Nanocarriers for cancer diagnosis and targeted cancer therapy

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Abstract : ***The intend of this study is to show the potential that nanotechnology has towards cancer diagnosis and targeted drug delivery. Various nanocarriers have been designed and manufactured to deliver the drug specifically and produce maximum therapeutic response. This shows the novel approach of nanocarriers by ruling out various disadvantages of conventional therapy. The study includes numerous nanocarriers such as liposomes, dendrimers, polymeric micelles etc. This study portrays the current scenario of nanocarriers around the globe. The review also explores the nanoparticles used in cancer diagnosis and imaging.***

Keywords - nanocarriers, liposomes, dendrimers, diagnosis, micelles.

I. INTRODUCTION

Cancer is the second leading cause of death globally, and was responsible for 8.8 million deaths in 2015. Globally, nearly 1 in 6 deaths is due to cancer. Cancer is the abnormal and uncontrolled proliferation of cells and in some cases can spread in different parts of the body. By the year 2030, World Health Organization (WHO) has estimated number of cancer related deaths as approximately 13.1 million. These situations are mostly being treated using conventional therapy, but this conventional approach has undesirable side effects on healthy body parts. Conventional drugs cause severe toxicities in our body, because of their low specificity. These drugs have low aqueous solubility which causes it to show less bioavailability and lower therapeutic action. Due to this drugs are required in higher doses and cause lethal toxicities. The growth in the field of nanotechnology has created a significant impact on cancer therapy.

Nano-sized drug carriers have been developed, which have the potential to deliver drug at the targeted site, thus showing high specificity. This has improved the efficiency of the treatment, thereby reducing the toxicity and side effects caused to the normal body cells. It shows high selectivity for tumors through enhanced permeability and retention (EPR) (Figure 1). The mechanism used is that, the drug is encapsulated within nanocarriers of 50-800nm, so that they do not cross the wall of healthy blood vessel (The space between normal cells is 15-30nm while that cells near the tumor is more). The EPR effect is the passive mechanism for targeted drug delivery. The active mechanism involves ligand or antibody mediated targeting. In ligand mediated strategy, the ligand molecule is grafted on the surface of nanocarrier while antibody is used as a surface modifier for active targeting (Figure 1). For example, folate-polymer coated nanocarriers can be used in targeted treatment of ovarian cancer due to the specificity for folate receptors.

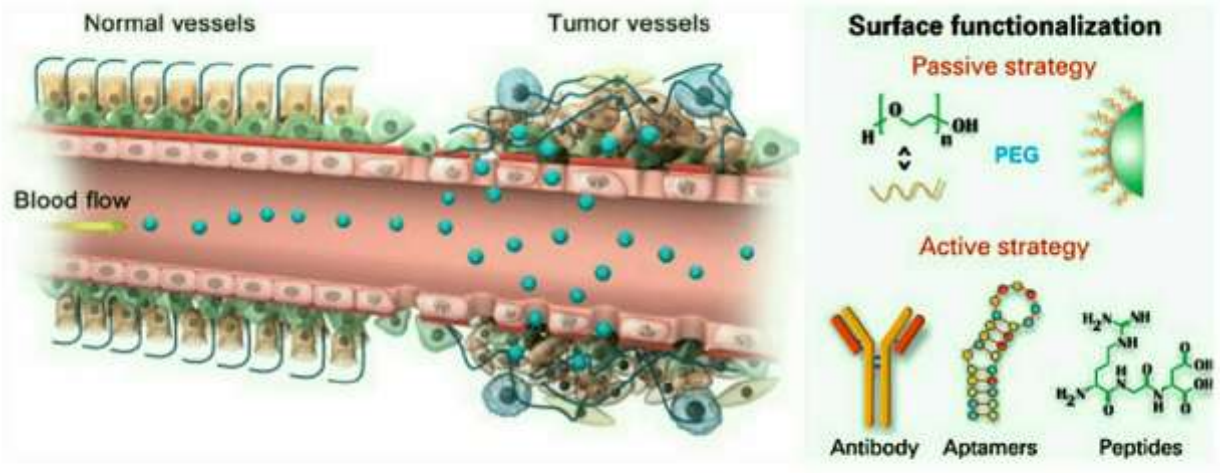

Figure 1. Mechanism for EPR and strategies for targeted drug delivery.

