ISSN: 2231-3656

International Journal of Pharmacy and Industrial Research (IJPIR)

IJPIR |Vol. 16 | Issue 3 | Jul – Sep 2026

www.ijpir.com

DOI: https://doi.org/10.61096/ijpir.v16.iss3.2026.1195.1213

Autologous Exosomes for Human Therapeutics: Biological Basis, Isolation Methodologies, Kit Development, and Translational Requirements

Dr. Leroy Rebello[1], Dr. Sreesudha Chepyala[2], Sahithi Polineni[3*], Dr. Rani Jangala[4]

[1,2,3,4] *Department of Research and Development, Biotex Life Solutions Pvt. Ltd., Secunderabad, Telangana, India*

Corresponding author: **Polineni Sahithi***

E-mail: sahithi.biotexlife@gmail.com

Published on: 12.08.2026

Published by: Futuristic Publications

Abstract: Autologous exosomes are extracellular vesicles obtained from a patient and intended for administration to the same patient. They are being investigated as cell-free biological materials for regenerative medicine, wound repair, aesthetic medicine, hair restoration, reproductive medicine, orthopaedic therapy, drug delivery, and immunomodulation. Their therapeutic rationale is based on extracellular vesicles' ability to transfer proteins, lipids, messenger RNA, microRNA, and other signalling molecules between cells. However, autologous origin does not establish complete safety, purity, therapeutic potency, or regulatory approval. The composition of a patient-derived preparation may vary depending on the source tissue, disease state, age, medications, inflammation, collection procedure, and isolation method. Current evidence also demonstrates that many published clinical studies involve allogeneic MSC-derived or platelet-derived EVs rather than autologous exosomes. Therefore, an autologous exosome kit should be developed as a validated, patient-specific small extracellular vesicle processing system, incorporating closed collection, controlled separation, purification, characterisation, contamination control, stability assessment, and indication-specific potency testing.

Keywords: Autologous exosomes; extracellular vesicles; patient-derived therapeutics; platelet-derived vesicles; regenerative medicine; size-exclusion chromatography; membrane filtration; platelet-rich plasma; wound healing; oocyte maturation.

Abbreviations

Abbreviation	Full term
EV	Extracellular vesicle
sEV	Small extracellular vesicle
MSC	Mesenchymal stromal/stem cell
MVB	Multivesicular body
ESCRT	Endosomal sorting complex required for transport
miRNA	MicroRNA
mRNA	Messenger RNA
TGF-β	Transforming growth factor beta
VEGF	Vascular endothelial growth factor
PDGF	Platelet-derived growth factor

IGF	Insulin-like growth factor
PRP	Platelet-rich plasma
NTA	Nanoparticle tracking analysis
DLS	Dynamic light scattering
ELISA	Enzyme-linked immunosorbent assay
SEC	Size-exclusion chromatography
TFF	Tangential-flow filtration
QC	Quality control
FDA	United States Food and Drug Administration
ISEV	International Society for Extracellular Vesicles
MISEV	Minimal Information for Studies of Extracellular Vesicles

Introduction

Extracellular vesicles are nanoscale, membrane-bound structures released by virtually all cell types and capable of modifying the phenotype and function of recipient cells through the transfer of proteins, lipids, messenger RNA, microRNA, and other signalling molecules [1,2]. They are increasingly studied as therapeutics, drug-delivery vehicles, disease biomarkers, and tools in regenerative medicine, with applications spanning wound healing, dermatology, orthopaedics, cardiology, neurology, nephrology, and reproductive biology [3–5]. The same molecular features that make extracellular vesicles attractive for therapy, however, also create substantial translational challenges related to heterogeneity, dose definition, purification, characterisation, contamination control, potency measurement, stability, and regulatory classification [6–8].

Within this broader landscape, autologous extracellular vesicles — vesicles isolated from the same patient who will receive them — occupy a distinct conceptual position. Because the donor and recipient are identical, autologous vesicles may reduce exposure to foreign antigens and avoid the donor-related pathogen concerns that apply to allogeneic preparations [9,10]. Their cell-free architecture additionally removes the engraftment, differentiation, and proliferative risks associated with live-cell therapies [3,8]. At the same time, autologous origin does not establish uniform purity, reproducible potency, or defined clinical efficacy. Variability in source tissue, age, disease state, medication, and processing method produces preparations that can differ substantially in particle count, cargo, and biological activity even when a single isolation workflow is followed [7,11].

The therapeutic promise of autologous vesicles has nonetheless driven the development of multiple point-of-care processing platforms intended for use in dermatology, aesthetic medicine, hair restoration, orthopaedics, reproductive medicine, and wound care [12–15]. The development of such kits has, in turn, raised a set of scientific and translational questions that are not specific to any one product but apply to all of them: how source material should be qualified, how the closed processing chain should be validated, how identity and purity should be demonstrated, how potency should be measured for a defined indication, how stability should be characterized, and what minimum regulatory and clinical evidence is required before therapeutic use [8,16–18]. The present manuscript has three objectives. First, it provides an integrated review of the biological basis, biogenesis, cargo composition, and potential therapeutic applications of autologous exosomes and related small extracellular vesicles. Second, it describes the principal isolation and extraction methodologies currently available for preparing patient-derived vesicle fractions and compares their advantages and limitations in the context of an injectable therapeutic product. Third, it proposes a translational framework for the design of an autologous exosome kit, with the Biotex platform used as an illustrative implementation of that framework. Throughout, the manuscript emphasises that autologous origin is a necessary but not sufficient condition for therapeutic readiness, and that clinical use of any autologous exosome kit must be supported by validated manufacturing, independent characterisation, indication-specific potency testing, and controlled human studies.

1. Terminology and scientific scope

In this manuscript, the term autologous exosome denotes that the source material and the recipient are the same patient. The term exosome refers specifically to vesicles generated through the endosomal pathway, whereas the broader term extracellular vesicles includes exosomes, microvesicles, ectosomes, apoptotic

bodies, and other cell-released membranous particles. Because vesicle subtypes can overlap in size and density, size alone cannot establish exosome identity. The International Society for Extracellular Vesicles recommends reporting the source, isolation procedure, particle characteristics, molecular markers, contaminants, and functional activity rather than assigning a specific vesicle biogenesis pathway without adequate evidence [16,17].

Accordingly, a kit may be more accurately described as an autologous small-extracellular-vesicle isolation and concentration kit unless the endosomal origin of the isolated particles has been demonstrated. This distinction is important for an academic publication, product labelling, regulatory submissions, and clinical-trial registration.

2. Biological rationale for autologous vesicle therapy

Extracellular vesicles are nanoscale, membrane-bound structures that carry nucleic acids and proteins from their cells of origin and can modify the function and phenotype of recipient cells. Their therapeutic potential arises from their ability to deliver a composite molecular signal rather than a single purified drug [1,16].

An autologous product may provide several potential advantages:

- reduced exposure to donor-derived antigens;
- reduced concern regarding transmission of donor-derived pathogens;
- compatibility with individualised treatment;
- access to patient-specific biological material;
- A non-cellular format that does not involve implantation of viable proliferating cells.

