REVIEW ARTICLE

Milk-Derived Exosomes: Innovative Nanocarriers for Enhanced Anticancer Drug Delivery

Gaurav Raghuwanshi, Harpritkaur Bagga, Gunjan Chaudhari, Ujwal Vyas*

Datta Meghe College of Pharmacy, Datta Meghe Institute of Higher Education & Research, Deemed to be University, Sawangi (M), Wardha (India).

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ABSTRACT

This in-depth review examines the recently emerging field of using exosomes from milk as anticancer medication nanocarriers. It gives a summary of the most current developments, difficulties, and opportunities in this cutting-edge therapeutic strategy. Exosomes are found in many different body fluids and are considered a promising option for precision medicine due to their biocompatibility and innate cell-targeting abilities. These extracellular vesicles are nanoscale. The review commences with a comprehensive synopsis of the composition and biogenesis of exosomes derived from milk, highlighting their distinct membrane properties and capacity to transport cargo. Interestingly, these naturally occurring nanocarriers hold a variety of bioactive substances that can be precisely delivered as anticancer medications. These substances include proteins, lipids, and nucleic acids. Because dietary(poly) phenols are rapidly metabolized, their ability to prevent cancer is limited. Extracellular vesicles called exosomes may shield polyphenols from metabolism. Our objective was to evaluate the anticancer effects of free curcumin and resveratrol in breast cancer cell lines compared to their encapsulation in extracellular matrix derived from milk. Breast tissue was disposed of kinetically using rats. Curcumin and resveratrol were assessed using UPLC-QTOF-MS and GV-MS, respectively. Dietary polyphenols have a limited capacity to prevent cancer due to their rapid metabolism. Extracellular vesicles called exosomes may shield polyphenols from metabolism. Our goal was to assess in breast tissue. UPLC-QTOF-MS and GV-MS were used to evaluate curcumin and resveratrol, respectively. Curcumin and Resveratrol anticancer activity and bioavailability were improved by milk extracellular urea, which served as Trojan horses to get around the ABC-mediated chemoresistance of cancer cells. Exosomes derived from milk are being studied for their potential as carriers of therapeutic and diagnostic agents, emphasizing the potential benefits of personalized and precision medicine approaches to cancer treatment. The review also covers the challenges that the clinical translation of milk-derived exosome-based drug delivery systems currently faces, including scalability, standardization and safety profiles. The article's conclusion presents an optimistic view of how milk-derived exosomes will develop in the future in terms of anticancer medication delivery. The review highlights the revolutionary potential of using milk-derived exosomes, nature's nanocarriers, to advance the field toward more precise and effective cancer treatments, anticipating future advancements and emerging trends.

Keywords: Exosomes, Curcumin, Milk, Isolation, Targeted drug delivery.

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INTRODUCTION

Abnormal cell division is the cause of cancer, which can spread to other parts of the body. One important characteristic is the rapid proliferation of abnormal cells beyond their typical boundaries, which may allow them to invade nearby tissues and move to other organs—a process called metastasis. In cancer instances, metastases are the primary cause of death.[1] Under the direction of Aleksandra Sochacka-Cwikła, scientists synthesized derivatives of 7-aminooxazolo [5,4-d] pyrimidines and assessed their antiviral, anticancer, and immunological properties. Interestingly, compound 1 and compound 2, two of these recently synthesized compounds, have remarkable anticancer activities.[2] EXOs can influence the response of distant recipient cells by conveying their cargo, which includes a range of metabolites, lipids, functional proteins, and nucleic acids.[3-5] EXOs affect both healthy and pathological processes, including inflammation, cancer, neurodegeneration, and cardiovascular disorders. They can also regulate immunological response, tissue healing, trafficking, and cell maintenance.[6-9] In addition to physical barriers, EXOs can

*Author for Correspondence: ujwal.pharmacy@dmiher.edu.in

also cross the placenta and the blood-brain barrier.[10] Under these circumstances, EXOs can be helpful delivery systems for prescription drugs, naturally occurring bioactive, and potentially beneficial nucleic acids for application in clinical settings.[11-14] Because cancer death rates are among the highest of emerging disorders, medicinal chemists' primary goals are to develop anticancer and chemotherapy medications.[15] Chemotherapy is used to treat malignancies, however, it has drawbacks such as low sensitivity, poor selectivity, and serious side effects. It is also resistant to several medications.[16]

