number of studies that compared the efficiency of active and passive targeting.

2. ACTIVE TARGETING

It is very important that in the treatment of cancer or other diseases, drugs or drug formulations reach the target tissues and cells in a very specific way and do not have any adverse effect on the surrounding normal cells. In active drug targeting, drug-containing nanoparticles reach specifically to the target tissue or cells by attaching ligands that have over-expressed receptors on the target cells surface. Cancer cell receptors that are overexpressed on cancer cells to receive nutrients are different from healthy cell receptors [4, 5]. Many of these receptors have been identified and their associated ligands have been made [3]. Interaction between attached ligands to the nanoparticles surface and related receptors on the cell surface facilitates the uptake and internalization process of drug-containing nanoparticles into the cells [6]. Actually, using this targeting strategy increases the specificity of drug delivery and avoiding the side effects.

2.1. Receptor-Mediated Active Targeting

The development of targeted drug delivery methods has led to increased drug uptake by the target cells [7]. One amazing strategy is to bind ligands to the drug carrier that interacts specifically with the target region (receptors that are overexpressed on the diseased cells) and thus the drug is specifically delivered to the target region. Drug delivery through targeting of receptors on the cell surface is a wonderful way to specific drug delivery and also to accumulate drug in the diseased site [8]. A key issue that ensures the safety of the targeted drug is the high expression of the targeted receptor in the target cells relative to the surrounding normal cells. Target receptor expression levels must be more than three times higher than a normal condition to deliver the drug formulation specifically to the target region [9]. In selecting the appropriate ligand for targeting a receptor, the ligand size is an important factor because this feature may lead to a good or bad event in conjunction with other factors [10–12]. In receptor-mediated drug delivery, a thorough understanding of the structure and biochemistry of the target receptor is essential. A number of receptors that can be used as therapeutic targets on different types of cancer cells including FA receptor, integrin αvβ3 and epidermal growth factor receptor (EGFR), which have high expression on the cancer cells surface, such as lung, breast, ovary, brain, and colon cancer.

2.1.1. Folic acid receptor

The FA receptor (40-40 kDa) is a member of the glycoprotein family and has three isoforms including alpha (α), beta (β), and gamma (γ). The first two isoforms are attached to the cell membrane but the third isoform is found in hematopoietic cells [9, 13, 14]. Actually, the FA receptor is a cysteine-rich glycoprotein and its normal function is to bind to the FA and internalize it into the cell. FA is essential for the synthesis, methylation, and repair of DNA molecules. The alpha isoform of the FA receptor is overexpressed in a number of cancers on the surface of cells [15, 16]. As will be discussed in this chapter, FA receptor on cancer cells has been studied as a therapeutic target in a number of studies.

2.1.2. Integrin αvβ3

Integrins are cell surface proteins that are involved in cell attachment to the extracellular matrix (ECM). Moreover, integrin receptors play an important role in sending messages to cells, regulating cell morphology, cell migration and also metastasis of cancer cells. Integrins are heterodimers of alpha and beta subunits. The αVβ3 integrin which expressed by platelets is composed of two parts: integrin alpha V and integrin beta 3 and is a receptor for vitronectin. Abnormal expression of v3 is associated with the prevalence of many diseases so it can be used as a therapeutic target in the treatment of various diseases [17–20].

2.1.3. Epidermal growth factor-receptor

EGFR, also known in human as human epidermal growth factor receptor 1 (HER1) or ErbB-1, is a transmembrane protein that is a member of the ErbB family of tyrosine kinase receptors. This receptor is often highly expressed on the surface of epithelial cancer cells. Binding of ligands such as EGF to EGFR leads to EGFR dimerization and tyrosine autophosphorylation, which activates intracellular pathways that are critical for the maintenance of malignant phenotypes. Defective signaling of tyrosine kinase receptors, especially EGFR, leads to diseases such as Alzheimer's disease, whereas overexpression of these receptors is associated with cancer [21–26]

2.2. Peptides

Peptides are either synthetic or originate from nature and have wide applications in drug delivery, cancer treatment, and diagnosis. Peptides can be used in a variety of roles, such as antibiotics, inhibitors, and hormones [27]. Peptides have attracted much attention because of their superiorities such as small size, lower immunogenicity, stability, easy synthesis and low cost, and most importantly easy attachment on the surface