlighted. Furthermore, their therapeutic potential is explored in the context of regenerative medicine, immunomodulation, and targeted drug delivery, underscoring their advantages as natural nanocarriers with biocompatibility and low immunogenicity. Advances in exosome-based therapies, challenges in clinical translation, and the regulatory landscape, including FDA status, are critically discussed. Finally, future directions emphasize personalized medicine, large-scale production, and emerging applications in diagnostics, aesthetics, and wellness. Collectively, exosomes represent a transformative frontier in modern medicine, bridging fundamental biology with translational therapeutics.

INTRODUCTION

Exosomes are small extracellular vesicles (30–150 nm) secreted by a wide variety of cell types into the extracellular matrix. Once considered merely cellular waste products, they are now understood to play a crucial role in intercellular communication by transporting proteins, lipids, and nucleic acids to recipient cells, thereby influencing cellular behavior and function. Their natural ability to deliver bioactive molecules with high biocompatibility, low immunogenicity, and stability makes them highly attractive candidates for therapeutic applications. Compared to synthetic delivery systems such as liposomes or polymers, exosomes offer superior advantages in

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targeting specificity, reduced toxicity, and prolonged circulation.

Despite their promise, isolating exosomes remains a technical challenge due to their heterogeneity of origin and variability in shape. Advances in proteomics and isolation technologies are steadily addressing these issues, enhancing yield, purity, and characterization. Functionally, exosomes are implicated in both physiological regulation and pathological processes, including cancer progression, cardiovascular disease, neurological disorders, and liver disease, through mechanisms such as modulation of protein function, gene expression, and immune signaling. In therapeutic contexts, exosomes represent a safer and less invasive alternative to conventional treatments, with potential applications in diagnostics, regenerative medicine, drug delivery, and personalized therapy. They hold the capacity to transform disease understanding, improve drug discovery, and revolutionize modern medicine. However, significant gaps remain in understanding their biology, mechanisms, and clinical translation, highlighting the need for further research to overcome technical, biological, and regulatory barriers.

Biogenesis Of Exosomes

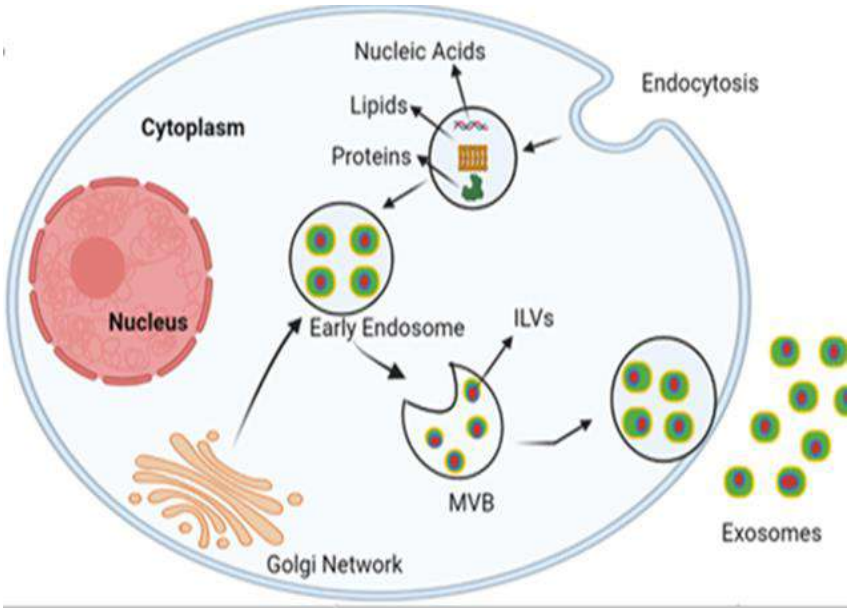

Fig No:1 Biogenesis of exosomes

Exosomes are small extracellular vesicles generated within multivesicular bodies (MVBs) through inward budding of late endosomal membranes, which produce intraluminal vesicles (ILVs). These ILVs encapsulate proteins and cytosolic components and are either released as exosomes upon fusion of MVBs with the plasma membrane or sent to lysosomes for degradation. Exosomes typically appear cup-shaped under preparation artifacts but spheroid under TEM and exhibit densities ranging from 1.13 g/mL (B cell-derived) to 1.19 g/mL (epithelial cell-derived). Their formation is mainly attributed to the endosomal sorting complex required for transport (ESCRT) pathway, a coordinated protein machinery. ESCRT-0 recognizes ubiquitinated cargo, ESCRT-I and -II promote membrane deformation, and ESCRT-III drives vesicle budding and scission with the help of the ATPase Vps4. Proteins such as Alix, TSG101, and CHMP4 play crucial roles in both membrane remodeling and selective cargo sorting. However, alternative ESCRT-independent mechanisms also exist.

