Indian Journal of Advances in Chemical Science

Review Article

Nanotechnology: A Modern Weapon to Conquer Cancer

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ABSTRACT

Cancer is one of the most serious fatal diseases that kill millions of people every year. It involves abnormal growth of cells which can easily invade the neighboring cells. To improve the lifespan of cancer patients', new technologies are always under consideration. Nanotechnology is one of the innovative methods which target the tumor site without affecting normal cells. More recently revolutionary advancement has been made using nanotechnology for cancer diagnosis and treatment. This review paper highlights the potential use of nanotechnology in cancer. This paper also emphasizes cancer drug delivery, cancer drug targeting, applications in cancer diagnosis, and treatment with their benefits. Recent advances in nanoparticles probes for molecular and cellular imaging might help the oncologist to detect and treat cancer patients with an eagle eye view.

Key words: Nanotechnology, Cancer, Nanoparticles, Passive targeting, Active targeting, Nanomedicine.

1. INTRODUCTION

Cancer is the rapid multiplication of abnormal cells that grow beyond their usual boundaries and spread to other parts of the body. In the human body, which is made up of trillions of cells, cancer can start almost anywhere. It is a genetic disease that is caused due to changes in genes that control the functioning of cells, especially their growth and division [1]. Radiation therapy, chemotherapy, and surgery are the major procedure in cancer treatment. All these three methods (surgery, radiation, and chemotherapy) are currently used in cancer therapies and all these methods are very risky because they may damage the normal tissues or there may be incomplete eradication of cancer [2,3].

When it comes to the innovation of new technologies, drug treatments are always under consideration to improve the symptoms and lifespan of cancer patients [2]. Nanotechnology has the ability to engineer materials that can be at the scale of nanometer (nm) [4]. The nanoparticles are used in medical treatment which has specific shapes, sizes, and surface characteristics; these three aspects influence the efficiency of nano-drug delivery and also control the therapeutic efficiency [5].

Nanotechnology offers the means to aim chemotherapies straightaway and selectively to cancerous cells or neoplasm upgrade the therapeutics efficiency of radiation-based or lead in surgical resection of the tumors.

A chemically modifiable surface to adhere with lots of ligands that could convert them into biosensors, molecular-scale fluorescent tags, targeted molecular delivery vehicles, imaging agents, and different beneficial biological tools are designed in nanoparticles [6]. Some therapeutic uses of nanotechnology in cancer are shown in Figure 1.

Nanotechnology has majorly revolutionized the diagnosis and treatment of cancer. Tumor localization, tumor margin detection, identification of important adjacent structures, mapping of sentinel lymph nodes, and detection of residual tumor cells or micro-metastases are the processes of cancer diagnosis that includes nanotechnology. During the treatment process, the nanoparticles' goal is to transport drugs, radiotherapy, phototherapy, and immunotherapy [5,6].

2. CANCER DIAGNOSIS THROUGH NANOPARTICLES

Nanotechnology comes up with high specificity, sensitivity, and complex measurement capacity. Therefore, it helps in the detection of extracellular cancer biomarkers and *in vivo* imaging. At present, imaging techniques, histopathology, or cytology facilitate in early detection of cancer. The most used imaging techniques, such as endoscopy, X-ray, magnetic resonance imaging, computed tomography, and ultrasound can diagnose cancer. For diagnosis of cancer, nanoparticles are applied to seize cancer biomarkers such as circulating tumor cells, circulating tumor DNA, and exosomes. The large surface area of nanoparticles facilitates easy adhesion of peptides, antibodies, small molecules, and other components. These components later can bind and recognize specific cancer molecules. Nanotechnology-based detection methods are developed as an encouraging tool for cost-effective cancer diagnosis [7].

3. DIFFERENT STRATEGIES TO TARGET CANCER CELLS USING NANOPARTICLES

Nanomaterials are highly useful in targeted delivery and can overcome complications associated with conventional free anticancer drugs treatment. Several studies have explored different strategies such as passive and active targeting cancer cells [8]. Figure 2 shows the mechanism of passive and active targeting of cancer cells using nanoparticles.

3.1. Passive Targeting

Passive targeting is the assemblage of macromolecules including nanoparticles in the neoplastic tissues. This process depends on enhanced

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ISSN NO: 2320-0898 (p); 2320-0928 (e)
DOI: 10.22607/IJACS.2021.904025

Received: 08th October 2021;
Revised: 12th October 2021;
Accepted: 21st October 2021

permeability and retention (EPR) effect, tumor microenvironment, and tumor pH to deliver therapeutics agents from the nanocarrier. In this technique, drug targeting occurs because of the body's natural response to physicochemical characteristics of the drug or drug carrier system. Pioneer nanoscale technology for passive targeting was based on liposomes. In advanced studies, liposomes are coated with a synthetic polymer that protects the agents from immune destruction. Although, passive targeting forms the basis of clinical therapy it has some limitations like in tumors, targeting cells are not always feasible diffuse because of the gap between endothelial cells [9,10].

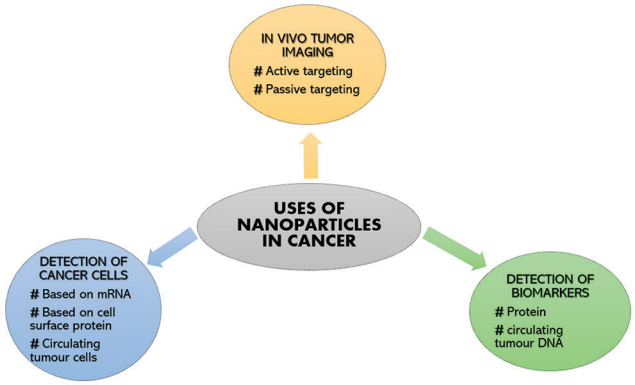

Figure 1: Therapeutic uses of nanotechnology in cancer.

