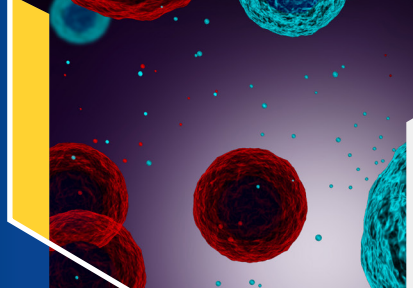
CAS INSIGHTS

R&D TRENDS: EXOSOMES IN DRUG DELIVERY AND DIAGNOSTICS



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Overview

Exosomes are poised for tremendous growth as they redefine drug delivery, diagnostics, and therapeutic applications. Key challenges in isolating, purifying, and standardizing exosomes need to be overcome for their potential to be fullfilled.

Background: Exosomes are small extracellular vesicles released by cells that transmit cargo and signals to other cells through nucleic acids, proteins, and lipids. They play a significant role in many physiological processes, including immunity, tissue homeostasis, and regeneration.

Market potential: The global market size of exosome therapeutics and diagnostics is likely to reach $1.4 billion by 2028.

Applications: Exosomes have drug delivery, diagnostic, and therapeutic applications in cancer, infectious diseases, cardiovascular, and neurodegenerative diseases. Applications in cosmetics and food are also being developed.

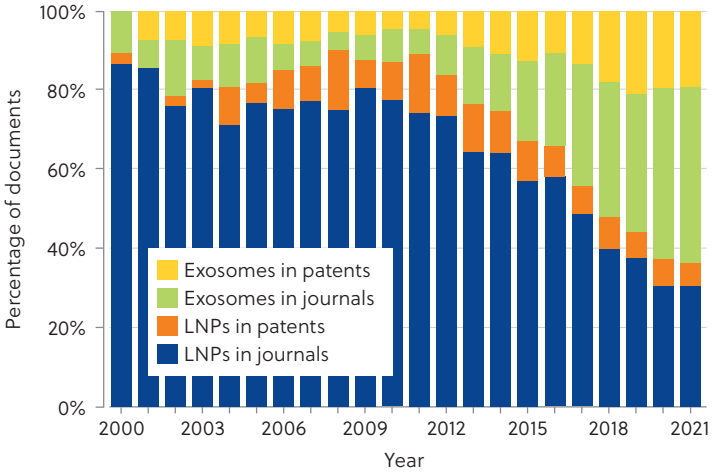
Key benefits: Exosomes can cross the blood-brain barrier, and have good bioavailability, low immunogenicity, and toxicity.

Key challenges: Inefficient methods of isolation, purification, and standardization must be overcome before scaling up.

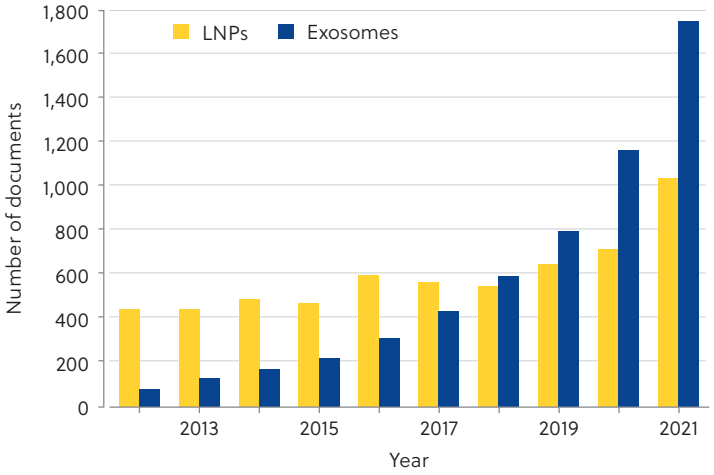
Emerging trends: exosomes overtake LNPs

The past decade has seen steady, exponential growth in journal articles and patents related to exosomes/extracellular vesicles. In the last 3–4 years, exosomes have overtaken lipid nanoparticles (LNP), as shown by the relative publication trends.

Journal articles and patent applications



Exosome and LNP publication trend



Opportunity: a more natural option to LNPs

Exosomes exhibit certain advantages over synthetic drug nanocarriers that make them a preferable drug delivery vehicle. Yet, certain limitations need to be overcome before exosomes can overtake LNPs in utility.

