Chapter 12
Targeted Drug Delivery in Cancer Treatment

Farhad Bano
National Institute of Immunology, New Delhi, India

Khalid Umar Fakhri
https://orcid.org/0000-0001-6978-8172
Department of Biosciences, Jamia Millia Islamia, New Delhi, India

M. Moshahid Alam Rizvi
Department of Biosciences, Jamia Millia Islamia, New Delhi, India

ABSTRACT

In a conventional oral or intravascular drug delivery approach, therapeutic factors are distributed throughout the body and only a limited part of the drug reaches to tumor site. Packaging of cytotoxic agents in drug delivery systems like nanoparticles could enhance its delivery to specific targets in the tumors and could be potential candidate for therapeutics advancement. Targeted drug delivery holds the potential to overcome the present therapeutics of cancer by selective delivery of an arbitrary amount of drug at the tumor site. Loading of cytotoxic agents in drug delivery systems could enhance its delivery to specific targets based on strategy to reach the tumor site. This chapter explores the detailed of innovative methods of drug delivery, challenges of targeted drug delivery, and their implications.

INTRODUCTION

Cancer is the second most leading cause of death in the world, estimated 9.6 million deaths in 2018 (World Health Organization). The treatment of cancer is based on surgery, radiotherapy, hormone therapy, and mainly chemotherapy. The radiation therapy induces DNA damage and kills cells within the localized tumor microenvironment. (Baudino et al. 2015). Chemotherapy is widely used treatment for cancer patients, produce systemic toxicity to not only growing and dividing cancer cells but also to proliferating normal cells. Success rate of present therapeutics remains low due to limited accessibility

DOI: 10.4018/978-1-7998-6530-8.ch012

of therapeutic drugs at tumor site, non-target killing of normal cells, undesirable side effects, intolerable toxicity, development of multi-drug resistance and the dynamic heterogeneity of the growing tumors (Vasir and Labhasetwar, 2005; Bahrami et al., 2017).

Targeted drug delivery holds potential to overcome the demerits of present therapeutics of cancer by accumulating the arbitrary amount of drug at particular tumor site translating the Paul Ehrlich's "magic bullet" concept in cancer therapy (Strebhardt and Ullrich, 2008). The magic bullet strategy of drug delivery in cancer seeks attraction in the preferential killing of cancer cells without any toxicity to normal healthy cells. This could be achieved by coupling cytotoxic agents with targeting ligands or entrapment of the drug into ligand-directed delivery systems to enhance its accumulation at designated target (Bahrami et al., 2017; Senapati et al., 2018). Furthermore, direct conjugation of drugs to the targeting ligand could directly impact the ligand and receptor interaction and potentially able to alter the characteristics of the drug. A receptor-directed drug delivery system is an emerging strategy in development of cancer therapy (Yu et al., 2010). The therapeutic efficacy of present drugs could be improved through this approach by specifically killing of the cancer cells by direct toxic action of drug or indirectly due to bystander effect of the therapy. This chapter explores the detailed of innovative methods of drug delivery, challenges of targeted drug delivery and their implications.

STRATEGY OF DRUG DELIVERY

The loading of cytotoxic agents in drug delivery systems increase its penetrance to cellular barriers, prevent the leakage to normal healthy cells, enhance controlled drug release and reduce side effect. Moreover, delivery of drugs through carriers overcome the multidrug resistance (MDR) caused by P-glycoprotein, drug efflux transporters frequently overexpressed in tumor cells (Piddock 2006; Yu et al., 2010). The delivery of drug carriers to specific targets is based on different strategy to reach the tumor site: Passive targeting or active targeting.

Passive Targeting

Passive targeting of drugs carriers could be done due to its specific physiological conditions of tumors including hypoxia, abnormal vasculature, temperature, pH, and surface charge of tumor cells. The increased penetrance of drug carriers in tumors is favored by enhanced permeability and retention (EPR) effect, which is firstly reported in 1986 (Matsumura and Maeda, 1986). The unchecked growth of tumor requires continuous oxygen and nutrient supply that is fueled by continued angiogenesis resulting poor vascularization (Hanahan and Weinberg, 2000). The chaotic and poorly formed new blood vessels often got leaky and allow increased mass transport of macromolecules, such as drug carriers, into the tumor (Maeda et al., 2000). This is coupled with impaired lymphatic drainage that enhanced the accumulation and retention of drug carriers in tumor cells (Leu et al., 2000).

Although passive targeting is interesting approach, however, it suffers from the serious limitations such as limited drug diffusion into tumor cells, the random nature of targeting, and the lack of EPR effect in some tumors.