These advantages should be presented as potential benefits, not guarantees. Autologous material may still contain inflammatory mediators, residual cells, blood-borne pathogens, disease-associated molecules, protein aggregates, lipoproteins, and other contaminants. In addition, a patient's disease state may influence the cargo and biological activity of the vesicles. Reviews of EV therapeutics emphasise that source-cell heterogeneity, cargo variability, incomplete characterisation, and uncertain potency remain major obstacles to clinical translation [6,7].

The term "zero immune rejection" should therefore be avoided. Autologous origin may reduce donor-recognition concerns, but it does not eliminate the possibility of innate immune activation, inflammatory responses, complement activation, coagulation effects, or adverse responses to contaminants or formulation components.

3. Biogenesis of exosomes

3.1 Endosomal pathway

Canonical exosome biogenesis occurs through the endosomal system. The plasma membrane undergoes inward internalisation to generate early endosomes. These endosomes mature and accumulate intraluminal vesicles through inward budding of the endosomal limiting membrane. Endosomes containing multiple intraluminal vesicles are termed multivesicular bodies [19].

Multivesicular bodies have at least two principal fates. They may fuse with lysosomes, leading to degradation of their contents, or they may fuse with the plasma membrane and release intraluminal vesicles into the extracellular environment. The released vesicles are conventionally called exosomes when their endosomal origin has been established [19].

3.2 Molecular regulators

The endosomal sorting complex required for transport, or ESCRT machinery, contributes to membrane remodelling and cargo selection. ESCRT-0, ESCRT-I, ESCRT-II, and ESCRT-III participate in the formation of intraluminal vesicles. Tetraspanins, particularly CD9 and CD63, are associated with exosome formation, membrane organisation, and cargo sorting [19].

Exosome formation may also occur through ESCRT-independent pathways. These include lipid-dependent mechanisms involving neutral sphingomyelinase 2, ceramide generation, membrane curvature,

and sphingosine-1-phosphate signalling. Syntenin, ALIX, Rab proteins, tetraspanins, and phospholipase-associated mechanisms have also been implicated in EV formation and release [2,4].

3.3 Molecular cargo

The vesicle membrane consists primarily of a lipid bilayer that protects internal cargo and participates in interactions with recipient cells. Reported cargo includes:

- proteins and peptides;
- membrane-associated tetraspanins;
- heat-shock proteins;
- growth-associated and angiogenesis-associated proteins;
- messenger RNA;
- microRNA;
- other non-coding RNA;
- cholesterol and sphingolipids;
- ceramide and other bioactive lipids;
- Metabolites.

The cargo is determined by the parent cell and its environment. It can change in response to inflammation, hypoxia, oxidative stress, tissue injury, ageing, disease, and pharmacological exposure. Exosomes therefore should not be treated as chemically uniform particles. Their biological action is dependent on both the vesicle source and the recipient tissue [4,19].

4. Potential autologous sources

4.1 Plasma and serum

Plasma and serum are practical sources for a point-of-care autologous platform because they can be obtained through blood collection. However, blood-derived samples are complex matrices containing EVs from platelets, leukocytes, endothelial cells, erythrocytes, and other cells, as well as abundant soluble proteins and lipoproteins. Co-isolation of these components can affect particle counts, molecular measurements, and therapeutic activity. A comparative study found that no method generated a completely pure EV preparation across plasma, urine, and cell-culture medium because non-EV particles overlap with EVs in size and density [11].

Autologous serum-derived EVs have been examined in a pilot case-control study involving chronic venous ulcers. The treated lesions showed more granulation tissue than sham-treated lesions. The reported median surface reduction was 151 mm^2 in the EV-treated group compared with 84 mm^2 in the sham group, and the day-30 values were 385 mm^2 and 106 mm^2, respectively, with a reported p-value of 0.004. These results are relevant to the concept of patient-derived EV therapy, but the study was a pilot investigation and does not establish effectiveness for all wound types or other therapeutic indications [10].

4.2 Platelet-derived vesicles

Activated platelets release EVs enriched in growth factors, cytokines, extracellular-matrix modifiers, proteins, lipids, and RNA. These vesicles may influence fibroblast proliferation and migration, endothelial-cell behaviour, angiogenesis, and wound healing [9].

The platelet source requires careful control because the final preparation can be influenced by platelet count, activation method, anticoagulant, processing time, residual intact platelets, and storage. Evidence from a first-in-human phase I trial concerned an allogeneic platelet-derived EV product purified using ligand-based exosome affinity purification. The product was reported to be safe and well tolerated, but treated and untreated wounds healed rapidly and did not differ in closure time in that healthy-volunteer model [9]. This evidence supports the feasibility of a particular purified platelet-EV process, not the universal efficacy of autologous platelet-derived exosomes.

4.3 Adipose tissue and bone marrow

Adipose and bone marrow are important sources of mesenchymal stromal/stem-cell-derived EVs. These products are generally manufactured by isolating cells, expanding them under controlled culture conditions, collecting conditioned medium, and purifying the EVs released by the cells. This approach differs from direct isolation of vesicles from a patient's plasma or serum [15].

MSC-derived EVs have been investigated in orthopaedic, reproductive, wound-healing, neurological, renal, cardiovascular, and other applications. However, a substantial proportion of the clinical literature involves allogeneic MSC-derived products rather than patient-derived autologous preparations [3,15].

5. Isolation and extraction methodologies

5.1 Differential ultracentrifugation

Differential ultracentrifugation separates particles according to differences in size and density. Sequential centrifugation steps remove intact cells, cellular debris, and larger particles before a high-speed step enriches small vesicles. Density-gradient ultracentrifugation may improve separation from some contaminants [20,21].

Advantages include extensive historical use and compatibility with laboratory-scale research. Limitations include high equipment cost, lengthy processing, operator dependence, variable recovery, possible vesicle aggregation, mechanical stress, and co-pelleting of soluble proteins, lipoproteins, and other particles. The final result depends on the sample type, rotor, centrifugal force, viscosity, acceleration and braking conditions, and resuspension procedure [11,20].

For these reasons, ultracentrifugation should not be described as an uncontested universal "gold standard." It is an established research method, but a therapeutic kit may require a more reproducible, closed, scalable, and automated process.

5.2 Size-exclusion chromatography

Size-exclusion chromatography separates material according to hydrodynamic size using a porous stationary phase. Small soluble molecules enter the pores and generally elute later, whereas larger vesicles and particles are excluded from some pores and elute earlier [21].

SEC can preserve vesicle structure and reduce exposure to high centrifugal forces. It is useful for removing soluble proteins and may be combined with a concentration step. Its limitations include sample dilution, finite column capacity, potential co-elution of similarly sized contaminants, and the need for additional concentration or buffer exchange. In therapeutic manufacturing, SEC is therefore often considered part of a multi-step process rather than a complete purification solution [21,22].

5.3 Membrane filtration and ultrafiltration

Membrane filtration can remove cells and large debris while allowing smaller vesicles to pass or can retain vesicles for concentration, depending on membrane configuration. Ultrafiltration is technically attractive for a kit because it can be implemented in a compact, closed processing path.

Important design variables include membrane material, nominal molecular-weight cutoff, pore geometry, transmembrane pressure, flow rate, membrane adsorption, sample viscosity, and recovery of vesicles from the membrane. Membrane filtration does not automatically remove all lipoproteins or soluble proteins because some contaminants have overlapping physical properties with EVs.