The ability of milk to transfer macromolecules that are both lipophilic and hydrophilic, and its capacity to pass the blood-brain barrier and its biocompatibility with a broad variety of species are two of its unique advantages.[17] In an attempt to shed light on the complex interactions between the inherent qualities of these materials and the demands of targeted drug administration, this review aims to thoroughly investigate the potential of milk-derived exosomes as anticancer medication nanocarriers.[18] The biogenesis, composition, and intricate mechanisms governing the generation and cargo loading of exosomes produced from milk are examined in the first half of this review.[19] These exosomes are a viable choice for anticancer therapies because they include a wide range of chemicals typical of their biological origin[20] and because they naturally have qualities that allow effective medication administration. Extracellular matrix (EXOs) generated from milk has been used in earlier research to encapsulate and distribute microRNAs, chemotherapeutic drugs, and natural substances.[21-23] Generally speaking, EXOs protect their cargo from gastrointestinal tract breakdown, metabolism, and digestion, which may allow systemic tissue biodistribution, including brain tissue.[24-26] It has been established that dietary (poly)phenols have many biological advantages.[27] One of its many uses is the prevention of cancer. This action in animal models has been found to be mediated by a variety of pathways, including an increase in caspases activation, endostatin, and p21, and a decrease in angiogenesis, matrix metalloproteinases, K67, and the Bcl-2/Bax ratio.[28] However, only a tiny percentage of the consumed intact (poly)phenolics enter the bloodstream due to their limited bioavailability.[29] Moreover, (poly)phenols are significantly metabolized by phase-II enzymes after absorption, mainly glucuronyl, sulfate, and catechol-methyl transferases. As a result, conjugated metabolites are produced that are significantly less active than the phenolic precursors found in food, namely glucuronides and sulfates.[30-32] Due to phase-II metabolism and generally moderate dietary polyphenol dosages, humans are not able to demonstrate robust polyphenol-related activity, in contrast to animal models. In order to boost the anticancer bioactivity of (poly)phenols like resveratrol (RSV) and curcumin (CUR) in systemic tissues, it is therefore desirable to block their metabolism. As dietary supplements, the polyphenols CUR and RSV have been shown to have chemo-preventive actions against cancer and to alleviate a variety of inflammatory disorders.[33,34] Nevertheless, as free, unconjugated polyphenols, they are rarely absorbed by the human body and have a low bioavailability. The paper then covers the latest advancements in milk-derived exosome engineering for drug delivery applications. Using molecular modification and bioengineering approaches, researchers have attempted to optimize the efficiency and selectivity of medication loading onto exosomes in an attempt to create tailored nanocarriers that can transcend biological barriers and precisely target cancer cells. Because exosomes like this can encapsulate a range of anticancer medicines like chemotherapeutics and nucleic acid therapies, personalized medicine is progressing. In addition to metabolism, the ATP-binding cassette (ABC) transporters can also limit the anticancer effect of drugs and (poly)phenols.[35] The overexpression of these transporters in cancer cells, particularly breast cancer cells, limits the amount of conjugated and free (poly)phenols that may enter the cell and determines whether they are forced to be effluxed back into the extracellular space.[36,37] The milk-derived exosomes from the animals are depicted in Figure 1.

Compositions and Characteristics of Milk-derived Exosomes

Lipid bilayer structure

Composition: Like cell membranes, the basic structure of milk exosomes is a lipid bilayer. Phospholipids, cholesterol, and proteins make up this bilayer. Their lipid composition influences the stability and integrity of the exosomes.

Proteins

- *Surface proteins*

One group of surficial indicators often used for exosomes consists of tetraspanins (CD9, CD63, and CD81). These proteins are responsible for recognition by target cells that labelised them, allowing for simple physical connection with the target cells which had their own unique personality.

- *Internal proteins*

There are many different types of proteins in the exosome, such as cytoskeletal ones, heat shock ones, and enzyme proteins. The physiological environment and origin cell influence these internal proteins.