These involve ceramide-enriched lipid microdomains, which induce negative membrane curvature and promote budding, as well as tetraspanins (CD81, CD9, CD63) that regulate receptor organization and cargo loading. Thus, both protein- and lipid-driven processes contribute to exosome biogenesis, varying with cell type and context. In contrast, other extracellular vesicles differ in origin and properties. Microvesicles (100–1000 nm, density 1.25–1.30 g/mL) bud directly from the plasma membrane, often produced by platelets, endothelial cells, or red blood cells. Apoptotic bodies (1–5 μm, density 1.18–1.28 g/mL) are released during apoptosis and contain organelles, membranes, and cytosolic fragments. Unlike these larger and heterogeneous vesicles, exosomes' small, uniform structure allows them to avoid rapid clearance by the mononuclear phagocyte system, remain longer in circulation, and serve as highly effective mediators of cell–cell communication.

Isolation And Characterization of Exosomes

The isolation and characterization of exosomes are crucial steps in both research and clinical applications, as they enable the accurate study of vesicle composition and function. A variety of isolation techniques are used, each offering a balance between yield, purity, and scalability. Ultracentrifugation-based methods remain the most widely adopted; differential ultracentrifugation separates vesicles based on size and density through sequential spins, though contamination with lipoproteins is a persistent issue. Density-gradient centrifugation, often using sucrose or iodixanol layers, improves purity but is labor-intensive and time-consuming. Size-based methods such as ultrafiltration employ membranes with defined pore sizes for rapid separation, while tangential flow filtration minimizes clogging and preserves vesicle integrity. Size-exclusion chromatography (SEC) uses porous gel matrices to separate exosomes from smaller contaminants like proteins and cytokines, and when combined with ultracentrifugation, further enhances purity. Polymer precipitation with polyethylene glycol (PEG) provides a simple and cost-effective approach but carries the risk of co-precipitating non-exosomal components such as lipoproteins and viruses. Immunoaffinity capture techniques use antibodies against surface markers like CD9 or CD63, immobilized on magnetic beads, to selectively isolate high-purity exosome subpopulations, although they may exclude vesicles lacking those specific markers. Recently, emerging technologies such as microfluidic platforms, nanolithography, and electro-deposition have enabled integrated isolation and analysis, offering high sensitivity and minimal sample requirements, and are increasingly applied in areas like cancer diagnostics. Once isolated, exosomes are characterized using complementary analytical techniques. Biophysical methods such as nanoparticle tracking analysis (NTA) measure size and concentration based on Brownian motion, while dynamic light scattering (DLS) provides size distribution data but is less reliable for heterogeneous samples. Imaging approaches including transmission electron microscopy (TEM), scanning electron microscopy (SEM), and atomic force microscopy (AFM) validate vesicle morphology, size, and surface topology at nanometer resolution. Molecular profiling techniques, such as flow cytometry, identify surface antigens but are limited by the detection threshold of conventional cytometers for particles below 300 nm, whereas western blotting confirms the presence of characteristic exosomal proteins like Alix and TSG101 to verify origin. Advanced analytical tools such as Raman spectroscopy allow non-destructive chemical fingerprinting of vesicles, and microfluidic biosensors enable real-time, high-throughput profiling of exosomal

cargo. Together, these diverse strategies provide a comprehensive toolkit for the efficient isolation and detailed characterization of exosomes, supporting their growing relevance in diagnostics, prognostics, and therapeutic delivery systems.