5.4 Tangential-flow filtration

Tangential-flow filtration directs the sample parallel to the membrane rather than directly toward it. This can reduce fouling and support concentration and diafiltration. Manufacturing studies have described filtration-based recovery followed by chromatography-based purification as a promising approach for reducing processing volume and improving scalability. Tangential-flow filtration concentrated MSC-secreted exosomes up to 125-fold in one reported context [22].

For an autologous kit, tangential-flow processing may offer better scalability and automation than ultracentrifugation, but it requires validation of pressure, flow, membrane compatibility, vesicle recovery, and removal of non-EV contaminants.

5.5 Polymer precipitation

Polymer precipitation is rapid and simple but can retain polymer residues, protein aggregates, and non-EV particles. Comparative analysis of plasma, urine, and cell-culture medium found that precipitation produced the lowest sample purity among the methods examined [11]. It is therefore generally more appropriate for exploratory research than for an injectable therapeutic product unless a subsequent validated purification step removes the residual contaminants.

5.6 Immunoaffinity purification

Immunoaffinity purification uses antibodies or ligands that bind particular surface molecules. It can enrich a selected vesicle population but may have limited capacity, high consumable cost, and possible effects on vesicle integrity or biological activity.

Ligand-based exosome affinity purification has been used to produce clinical-grade platelet EVs carrying wound-healing-associated proteins such as insulin-like growth factor and transforming growth factor beta [9]. However, affinity capture is not necessarily ideal for a broad autologous product because it may selectively remove vesicles lacking the chosen marker and may produce a product whose biological activity depends on the capture ligand.

5.7 Microfluidic and point-of-care processing

Microfluidic systems can integrate plasma separation, filtration, concentration, and analysis. Exodisc was reported to isolate EVs in the 20–600 nm range within 30 minutes and achieved greater than 95% recovery from cell-culture supernatant in the cited study [23]. A related Exodisc-B/P system processed whole-blood samples of 30–600 μL and enriched EVs within 40 minutes using a small bench-top system [24].

These findings demonstrate the potential of automated miniaturised processing, but diagnostic or research-grade recovery cannot automatically be equated with clinical-grade therapeutic purity. A point-of-care kit must additionally demonstrate sterility, endotoxin control, reproducible identity, acceptable residual protein and lipoprotein levels, potency, stability, and clinical safety.

6. Proposed Design of an Autologous Exosome Kit

6.1 Intended use

The kit should define whether it is intended for research use, laboratory development, investigational clinical use, or preparation of a product for a specified therapeutic indication. It must also specify the source material, collection volume, processing time, target particle class, administration route, allowable storage interval, and release criteria before patient administration. A kit intended for plasma-derived vesicles should not automatically be labelled as producing purified exosomes unless exosome biogenesis, particle purity, and biological activity have been demonstrated using validated analytical criteria [16,17].

The Biotex autologous exosome kit is designed as a closed, point-of-care processing platform for the preparation of patient-derived small extracellular vesicles directly from a peripheral whole-blood sample. Its intended clinical use is the preparation, within a single session, of a sterile autologous plasma-derived vesicle fraction intended for administration to the same patient according to the relevant indication and the prescribing clinician's protocol.

6.2 Integrated workflow

A clinically oriented autologous kit should ideally incorporate the following functional modules, several of which are combined within a single integrated session in the Biotex workflow: [8,22]

1. Patient identification and traceability: Patient matching, barcode or electronic tracking, lot identification, and operator documentation.
2. Sterile sample collection: A validated blood, serum, plasma, platelet, or tissue collection container compatible with the selected anticoagulant and downstream process.

3. Primary clarification: Removal of intact cells, large debris, and gross particulate matter.
4. Vesicle enrichment: Membrane filtration, ultrafiltration, tangential-flow filtration, size-exclusion chromatography, or a validated combination.
5. Purification and buffer exchange: Reduction of soluble proteins, lipoproteins, free nucleic acids, anticoagulants, and process-related residues.
6. Controlled formulation: Adjustment of concentration, buffer, pH, osmolality, and container compatibility.
7. Aseptic transfer: Closed transfer to the administration or storage container.
8. Quality-control sampling: Collection of a representative sample for particle count, size distribution, markers, contaminants, sterility, endotoxin, and potency testing.

The process should minimise open handling, uncontrolled temperature changes, excessive shear, repeated transfers, and unnecessary freeze–thaw cycles. The remainder of this section describes how these modules are operationalised in the Biotex kit.

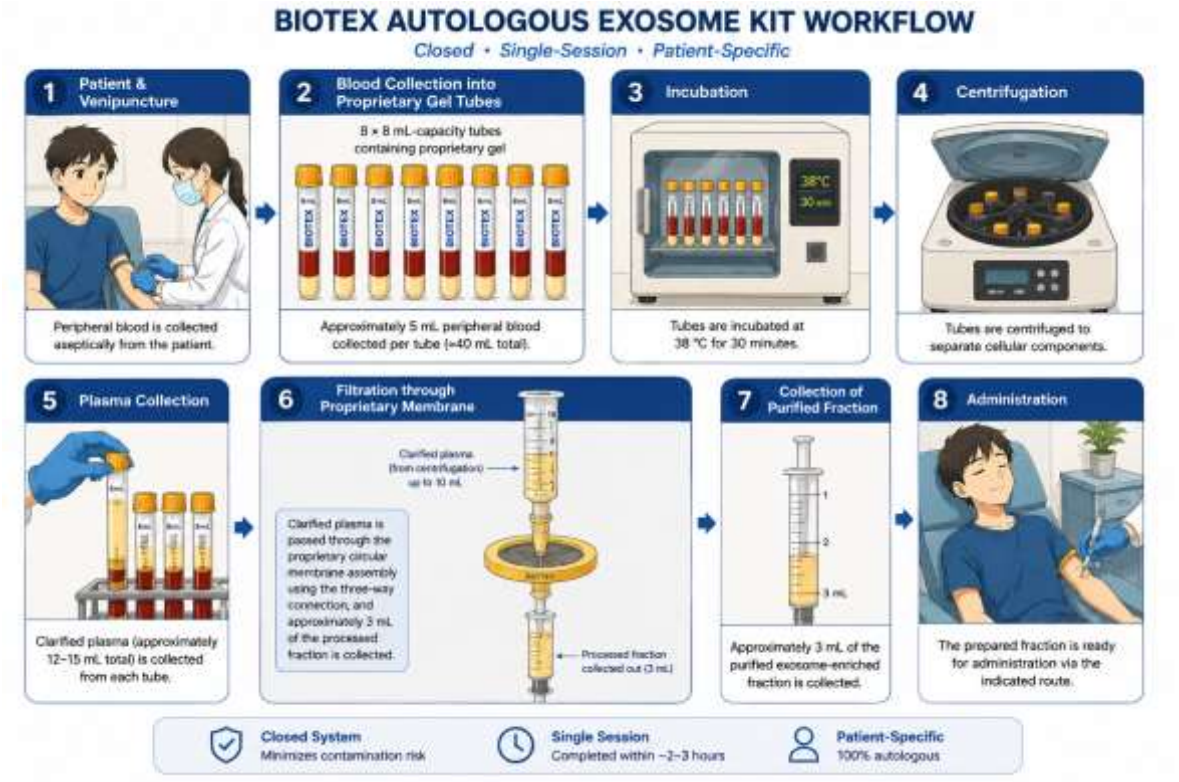

Fig 1: Schematic representation of the closed, single-session Biotex autologous exosome kit workflow, from peripheral blood collection through thermal incubation, centrifugation, gel-filtration purification, and syringeable finished product ready for the indicated route of administration.

