Introduction

In today’s day and age, various drug delivery systems have evolved along with the development and research of varied chemotherapeutic agents to ensure safer delivery of these agents to achieve optimal clinically efficacious response. Currently used anticancer drugs suffer from a myriad of problems such as extremely low aqueous solubility, lack of stability, nonspecific drug accumulation, which eventually leads to toxicity issues. Additionally, low bioavailability along with organ toxicity causes a major limiting factor for the maximum tolerated dose. These combinations of drug delivery systems along with the chemotherapeutic agents have led to the alleviation of multiple indications in various cancers, thus leading to a more clinically enhanced response, as compared to the chemotherapeutic agents alone [1]. One of the classic examples is liposomal Doxorubicin used to treat AIDS-related Kaposi’s sarcoma and ovarian cancer which has undergone clinical approval [2,3]. Other drugs encapsulated in liposomes are currently undergoing clinical trials or have been approved for clinical use such as Daunoxome (Liposomal Doxorubicin) used to treat AIDS-related Kaposi’s sarcoma [4,5] or Depocyt (Liposomal Cytarabine) used to treat lymphomatous meningitis [6]. Other approved products include Abraxane (Albumin bound Paclitaxel) used to treat metastatic breast cancer [7] and Marqibo (Liposomal Vincristine) used to treat acute lymphoblastic leukemia [8]. Other approved products include Genexol-PM [(Methoxy-PEG-poly (D,L-lactide) taxol] which has been approved in S. Korea for metastatic breast cancer and Oncaspar® (PEG-L-asparaginase; Enzon) which was approved by FDA in 2006 for Acute Lymphoblastic Leukemia.

Nanoparticulate Systems in Tumor Targeting

Nanoparticles will be able to deliver a precise dose of the drug in the tumor region due to the enhanced permeability and retention effect. General features of the tumors include leaky blood vessels and extremely poor lymphatic drainage. Free drugs are known to diffuse non-specifically; however, nanoparticles accumulate at the specific target site with the aforementioned enhanced permeability and retention effect.

With the aid of optimized targeting ligands on their surface, nanoparticles will be able to deliver the payload at the tumor site and even reduce its distribution to the peripheral tissues. For example, in a breast cancer model, a receptor density of not less than 12 drug-polymer conjugates have entered Phase I and II clinical trials for targeting blood vessels in tumors. Despite the myriad drug targets and a host of chemistries available, only four drugs namely Doxorubicin, Camptothecin, Paclitaxel and Platinate and some polymers such as Polyethylene Glycol (PEG), poly-L-glutamic acid, and HPMA and Dextran have been often used to develop polymer-drug conjugates [16].

Conclusion

The choice of optimal nanocarriers has to be extremely judicious considering its overall pharmacokinetic profile and factors which may influence the efficacy and biodistribution of the delivery system. Developing robust methods for high throughput screening of these nanocarriers is extremely laborious and time consuming. In addition, strategies have to be designed in the initial phases to avoid the uptake of these nanocarriers by the Reticulo-Endothelial System (RES). However, because of the diligent investigative research, a large number of clinical
trials are underway with various antibody containing nanocarriers formulations. Biological targets, whether it be cell surface markers or tumor vasculature or the extracellular matrix surrounding the tumor microenvironment always pose monumental challenges. An optimistic era of research will usher in significant amounts of progress in both the diagnostic and therapeutic potential of these nanocarriers.

References