Protein Composition O Exosomes

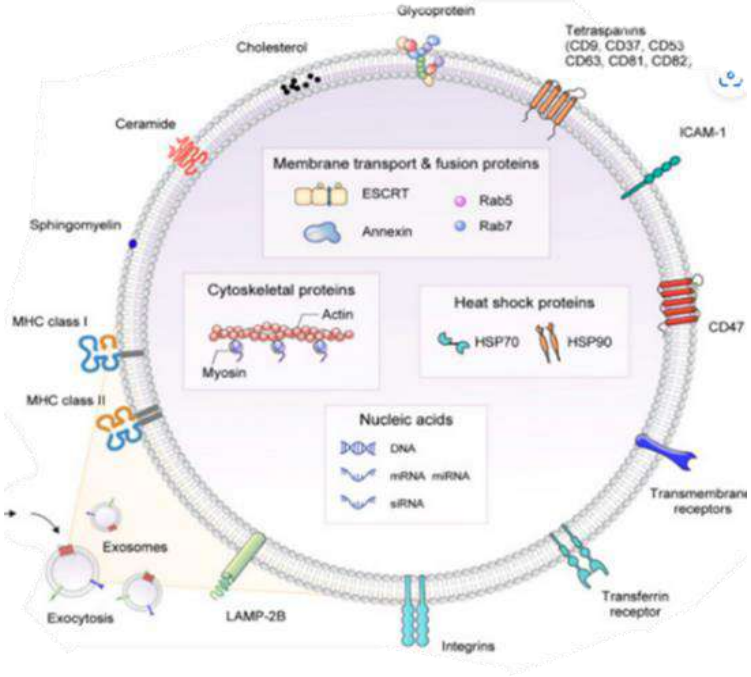

Fig No:2 Protein composition of exosomes

The protein composition of exosomes is highly specialized and reflects their biogenetic origin. Central protein families consistently identified in exosomes include **tetraspanins** (CD9, CD63, CD81), ESCRT-related proteins (e.g., Alix, TSG101), syntenin-1, and cytoskeletal proteins, which together contribute to exosomal structure and trafficking. In addition, other functionally relevant groups such as Rab GTPases, SNARE proteins, and cell type–specific proteins are frequently enriched. Exosomes are known to contain selected membrane and cytosolic proteins but are generally devoid of nuclear proteins when compared with their parental cells. Quantitative estimates suggest that a single exosome may contain approximately 20,000 protein molecules, although this number is influenced by vesicle size and the molecular packing parameters. Functionally, exosomal proteins participate in multiple steps of the tightly regulated process of exosome biogenesis. Endosomes, formed by the invagination of the plasma membrane, represent the precursors of exosomes. In the ESCRT-dependent pathway, the endosomal sorting complex required for transport (ESCRT) machinery is essential for the progression of early endosomes into multivesicular bodies (MVBs), which subsequently release intraluminal vesicles as exosomes.

Exosomes As Mediators of Cellular Communication and Disease Pathogenesis

Exosomes serve as critical mediators of intercellular communication by transporting a wide range of bioactive molecules, including proteins, lipids, mRNAs, miRNAs, and DNA, thereby regulating the fate and behaviour of recipient cells at both local and systemic levels. Communication occurs through several mechanisms: exosomes may interact with recipient cells via adhesion molecules that activate

signalling cascades, fuse directly with the plasma membrane to release their cargo, or undergo internalization through receptor-mediated endocytosis, phagocytosis, or macropinocytosis. Through these pathways, exosomes deliver genetic material, proteins, and lipids that modulate gene expression and signalling networks, thereby influencing a broad spectrum of physiological and pathological processes. Their functions extend to immune modulation, cell proliferation and survival, tissue remodelling and angiogenesis, and the progression of diseases such as tumour growth and metastasis. Importantly, exosomal communication demonstrates greater specificity and targeting than classical paracrine or endocrine signalling, as they are capable of transmitting complex molecular "messages" to distant recipient cells. Beyond their roles in physiological regulation, exosomes are deeply implicated in disease pathogenesis, where they act as conveyors of pathogenic molecules and modulators of cellular responses. In cancer, tumour-derived exosomes transfer oncogenic proteins, RNAs, and regulatory factors that remodel the tumour microenvironment, enhance angiogenesis, drive epithelial–mesenchymal transition (EMT), and promote metastasis. For example, hepatocellular carcinoma (HCC)-derived exosomes activate the FAK/Src–p38 MAPK and Wnt/β-catenin pathways to stimulate EMT while simultaneously suppressing immune surveillance by impairing NK cell activity, inducing T-cell apoptosis, and promoting M2 macrophage polarization. In neurodegenerative diseases such as Alzheimer's and Parkinson's, exosomes facilitate the spread of β-amyloid and α-synuclein aggregates between neurons, disrupting proteostasis and accelerating disease progression. Similarly, in fibrotic diseases, exosomes regulate fibroblast activation, immune cell migration, and extracellular matrix deposition. Macrophage-derived exosomes, for instance, deliver angiotensin II receptors to fibroblasts, driving myofibroblast differentiation in pulmonary fibrosis, while hepatocyte-stromal exosomal crosstalk promotes fibrotic remodelling and tumour progression in liver disease. Moreover, exosomes exert dual roles in immune regulation, either stimulating immune responses through MHC–antigen presentation or dampening immunity by transferring immunosuppressive cargo such as PD-L1 and TGF-β. Given their stability, targeting specificity, and ability to carry diverse molecular cargo, exosomes are increasingly being explored as therapeutic agents and diagnostic biomarkers. Strategies such as blocking oncogenic exosomal miRNAs (e.g., miRNA-21) or enhancing tumour-suppressive exosomal miRNAs (e.g., let-7) show promise in treating fibrosis and cancer. Collectively, these findings highlight exosomes as multifaceted regulators of cell communication that function not only as drivers of pathogenesis but also as potential targets and vehicles for therapy, underscoring their profound importance in both health and disease.

Therapeutic Potential of Exosomes in Regenerative Medicine and Targeted Drug Delivery

