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Nanoparticles -Based drug delivery system for cancer therapy

Sejal Bhosale[1*], Jayesh Pati[2]
[1] Department of Pharmaceutics, Delonix Society's Baramati College of Pharmacy, Barhanpur, Madhya Pradesh, India
[2] Department of Pharmaceutics, Dr. Babasaheb Ambedkar Technological University, Lonere, Madhya Pradesh, India

Abstract
Nanoparticle based drug delivery system is considered optimistic for neoplasia treatment. It shows greater potency by enhancing half life of drug and proteins by enhancing the solubility of lipophilic drugs by permeating controlled and targeted release of drug in diseased site. Nanoparticle based drug delivery system is mostly beneficial for tumor treatment. The ability to treat tumor by agiogenesis also discussed. Patients treated with conventional drug therapy for tumor surfers from adverse impact of drugs due to non- selective action of chemotherapeutic drugs to normal cells.

Keywords: Nanoparticle, malignant tumor, neoplasia, chemotherapy, oncogenes, agiogenesis

Introduction

Cancer is also known as Malignant Tumor, tumor means the swelling or the mass of cells. In the tumor condition a normal cell abundantly grow and spread in all over the body. It is a genetic disorder, there are some reasons that are responsible for the formation of malignant tumor, that are:
Delusion that causes cell division.
Damage to DNA by harmful substances present in environment such as tobacco, smoking, UVRadiations from sun.
It is genetic from our parents.
Cancer is the world's deadliest disease of human beings [1]. In GLOBOCAN 2012 approximately 14.1million new cancer cases per year in world which would be expected to increases to 19.3 million new cancer causes per year by 2025 [1]. In the drug therapy for cancer four methods are involved that are "Surgery, radiation, chemotherapy and immunotherapy" which are globally used for cancer therapy. However high toxicity, low oral bioavailability, poorly water solubility, narrow therapeutic index, inconsistency in circulation, delivery of an antineoplastic drug to normal and tumor cells are the key shortcoming of convention Cancer therapy. [2, 3] Main objective of chemotherapy and radiation is to destroy the tumor cells are more vulnerable to action of these drugs and methods because of their growth as much rapid than normal healthy cells at least in adults.In all cases, the benefit of the treatment is directly related to the treatment's ability to target and to destroy the cancer cells while affecting as few healthy cells as possible. The degree of alteration in the patient's quality of life and ultimately life expectancy is directlyrelated to this targeting ability of the treatment.

Types of genes that causes cancer

Change in the genetic structure contribute to cancer leads to affect main three types of genes- proto-oncogenes, tumor suppressor genes and the DNA repair genes.

1. Proto-oncogenes related to the normal cell growth and cell division. If these genes are changes to cancer causing genes or oncogenes permeating the cells to grow and remain alive when they should not.
2. Tumour suppressor genes also get participated to normal cell growth and cell division. Cells with certain changes in these genes may divide in an uncontrolled manner.
3. In the DNA repair genes they get involved in the repairing damaged DNA.

Metastatic

In metastasis, the tumor cells break from where they formed first and forms a new tumors to the other body parts.

Types of cancer

1. Carcinoma: It is the most general type of cancer. Formed by epithelial cells, that cover the inside and outside surface of body.

Different types of carcinoma

- **Adenocarcinoma:** Form in epithelial cells which forms fluids or mucus. Basal cell carcinoma- Begins in lower layer of epidermis that is a outer layer of a skin.
- **Squamous cell carcinoma:** Forms in a squamous cells that are present beneath the outer layer of the skin.
- **Transitional cell carcinoma:** Forms in the transitional epithelium or urothelium

2. Sarcoma: These type of cancer that forms in bone and the soft tissues, including muscles, fat, blood vessels, lymph vessels and fibrous tissues.

3. Leukemia: it is started in the blood forming tissues of bone marrow know as leukaemias. In these type of cancer there is not a formation of solid tumors instead of that huge number of abnormal white blood cells are formed in blood and the bone marrow.

4. Lymphoma: Started in lymphovytesi.e T cells and B cells. There is abnormal lymphocytes forms in lymph nodes and lymph vessels and also in organs in the body.

5. Multiple Myeloma: Cancer in plasma cells.
Abnormal growth of plasma cells know as Myeloma cells which are built up in bone marrow and forms tumor in bone throughout the body.

6. Myeloma: Cancer begins in melanocytes that are the special cells which makes melanin (pigment responsible for the color of the skin).

