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Nano-Sized Drug Delivery

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In the last few decades, pharmacists focused to develop targeted drug delivery systems. The basic aim is to deliver drug molecules directly to the target tissues which Paul Ehrlich in about a century ago mentioned and named it as magic bullets of medicine [1,2]. Generally, pharmaceutical agents tend to distribute equally throughout the body. In addition, to reach the site of action, the drug has to cross vast majority of physiological and biochemical barriers which reduce the bioavailability of drugs. more importantly, After crossing through these barriers drugs should be able to elicit pharmacological action [3,4]. However, Nowadays, rapid advances in molecular biology, chemistry, pharmacy and nanotechnology enable a number of targeted drug delivery systems which can reach the malignant tissues selectively and accurately to the affected sites of the body [2,5].

Targeted drug delivery augments the therapeutic range of drugs in the tissues of interest while reducing the relative concentration of those in the other parts of the body. Targeting of drugs to affected site of the body offers enormous advantages [2,6-8]:

- Provide drug levels within the therapeutic range
- Vastly decrease in toxicity and side effects
- Increase in efficacy of drugs and bioavailability
- Increase drug concentration in the target organ
- Decrease the dosage of drug

There are numerous research and review articles in the literature on targeted drug delivery for cancer, inflammations, HIV in tissues such as brain, prostate, lung, heart, liver, ocular and blood [2,9-13]. Amongst those, cancer has much more attention than other diseases. Different types of drug carriers, varied targeting systems were developed a way to provide effective treatment for this fatal disease [11].

Types of Carriers

There are 2 broad drug carriers namely: Particulate drug carriers and macromolecular conjugates. Use of appropriate carriers is one of the most important steps to devise targeting agents [14]. Several carriers such as liposomes, micelles, polymeric nanoparticles, dendrimers, solid lipid nanoparticles, proteins, viruses, Carbon nanotubes, Gold nanoparticles , chitosan nanoparticles metallic nanoparticles are reported for drug targeting [9-17]. A carrier should be biocompatible, biodegradable, hydrophilic and have potential for surface modification. However, the most important aim for this modification is to increase solubility, stability and extended duration of drugs in blood circulation and add a passive or active targeting option to these nanocarriers. Based on physico chemical property of drugs, its target, targeting moiety, better drug loading and release profile are required [15,16,18,19].

Principles of drug targeting

Recognizing the morphological and physiological differences between malignant and normal tissues is essential to achieve effective drug delivery to the tumor tissues. Many different types of nano-systems have been designed and evaluated for drug targeting to tumors. There are 2 main types of targeted therapy drugs which are discussed below [2,20,21].

Passive targeting

Passive targeting is to target anatomical and patho-physiological differences of malfunction tissues from normal ones, for example angiogenesis leads to elevated vascular density in tumors, and because of that the gaps between endothelial cells are much larger than endothelial gaps in normal cells. This unique phenomenon called as enhanced permeability and retention (EPR) effect. To take advantage of this effect, nanoparticles must be engineered with ideal size and long circulation [7,14,20,21].

For passive targeting, nanoparticles circulate in vessels to meet a leaky vessel of tumor and go through them to reach the tumor site [7,20,22].

Another types of passive targeting is to track Tumor microenvironment, likewise change in PH, temperature and some enzymes [21,23-25]. The excessive metabolic rates in tumors provide an acidic environment around that the tumor. Shnitzky in 1980 prepared PH-sensitive liposomes [26]. The other approach is temperature-sensitive liposomes. In these kinds of nanoparticles, thermo-sensitive polymer were used which exhibit a lower critical solution temperature (LCST). Surface Modification of liposomes with these polymers give temperature-sensitive functionalities to the liposomes [24,27].

Active targeting

The active targeting involves surface modification of drug carriers by conjugating ligands including proteins, glycolipids, peptides, polysaccharides, glycoproteins, aptamers and monoclonal antibodies which specifically attach to receptors exist at the target site [7,14,20,28].

MAbs are amongst one of the most frequently used legends as active targeting agents [7,18,29].

In summary, as a result of research for the half century on different approaches to develop targeted drug delivery systems and multifunctional nanoparticles, the advantages are clearly demonstrated. However, still there are long way to achieve an ideal targeted drug delivery systems for clinical use [21,30].

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