6.3 Source-material collection

The Biotex kit provides eight sterile blood-collection tubes, each with an 8 mL nominal capacity and individually validated to hold approximately 5 mL of peripheral whole blood per tube. The 8 mL tubes are pre-filled with a Biotex proprietary separator gel that, during centrifugation, migrates upward to form a stable physical barrier between the cellular fraction and the plasma fraction, supporting cleaner plasma recovery and minimising cellular resuspension during aspiration. At full collection capacity, the eight tubes together provide a 40 mL whole-blood sample. Blood is drawn from the patient using a standard peripheral venipuncture needle; when the therapy is delivered intravenously, a scalp-vein (winged infusion) set may be used to streamline collection and immediate downstream administration. The dual-route compatibility of the kit allows the same collection procedure to serve either local administration protocols (such as

intradermal, intra-articular, or intralesional injection) or systemic intravenous administration, contingent upon the indication and the prescribing protocol [9,10].

The 40 mL total collection volume is a deliberate compromise between clinical practicality and downstream yield. It is sufficient to recover an adequate plasma volume after centrifugation, while remaining within volumes commonly tolerated by point-of-care autologous procedures and consistent with volumes used in autologous regenerative protocols [10,12].

Fig 2: Biotex autologous exosome kit

6.4 Thermal incubation for exosome generation

Following collection, the eight tubes are incubated under controlled thermal conditions to promote exosome generation and release from blood-resident cellular sources, including platelets, leukocytes, and erythrocytes. The Biotex protocol specifies an incubation temperature of 38 °C for approximately 30 minutes. Both the elevated temperature and the duration of incubation are intended to optimise extracellular vesicle release: minor deviations from baseline physiological temperatures within an extended range are associated with altered vesicle shedding kinetics, with controlled thermal stress enhancing the release of small extracellular vesicles from blood cells into the surrounding plasma. The exact temperature-duration profile should be reported as part of the kit's standard operating procedure so that any variation can be traced in the batch record [2,4,19].

The biological rationale for elevated-temperature incubation is consistent with established observations that exosome and microvesicle release is sensitive to temperature, cellular activation state, and incubation time. Platelet activation, in particular, is known to release extracellular vesicles enriched in growth factors, cytokines, and signalling lipids, and the rate of release can be modulated by incubation conditions. The Biotex protocol therefore explicitly defines both temperature (38 °C) and time (30 minutes) to ensure reproducible batch-to-batch vesicle yields [9,19].

6.5 Primary clarification by centrifugation

After incubation, the tubes are centrifuged under controlled conditions to separate the cellular components from the plasma fraction. From a 40 mL whole-blood sample, the centrifugation step is expected to recover approximately 12–15 mL of plasma, in line with standard hematocrit-dependent yields. The plasma fraction is carefully aspirated from each tube under aseptic conditions, pooled when appropriate, and transferred for downstream processing [11].

The centrifugation step serves multiple functions:

- removal of intact erythrocytes, leukocytes, and platelets;
- reduction of large cell debris and apoptotic bodies;
- reduction of gross particulate matter that could otherwise foul the downstream filtration matrix;
- concentration of the small extracellular vesicle population within the plasma fraction, consistent with reported plasma-EV processing workflows [11,20].

Comparative studies have shown that centrifugation-based clarification combined with subsequent filtration or chromatography yields higher small-vesicle purity than precipitation-based approaches, particularly for plasma-derived material where lipoprotein and protein contamination is substantial [11,21].

6.6 Proprietary gel filtration and three-way manifold

The clarified plasma is then passed through a Biotex proprietary filtration membrane housed in a sterile single-use cartridge, which retains larger contaminants — including residual cellular fragments, protein aggregates, lipoproteins, and free nucleic acids — while allowing small extracellular vesicles within the target size range to pass through. The cartridge is connected on one end to a three-way stopcock manifold and on the other end to the pooled plasma reservoir; a 3 mL syringe is attached to the third port of the three-way manifold to draw the purified filtrate under controlled pressure. The proprietary gel matrix is engineered to retain larger contaminants — including residual cellular fragments, protein aggregates, lipoproteins, and free nucleic acids — while allowing small extracellular vesicles within the target size range to pass through. The Biotex protocol reports approximately 90% purification efficiency at this stage, meaning that approximately 90% of the non-vesicular and oversized contaminants present in the clarified plasma are removed by the gel filtration matrix [20,21,23].

Filtration-based purification is consistent with the published Exodisc workflow, which demonstrated rapid, size-selective isolation of nanoscale extracellular vesicles from biological samples within short processing times and with recovery exceeding 95% from cell-culture supernatant. The Biotex three-way manifold design is a closed-system adaptation of this principle, allowing plasma-derived vesicles to be processed, purified, and reconcentrated into a syringeable format without breaking sterility [23,24].

The use of a 3 mL syringe at the collection port serves three functional objectives:

- conversion of the filtered plasma into an immediately syringeable formulation;
- precise volumetric control of the final injectable dose;
- preservation of a closed system through which the resulting product is transferred directly to the administration device [22].

6.7 Final formulation and administration

After gel filtration, the resulting filtrate constitutes the prepared autologous exosome fraction intended for administration. The product is delivered to the patient through the route appropriate to the therapeutic indication:

- intradermal or subcutaneous injection for aesthetic medicine and skin regeneration indications;
- intradermal microinjection into the scalp for alopecia-related indications;
- intra-articular injection for orthopaedic indications;
- intravenous administration, particularly when the scalp-vein collection route has been used, and the therapeutic protocol calls for systemic delivery;

- Intralesional or peri-lesional injection for wound-healing indications [10,12,14,15].

The same kit and same upstream processing therefore supports multiple downstream therapeutic indications, provided that the per-indication dose, administration route, and treatment schedule are defined by the prescribing protocol and supported by indication-specific potency testing [8,25].

6.8 Integrated timeline and operational characteristics

The complete Biotex procedure, from phlebotomy to syringeable finished product, is performed within a single closed session. The principal sequential steps, their inputs, processing conditions, outputs, and approximate durations are summarised in Table 1.

Table 1. Step-by-step operational parameters of the Biotex autologous exosome kit, summarising input volume, processing conditions, expected output, and approximate duration for a single closed session.