Nucleic acid

The exosomes found in milk have many nucleic acids like mRNA and miRNA, among others, that are all particles

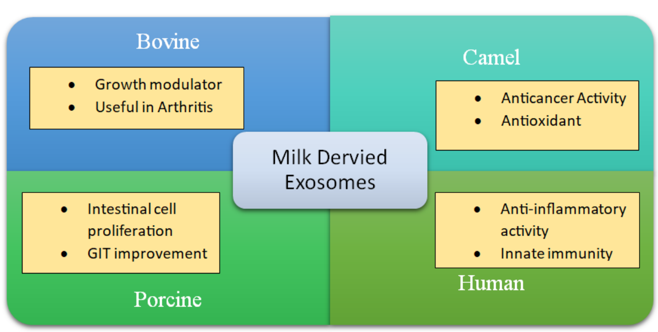

Figure 1: Milk derived exosomes from animals

containing messenger RNAs (mRNA) and small ribonucleic acids (miRNAs) Milk exosome has a range of different nucleic acids including mRNA and miRNA. Through exosome fusion, these nucleic acids may be transferred into recipient cells, thereby interfering with cellular functioning and gene expression.

Lipids

Cholesterol and Phospholipids: The composition of milk exosomes is similar to other cell membranes and contains both phospholipids and cholesterol. This lipid bilayer structure safeguards the payload of an exosome while maintaining its stability.

Size and morphology

Milk exosomes in diameter typically have a size that varies between 30 nanometers to 150 nanometers. Their extremely small size makes them ideal for several applications, including drug administration and intracellular signaling. What do milk exosomes look like? Milk exosomes appear as spherical vesicles with a lipid bilayer when examined using electron microscopy. Their unique shape distinguishes them from all other forms of extracellular vesicles.

Origin and cargo loading

- *Cellular origin*

They come from the very cells that made them; hence, the milk exosomes have a similar composition to the cells that formed them. They are produced by mammary epithelial cells when it comes to milk.

- *Payload loading*

Exosomes are engineered or created in nature to serve a specific purpose such as carrying DNA or medicines. This ability for cargo loading makes them ideal candidates for delivering drugs.

Biological function

- *Intercellular communication*

Milk exosomes primarily facilitate intercellular communication. Through these nano-sized vesicles, proteins and nucleic acids their bioactive substances are transported between cells, influencing many physiological functions. General targeted drug delivery methods are mentioned in Table 1.

Enhancing Curcumin's Functional Activities Application of Milk Proteins as Nanocarrier

Curcuma longa plants yield curcumin, a vivid yellow powder. It is the main curcuminoid found in turmeric, also known as Curcuma longa, a herb used as a flavoring, food coloring, and herbal supplement.[38] Researchers have found that curcumin has a wide range of biological properties, including antibiofilm, antibacterial, anti-inflammatory, wound healing, and anti-amyloid effects.[39] Regretfully, curcumin's poor water solubility, bioavailability, and quick breakdown at neutral and alkaline pH levels account for its restricted

Table 1: Description of targeted drug delivery methods

S. No.	*Targeted drug delivery*	*Description*
1	Engineering for specificity	Exosomes derived from milk can be altered to contain specific ligands that bind and recognize the receptors which are overexpressed on the surfaces of cancerous cells. By doing so, these exosomes have an increased tendency to stick onto tumor cells thereby improving their targeting capabilities for these cell lines.
2	Minimizing off-target effects	Diminished Systemic Toxicity: Targeted delivery of drugs to cancer cells minimizes the extent of unwanted actions on healthy tissues. This is crucial as systemic toxicity is often an issue with standard chemotherapy because it regularly induces damage to non-cancerous cells and tissues.
3	Improved therapeutic efficacy	Increased Therapeutic Drug Concentration: Targeted administration stimulates cancer medicines' dose, such as anticancer drugs, at a particular spot where tumors are located. The concentration can increase its effectiveness against malignancies lessening any damage caused to normal tissues by assuring higher local doses.
4	Overcoming biological barriers	More Active Infiltration: Due to their tiny size, milk exosomes can traverse biological barriers more easily. It goes through the leaky blood vessels which are connected with tumor tissues giving rise to the increased permeability and retention (EPR) effect.
5	Cellular internalization	The biological event that allows for the absorption of milk exosomes into a target cancer cell is called endocytosis. Endocytosis occurs when the exosome binds to a cancer cell and causes it to internalize, releasing its drug more easily for therapy.
6	Customization for specific cancer types	Specific ligands: The cancer properties of various class types match precisely within an exosome surface ligand selection. This customization makes it possible for cancer care considering thus precision medicine.
7	Combination therapies	Multiple Drug Loading: The ability of milk exosomes to carry several drugs at once makes combination therapy possible. This is crucial for attacking angiogenesis, cell division and resistance mechanisms together that are the pillars of cancer biology.
8	Realizing the potential of immunotherapy	Immunomodulation: There is potential for milk exosomes to have innate immune-modulating properties. If immunomodulatory drugs are given directly into tumor niches, they could enhance the immune response of the host against cancer.
9	Monitoring and imaging	Coalescing Foreign Ingress Particles: As the power to load imaging agents into exosomes lets the real-time watching of drug delivery. This enhances chemotherapy programs and establishes distribution patterns of a particular drug through malignant growth.