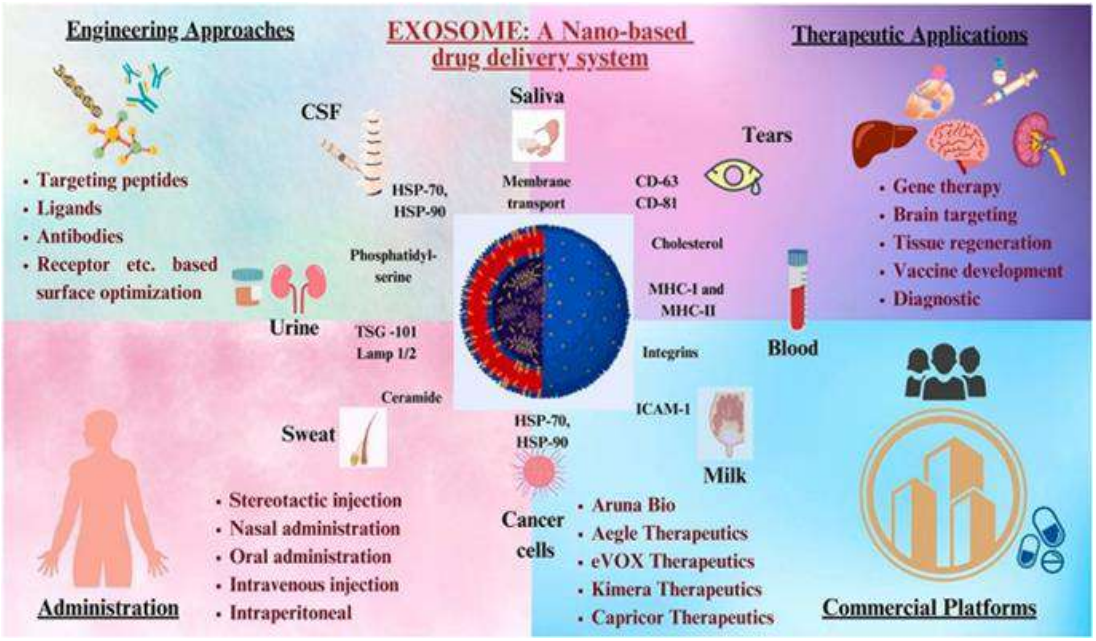

Fig No.3 Therapeutic Potential of Exosomes

Exosomes are increasingly recognized as powerful therapeutic tools due to their capacity to deliver bioactive molecules, regulate immune responses, and cross biological barriers. Their applications span regenerative medicine, immunomodulation, targeted drug delivery, and cancer therapy. In regenerative medicine, stem cell-derived exosomes (mesenchymal and neural) facilitate tissue repair, neuroprotection, and angiogenesis. For instance, MSC-derived exosomes aid spinal cord injury recovery by shifting microglial polarization (M1 to M2) through TLR4/NF-κB/PI3K/Akt signaling and promoting angiogenesis via VEGF-A delivery, while neural stem cell-derived exosomes reduce neuroinflammation in Alzheimer's and Parkinson's disease through anti-inflammatory miRNAs such as miR-216a-5p. In cardiovascular repair, they mitigate atherosclerosis and heart failure by modulating macrophage activity and suppressing inflammation. Their immunomodulatory potential is equally significant. In multiple sclerosis, MSC-derived exosomes inhibit TLR2/IRAK1/NF-κB signaling to reduce demyelination while promoting oligodendrocyte regeneration. In pulmonary disorders like ARDS, they suppress alveolar inflammation and enhance epithelial regeneration, supporting their role in autoimmune and inflammatory diseases. A major therapeutic frontier is drug delivery, where exosomes outperform synthetic carriers owing to their biocompatibility, stability, natural targeting capacity, and ability to traverse the blood–brain barrier. They can be engineered via passive loading, active loading (electroporation, sonication), or cell engineering to deliver chemotherapeutics (e.g., doxorubicin), nucleic acids (miRNAs, mRNAs), proteins, or gene-editing agents such as CRISPR-Cas systems. This flexibility has fueled interest in their use for neurological therapy, cancer treatment, and gene therapy. In oncology, engineered exosomes can deliver PD-1/PD-L1 inhibitors, tumor antigens, and immunostimulatory molecules, enhancing T-cell activation and reducing tumor immunosuppression. Furthermore, hybrid exosome–nanoparticle systems improve stability, loading efficiency, and pharmacokinetics, broadening therapeutic scope. In summary, exosomes offer unique advantages—low

immunogenicity, cargo protection, precise targeting, and barrier-crossing ability—making them an exceptional platform for next-generation therapies in regenerative medicine, oncology, neurology, cardiovascular repair, and immunomodulation.

Exosome-Based Therapy

Exosome based therapy is an emerging opportunity in targeted drug delivery, regenerative medicine and it is a natural extracellular vesicle to treat various diseases.

The exosome-based therapy has various advantages

Major advantages over Traditional Therapies

- Low immunogenicity and toxicity: Exosomes escape immune rejection and infusion-related disorders, unlike cell-based therapies.
- Improved targeting: Naturally home to targeted tissues and cross biological barriers (e.g., blood-brain barrier).
- Stability and storage: Easier to store and deliver than live cells.

Ethical safety: Avoid controversies surrounding stem cell utilization.

Clinical Applications:

Regenerative Medicine

- Tissue Repair: Mesenchymal stem cell (MSC)-derived exosomes, particularly from adipose tissue, promote angiogenesis, reduce inflammation, and enhance wound healing as well as orthopedic repair.
- Neurological Repair: Neural stem cell-derived exosomes show promise in stroke recovery and the management of neurodegenerative diseases by supporting neural regeneration and functional recovery.