Step	Input	Conditions	Output
Blood collection	Patient peripheral whole blood	Venipuncture or scalp-vein set; ≈ 5–10 min	40 mL whole blood across 8 × 5 mL tubes
Thermal incubation	40 mL whole blood in 8 sealed tubes	38 °C, ~30 min, closed	Vesicle-enriched whole blood
Centrifugation + plasma recovery	40 mL whole blood in tubes pre-filled with Biotex proprietary separator gel	Standard clinical centrifugation; ≈ 10–15 min	12–15 mL clarified plasma
Membrane filtration and purification	12–15 mL plasma via three-way manifold	Closed system, proprietary gel cartridge; ≈ 10–20 min	≈ 90% removal of non-vesicular contaminants
Final reconstitution	Filtrate drawn into 3 mL syringe	Closed aseptic transfer; ≈ 5 min	Syringeable autologous EV fraction
End-to-end session	—	≈ 2–3 hours	Same-visit injectable product

The estimated end-to-end procedural time of approximately 2–3 hours is consistent with the rapid point-of-care turnaround reported for related microfluidic and centrifugal EV-isolation systems [23,24].

6.9 Quality control within the kit workflow

Even within a closed point-of-care workflow, every batch of the kit should be sampled for post-process quality control. The recommended QC parameters for the Biotex output include:

- particle concentration by nanoparticle-tracking analysis or equivalent;
- particle size distribution within the expected small-EV window;
- tetraspanin markers (CD9, CD63, CD81) and a source-appropriate positive marker;
- negative markers appropriate to plasma, including albumin and lipoprotein markers;
- residual protein and lipoprotein content;
- endotoxin;
- sterility (bacterial and fungal);
- pH and osmolality of the final filtrate;
- An indication-appropriate potency assay where feasible [8,16–18].

MISEV2023 emphasises that minimal reporting standards should be applied even in a point-of-care product and that orthogonal analytical methods should accompany any single-particle measurement to control for non-EV particles such as lipoproteins and protein aggregates [16,18].

6.10 Strengths and recognised limitations of the Biotex design

Strengths:

- closed, single-session workflow minimises contamination risk and operator dependency;
- autologous origin eliminates donor-antigen exposure;
- integrated collection-to-injection transfer through the three-way manifold preserves sterility;
- rapid turnaround of approximately 2–3 hours supports same-visit clinical use;
- standardised 40 mL collection volume supports reproducible plasma recovery;
- filtration-based purification avoids the equipment burden of ultracentrifugation [22,23].

Recognised limitations that must be addressed before routine clinical use:

- Exosome identity, as opposed to generic small-EV identity, should be confirmed by endosomal-pathway markers.
- Particle counts should be accompanied by protein- and lipoprotein-contamination data because plasma-derived particle counts can be inflated by non-vesicular material.
- 90% purification reporting should be paired with a quantitative residual-contaminant specification (protein, lipoprotein, endotoxin).
- Indication-specific potency assays should be developed and validated.
- Clinical efficacy must be established through controlled human trials, not inferred from procedural feasibility alone [11,13,16,18].

6.11 Summary role within the broader development strategy

The Biotex kit represents the operational embodiment of the design principles outlined in sections 6.1–6.2: a patient-specific, closed, traceable, and quality-controlled autologous small-EV processing platform. The kit addresses source, clarity, enrichment, purification, formulation, aseptic transfer, and quality control within a single integrated session. However, the kit is best understood as a manufacturing platform whose clinical readiness depends on subsequent characterisation, potency-validation, stability data, regulatory alignment, and controlled human studies, rather than as a finished therapeutic product in itself. Its inclusion in the article is therefore positioned as a representative implementation of the autologous exosome kit concept described throughout section 6 [8,22].

7. Manufacturing standards and quality control

7.1 Identity

Identity should be established using multiple orthogonal measurements. Recommended categories include:

- particle size and concentration;
- morphology;
- membrane-associated markers;
- luminal or cytosolic markers;
- source-related markers;
- Negative or depleted contaminant markers.

MISEV2023 recommends estimating EV number, characterising the degree of contamination, reporting the complete particle-size distribution, and describing the analytical method's detection limits [18].

7.2 Molecular characterization

Analytical methods may include nanoparticle-tracking analysis, dynamic light scattering, tunable resistive-pulse sensing, electron microscopy, immunoblotting, flow-based assays, ELISA, mass spectrometry, RNA

sequencing, RT-qPCR, and lipid analysis. No single method is sufficient for complete characterisation [8,18].

At least two EV-associated proteins should be measured, including one membrane or membrane-anchored protein and one cytosolic or luminal protein. Negative markers should be selected according to the source material. Albumin is particularly relevant for plasma-derived products, while other contaminants may arise from intracellular organelles, cell death, culture media, or lipoprotein fractions [8,25].

7.3 Purity

Purity assessment should examine:

- residual intact cells;
- platelets;
- apoptotic bodies;
- protein aggregates;
- albumin and immunoglobulins;
- lipoproteins;
- free DNA and RNA;
- membrane or process residues;
- endotoxin;
- bacteria, fungi, and mycoplasma;
- Relevant viruses.

A high particle count may reflect lipoproteins or other non-EV particles rather than therapeutic vesicles. The study comparing plasma, urine, and cell-culture methods found that all methods co-isolated some non-EV material and that purity depended on both the sample type and the isolation method [11].

7.4 Potency

Particle number is not a validated surrogate for biological potency. Potency testing should be linked to the proposed indication. Possible assays include:

- fibroblast migration and proliferation for wound repair;
- endothelial-cell angiogenesis assays;
- inflammatory cytokine modulation;
- chondrocyte or osteoblast response;
- follicular-cell survival and hair-cycle assays;
- Ovarian or oocyte-related assays where ethically and scientifically justified.

MISEV2023 recommends dose-response studies, time-course analysis, suitable negative EV controls, and non-EV controls before a biological effect is attributed specifically to EVs [18].

7.5 Stability

Stability testing should monitor:

- particle count;
- size distribution;
- aggregation;
- morphology;
- marker retention;
- RNA integrity;
- potency;
- sterility;

- endotoxin;
- Container compatibility.

The product should have a defined maximum period between collection, isolation, quality-control release, and administration. Claims that the process preserves microRNA or other fragile cargo require direct measurement.

8. Therapeutic applications

8.1 Aesthetic medicine and skin regeneration

EVs are being investigated for wound healing, skin regeneration, scar modulation, pigmentation, inflammation, angiogenesis, and extracellular-matrix remodelling. A recent dermatology-focused review described early human studies involving wounds, rejuvenation, scars, and alopecia, but emphasised that products, doses, outcome measures, and administration methods remain heterogeneous [12].

Exosomes used with micro needling, laser procedures, topical treatment, or local administration should therefore be described as investigational or adjunctive unless supported by controlled clinical evidence for the exact product and indication. The existence of biological plausibility or positive preclinical data does not establish clinical effectiveness.

8.2 Alopecia and hair restoration

EVs may influence hair biology through effects on follicular-cell survival, dermal-papilla-cell signalling, angiogenesis, inflammation, and hair-cycle regulation. However, the clinical evidence remains limited. One review reported that no ClinicalTrials.gov studies were identified using the combined terms & quot; extracellular vesicles, & quot; & quot; exosomes, & quot; & quot; hair loss, & quot; and & quot; alopecia, & quot; and concluded that more robust clinical research is required [14].

The proposed kit should not claim that autologous exosomes "dramatically" activate dormant follicles or reliably induce anagen unless such effects have been demonstrated in a controlled human study using the same product, dose, route, and treatment schedule.