use in functional food formulations.[40] Curcumin's solubility and bioavailability have been improved through numerous attempts, such as the use of emulsions, liposomes, and nanoparticles. An important strategy is to use nanotechnology to increase curcumin's solubility and bioavailability.[41] Several nanoparticle formulations of curcumin have been developed to improve its functional properties.[42,43] In this context, a range of nanocarriers have been used; these are generally composed of biodegradable substances like proteins, polysaccharides (i.e., chitosan), carbohydrates, and proteins (including milk proteins).[44-46] Because of their distinct structural and functional diversity, milk proteins can be used as encapsulation agents and carriers of bioactive molecules. Milk proteins are good interfacial agents that help form and stabilize emulsions containing hydrophobic molecules because they transport ions or hydrophobic molecules. Furthermore, milk proteins have the ability to gel and ensnare bioactives by binding to target molecules to form covalent or electrostatic complexes. Furthermore, milk proteins can self- or co-assemble into supra-structures that help to encapsulate and transport a variety of small molecules.[47]

Milk Exosomes as Potential Agents for the Delivery of Anticancer Drugs

Exosomes are naturally occurring extracellular nanovesicles that are involved in intercellular communication. They carry biologically active molecules like microRNA, mRNA, DNA, and proteins.[48,49] Exosomes have the ability to carry the carried compounds both inside and outside of them.[50] Because of their 40–100 nm diameter, exosomes are a promising drug delivery system.[51] The production of synthetic exosomes is still unattainable, so a major challenge is safely and effectively extracting exosomes from natural sources on a large scale. Tumor cell cultures are not a dependable source of vesicles for pharmacological applications. Exosomes have been found in a wide range of biological fluids, including blood plasma, urine, saliva, milk, amniotic fluid, ascites, cerebrospinal fluid, and others. The only biological liquid with exosomes that is suitable for industrial use is milk. Exosomes from human milk were first reported in 2007. The following species, in chronological order, have had exosomes isolated from them: human[52] or bovine[53]or porcine[54] or wallaby[55] or camel[56] or rat[57] or horse[58] or panda[59] or yak[60] or sheep[61] or and goat milk.[62] More than 100 articles about exosomes and other milk vesicles can be found in databases; the majority of these articles discuss vesicles found in human and cow milk. A horse, sheep, goat, and camel can also produce comparatively large amounts of milk, in addition to a cow. Because of the possible prion content, cow's milk shouldn't be considered a source of protein-containing structures.[63] Milk exosomes are cutting-edge therapeutic candidates with the potential to treat cancer among other illnesses. However, the information regarding the delivery of biologically active molecules—exosomes in particular—through milk vesicles to cells is currently scarce in the literature.[64] Important uses of milk exosomes in cancer therapy include the delivery of therapeutic antitumor drugs[65] and nucleic acids.[66,67] Among the unsolved issues with cancer chemotherapy are the numerous side effects that could arise from the use of cytotoxic and cytostatic agents.[68]