Cancer Therapy

- **Drug Delivery:** Exosomes engineered to carry chemotherapeutics improve tumor targeting while minimizing systemic toxicity. For instance, milk-derived exosomes delivering paclitaxel orally have been shown to inhibit lung tumor growth in mice with reduced side effects.
- **Immunomodulation:** Exosomes are being utilized to strengthen anti-tumor immunity, either through cancer vaccines or as vehicles for checkpoint inhibitors, thereby enhancing immunotherapeutic outcomes.

Disease-Specific Treatments

- Cardiovascular Disorders: Endothelial stem cell-derived exosomes facilitate cardiac tissue repair and functional recovery after injury.
- Urological Disorders: MSC-derived exosomes demonstrate protective effects against bladder trauma and kidney-related diseases.
- Hair Restoration: Exosome-based scalp injections can stimulate dormant hair follicles and promote new hair growth without the side effects commonly associated with conventional therapies.
- Diabetes and Metabolic Disorders: Exosomes are being investigated for their role in modulating immune responses and restoring pancreatic β-cell mass, offering potential benefits in type 1 diabetes management.

Recent Advancements

- Next-Generation Stem Cell-Derived Exosomes: Highly purified formulations enriched with growth factors and anti-inflammatory molecules are being developed to maximize therapeutic potential in tissue repair and inflammation control.

- Personalized Therapies: Patient-specific, biomarker-guided exosome preparations are emerging, allowing tailored interventions for aging, immune deficiencies, and neurological conditions.

- Cosmetic and Dermatologic Uses: Exosomes are increasingly integrated with aesthetic procedures such as microneedling and platelet-rich plasma (PRP), enhancing outcomes in skin rejuvenation and wound healing.

Challenges And Limitations of Exosome Based Therapy

1**. Manufacturing and Standardization Challenges**

- Lack of Standardized Protocols: There is no universally accepted method for exosome isolation, purification, or characterization, leading to variability in product quality and therapeutic performance.

- Scalability Issues: Large-scale production remains technically difficult, and replicating the same exosome quality and phenotype during scale-up is a significant obstacle.

- Contamination Risks: Current isolation practices carry risks of microbial or protein contamination, which can compromise safety and therapeutic reliability.

2. Biological and Technical Limitations

- Heterogeneity: Exosome composition varies depending on the source cell type, donor, and culture conditions, creating batch-to-batch inconsistency.

- Limited Drug Loading Efficiency: Incorporating therapeutic cargo into exosomes remains inefficient, reducing treatment potency and reproducibility.

- Short Half-Life and Rapid Clearance: Exosomes are quickly removed from circulation, limiting their bioavailability and target accumulation.

- Suboptimal Tissue Targeting: Despite engineering efforts, exosomes often accumulate in non-target tissues such as the liver and spleen, reducing therapeutic specificity.

3. **Regulatory and Clinical Challenges**

- **Regulatory Ambiguity:** Clear regulatory frameworks are still evolving, and currently no FDA-approved exosome-based intravenous drugs are available.

- **High Development Costs:** Isolation, characterization, and manufacturing are resource-intensive, making clinical development costly and time-consuming.

- **Limited Clinical Evidence:** Most clinical trials are small-scale and early-phase, with insufficient data on long-term safety, efficacy, and standardized dosing.

4. **Additional Considerations**

- Off-Target Effects: Unintended delivery of therapeutic cargo may cause unwanted biological effects in non-target tissues.

Column 1: Sr No, Column 2: Challenge type, Column 3: Description.

Sr, No.	Challenge Type	Description
1	Manufacturing	Standardization, scalability problems, potential for contamination
2	Biological/Technical	Heterogeneity, constrained drug loading, short half-life, inadequate tissue targeting
3	Regulatory/Clinical	Regulatory uncertainty, expense of clinical trials, limited large-scale data
4	Ethical/Quality	Ethical sourcing, high-quality control demands
5	Potential for Off-Target Effects	Nonspecific cargo loading

FDA Approval Status

- To date, no exosome-based therapeutic, diagnostic, or preventive product has been approved by the U.S. Food and Drug Administration (FDA).
- **Regulatory Classification**: Exosome products intended for the treatment, prevention, or cure of diseases are regulated as drugs and biological products under the *Public Health Service Act* and the *Federal Food, Drug, and Cosmetic Act*. Such products require FDA premarket review and approval before commercial distribution.
- **Investigational Use Only**: Exosomes can be used in humans strictly under clinical research settings when supported by an Investigational New Drug (IND) application or an Investigational Device Exemption (IDE).
- **Illegal Marketing Concerns:** Several clinics and businesses are marketing unapproved exosome therapies, often making unsubstantiated claims. The FDA has issued public health warnings regarding such activities, citing reports of serious adverse events.
- **Cosmetic Products**: While exosome-based formulations are increasingly marketed in skincare, the FDA does not recognize or approve these as cosmetics for medical use. Their clinical safety and efficacy remain unverified.
- **Recent Advances in Cell Therapy:** The FDA's approval of *Ryoncil (remestemcel-L)*, an allogeneic mesenchymal stromal cell therapy, was a milestone for regenerative medicine but does not include exosome products, underscoring the regulatory gap in exosome therapeutics.