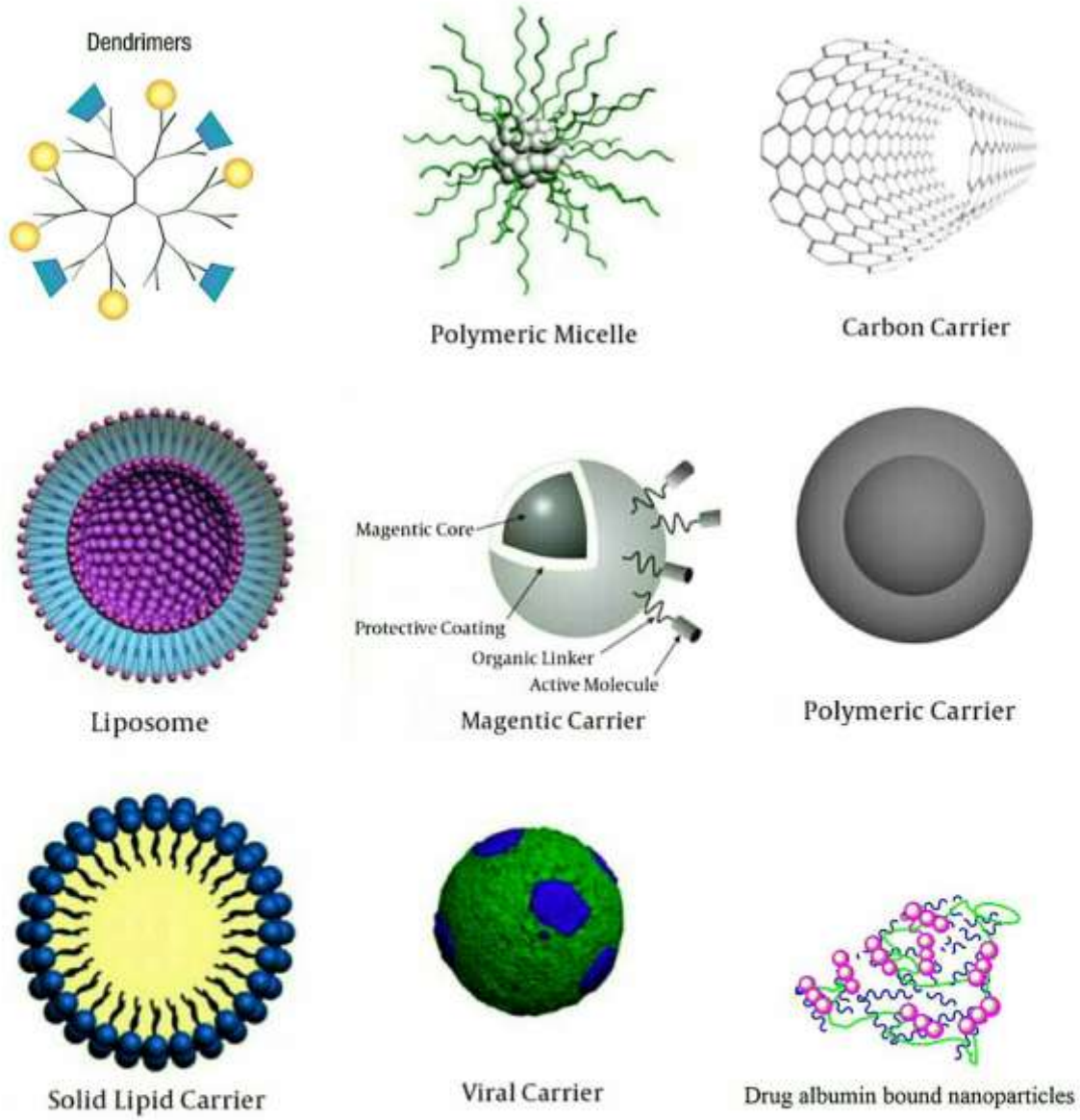

Figure 2. Various nano-vehicles.

II. VARIOUS NANO-VEHICLES

2.1 Dendrimers

It is a polymer consisting of monomers linked to each other by extensive branching. This macromolecule has improvisable surface characteristics, defined molecular weight, uniform size and distribution which makes dendrimer a potent vehicle for targeted therapy (Figure 2). It was found that cationic dendrimers cause cytotoxicity and hemolysis. The number of surface attachments increase the level of toxicity produced. Some anionic dendrimers were found to be non-cytotoxic though they have longer circulation period than cationic. For cancer diagnosis dendrimers are used as an agent in MRI and also for in-vitro diagnosis. For therapy, it is used as a gene carrier e.g. polyamidoamine dendrimer (PAMAM), and also used in photodynamic therapy (PDT).