LNPs		Exosomes	
Advantages	**Challenges**	**Advantages**	**Challenges**
Drug protection from dilution, degradation, or inactivation in the blood	Low bioavailability, cytotoxicity	Ability to cross the blood-brain barrier	Lower yield due to inefficient methods for isolation and purification
Significant enhancement of drug pharmacokinetics	Rapid bloodstream clearance	Negligible immunogenicity and toxicity	Limited cargo-loading efficiency
Improvements in efficiency, selectivity, residence time, and biodistribution	Triggering of innate immune responses	Large variety of peripheral and integral proteins	Challenges with quality control of exosomes compared with LNPs

Therapeutic and diagnostic applications

Therapeutic

Exosomes are unique in that they reflect the molecular make up of the parent cell but cannot include components not in the parent cell.

Key advantages over conventional methods include good bioavailability and low immunogenicity due to heterogeneous, asymmetric, native lipid composition.

Exosomes can be applied to a wide range of diseases such as cancers, various infections, and neurodegenerative disorders.

ExoFlo

Direct Biologics therapeutic is currently available under the U.S. Food and Drug Administration (FDA) expanded use protocol for the treatment of COVID-19 acute respiratory distress syndrome. It is also being evaluated in inflammatory bowel disease, solid organ transplant rejection, and mild/moderate COVID-19.

Diagnostic

Conventional diagnostic approaches, such as solid biopsy biomarkers, can be invasive, with limited diagnostic sensitivity and accuracy.

Exosomes are easily isolated and reflect the molecular composition of parent cells. They can provide insights into the pathological status of cells more accurately than conventional biomarkers.

ExoDx

A urine-based liquid biopsy test was granted FDA Breakthrough Device Designation in 2019 and is now commercially available. It is used to predict the likelihood of a patient developing prostate cancer.

Exosomes in clinical trials

Several clinical trials are currently underway in exosome therapeutics and diagnostics. Though most exosome therapeutics utilize mesenchymal stem cell-derived exosomes, exosomes from other sources (e.g., amniotic fluid) are increasingly being explored.

Therapeutic

Clinical trial status	Recruiting	Recruiting	Expanded Access	Expanded Access
	2018	2020		
Organization	M.D. Anderson Cancer Center (USA)	Ruijin Hospital (China)	Organicell Regenerative Medicine (USA)	Direct Biologics (USA)
Exosome	MSC-derived exosomes with KrasG12D siRNA (iExosomes)	Adipose mesenchymal MSC-Exos	Amniotic fluid-derived exosomes/Zofin (Organicell Flow)	Bone marrow MSC-derived exosomes/DB-001/ExoFlo
Disease	Metastatic pancreatic cancer with KrasG12D mutation	Alzheimer's Disease induced dementia	Mild/moderate COVID-19	COVID-19 ARDS

Diagnostic

Clinical trial status	Completed	Active	Completed	Recruiting
	2013	2016		2020
Organization	University of Alabama at Birmingham (USA)	Boston University (USA)	Exosome Diagnostics (USA)	Lithuanian University of Health Sciences (Lithuania)
Exosome	Blood or urine-derived exosomes (LRRK2)	Plasma-derived exosome (tau)	Urine-derived exosome (ERG, PCA3, and SPDEF)	Eosinophil-derived exosome
Disease	Parkinson's disease	CTE	Prostate cancer	Asthma

Abbreviations: ARDS = acute respiratory distress syndrome; CTE = chronic traumatic encephalopathy; ERG = V-ets erythroblastosis virus E26 oncogene homologs; Exos = exosomes; LRKK2 = Leucine-rich repeat kinase 2; MSC = mesenchymal stem cells; PCA3 = prostate cancer antigen 3A; siRNA = small interfering RNA; SPDEF = SAM pointed domain containing ETS transcription factor

Looking ahead

There are immense opportunities for exosome research and development, particularly in therapeutics and diagnostics. Exploration of exosomal RNAs as diagnostic biomarkers is a key opportunity in research, with companies beginning to commercialize assays. Breakthroughs in scalable isolation and standardization are still needed to enable a large-scale application of this technology. Only by addressing these challenges can the full potential of exosomes be realized.

Comprehensive references can be found at cas.org/exosome-report

Learn more at cas.org/insights

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