8.3 Reproductive medicine and oocyte maturation

Reproductive applications include the study of follicular-fluid EVs, ovarian tissue signalling, oocyte maturation, diminished ovarian reserve, and embryo development. These applications require particularly rigorous evidence because they involve reproductive tissue and potential effects on embryos and offspring.

A human laboratory study of follicular-fluid-derived EVs reported maturation of 77.8% of EV-supplemented oocytes compared with 55% in controls, corresponding to a difference of 22.8 ± 9.4%. The study used EVs isolated from human follicular fluid and evaluated rescue in-vitro maturation; it did not evidence for a broadly validated autologous therapeutic injection [26].

Other reproductive reports have studied human umbilical-cord MSC-derived EVs, which are allogeneic, or compared MSC-derived EVs with autologous platelet-rich plasma. These studies should not be represented as evidence for patient-derived autologous exosomes [27,28].

8.4 Orthopaedic and cartilage applications

MSC-derived EVs are being investigated for osteoarthritis, cartilage repair, fracture healing, tendon injury, bone regeneration, and spinal injury. Proposed mechanisms include immunomodulation, regulation of inflammatory signalling, support of chondrocyte and osteoblast activity, angiogenesis, and transfer of regulatory RNA [3,5].

However, the clinical literature includes heterogeneous sources, routes, doses, purification methods, and study designs. A review of MSC-derived exosome clinical trials identified studies in osteoarthritis and other indications but emphasised the variability of source and administration parameters [15]. For an autologous orthopaedic kit, the product would require indication-specific potency assays, particle and contaminant characterisation, endotoxin control, and a validated local-delivery procedure.

8.5 Targeted drug and gene delivery

EVs can carry or be engineered to carry proteins, RNA, and other therapeutic molecules. Their membrane structure and natural cellular uptake have encouraged investigation as delivery vehicles for gene therapy and other biologic agents [1,5].

Nevertheless, targeted delivery remains experimental. Engineering, loading, or surface modification changes the product's manufacturing and regulatory profile. Claims that autologous exosomes can reliably cross the blood–brain barrier or deliver bone morphogenetic proteins to joints require indication-specific pharmacokinetic, biodistribution, potency, and safety evidence.

9. Autologous versus allogeneic products and cellular therapies

Feature	Autologous EVs	Allogeneic EVs	Live-cell therapy
Source	Patient's own blood, tissue, serum, plasma, or cells	Human donor cells, platelets, placenta, umbilical tissue, or other sources	Patient-derived or donor-derived viable cells
Main potential advantage	Patient-specific source and reduced donor-recognition concern	Greater scalability and potential batch standardisation	Capacity for engraftment, differentiation, and paracrine signalling
Main limitation	Patient-to-patient variability and limited manufacturing scalability	Donor screening, pathogen control, and possible immunological effects	Viability, engraftment, differentiation, migration, and proliferative risks
Identity challenge	Disease state may alter cargo and purity	Donor and culture conditions influence cargo	Cell identity, viability, phenotype, and potency must be controlled
Dose challenge	No universally accepted particle or potency metric	Same challenge, although batch production may improve consistency	Cell number and viability can be quantified but do not fully define potency

The table summarises conceptual differences rather than regulatory conclusions. Autologous EVs should not be described as having "none" for tumorigenesis or immune risk. EVs are biologically active and may influence recipient-cell signalling, immune responses, angiogenesis, and other pathways. Regulatory and safety assessment must therefore be product-specific [6,8].

10. Regulatory status

There are currently no FDA-approved exosome therapeutic products. The FDA has issued public safety warnings concerning unapproved products marketed as containing exosomes following reports of adverse events [6,29].

The regulatory classification of an autologous product depends on its source, processing, intended use, route of administration, biological claims, manufacturing controls, and clinical evidence. A product does not become exempt from regulatory requirements merely because it is prepared from the same patient who receives it.

Regulatory evaluation is complicated by:

- heterogeneous vesicle populations;
- uncertain dose units;
- incomplete potency assays;
- variable isolation procedures;
- uncertain biodistribution;
- inconsistent reporting of adverse events;
- limited long-term human follow-up.

The appropriate development pathway should therefore include regulatory consultation before human therapeutic use, together with a defined chemistry, manufacturing, and controls strategy.

11. Principal challenges for clinical translation

Standardization

The same biological source can produce different EV preparations depending on collection conditions, processing time, centrifugation or filtration settings, membrane composition, temperature, and storage. MISEV guidance emphasises standardised reporting and orthogonal characterisation because crude preparations may contain heterogeneous and contaminating particles [16,17].

Product variability

Autologous products are especially vulnerable to variability because the starting material differs between patients. Age, disease, medications, inflammation, metabolic status, platelet activation, and tissue condition may alter both particle yield and cargo.

Contamination control

Blood- and tissue-derived materials may contain pathogens, residual cells, free nucleic acids, protein aggregates, lipoproteins, and inflammatory components. The rapid nature of a point-of-care process must not replace validated quality-control testing [8,11].

Dose and potency

The EV field lacks a universally accepted therapeutic dose metric. Particle number, protein amount, volume, and functional activity may provide different estimates of dose. A clinically meaningful product specification should therefore combine particle characterisation with a validated potency assay [6].

Stability

Storage and handling may change membrane integrity, aggregation, RNA content, marker expression, and biological activity. Stability must be evaluated for the specific formulation and container rather than inferred from studies of unrelated EV products.

Clinical evidence

Human EV studies remain predominantly small pilot studies with heterogeneous routes, doses, manufacturing methods, and endpoints. A 2024 scoping review found 40 published human therapeutic studies and concluded that the lack of placebo controls in many studies, inconsistent dose metrics, and heterogeneity of administration prevent firm conclusions about efficacy [13].

12. Recommended scientific positioning of the proposed kit

The kit should be positioned as a patient-specific, closed-system platform for the controlled preparation of autologous small extracellular vesicles, not as a universally validated exosome treatment. The development program should include:

1. source-material qualification;
2. closed-system engineering;
3. process validation;
4. analytical characterisation;
5. contaminant and sterility testing;
6. indication-specific potency testing;
7. stability studies;
8. preclinical safety assessment;
9. regulatory consultation;
10. controlled human clinical trials.

The publication should avoid unsupported claims that autologous exosomes have "zero immune rejection," "no tumorigenesis risk," guaranteed therapeutic efficacy, or FDA approval. The scientifically supportable conclusion is that autologous EVs are a promising but still investigational platform whose principal opportunities are personalised regenerative medicine and cell-free delivery, while its principal obstacles are product heterogeneity, purification, potency measurement, contamination control, stability, dose definition, and clinical validation.

Conclusion

Autologous exosomes and other patient-derived small extracellular vesicles represent a potentially important class of personalised biologic therapeutics. Their ability to transfer proteins, lipids, RNA, and other signalling molecules provides a mechanistic basis for applications in wound repair, skin regeneration, hair biology, reproductive medicine, orthopaedics, and drug delivery. Human studies provide early evidence of feasibility, including a pilot study of autologous serum-derived EVs for chronic venous ulcers, but the broader clinical evidence remains limited and heterogeneous [10,13].

A clinically credible autologous exosome kit must therefore integrate sample traceability, sterile closed processing, reproducible enrichment, purification, orthogonal characterisation, contaminant testing, stability assessment, and indication-specific potency testing. The central scientific objective is not merely to obtain a high particle count, but to produce a consistently characterised and biologically active preparation whose safety and efficacy can be demonstrated for a defined human therapeutic indication.