Major Types and Strategies of Exosome Formulations

- **Thermoresponsive Hydrogel-Embedded Exosomes:**
  Encapsulation in temperature-sensitive hydrogels allows localized delivery, particularly for wound healing and gastrointestinal repair. These hydrogels

transition from liquid to gel at body temperature, improving site retention and enabling delivery into irregular or difficult-to-access regions.

- **Systemic Formulations:**

Intravenous administration results in rapid hepatic clearance, making exosomes particularly useful for liver-targeted therapies. To expand systemic applications, novel strategies are under investigation to minimize liver capture and enhance targeting to other organs.

- **Engineered Exosomes:**

Exosomes can be bioengineered to carry therapeutic RNAs, proteins, or small molecules, and may be modified to display targeting ligands on their surface. These strategies improve selective tissue targeting, intracellular uptake, and therapeutic activity.

- **Exosome-Mimetics:**

Synthetic or semi-synthetic vesicles designed to mimic the structure and function of natural exosomes. They address challenges such as low natural yield, immunogenicity, and toxicity while allowing scalable, reproducible production.

- **Drug-Loaded Exosomes:**

Therapeutics may be incorporated into exosomes either indirectly (loading parental cells, which then release drug-loaded exosomes) or directly (loading isolated exosomes through techniques such as co-incubation or electroporation). Challenges remain regarding loading efficiency, membrane integrity, and drug stability.

- **Stabilized Exosome Formulations:**

Advanced purification methods (e.g., anion-exchange chromatography) and removal of impurities improve exosome shelf-life and product stability, which is critical for commercial scalability and clinical reliability.

- **Disease-Specific Formulations:**

Specialized exosome formulations are under development for targeted indications—for example, regulatory T-cell-derived exosomes engineered to deliver VEGF antibodies for ocular disorders such as choroidal neovascularization, improving precision and efficacy.

Column 1: Sr No, Colum 2: Brand or Product Nate, Column 3: Company/Developer, Column 4: Source/Type, Column 5: Main Application/Indication, Column 6: Status/Notes.

Sr. No.	Brand/ Product Name	Company/ Developer	Source/ Type	Main Application/ Indication	Status / Notes
1	XoGlo®	Kimera Labs	MSC-derived exosomes	Regenerative, anti-inflammatory, cosmeceuticals	not FDA-approved
2	ExoFlo	Direct Biologics	Bone marrow MSC-derived EVs	Anti-inflammatory, regenerative	Clinical trials; not FDA-approved
3	DeliverEX platform	Evox Therapeutics	Engineered exosomes	Rare genetic/metabolic diseases	Pipeline; multiple candidates
4	AGLE-102	Aegle Therapeutics	Not Specified	Dermatology, Wound healing	Clinical pipeline

			(likely MSC derived)		
5	EXO-CD24 (Nano24)	Nano 24 (OBCTCD 24)	Not Specified	Inflammatory/immune modulation	Clinical pipeline
6	CAP-1002	Capricor therapeutics	Cardio sphere-derived exosomes	Cardiovascular, Duchenne muscular dystrophy	Clinical pipeline
7	Exo-101	Exogenous Therapeutics	Umbilical cord blood derived exosomes	Tissue regeneration, inflammatory diseases	Preclinical/clinical GMP manufacturing
8	CALECIM Professional Serum	Cell Research Corporation	Umbilical cord lining-derived exosomes	Skin rejuvenation (cosmetic)	Cosmetceutical;not FDA-approved
9	Lifeline Intense Moisture Serum	Lifeline Skin Care	Stem cell-derived exosomes	Skin care (cosmetic)	cosmetceutical

Future Directions and Clinical Trial Landscape of Exosome-Based Therapies

Exosomes are rapidly emerging as versatile platforms for therapeutics, diagnostics, and regenerative applications, with ongoing research pointing to a transformative future in precision medicine.

Personalized Drug Delivery and Targeted Therapies: Advances in exosome engineering are enhancing cargo loading, targeting specificity, and therapeutic potency, allowing for precise delivery of drugs, genes, and immune modulators. Integration with gene editing tools such as CRISPR/Cas9 and parent cell engineering further expands their potential.

Diagnostics and Liquid Biopsy: Exosomes are increasingly studied as non-invasive biomarkers for cancer detection, prognosis, and disease monitoring, particularly in breast, lung, colorectal, and prostate cancers. Coupled with AI and big data analytics, exosome-assisted multiplexed detection promises greater diagnostic precision and early intervention capabilities.

Regenerative Medicine and Tissue Repair: Clinical trials are underway testing exosome therapies for osteoarthritis, myocardial infarction, wound healing, and organ regeneration. Their ability to regulate inflammation and promote tissue repair positions exosomes as promising candidates for next-generation regenerative medicine.

Neurological and Immune Disorders : Exosome therapies are in development for neurodegenerative diseases (e.g., Parkinson's, Alzheimer's, stroke) and immune-mediated disorders, leveraging their neuroprotective and immunomodulatory activities to achieve therapeutic benefits.

