Research and Reviews: Drug Delivery

Targeting Methods of Drug Delivery and its Consequences

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Perspective

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DESCRIPTION

In order to delivery drug to the desired destination, targeting is an important subject in drug delivery. Ligand is a substance that forms a complex with a biomolecule to serve for a biological purpose. There are three classes of ligands that are commonly used for drug delivery targeting. Antibodies and/or antibody fragments, peptides, and aptamers. Depending upon the situation of targeting, different type of ligand is used.

Passive targeting

Passive targeting is achieved by incorporating the therapeutic agent into a macromolecule or nanoparticle that passively reaches the target organ. In passive targeting, the drug's success is directly related to circulation time. This is achieved by cloaking the nanoparticle with some sort of coating. Several substances can achieve this, with one of them being Polyethylene Glycol (PEG). By adding PEG to the surface of the nanoparticle, it is rendered hydrophilic, thus allowing water molecules to bind to the oxygen molecules on PEG *via* hydrogen bonding. The result of this bond is a film of hydration around the nanoparticle which makes the substance antiphagocytic. The particles

obtain this property due to the hydrophobic interactions that are natural to the Reticuloendothelial System (RES), thus the drug-loaded nanoparticle is able to stay in circulation for a longer period of time. To work in conjunction with this mechanism of passive targeting, nanoparticles that are between 10 and 100 nanometers in size have been found to circulate systemically for longer periods of time.

Active targeting

Active targeting of drug-loaded nanoparticles enhances the effects of passive targeting to make the nanoparticle more specific to a target site. There are several ways that active targeting can be accomplished. One way to actively target solely diseased tissue in the body is to know the nature of a receptor on the cell for which the drug will be targeted to. Researchers can then utilize cell-specific ligands that will allow the nanoparticle to bind specifically to the cell that has the complementary receptor. This form of active targeting was found to be successful when utilizing transferrin as the cell-specific ligand. The transferrin was conjugated to the nanoparticle to target tumor cells that possess transferrin-receptor mediated endocytosis mechanisms on their membrane. This means of targeting was found to increase uptake, as opposed to non-conjugated nanoparticles. Another cell-specific ligand is the RGD motif which binds to the integrin αvβ3. This integrin is upregulated in tumor and activated endothelial cells. Conjugation of RGD to chemotherapeutic-loaded nanoparticles has been shown to increase cancer cell uptake *in vitro* and therapeutic efficacy *in vivo*.

Active targeting can also be achieved by utilizing magnetoliposomes, which usually serves as a contrast agent in magnetic resonance imaging. Thus, by grafting these liposomes with a desired drug to deliver to a region of the body, magnetic positioning could aid with this process.

Furthermore, a nanoparticle could possess the capability to be activated by a trigger that is specific to the target site, such as utilizing materials that are pH responsive. Most of the body has a consistent, neutral pH. However, some areas of the body are naturally more acidic than others, and, thus, nanoparticles can take advantage of this ability by releasing the drug when it encounters a specific pH. Another specific triggering mechanism is based on the redox potential. One of the side effects of tumors is hypoxia, which alters the redox potential in the vicinity of the tumor. By modifying the redox potential that triggers the payload release the vesicles can be selective to different types of tumors.

By utilizing both passive and active targeting, a drug-loaded nanoparticle has a heightened advantage over a conventional drug. It is able to circulate throughout the body for an extended period of time until it is successfully attracted to its target through the use of cell-specific ligands, magnetic positioning, or pH responsive materials. Because of these advantages, side effects from conventional drugs will be largely reduced as a result of the drug-loaded nanoparticles affecting only diseased tissue. However, an emerging field known as nanotoxicology has concerns that the nanoparticles themselves could pose a threat to both the environment and human health with side effects of their own. Active targeting can also be achieved through peptide based drug targeting system.

Mainly, pharmaceuticals are more concerned with what would happen if a drug meant for the kidney ends up near the lungs, or something similar to this. This could be called side effects. Often this is solved by observing the carbohydrate chains on the surface of cell membranes to discover what receptors cells of specific organs have. Developing a drug that fits into most of these receptors (a broad and commonly structured drug) would increase the chances of side effects. It is therefore crucial to develop a drug that binds to a cell's receptor as specifically as possible to reduce side effects. Discovering side effects and minimizing these side effects is a big part of getting a drug pass the examination tests and get on the shelves of pharmacies.