Declaration

Funding

This manuscript was prepared with the support of Biotex Life Solutions Pvt Ltd, the developer of the autologous exosome processing platform referenced in this work. The company provided logistical and editorial support for the conceptualisation, drafting, and revision of the manuscript, including access to internal technical documentation describing the Biotex autologous exosome kit and its processing workflow. No external funding, grant, or financial support from any other agency, institution, ministry, or non-governmental organisation was received for the preparation of this work. The funder did not influence the scientific interpretation of the cited literature, the mechanistic descriptions of extracellular vesicle biology, the regulatory discussion, or the conclusions drawn in this manuscript. The authors retained full intellectual independence in writing and approving the final version of the article.

Conflict of interest

The authors are employees of Biotex Life Solutions Pvt Ltd, which develops, manufactures, and markets the autologous exosome kit described in Section 6 of this manuscript. Because the manuscript includes a substantive description of the Biotex kit's design, processing parameters, and clinical positioning, the authors disclose this employment relationship as a direct and material competing interest. This affiliation has been disclosed in full transparency so that readers can independently evaluate the technical descriptions and scientific claims in the article.

Author contributions

All listed authors are employed by Biotex Life Solutions Pvt Ltd and contributed substantively and collaboratively to the preparation of this manuscript. Each author participated in the conceptualisation of the manuscript scope, the drafting of one or more sections, the critical review of the literature, the integration of the biological, methodological, manufacturing, regulatory, and clinical-translational content, and the final approval of the version submitted for publication. Each author has read and approved the submitted manuscript and agrees to be jointly accountable for the integrity, accuracy, and originality of the work, in accordance with the authorship requirements of the target journal.

Data availability

This manuscript is a narrative and methodology-focused review of published peer-reviewed literature, combined with the in-house technical specification of the Biotex autologous exosome kit, which is the

proprietary product of Biotex Life Solutions Pvt Ltd. No new primary experimental data, clinical datasets, genomic datasets, imaging datasets, or patient-level information were generated or analysed by the authors for this work. All scientific claims, mechanistic descriptions, therapeutic statements, and clinical data referenced in the manuscript are attributable to the published literature cited in the reference list and are publicly available through the cited publishers and databases. Detailed engineering specifications of the Biotex kit (tube geometry, separator-gel composition, filtration-membrane characteristics, three-way manifold layout, and processing parameters) are described at the design-concept level and do not constitute the proprietary manufacturing dossier of Biotex Life Solutions Pvt Ltd. Requests for additional technical or scientific information about the Biotex kit should be directed to the corresponding author at the corporate contact address.

Ethics approval and consent to participate

This manuscript is a review and methodology article that does not report new experiments performed by the authors on human participants, human tissue, human blood products, animal subjects, or identifiable personal data. No additional institutional review board, ethics committee, or regulatory-body approval was therefore required for the preparation of this work. Any primary studies cited in the manuscript (animal wound-healing studies, clinical pilot case-control trials, in-vitro oocyte-maturation experiments, and clinical-trial summaries) are the responsibility of their original investigators and were subject to the ethical approvals, patient-consent procedures, and institutional oversight reported in those original publications. The authors have relied solely on the ethical frameworks of those primary publications and have not re-analysed, re-aggregated, or reinterpreted any patient-level data. The Biotex kit itself is described in this manuscript at the design and intended-use level only; no in-house clinical outcomes from Biotex-sponsored studies are reported.

AI tool usage and permissions

Generative artificial-intelligence tools were used during the preparation of this manuscript for language-level drafting assistance, grammar, and editorial consistency checking. All scientific statements, mechanistic descriptions, claims about extracellular vesicle biology, descriptions of the Biotex kit's components and processing workflow, regulatory characterisations, and conclusions in this manuscript have been reviewed, verified against the cited primary literature, and finalised by the human authors at Biotex Life Solutions Pvt Ltd. Artificial-intelligence tools were not used to generate original scientific data, fabricate citations, fabricate clinical outcomes, misrepresent the contents of cited studies, or substitute for the authors' expert interpretation of the literature. The authors accept full responsibility for the content of this manuscript and confirm that all referenced works are accurately cited and that all quantitative claims originate from the cited primary sources.

References

1. Lee KWA, Chan LKW, Hung LC, Lam PKW, Park Y, Yi K. Clinical Applications of Exosomes: A Critical Review. International Journal of Molecular Sciences [Internet] 2024 [cited 2025 Nov]; 25(14):7794–7794. Available from: https://doi.org/10.3390/ijms25147794
2. Niel G van, D'Angelo G, Raposo G. Shedding light on the cell biology of extracellular vesicles. Nature Reviews Molecular Cell Biology [Internet] 2018 [cited 2026 Mar]; 19(4):213–28. Available from: https://doi.org/10.1038/nrm.2017.125
3. Tan F, Li X, Wang Z, Li J, Shahzad KA, Zheng J. Clinical applications of stem cell-derived exosomes. Signal Transduction and Targeted Therapy [Internet] 2024 [cited 2026 Jan]; 9(1):17–17. Available from: https://doi.org/10.1038/s41392-023-01704-0
4. Kumar MA, Baba SK, Sadida HQ, Marzooqi SA, Jerobin J, Altemani FH, et al. Extracellular vesicles as tools and targets in therapy for diseases. Signal Transduction and Targeted Therapy [Internet] 2024 [cited 2026 Jan];9(1):27–27. Available from: https://doi.org/10.1038/s41392-024-01735-1

