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Commentary

Targeting Liver Disorders through the Drug Delivery System

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DESCRIPTION

The liver is a mammalian organ that is implicated in metabolism, detoxification, protein and lipid synthesis, cytokine and growth factor release, and immune/inflammatory responses. The most prevalent liver disorders are hepatitis, alcoholic or non-alcoholic liver disease, hepatocellular carcinoma, liver fibrosis, and cirrhosis. It is critical to transfer therapeutic molecules (drugs, genes, or proteins) into the liver safely and efficiently in order to improve clinical efficacy and reduce adverse effects in other organs. Several drug delivery systems for liver cells have been designed and tested *in vivo*, *ex vivo* and *in vitro*. However, one of the most difficult study areas in pharmaceutical sciences is drug transport to the liver. Some physiological barriers and mechanical entrapment by the pulmonary vascular bed, and uptake by the Reticuloendothelial System (RES), pose an insurmountable challenge for a wide range of proteins and drugs, including antibiotics, antineoplastic agents, and antiviral agents are used to treat liver disorders.

The treatment of liver cancer and other disorders is a difficult issue for pharmaceutical science. Targeting ligands that can combine with nanocarriers or medication molecules are used in the novel targeting techniques. These conjugate systems can be passively or actively accumulated. Hepatitis B (viral HBV infections), liver fibrosis, and Hepatocellular Carcinoma (HCC) are the leading causes of disability and death around the world. These conditions necessitate long-term pharmacological therapy. Drug administration to the liver reduces side effects by drug distribution to non-target organs and increases therapeutic efficacy by increases drug concentration in target cells at the same time. Because the liver is the body's largest reticuloendothelial organ, macrophages in the liver (also known as kupffer cells) for the treatment of liver disease through effector cells in hepatic therapy.

The particle sizes and surface properties of colloidal drug carrier systems appear to influence their body distribution and opsonization by macrophages. The ability of particles with diameters ranging from 50 to 200 nanometers to achieve opening in the hepatic sinusoidal endothelium could result in hepatic accumulation. Although nanoparticles and liposomes could not directly reach hepatocytes, macrophage absorption of IV-injected particulate drug carriers could be the important factor in the efficient targeting of a drug to the kupffer cells in the liver.

When different carrier systems, such as liposomes and nanoparticles, enter the bloodstream, nonspecific interactions with serum proteins occur, resulting in the surface deposition of antibodies and complement proteins, a process known as opsonization. Due to various mechanical entrapments of aggregates in the alveoli and clearance by the reticuloendothelial system in the liver, spleen, and bone marrow, this interaction reduces overall dose and carrier circulation time, especially if the aggregate size is greater than 200 nm and a large surface negative charge is present.

The endothelial cells that line the sinusoids of the liver are another component of the RES scavenger receptors. Protein binding is minimized, and nonspecific scavenging of carriers by RES is reduced, thanks to steric stabilization and shielding of carriers with PEG molecule. In general, passive and active targeting used to achieve targeting. Nano carriers of a desired size and surface modification are used to achieve passive targeting. Passive targeting, which improves the local concentration of the medicine and lowers unwanted side effects, can be used to deliver treatments to specific locations. Surface modification of nanoparticles with specific ligands such as carbohydrates, peptides, proteins, and antibodies allows for active targeting.

Carrier molecules are designed for selective cellular uptake by utilizing specialized receptors or binding sites on the target cells surface membrane. Although hepatocytes account for more than 80% of the total number of resident hepatic cells, uptake in other cell types such as Kupffer cells can also occur, and high uptake of viruses, antibodies, or other biological compounds into these cells frequently results in complete degradation of these compounds, which in some cases renders them useless. As a result, there should be a particular delivery method and ligand for targeting each cell. Hepatocytes, Kupffer and sinusoidal endothelial cells, Hepatic Stellate Cells (HSC), bile duct epithelial cells, and hepatocellular carcinoma cells are the five cell types that may be present in the liver for active drug targeting. The aetiology of liver ailments encompasses a wide range of cells, rendering drug delivery challenges. The design and manufacture of appropriate polymeric materials to target specific liver cells are the most significant parts of improving treatment through drugs.

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