Aesthetics and Wellness : Beyond clinical medicine, exosomes are entering the aesthetics

sector, showing promise in skin rejuvenation, anti-aging, and wound healing. As production scalability improves, bioengineered exosomes are expected to become more accessible in routine skincare and wellness products.

Manufacturing and Scalability : Technological advances such as hollow-fiber bioreactors, microfluidic isolation, and scalable purification methods are addressing the challenges of low yield and high manufacturing costs. These developments pave the way for large-scale, GMP-grade production of exosome formulations suitable for widespread clinical use.

Challenges Ahead: Despite advances, key hurdles remain: standardizing quality control, improving reproducibility, enhancing targeting specificity, addressing immunogenicity concerns, and generating robust clinical trial data. Collaborative efforts between academia, industry, and regulatory bodies will be essential to ensure safe and effective clinical translation.

Pipeline and Clinical Trials (as of July 2025) : The global pipeline of exosome therapies is expanding rapidly, with over 100 active clinical trials exploring applications in oncology, neurology, immune modulation, and regenerative medicine. Notable programs include:

- Evox Therapeutics: DeliverEX™ platform advancing RNA therapeutics, antisense oligonucleotides, and enzyme replacement therapies in partnership with Eli Lilly.
- Kimera Labs: Investigating XoGlo® (MSC-derived exosomes) for wound repair, skin rejuvenation, orthopedic repair, and early ophthalmologic/neurologic uses.
- Aruna Bio: Developing exosome-based therapies for neurological diseases.
- Aegle Therapeutics: Focused on dermatology and wound healing applications.
- Codiak BioSciences: Engineering exosomes for targeted drug delivery in cancer and other diseases.
- Exosome Diagnostics (Bio-Techne): Leading exosome-based liquid biopsy trials in oncology.

Therapeutic Areas in Development

- Cancer: Exosomes as drug delivery systems and biomarkers in lung, prostate, and pancreatic cancers.
- Neurological Disorders: Applications in Alzheimer's, Parkinson's, and stroke.
- Regenerative Medicine: Trials in osteoarthritis, myocardial infarction, and cutaneous wound healing.
- Immune Modulation: Delivery of immunotherapeutic and chemotherapeutics.

CONCLUSION

Exosomes represent a transformative frontier in modern medicine, uniquely positioned at the intersection of cellular communication, diagnostics, and therapeutics. Their nanoscale architecture, ability to encapsulate diverse bioactive cargo, and natural biocompatibility provide significant advantages over synthetic delivery systems. Current evidence underscores their therapeutic promise in regenerative medicine, oncology, neurology, and immune modulation, with early clinical trials demonstrating safety and feasibility. However, the translation of exosome-based therapies into clinical practice is constrained by challenges in large-scale manufacturing, standardization, targeted delivery, and regulatory

approval. Advances in bioengineering, high-throughput isolation, and GMP-grade production are beginning to address these barriers, paving the way for next-generation, personalized, and disease-specific applications. As the clinical pipeline expands, collaborative efforts between academia, industry, and regulatory agencies will be critical to establish robust safety, efficacy, and quality frameworks. Collectively, exosomes hold immense potential to redefine therapeutic strategies, serving not only as powerful nanocarriers but also as biomarkers and active modulators of disease biology, thereby shaping the future of precision and regenerative medicine.

Conflict Of Interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Gao J, Li A, Hu JF, Feng L, Liu L, Zuo - Jun Max Shen : Recent developments in isolating methods for exosomes. Frontiers in Bioengineering and Biotechnology 2023 ; Jan 13;10.
2. Sen S, Xavier J, Kumar N, Ahmad MZ, Ranjan OP. Exosomes as natural nanocarrierbased drug delivery system: recent insights and future perspectives. 3 Biotech. 2023; 13:101.
3. Nikapitiya C, Jayathilaka EHTT, Edirisinghe SL, Rajapaksha DC, Wasana WP, Jayasinghe JNC, et al.: Isolation and Characterization of Plasma-Derived Exosomes from the Marine Fish Rock Bream (Oplegnathus fasciatus) by Two Isolation Techniques. Fishes 2022; 7(1), 36
4. Houssam Aheget, Loubna Mazini, Francisco Martin, Karim Benabdellah, Boutaïna Belqat ,et al: Exosomes: Their Role in Pathogenesis, Diagnosis and Treatment of Diseases. Cancers 2021; 13, 84
5. Zhang Y, Bi J, Huang J, Tang Y, Du S, Li P : Exosome: A Review of Its Classification, Isolation Techniques, Storage, Diagnostic and Targeted Therapy Applications. International Journal of Nanomedicine 2020 ;15:6917–34.
6. Sidhom K, Obi PO, Saleem A : A Review of Exosomal Isolation Methods: Is Size Exclusion Chromatography the Best Option?. International Journal of Molecular Sciences 2020 ; Sep 4;21(18):6466.
7. Zhang Y, Bi J, Huang J, Tang Y, Du S, Li P : Exosome: A Review of Its Classification, Isolation Techniques, Storage, Diagnostic and Targeted Therapy Applications. International Journal of Nanomedicine 2020 ; 15:6917–34.
8. Patel GK, Khan MA, Zubair H, Srivastava SK, Khushman M, Singh S, et al.: Comparative analysis of exosome isolation methods using culture supernatant for optimum yield, purity and downstream applications. Scientific Reports [Internet] 2019 ; 9(1):1–10.
9. Yuan Zhang, Yunfeng Liu, Haiying Liu and Wai Ho Tang : Exosomes: biogenesis, biologic function and clinical potential. Cell & Bioscience 2019 ; 9:19.
10. Gurunathan S, Kang MH, Jeyaraj M, Qasim M, Kim JH : Review of the Isolation, Characterization, Biological Function, and Multifarious Therapeutic Approaches of Exosomes. Cells 2019; Apr 3;8(4):307.
11. Chahar H, Bao X, Casola A : Exosomes and Their Role in the Life Cycle and Pathogenesis of RNA Viruses. Viruses 2015 ; Jun 19;7(6):3204–25.
12. Pospichalova, V.; Svoboda, J.; Dave, Z.; Kotrbova, A.; Kaiser, K.; Klemova, D.; Ilkovics, L.; Hampl, A.; Crha, I.; Jandakova, E. Simplified protocol for flow cytometry analysis of fluorescently labeled exosomes and microvesicles using dedicated flow cytometer. J. Extracell. Vesicles 2015, 4, 25530.