Isolation of Milk Exosomes

To extract exosomes from milk, a variety of physical, physicochemical, and immunological techniques are employed. The International Society has published guidelines for the general identification and separation of exosomes for Extracellular Vesicles.[69,70] Furthermore, sets of reagents that are patented and sold commercially are polymer sets that do not include volume. Two such sets are ExoQuick (System Biosciences, Palo Alto, CA, USA), which contains PEG 8000 kDa, and Total Exosome Isolation (Thermo Fisher Scientific, Waltham, MA, USA), which contains dextrans, polyethylene glycol, and polyvinyl with a molecular weight above 1000 kDa.[71] Two other methods for isolating exosomes are separation on immunomagnetic particles and filtering through a semipermeable membrane. As mentioned in many protocols, including,[72] it is considered necessary to centrifuge milk once or twice at low speeds, and then store milk plasma if desired before isolating exosomes. The possibility that nondeflated milk samples stored in storage cause contamination of exosome preparations with milk fat globule membrane (MFGM) cannot be ruled out, considering the numerous instances in which the nucleic acid, protein, and lipid compositions of milk exosomes and MFGM[73,74] coincide in different publications There's a possibility that exosomes will stick to MFGM and contaminate the extracted exosome samples when nondeflated milk samples are refrigerated. It has been demonstrated that gel filtration is a useful technique for separating exosomes from human,[75] cow,[76] and equine[77] milk. Ultracentrifugation can be used in place of or in addition to this method. This method works well for separating small sample volumes (less than 1%–5% of the column volume), but it is not appropriate for directly isolating exosomes from large volumes of milk. After ultrafiltration and/or ultracentrifugation, preparations can be obtained. The sample can be purified using gel filtration to remove co-isolating proteins.

Drug Delivery in Cancer therapy using Milk Exosomes

When antitumor drugs are applied to the surface of naturally occurring, biologically active structures, like proteins, their biological availability and efficacy are significantly enhanced.[78] Recently, there has been a lot of focus on exosomes' ability to cross physiological barriers, including the blood-brain barrier.[79,80] Many research facilities have used exosomes that have been isolated from different cell lines to accomplish targeted drug delivery.[81,82] The development of exosomes as pharmaceutical products is beset with significant obstacles, even in light of the encouraging results. When exosomes are administered systemically, their protein component is likely to trigger an immune response. Furthermore, exosomes generated from patient samples or cell lines cannot be extracted for use in commercial pharmaceutical manufacturing.[83] By utilizing readily available mass exosome sources, these can be overcome while addressing immune responses. Exosomes from cow's milk can be extracted in large quantities, according to research.[84,85] Moreover, injecting milk exosomes into mouse models did not result in anaphylactic reactions or systemic toxicity. Nonloaded camel milk exosomes significantly inhibited the growth of breast cancers, as shown by elevated apoptotic process markers, reduced oxidative stress and downregulation of several genes associated with the induction of the immune response and inflammatory processes.[86] Because human immune tolerance to milk proteins was probably developed as a result of the widespread consumption of milk and dairy products, milk exosomes can be used as delivery systems for oral drug administration.[87] For the first time, milk exosomes were demonstrated to be directed against a malignant tumour in 2016. Free medication did not work as well as exosomes containing medication when treating lung tumour xenografts and cell cultures in vivo. Milk exosomes demonstrated interspecific tolerance without inducing unfavorable immune or inflammatory reactions. The lack of recipient cell specificity in milk exosomes makes them a challenge to use for targeted drug delivery. It has been demonstrated that ligands can alter intact milk exosomes to increase their retention in target tissues after being absorbed from the gut.[88] Milk exosome-based vectors can be modified with particular ligands to bind tumour-specific receptors, just like liposome-based drug delivery systems.[89] Many distinct types of cancer cells frequently have an overexpression of the CD44 receptor on their surface, which binds to the specific ligand hyaluronan.[90] The lipid membrane of milk exosomes was modified to include hyaluronan molecules, which allowed doxorubicin a cytostatic medication to be delivered exclusively to cells that expressed CD44.

Application of Milk Derived Exosomes[91,92]

Nutritional supplement delivery

Exosomes made from milk can be used as delivery systems for bioactive substances like proteins, vitamins, and other nutrients. By increasing the compounds' stability and bioavailability, these exosomes may improve their absorption in the gastrointestinal system.

Therapeutic delivery

Exosomes contain a variety of biological molecules, including microRNAs, proteins and lipids. Scientists are studying how to use milk exosomes to carry different therapeutic agents such as drugs or genetic material selectively to certain cells. This may have ramifications in the management of several diseases.

Immunomodulation

Extensive studies have been conducted on milk exosomes and their role in functioning of immune system. These studies seek to establish if they suppress or enhance excessive immune responses. They comprise of varied immune-associated components.

Wound healing

Research has been done into the potential of milk-derived exosomes to speed up wound healing. Because they may contain certain constituents capable of tissue rebuilding, cell relocating as well as proliferation, they may be useful for wounds' therapies.