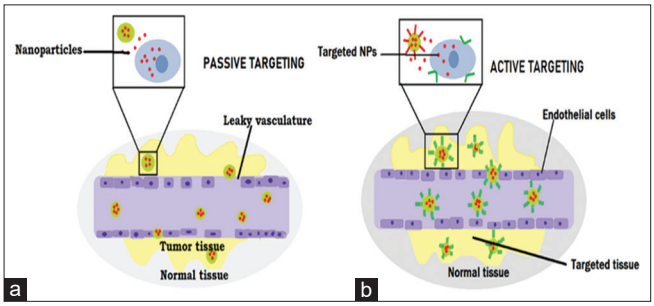

Figure 2: (a) The mechanism of passive targeting [9]. (b) The mechanism of active targeting [9].

3.2. Active Targeting

The term "active targeting" defines a specific interaction between ligand-receptors which occur at the target site after reaching through blood circulation and exudation. Active targeting overcomes the limitations of passive targeting is to attach affinity ligands (peptides, antigen-antibody interaction, ligand-receptor, and aptamers) that only bind to the surface of the nanocarrier by a variety of ligands. To gain high specificity, receptors should be highly expressed in tumor cells.

Despite the advantages, active targeting also faces some limitations. Mostly, the targeting ligand may expose the NP carrier system to reticuloendothelial system. As a result, a higher compilation of NPs occurs in unwanted organs over the expected ones. Nanodrugs are currently under clinical development lack specific targeting. To obtain clinical benefits, the active targeting with NPs may follow a disease-driven approach [11].

4. LIST OF SOME APPROVED NANOMEDICINES FOR CANCER

Newly developed TNPs have shown greater anticancer efficacy and lower toxicity than their corresponding free agents. Some TNPs are already approved by the FDA for clinical use (Table 1). Some advantages of nanomedicines over other cancer therapeutics –

- Nanosystems can attach to multivalent targeting ligands which succumb to high affinity or particularity for target cells.
- Nanosystems can bypass traditional drug resistance mechanisms by active or passive targeting.
- Nanosystems can have diagnostics and therapeutics properties [12].

5. CHALLENGES WHILE USING NANOPARTICLES

- Sometimes, oxidative stress and lung inflammations can result from the free radical or oxidative activity of nanoparticles [14].

Table 1: Some approved nanomedicines for cancer [13].

Year of approval	Drug name	Nanoparticle used	Product name	Approved against
1995	Doxorubicin	Liposomes	Doxil	Kaposi's sarcoma
1996	Daunorubicin	Liposomes	DaunoXome	Kaposi's sarcoma related to HIV
1998	Doxorubicin	Liposome	Lipo-dox	Ovarian and Breast cancer, Kaposi's sarcoma
1999	Cytarabine	Liposome	DepoCyt	Neoplastic/Lymphomatous meningitis
1999	Doxorubicin	Liposome	Doxil	Ovarian cancer
2000	Doxorubicin	Liposome	Myocet	Breast Cancer
2005	Paclitaxel	Nanoparticle-bound albumin	Abraxane	Metastatic breast (secondary) and Metastatic pancreatic (primary) cancer, Advanced non-small cell lung cancer
2006	L-Asparaginase	Polymeric conjugates	Oncaspar	Lymphoblastic Leukemia
2007	Doxorubicin	Liposomes	Doxil	Multiple myeloma and Breast cancer
2007	Paclitaxel	PEG-PLA Polymeric micelle	Genexol-PM	Ovarian and Breast cancer and Non-small cell lung cancer
2009	Mifamurtide	Liposome	Mepact	Osteosarcoma
2011	Eribulin Mesylate	Liposome	Halaven	Breast neoplasms and Liposarcoma
2012	Vincristine	Liposome	Marqibo	Acute Lymphoid Leukemia
2015	Irinotecan	Liposome	Onivyde	Pancreatic cancer
2016	Mitoxantrone	Liposome	Novantrone	Breast cancer and Lymphoma

- It may also lead to genotoxicity [15].
- Oxidative stress and cell injury, leading to alterations in hepatic production of clotting factors, inflammation, and systemic thrombosis is also caused by the nanodrugs which were induced in rat livers [16].
- Neurotoxicity may also occur when few nanoparticles tend to cross the blood-brain barrier through the intravenous route.
- Nanoparticle neurotoxicity both *in vitro* and *in vivo* can also be seen [17].

6. CONCLUSION

Nanotechnology has shown a lot of potential in cancer therapy over the years. By their improved pharmacodynamics and pharmacokinetic properties, nanotechnology has contributed to improved cancer diagnosis and therapy. Modern cancer treatment focuses on precise drug delivery to the cancerous cells and reduces the adverse effects on healthy cells. By improving the interaction between the physiochemical property of the nanotechnology working and more effective for diagnosis and therapy can be made available for cancer care. The future advancements and the therapeutic benefits of nanotechnology could make them a therapeutic potential to be used in other disease conditions. Nanoparticles can be considered as the future of cancer treatment. The prospering field of nanotheranostics is promising the convenient early diagnosis and therapy of various diseases, particularly cancer, and is providing personalized oncology/medicine, and is opening gates for further investigation of cancer. Biocompatibility and toxicity of nanoparticles are to be studied for safer use in biomedicine or cancer medicine. Oxidative distress and inflammation in the lung, coagulation factor production in rat liver, and neurotoxicity caused by nanoparticles are still part of the present research.

7. ACKNOWLEDGMENT

The authors are highly indebted to the President, Principal, and to the Department of Biotechnology, Isabella Thoburn College, Lucknow, India, for their great support and encouragement to complete this manuscript.

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