13. Li, K.; Chen, Y.; Li, A.; Tan, C.; Liu, X. Exosomes play roles in sequential processes of tumor metastasis. Int. J. Cancer 2019, 144, 1486–1495.
14. Emmanouilidou, E.; Melachroinou, K.; Roumeliotis, T.; Garbis, S.D.; Ntzouni, M.; Margaritis, L.H.; Stefanis, L.; Vekrellis, K. Cell-produced-synuclein is secreted in a calcium-dependent manner by exosomes and impacts neuronal survival. J. Neurosci. 2010, 30, 6838–6851.
15. Webber, J.; Steadman, R.; Mason, M.D.; Tabi, Z.; Clayton, A. Cancer exosomes trigger fibroblast to myofibroblast differentiation. Cancer Res. 2010, 70, 9621–9630.
16. Ratajczak, M.Z.; Ratajczak, J. Extracellular microvesicles/exosomes: Discovery, disbelief, acceptance, and the future? Leukemia 2020, 34, 3126–3136.
17. Aheget, H.; Tristán-Manzano, M.; Mazini, L.; Cortijo-Gutierrez, M.; Galindo-Moreno, P.; Herrera, C.; Martin, F.; Marchal, J.A.; Benabdellah, K. Exosome: A new player in translational nanomedicine. J. Clin. Med. 2020, 9, 2380.
18. Santucci, L.; Bruschi, M.; Del Zotto, G.; Antonini, F.; Ghiggeri, G.M.; Panfoli, I.; Candiano, G. Biological surface properties in extracellular vesicles and their effect on cargo proteins. Sci. Rep. 2019, 9, 13048.
19. Li, K.; Chen, Y.; Li, A.; Tan, C.; Liu, X. Exosomes play roles in sequential processes of tumor metastasis. Int. J. Cancer 2019, 144, 1486–1495.
20. Valadi, H.; Ekström, K.; Bossios, A.; Sjöstrand, M.; Lee, J.J.; Lötvall, J.O. Exosome-Mediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells. Nat. Cell Biol. 2007, 9, 654–659.
21. Thakur, B.K.; Zhang, H.; Becker, A.; Matei, I.; Huang, Y.; Costa-Silva, B.; Zheng, Y.; Hoshino, A.; Brazier, H.; Xiang, J. Double stranded DNA in exosomes: A novel biomarker in cancer detection. Cell Res. 2014, 24, 766–769.
22. Huang, X.; Yuan, T.; Tschannen, M.; Sun, Z.; Jacob, H.; Du, M.; Liang, M.; Dittmar, R.L.; Liu, Y.; Liang, M. Characterization of humanplasma-derived exosomal RNAs by deep sequencing. BMC Genom. 2013, 14, 319.
23. He, C.; Zheng, S.; Luo, Y.; Wang, B. Exosome theranostics: Biology and translational medicine. Theranostics 2018, 8, 237.
24. De Jong, O.G.; Verhaar, M.C.; Chen, Y.; Vader, P.; Gremmels, H.; Posthuma, G.; Schiffelers, R.M.; Gucek, M.; van Balkom, B.W. Cellular stress conditions are reflected in the protein and RNA content of endothelial cell-derived exosomes. J. Extracell. Vesicles 2012, 1, 18396.
25. Laulagnier, K.; Vincent-Schneider, H.; Hamdi, S.; Subra, C.; Lankar, D.; Record, M. Characterization of exosome subpopulations from RBL-2H3 cells using fluorescent lipids. Blood Cells Mol. Dis. 2005, 35, 116–121.

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