Therapy of cancer

One of the sources whose potential has been studied to aid targeted drug delivery in cancer treatment in milk exosomes. For this reason, they have a large ability for selecting and binding on tumor cells are among other properties that make them appropriate to be used in the delivery of anticancer medications.

Gut health

Milk exosomes could potentially influence the health of the intestine via their interactions with the digestive system. They may affect gut microbiome composition and contribute to gut homeostasis preservation.

Neurological disorders

Exosome function in neurological diseases has only just begun to be examined. In particular, certain components within milk exosomes may have neuroprotective or regenerative properties.

Disease diagnosis

Exosomes have different biomolecules that are unique to each parent cell. Analysis of milk exosome contents can provide helpful diagnostic information. Changes in exosomal composition can act as indicators for numerous diseases such as cancer, neurological disorders and metabolic problems.

Regenerative medicine

It's generally believed that milk-derived exosomes can be applied in regenerative therapy because they contain signaling molecules and growth factors. Research can, therefore be directed at their potential to enhance tissue regeneration and repair. They are especially pertinent in discussing wounds or degenerative diseases.

Maternal-infant health

When it comes to the relationship between mothers and their children, exosomes found in breast milk may play a significant role. Scientists are currently conducting studies on how these exosomes influence infant immunity and gut microbiota.

Anti-inflammatory effects

Zeroes made of milk are a kind of stuff that may exhibit some anti-inflammatory functions (this aspect can be useful for creating treaments that manage inflammatory responses). A case in point includes rheumatoid arthritis and/or bowel diseases.

Sports and exercise physiology

The possibility of how exosomes can influence muscle recovery and adaptation has caught sports medicine's attention. If research on the impact of exosomes found in milk on muscle healing and performance is pursued, new techniques for athletes could be developed.

Cosmetic and dermatological applications

The potential roles of exosomes in skin health and regeneration have been researched. For instance, milk-derived exosomes may be used in dermatological or cosmetic formulations to reduce wrinkles, enhance skin's overall health and improve skin's textures.

Agricultural applications

Livestock may benefit from using milk exosomes in farming to enhance their well-being and development. This research direction can investigate the advantages of incorporating milk exosomes into animal diets to support improved growth and feeding.

Environmental remediation

There might be applications for the environment in the future due to exosomes' capacity to carry diverse substances. Such as milk-derived exosomes could be utilized for environmental restoration as they transport specific elements to the soil or aquatic systems.

Vaccine development

Research has been conducted on the potential use of exosomes as vaccine delivery systems. The ability to stimulate the immune system or provide a basis for the vaccine development using exosomes derived from milk may be explored.

Various methods are used to isolate exosomes and their effects are depicted in Table 2.

Future Directions

Engineering strategies

Provide state-of-the-art engineering methods to enhance the medicine loading efficiency and selectivity into milk exosomes. This includes the use of genetic alteration and bioconjugation methods.

Combination therapies

Analyse the potential for using milk exosomes to deliver combination therapeutics, such as medication and chemotherapeutic agents or therapeutic nucleic acids.

Personalized medicine

Analyse whether using milk exosomes to study personalized medicine approaches is feasible. Customizing drug-loaded exosomes to each patient's specific cancer kind and genomic profile may improve treatment success.

Table 2: Different methods for isolating exosomes and their effects on recovery, purity, and time

S. No	*Method*	*Time (hours)*	*Recovery*	*Purity*
1	Size Exclusion Chromatography	5–10	Low	High
2	Polymer based Precipitation	0.5–12	Low	Low
3	Ultracentrifugation	5–10	High 5-25%	High to Low
4	Ultra- filtration	2–4	Low- High	High
5	Destiny Gradient Centrifugation	16–20	Very low	High

Clinical trials

Milk-derived exosomes as anticancer medication carriers need to undergo well-designed clinical trials in terms of their efficacy and safety. Moving forward with the next phase of development requires validating the preclinical studies done so far.

Imaging and diagnostic applications

See if liquid channels or anything like milk microscopic images is inside. Exosomes may be used as diagnostic indicators within the clinical framework, and additionally they may be used for drug administration.

Regulatory approval

Making an effort to comply with the necessary legal requirements for a milk exosome-based therapy to be approved is very important. A cooperative goal from three groups of people: the pharmaceutical industry, regulatory authority and scientists is needed for it to be possible.

Long term effect

Research extensively on the consequences of milk exosome-based treatments over time while taking into consideration the risk of cumulative toxicity that may develop, as well as unforeseen effects on regular cell operations.