Angiogenesis is a process vital to the continued Development of a tumormass.This process has been subject of intense research due to its role in Cancer development and has proven to be the result of numerous interactions between regulators, mediators and stimulatory molecules. Timeline for the development of nanoparticle drug delivery systems.Nanoparticles are currently studied for their use in detection of Cancer at its earlier stage The critical step in cancer treatment Is the detection of cancer at its initial stage of carcinogenesis. Results of the numerous researches done in nanotechnology are inspiring the scientific community to discover new innovative non- Invasive tools at the nanoscale level for such purposes. The most common examples of Nano carriers for the delivery of chemotherapeutics include liposomes, polymeric Angiogenesis–a process vital to the continued Development of a tumormass.This process has been subject of intense research due to its role in Cancer development and has proven to be the result of numerous interactions between regulators, mediators and stimulatory molecules. [4] Timeline for the development of nanoparticle drug delivery systems.Nanoparticles are currently studied for their use in detection of Cancer at its earlier stage The critical step in cancer treatment Is the detection of cancer at its initial stage of carcinogenesis. Results of the numerous researches done in nanotechnology are inspiring the scientific community to discover new innovative noninvasive tools at the nanoscale level for such purposes. [5, 6]

Antineoplastic agents

Calprotectin-based drugs, specifically irinotecanb (Composer) and topotecan (Hamptin) have been Approved by the FDA and are used most often either In conjunction with 5-fluorouracil as a first therapy or Sometimes used alone after 5fluorouracil has failed. Analogs of these molecules have shown up to 1000- Fold higher activity but are a great challenge to Delivery because of their extreme hydrophobicity [7]

Advantages of Nano technological drug delivery

Systems the most common examples of Nano carriers for the delivery of chemotherapeutics include liposomes, polymeric,nanoparticles, dendrites, Nano-shells, inorganic, nucleic acid based and magnetic nanoparticles improve the therapeutic index of the loaded chemotherapeutic agents compared to the drugs delivered via conventional dosage forms. Increase drug efficacy by achieving steady state therapeutic levels of drugs over an extended period. Lower drug toxicity due to controlled drug release and Improve drug's pharmacokinetics by increasing drug's Solubility and stability.

The engineered Nano carriers offer various other advantages compared to free.Drug administration, such as

1. Nanometre size range suitable For tumour targeting via EPR effect
2. Protective insulation of Drug molecules to enhance their stability and minimize their Systemic clearance
3. Ability for surface functionalization

Possibility of multiple drug delivery to achieve synergistic therapeutic response (iv) Opportunity for the application of combination therapy by utilizing chemotherapeutic and Photothermal effects, or creating magnetic nanostructures Making delivery of NPs easier with the application of an External magnetic field [8]. The parameters such as size, conformation, noncovalent Interactions and surface adsorption would have remarkable Effects and variations on the interaction between the Nanocarrier and the biological environment [9, 10]. For Example, size of the NPs is critical for their renal and liver Excretion: kidney filters particles smaller than 10 nm (about 70 kDa) and the liver can capture particles of diameter larger Than 50 nm. For this reason, the size of an ideal nanocarrier Must be in the range of 10–50 nm [11]. In addition, surface Characteristics of NPs influence their uptake and clearance *In vivo*. NP clearance occurs mainly via opsonization and Phagocytosis By macrophages following the mechanism of Receptor-mediated endocytosis [14, 12]. To delay degradation, Surface of the NPs has been decorated using a biocompatible and nonimmunogenic hydrophilic polymer, poly (ethylene Glycol) (PEG) that reduces nanoparticle binding to opsonins, Avoiding reticuloendothelial degradation [13]

Obstacles of nanoparticles for clinical use

1. Scaling up problems

Chitosan is also highly Susceptible to environmental factors: exposure to high relative humidity (>60%) can result in a significant Increase in water content of chitosan, Lowering its mechanical properties [15, 16]; exposure to high temperature (>40 C) can increase the degradation rate of chitosan [17, 18].

2. Toxicity and biodistribution

Nanoparticles have many unique properties that are different from Bulk materials. Therefore, the toxicological profile of the nanoparticles is Not the same as the bulk materials [19]

3. Poor control over loading and releasing of drugs

For many polymeric nanoparticles, a low rate of drug loading is one of The major pitfalls [20, 21]. Many studies have reported a loading rate of Less than 10% [22–23]. Initial burst release is also a big concern for Nanoparticles as drug delivery systems. It often happens during the first Few minutes when the nanoparticles contact the external environment [24]

Future of nanoparticles as drug delivery system

Nanoparticles have many advantages compared with traditional drug Delivery strategies. However, for wider application of nanoparticles in The pharmaceutical market, more *in vivo* studies and clinical trials are Needed to understand the toxicity And long-term biological behavior of Nanoparticles.

The development of multi-functional nanoparticles is also a blooming Research field. This field is driven by the growing medical needs. During cancer treatment, nanoparticles are needed to not only deliver Drugs but also to provide diagnosis and drug monitoring. One example Could be image-guided drug delivery, which incorporates magnetic Resonance imaging (MRI) with drug delivery nanoparticles to monitor the Bio distribution, circulation, and targeting behaviour of nanoparticles. The Formation of a hydrating layer on the nanoparticles can help increase the Circulation lifetimes after intravascular injection. Another top-down Biomimetic approach, cell membrane coated nanoparticles, has also Been intensively researched [25–30].

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