2.2 Micelles and polymer based nano-particles

Polymeric micelles are nano-particles with hydrophobic core and hydrophilic shell, they are self-assembled systems formed at optimum concentrations of amphiphilic surfactants, optimum temperature, pH and ionic strength (Figure 2). This is specifically used for the drugs with poor aqueous solubility, these drugs are loaded into the hydrophobic core for better delivery. Even combination of drugs can be given using these nanocarriers. Advantages of using micelles as vehicle are significant, due to their hydrophilic shell it shows reduced uptake by mono-nuclear phagocytes (MNP). The molecule shows great result on surface attachment of peptides, monoclonal antibodies, DNA/RNA oligonulceotide thereby increasing specificity and bioavailability. Renal excretion is lowered down as the molecular weight of these nano-vehicles is considerably high. Various clinical trials are under process using polymeric micelles for targeted cancer therapy e.g. Docetaxel-PM

2.3 Carbon-based nanocarriers

Carbon skeleton forms a nanotube which consists of rolled benzene rings (related to fullerene family). It forms extremely light weight but a rigid structure with a high penetrating capacity. The carbon nanotubes (CNT) used for single drug therapy are usually single-walled, made up of single layer of graphene (Figure 2). The multi-layered nanotubes have concentric layering of graphene sheet, multiple drugs can be incorporated within the layers. These tubes penetrate like needle through almost all type of cells, hence can be used for those drugs which are potent for cancer therapy, but have less penetration power. This tube-like structure makes it easy for loading the drugs and has high loading capacity, for e.g. nanotubes shows up to 400% increased loading capacity for doxorubicin. Few other advantages of CNTs are that, they provide a larger surface area, high thermal and electrical conductivity. Some drawbacks of CNTs are that, bulky drugs such as paclitaxel show lower absorption and multi-drug therapy is also limited due to instability on multiple drug attachment.

2.4 Liposomes

Liposomes are lipoidal vesicles containing phospholipids which are self-assembled, forming a spherical shape (Figure 2). Liposomes have hydrophilic core and outer part as a phospholipid bilayer. Hydrophilic drugs are encapsulated within the core, and hydrophobic drugs are embedded within the bilayer. Liposomes can be extremely useful in multi-drug therapy, however, liposomes show less rate of drug release and slow accumulation due to the EPR effect. These nano-vehicles require low production cost and has the ability to thwart immunological response, thereby increasing patient compliance. Doxil® is one of the early approved liposomal nanocarrier. Many new liposomes are currently under clinical trials, one of the example is AVB-S6-500 for the treatment of ovarian cancer.

2.5 Metallic and Super-paramagnetic nanoparticles

These are the most innovative approach of nano-science towards the cancer therapy. Gold and silver is used to form metallic nanoparticles, they have electronic and optical properties which help them act as a chemical sensor in cancer therapy. These metallic nanoparticles readily conjugate with antibodies, enzymes and DNA, which help them act with increased potency for cancer therapy. Recently, magnetic properties are being used in the form of super-paramagnetic nanoparticles for cancer treatment (Figure 2). These particles are concentrated into the tumor by applying magnetic field from the external environment on the affected region. Magnetic nano-spheres are made up of Fe_3O_4 (iron oxide) and polystyrene. Feridex is an example of super-paramagnetic nanoparticle, used as a contrasting agent in MRI.

2.6 Miscellaneous

Few other nanocarriers include solid-lipid carrier, which are oil in water (o/w) emulsifying systems. They consist of solid lipid particles instead of oil (waxes, fatty acid, triglycerols). SLCs are biodegradable and cause less cytotoxicity. The drug is incorporated within the lipophilic matrix, it shows enhanced absorption and bioavailability. Second, viral carriers that are obtained from plants and bacteria, it acts as a highly efficient drug delivery system. The benefit of viral carrier is that, they are biodegradable and cause no toxicity or infection in mammals. Finally, albumin carriers made out of albumin, which is a globular protein also present in human body as serum albumin. Due to this, they are well-tolerated by immune system and cause less toxicity. Ambraxane is the first drug based on albumin carrier. It is a protein-bound paclitaxel, which shows increased half life and avoid hypersensitiviy reaction.

III. Conclusion

This review specifies the benefits of nanocarriers over the conventional treatment for cancer (chemotherapy). The presented data provides the pros and cons of nanomedicine. Many evidences have been stated in the review for advocating the fact that nanomedicine is coming forward as one of the advanced technique for diagnosis and medication for cancer. This study shows, how close we have reached towards the Paul Ehrlich's idea of 'Magic bullet'.

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