

Supplementary Table. Comparison of Plant and other-Derived Types of Exosomes. (**Abbreviations:** DUC, differential ultracentrifugation; GUC, gradient Ultracentrifugation; SEC, size exclusion chromatography; UF, centrifugal ultrafiltration.)

| Feature | Plant-Derived Exosomes | Mammalian-Derived Exosomes | Bacterial-Derived Exosomes | Fungal-Derived Exosomes | Synthetic/Engineered Exosomes | Milk-Derived Exosomes | Parasitic-Derived Exosomes |
|------------------|--|--|---|-------------------------------------|--|-----------------------------------|---|
| Source | Plants (e.g., fruits, vegetables) | Mammalian cells (e.g., immune, stem, tumor cells) | Bacteria (e.g., Gram-positive or Gram-negative bacteria) | Fungi (e.g., Candida, Cryptococcus) | Artificially synthesized or engineered from natural exosomes | Mammalian milk (e.g., cow, human) | Parasites (e.g., Leishmania, Plasmodium) |
| Size | 50–200 nm | 30–150 nm | 20–300 nm | 40–250 nm | Variable, depending on design parameters | 50–200 nm | 50–150 nm |
| Composition | Lipids Proteins RNAs, Bioactive compounds (e.g., polyphenols) | Lipids Proteins (e.g. Tetraspanins) miRNAs | Lipids (e.g., lipopolysaccharides) Proteins DNA/RNA | Lipids proteins RNAs | Customizable; can include specific lipids, proteins, and nucleic acids | Lipids Proteins, miRNAs | Lipids Proteins RNAs |
| Biocompatibility | High; low immunogenicity | High; potential immunogenicity depending on the source | Can be immunogenic due to bacterial components (e.g., endotoxins) | Moderate; potential immunogenicity | Designed for high biocompatibility; depends on engineering | High; generally well-tolerated | Moderate to low; potential immunogenicity |



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| Therapeutic Potential | Rich in bioactive compounds Used in drug delivery and disease modulation | Used for cell signaling Immune modulation Drug delivery | Emerging applications in immunotherapy and vaccine delivery | Potential in antifungal therapies and immune modulation | Tailored for specific therapeutic applications, including targeted drug delivery | Applications in nutraceuticals and drug delivery systems | Potential in vaccine development Modulating immune responses |
| Ease of Production | Easily isolated from plant materials Scalable | Requires cell culture systems More complex and costly | Requires bacterial culture systems Moderate complexity | Requires fungal culture systems Moderate complexity | Production depends on synthesis methods; can be complex | Easily isolated from milk Scalable | Requires parasitic cultures Complex and potentially hazardous |
| Stability | High stability under various conditions (e.g., pH, temperature) | Sensitive to pH, temperature, and storage conditions | Moderate stability; depends on bacterial species and preparation | Moderate stability; influenced by fungal species | Stability varies; can be engineered for enhanced stability | High stability; suitable for various applications | Moderate stability; depends on parasite species |



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| Cost | Low cost; plant materials are abundant and inexpensive | Higher cost due to complex isolation and purification processes | Moderate cost; bacterial cultures are relatively inexpensive | Moderate cost; requires specialized fungal cultures | Variable cost; depends on materials and methods used | Low cost; milk is readily available | High cost; parasitic cultures are complex and require specialized facilities |
| Safety Concerns | Generally safe Minimal risk of pathogen transmission | Potential risks include contamination or tumorigenicity | Risk of endotoxin contamination (e.g., lipopolysaccharides) | Potential presence of pathogenic fungal components | Safety depends on design Off-target effects are possible | Generally safe Minimal risk of contamination | Potential safety risks due to pathogenic content |
| Applications | Nutraceuticals Drug deliver Immune modulation | Cancer therapy Regenerative medicine Vaccine delivery | Immunotherapy Vaccines, antimicrobial therapies | Vaccine development Anti-fungal targets Immune modulation | Targeted drug delivery Gene therapy Precision medicine | Gut health Nutraceuticals Drug delivery | Vaccine development Immune response modulation |
| References | (128-131) | (26, 116-118, 132, 133) | (124, 134-137) | (125, 126, 138-140) | (120, 121, 141-143) | (122, 123, 144-146) | (127, 147-149) |