5. Miron RJ, Estrin NE, Sculean A, Zhang Y. Understanding exosomes: Part 2—Emerging leaders in regenerative medicine. Periodontology 2000 [Internet] 2024 [cited 2025 Nov];94(1):257–414. Available from: https://doi.org/10.1111/prd.12561
6. Killingsworth B, Welsh JA, Jones J. EV Translational Horizons as Viewed Across the Complex Landscape of Liquid Biopsies. Frontiers in Cell and Developmental Biology [Internet] 2021 [cited 2026 Jan]; 9:556837–556837. Available from: https://doi.org/10.3389/fcell.2021.556837
7. Delen MV, Derdelinckx J, Wouters K, Nelissen I, Cools N. A systematic review and meta-analysis of clinical trials assessing safety and efficacy of human extracellular vesicle-based therapy. Journal of Extracellular Vesicles [Internet] 2024 [cited 2025 Nov]; 13(7). Available from: https://doi.org/10.1002/jev2.12458
8. Takakura Y, Hanayama R, Akiyoshi K, Futaki S, Hida K, Ichiki T, et al. Quality and Safety Considerations for Therapeutic Products Based on Extracellular Vesicles. Pharmaceutical Research [Internet] 2024 [cited 2026 Jan]; 41(8):1573–94. Available from: https://doi.org/10.1007/s11095-024-03757-4
9. Johnson J, Law SQK, Shojaee M, Hall A, Bhuiyan S, Lim MBL, et al. First-in-human clinical trial of allogeneic, platelet-derived extracellular vesicles as a potential therapeutic for delayed wound healing. Journal of Extracellular Vesicles [Internet] 2023 [cited 2026 Jan]; 12(7). Available from: https://doi.org/10.1002/jev2.12332
10. Gibello L, D'Antico S, Salafia M, Senetta R, Pomatto MAC, Orlando G, et al. First pilot case-control interventional study using autologous extracellular vesicles to treat chronic venous ulcers unresponsive to conventional treatments. Pharmacological Research [Internet] 2023 [cited 2026 Jan]; 190: 106718–106718. Available from: https://doi.org/10.1016/j.phrs.2023.106718
11. Dong L, Zieren RC, Horie K, Kim C, Mallick ER, Jing Y, et al. Comprehensive evaluation of methods for small extracellular vesicles separation from human plasma, urine and cell culture medium. Journal of Extracellular Vesicles [Internet] 2020 [cited 2025 Nov]; 10(2). Available from: https://doi.org/10.1002/jev2.12044
12. Pham GM. Exosome-Based Therapeutics in Dermatology and Beyond: A Narrative Review. Biomedicines [Internet] 2026 [cited 2026 Mar]; 14(2):338–338. Available from: https://doi.org/10.3390/biomedicines14020338
13. Fusco C, Rosa GD, Spatocco I, Vitiello E, Procaccini C, Frigé C, et al. Extracellular vesicles as human therapeutics: A scoping review of the literature. Journal of Extracellular Vesicles [Internet] 2024 [cited 2026 Mar]; 13(5). Available from: https://doi.org/10.1002/jev2.12433
14. Gangadaran P, Rajendran RL, Kwack MH, Jeyaraman M, Hong CM, Sung YK, et al. Application of Cell-Derived Extracellular Vesicles and Engineered Nanovesicles for Hair Growth: From Mechanisms to Therapeutics. Frontiers in Cell and Developmental Biology [Internet] 2022 [cited 2026 Jan]; 10: 963278–963278. Available from: https://doi.org/10.3389/fcell.2022.963278
15. Lotfy A, AboQuella NM, Wang H. Mesenchymal stromal/stem cell (MSC)-derived exosomes in clinical trials. Stem Cell Research & Therapy [Internet] 2023 [cited 2026 Mar]; 14(1):66–66. Available from: https://doi.org/10.1186/s13287-023-03287-7
16. Welsh JA, Goberdhan DCI, O'Driscoll L, Buzás EI, Blenkiron C, Bussolati B, et al. Minimal information for studies of extracellular vesicles (MISEV2023): From basic to advanced approaches. Archivio istituzionale della ricerca (Alma Mater Studiorum Università di Bologna) [Internet] 2024 [cited 2026 Mar]; 13(2). Available from: https://hdl.handle.net/11585/961943
17. Théry C, Witwer KW, Aïkawa E, Alcaraz MJ, Anderson JD, Andriantsitohaina R, et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. Journal of

Extracellular Vesicles [Internet] 2018 [cited 2026 Mar]; 7(1):1535750–1535750. Available from: https://doi.org/10.1080/20013078.2018.1535750

18. Samuels M, Giamas G. MISEV2023: Shaping the Future of EV Research by Enhancing Rigour, Reproducibility and Transparency. Cancer Gene Therapy [Internet] 2024 [cited 2026 Jan]; 31(5):649–51. Available from: https://doi.org/10.1038/s41417-024-00759-7
19. Abels ER, Breakefield XO. Introduction to Extracellular Vesicles: Biogenesis, RNA Cargo Selection, Content, Release, and Uptake. Cellular and Molecular Neurobiology [Internet] 2016 [cited 2026 Jan]; 36(3):301–12. Available from: https://doi.org/10.1007/s10571-016-0366-z
20. Chen J, Li P, Zhang T, Xu Z, Huang X, Wang R, et al. Review on Strategies and Technologies for Exosome Isolation and Purification. Frontiers in Bioengineering and Biotechnology [Internet] 2022 [cited 2026 Jan]; 9: 811971–811971. Available from: https://doi.org/10.3389/fbioe.2021.811971
21. Li P, Kaslan M, Lee SH, Yao JD, Gao Z. Progress in Exosome Isolation Techniques. Theranostics [Internet] 2017 [cited 2026 Jan]; 7(3):789–804. Available from: https://doi.org/10.7150/thno.18133
22. Colao IL, Corteling R, Bracewell DG, Wall I. Manufacturing Exosomes: A Promising Therapeutic Platform. Trends in Molecular Medicine [Internet] 2018 [cited 2026 Jan];24(3):242–56. Available from: https://doi.org/10.1016/j.molmed.2018.01.006
23. Woo H, Sunkara V, Park J, Kim TH, Han JR, Kim C, et al. Exodisc for Rapid, Size-Selective, and Efficient Isolation and Analysis of Nanoscale Extracellular Vesicles from Biological Samples. ACS Nano [Internet] 2017 [cited 2025 Nov]; 11(2):1360–70. Available from: https://doi.org/10.1021/acsnano.6b06131
24. Sunkara V, Kim C, Park J, Woo H, Kim D, Ha HK, et al. Fully Automated, Label-Free Isolation of Extracellular Vesicles from Whole Blood for Cancer Diagnosis and Monitoring. Theranostics [Internet] 2019 [cited 2025 Nov]; 9(7):1851–63. Available from: https://doi.org/10.7150/thno.32438
25. Al-Masawa ME, Alshawsh MA, Ng CY, Ng MH, Foo JB, Vijakumaran U, et al. Efficacy and safety of small extracellular vesicle interventions in wound healing and skin regeneration: A systematic review and meta-analysis of animal studies. Theranostics [Internet] 2022 [cited 2026 Jan]; 12(15):6455–508. Available from: https://doi.org/10.7150/thno.73436
26. Makieva S, de-Juano MDS, Almiñana C, Bauersachs S, Bernal-Ulloa S, Xie M, et al. Treatment of human oocytes with extracellular vesicles from follicular fluid during rescue in vitro maturation enhances maturation rates and modulates oocyte proteome and ultrastructure. Human Reproduction Open [Internet] 2026 [cited 2026 Mar];Available from: https://doi.org/10.1093/hropen/hoag021
27. Martirosyan Y, Biryukova A, Назаренко ТА, Силачев ДН, Sukhih G. P-800 Possibilities for improving IVF outcomes in women with unexplained infertility and diminished ovarian reserve. Human Reproduction [Internet] 2025 [cited 2025 Nov]; 40. Available from: https://doi.org/10.1093/humrep/deaf097.1104
28. Martirosyan Y, Назаренко ТА, Силачев ДН, Kadaeva AI, Biryukova A, Сухих ГТ. P-793 New approaches for treating diminished ovarian reserve: MSC-derived extracellular vesicles and autologous platelet rich plasma. Human Reproduction [Internet] 2024 [cited 2025 Nov]; 39. Available from: https://doi.org/10.1093/humrep/deae108.1105
29. Soltanmohammadi F, Maghsoodi M, Alizadeh E, Adibkia K, Azarmi Y, Gharehbaba AM, et al. Bio fluid exosomes: promises, challenges, and future directions in translational medicine. Journal of Translational Medicine [Internet] 2025 [cited 2026 Jan]; 23(1):993–993. Available from: https://doi.org/10.1186/s12967-025-06886-5