Exosomes as drug delivery system

Editorial Article

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There are many factors that need to be taken into consideration when converting an active substance into a drug, such as the properties of the molecule, biological barriers, pathological condition, and technical problems.

However, the most important among these factors is the transportation of the molecule with pharmacological activity to the required region with an appropriate carrier system. The carriers developed for the active substance to date have different problems and cause difficulties in treatment. These include those that pose serious problems in drug administration, such as the blood-brain barrier, in reaching the active substance to the brain.

The main purpose of drug delivery systems is the entry of the therapeutic molecule into the cell. Today new dosage forms such as liposomes and polymeric nanoparticles are the most preferred drug delivery systems. Nevertheless, the circulatory capacity and stability of the liposomal system as well as its ability to invade the host immune system without toxicity remain elusive. Although polymeric nanoparticles solve the stability problem, their toxicity and biocompatibility remain a significant problem, especially when non-biodegradable polymers are used. Secreted membrane vesicles, which are essentially nature-derived liposomes, can potentially overcome some of the limitations of synthetic liposomes, such as the toxicity of lipid membranes. Among the different secreted membrane vesicles, exosomes are the most clearly defined and are most amenable to development as drug delivery vehicles.

Extracellular vesicles are cell-derived nanoparticles that are important mediators in intercellular communication. This function makes them auspicious candidates for therapeutic and drug-delivery applications and this function makes them convenient candidates for therapeutic and drug delivery applications.

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Among the most highly researched extracellular vesicles are exosome. Recent studies show that exosomes derived from cells have different roles and targets.

Exosomes, have intercellular material derived from endosomes of parent cells. Exosomes have a wide variety of components, such as, heat shock proteins surface proteins, lysosomal proteins, tumor-responsive gene, fusion proteins, and nucleic acids, each with specific functions. Proteins exhibit a distinct function in biogenesis and transport mechanisms in exosomes. These are phospholipid bilayer microparticles with a size of 50-100 nm.

Exosomes have many characteristics of an ideal drug delivery vehicle. First, the presence of proteins and genetic materials in exosomes means that such biological materials can be loaded into exosomes. Secondly, exosomes are well tolerated in the body and their distribution in biological fluids such as blood, urine and breast milk has also been demonstrated.

Therefore, exosome-derived drug delivery systems will likely be better tolerated, resulting in longer circulating half-life and increased efficacy. Third, exosomes have been shown to cross the plasma membrane to deliver their cargo to target cells. Fourth, exosomes have an inherent ability to target tissues. Much circumstantial evidence suggests that exosomes have preferential homing targets depending on their cellular source. Finally, exosomes are suitable for membrane modifications that enhance cell type-specific targeting.

Although most cell types produce exosomes, but the amount of exosomes produced by each cell type is variable. Exosomes express cell recognition molecules on their surface that facilitate selective targeting and uptake by recipient cells. The process of exosomes entering cells occurs by transferring their signals to the cell through a 3-step mechanism; receptor interaction, membrane fusion and endocytosis/phagocytosis. Currently, different methods are applied for exosome isolation; differential centrifugation, filtration, size-exclusion chromatography, and polymer precipitation.

An exosome-based delivery system has specific benefits such as specificity, stability, and safety, they can deliver their cargo to specific targets over long distances. Exosomes can also be used to deliver small and large molecules such as proteins and peptides. Exosomes naturally transport nucleic acids such as DNA, RNA, and siRNA to targeted cells and cause genetic modifications in both biological and pathogenic processes. Researchers have shown that doxorubicin loaded exosomes were readily up taken by cells and re-distributed. In another study, exosomal system evaluated for delivery of paclitaxel. Exosome-based carrier systems have been used for gemcitabine in the treatment of pan-

creatic cancer and for dopamine in the treatment of Parkinson's disease. For exosomes to be used effectively as drug delivery systems, drugs must be efficiently loaded into exosomes. They are introduced into exosomes via two ways: active or passive loading/encapsulation.

On the contrary traditional nanoparticulate system, exosomes can possibly avoid the endosomal pathway and lysosomal degradation and deliver cargos directly to the cytoplasm.

If exosomes are to be used as drug delivery carriers on a large scale, large-scale isolation, and separation of exosomes with high purity is important. However, it is not yet possible to isolate and separate exosomes in high purity on a large scale. This is an important challenge. Exosomes role in disease must be investigated in detail to enable clinical translation. Few clinical studies using exosomes as drug delivery systems are ongoing.

Recent literature shows continued exploration and promise of exosomes as drug delivery carriers for various diseases including solid tumors, bone regeneration, cardiac diseases, Parkinson's amongst others.

Briefly, it can be said that exosomes as a drug delivery system with minimal toxicity, biocompatibility, tissue and tumor targeting, and long circulating half-life is appearing as a superior choice, overcoming the shortcomings of liposomes or polymeric nanoparticles.

Keywords: exosome, delivery vehicle, nanoparticles, extracellular vesicles, drug

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