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Advances in Drug Delivery Strategies for Cancer Therapeutics

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Introduction

In spite of intensive research is being reported on cancer and its therapy, still it is identified as a leading killer worldwide. It is reported that around 7 million deaths occur every year and WHO (2007) estimated that around 16 million new cancer cases will be detected every year by 2020. The major cancer mortality by all types of cancer is stomach, lung, colon, liver and breast cancers. The carcinogens such as tobacco, smoke, infectious or chemical agents and radiation leads to genetic abnormalities and causes cancer. Different treatment approaches available currently and under evolution are based on surgical removal of malignant cells, radiation therapy, chemotherapy, target and immunotherapy [1]. The treatment approach is decided based on location, stage and grade of the tumor including general state of the patient, but chemotherapy has been observed as one of the best way to treat cancer. The success of treatment depends on types of drug delivery carrier system selected and their target approach.

Ideal Characteristics of Cancer Chemotherapy

Although many approaches are in use for cancer therapy, chemotherapy is considered as best approach to treat cancer. The main objective of ideal cancer chemotherapy is delivering the adequate amount of drug in a predetermined rate and time to the infected cells or organs without affecting the normal cells to get the required therapeutic action. To achieve this goal, drug delivery systems are designed in such a way that, they must maintain sufficient amount of therapeutic agent at the site of action without producing drug resistance either on cellular or non-cellular mechanism, distorted bio distribution / bio transformation and exit of drug from the biological system. In this context, drug delivery systems must be able to prolong the systemic circulation, sufficient tumor accumulation and controlled release pattern without altering the pharmacodynamics of the therapeutic agents. The intravenous injection of cancer therapeutics by conventional chemotherapy are assumed to be distributed throughout the body via systemic circulation, and affects both tumor and non-tumor normal cells [2]. But, such conventional chemotherapy with intravenous administration leads to severe side effects, high patient risks, repeated treatments, distorted bio distribution and the acquisition of multidrug resistance by the cancer cells [3]. Development of multi drug resistance by malignant cells limits the successful treatment of cancer chemotherapy. Inclusion or co-administration of P-glycoprotein inhibitors with encapsulated anticancer drugs in nanoparticles have been proposed to prevent P-glycoprotein mediated multi drug resistance [4]. Cancer chemotherapeutics exhibit a nature of rapid blood clearance by the reticuloendothelial system which leads to poor cancer therapy. This problem can be rectified by PEGylation of the delivery system. The polyethyleneglycol (PEG) coated liposome was found to be had significantly increased half-life of cancer chemotherapeutics in the blood [5].

Chemotherapy via Drug Targeting

The limitations of conventional chemotherapy with anticancer drugs namely lack of tumor selectivity, random distribution and low therapeutic index generally leads to severe side effects. The tumor selectivity of anticancer drugs can be improved by developing conjugates bearing tumor-specific antibodies or peptides [6]. However, even in absence of targeting approach of macromolecular drug delivery system with prolonged systemic circulation can also be accumulated by passive retention action [7]. In order to avoid problems associated conventional cancer chemotherapy advanced nanotechnological based targeted therapy has been exploited. The nanotechnological based target system includes nanocrystals, nanotubes, liposomes, nanofibers, nanorods, etc., which are said to be able to selective and effective retention of cancer therapeutics at pre-identified targets in sufficient therapeutic amount without affecting normal non-targeted cells and thus reduce toxicity, maximize therapeutic index and improves the bio distribution of drug which is a major factor in success of cancer chemotherapy. Therapeutic monoclonal antibodies have mostly been utilized without any conjugates in cancer therapy [8]. The concept of therapeutic monoclonal antibodies was reported by Nadler et al. against lymphoma cells for effective human cancer therapy [9] and the Orthoclone OKT3®) a first FDA approved TMA came in existence in September 1992 with slow but steady introduction of additional antibodies into the clinic. The development of antibody drug conjugates was considered parallel to therapeutic monoclonal antibodies which are considered much better for their targeting advantages with cytotoxic potential of chemotherapy. During early eighties intensive research effort was put in the development of peptide therapeutics, but only selected products came in the market. To date several peptide drug conjugates for tumor therapy have been developed but yet to receive regulatory approval. The peptide drug conjugate to be used for the treatment of advanced solid tumor in brain metastases is under clinical trial [10].

Conclusion

With the above brief discussion about cancer therapy via targeting approach it can be clearly concluded that targeted therapy is on the edge for vivid future. The various approaches such as therapeutic monoclonal antibodies, antibody drug conjugates and peptide drug conjugates shows their own merits and demerits and better understanding of these strategies may allow a more rational selection of therapy approaches. The issues related with safety, efficacy, toxicity accumulation and removal of cancer therapeutic moiety are significant aspects of targeted drug delivery systems. Thus, in near future, the

entire health care team along with patients can expect a variety of alternatives from which to select a more effective and economic targeted treatment for a particular cancer type.

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