Advantages of using Milk Exosomes as Nanocarriers for Anticancer Drugs[93,94]

Cellular targeting

A modern way of treating cancerous cell is by cellular targeting which makes use of exosomes that are designed to display certain ligands or membrane proteins. Such an approach reduces the damage inflicted upon normal cells while making drug delivery more precise.

Stability and protection

Drugs enclosed in exosomes are shielded from being degraded by enzymes, or anything else that would otherwise cause them to break down. This stability allows drugs to remain in the bloodstream longer.

Transcending biological barriers

Exosomes possess the unique property of crossing several biological barriers including blood-brain barrier; thus facilitating delivery of anticancer agents to sites that would be difficult to access via traditional means of drug delivery.

Diminished immunogenicity

Are you aware that the base for these artificial nanocarriers is mainly made out of milk? Unlike these synthetic nanocarriers which possess central nervous system toxicity, milk exosomes do not have it, hence they are likely to trigger less reaction from our immune system. This feature will minimize possible immune responses that may lead to the decreasing operation of this therapeutic vehicle.

Diversity of payload

Milk exosomes carry a wide range of bioactive chemicals in their payload, including proteins and nucleic acids. Different anticancer drugs, therapeutic nucleic acids, or combination therapies can all be encapsulated within a single carrier due to their diversity.

Enhancement of bioavailability

Drugs can be made more readily available by milk exosomes due to their ability of prolonging the time they remain in circulation and preventing them from dissolving. As a result, this might lead to improving therapeutic effectiveness while reducing required dosage levels.

Natural origin

As milk exosomes come from an inherent and regrowing source, their production methods may be uncomplicated and manufacturing costs may be lowered in contrast with synthetic nanoparticles. The increasing focus on sustainable and ecologically friendly medical solutions enhances this natural origin.

Intercellular communication properties

Potentially, exosomes could offer additional advantages in terms of utilizing their ability for medication delivery through intercellular signaling promotion. It might impact the tumor microenvironment and facilitate directing treatment drugs to distinct cellular targets.

Disadvantages of using Milk exosomes as a Nanocarriers for Anticancer Drugs

Separation and cleaning difficulties

In the case of procedures to isolate and purify milk exosomes, they can be quite complex from a technical point of view, while it is worth noting that different methods would yield different results. Therefore, it is very important to have highly purified materials which are consistently available for use in clinics.

Limited drug loading capacity

The ability of exosomes, including milk exosomes, to load drugs may be limited. It is very difficult to optimize drug loading without sacrificing the integrity and stability of exosomes.

Biological and biodistribution

Even though exosomes can pass through some biological barriers, it is still difficult to distribute them uniformly and effectively throughout the body. An uneven distribution could reduce medication delivery's effectiveness.

CONCLUSION

Molecular pharmacology depends on the development of biocompatible techniques for the in vivo and in vitro delivery of therapeutically relevant drugs. In 1994. Sheep, goat, and horse milk exosomes are very promising for use in medicine because they do not contain prion proteins. Before using them in therapy, a few things must be taken care of. A few of these include the fact that milk exosomes are specific to different cells and tissues, the development of techniques for altering their surface for target delivery, and our ignorance of the nucleic acids and proteins that are intrinsic components of exosomes and that are co-isolated during purification. When it comes to drug delivery, natural exosomes and artificially generated liposomes are often compared. There are several arguments in favor of and against the use of natural vesicles over liposomes and other synthetic nanoparticles. For example, milk exosomes have lower immunogenicity and cytotoxicity due to their chemical similarity to cell membranes, and they have higher biocompatibility. Compared to the more costly and scalable methods of isolating blood plasma or culture fluid, milk exosomes are able to move molecules that are hydrophilic or hydrophobic. Oral medication delivery is possible with milk exosomes because their biologically active molecules remain stable in the digestive tract's harsh environment. Gene therapy holds great promise for exosomes, especially in the treatment of cancer. This is because it has been found that different miRNAs affect how genetic information is delivered to recipient cells and are part of the makeup of milk exosomes. Less research has also been done on the lipid composition of milk exosomes, which is crucial for the delivery of medications and other physiologically active materials. The information shown above suggests that additional research is required to completely comprehend the biochemical makeup of milk exosomes. Milk exosomes can carry therapeutic nucleic acids and antitumor medications.

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