An Overview of the Application of Nanoscience in Cancer Diagnosis and Treatment

Salman Sheikhi Master's Degree in Medical Nanotechnology, Islamic Azad

University, Medical Sciences Branch, Tehran.

Negar Asghari Hosori Master's Degree in Nanobiotechnology, Shahid Beheshti

University, Tehran.

Saeed Yari Ph.D. of Environmental Engineering-Air Pollution, Tehran

University, Tehran, Iran.

Cancer is one of the most common causes of death. One of the most important problems in cancer treatment is the side effects of drugs and treatments. The limiting factor in cancer treatment is the lack of selectivity of drugs against cancer cells. Today, nanotechnology has been able to help in the diagnosis and treatment of this disease because most biological processes such as the creation of cancer occur in nano dimensions, therefore, in order to reduce side effects and improve existing drugs, various drug delivery systems based on nanotechnology have been developed. Cancer researchers use the ability of nanotechnology to evaluate cells and achieve the following goals: 1- Simulating the reaction of cells with protein and nucleic acids at the molecular level, and then obtaining a proper knowledge of cell behavior. 2- Studying the structure and function of intracellular proteins and research in the field of proteomics. 3- Initial determination of cancer. This article is written based on reviews of various articles in reputable journals and books related to the use of nanotechnology in cancer treatment. The selection of sources is based on suitability to the topic, year of research, non-repetition and comprehensiveness of the content. The effective treatment of cancer with the least side effects is considered one of the challenges of medical and pharmaceutical sciences, and the introduction of nanotechnology into therapeutic fields promises the production of a new group of anti-cancer drugs that provide diagnostic and therapeutic capabilities simultaneously. These structures have a special place in cancer treatment as drug carriers and optically and thermally active substance

Introduction

Cancer is a complex disease characterized by the uncontrolled growth of cells and the spread of these abnormal cells in the body, causing the death of more than 9.6 million people worldwide. world only in 2017 [1]. The application of nanotechnology to medical science involves the use of very small particles from 1 to 100 nm, which has created a new branch of cancer science called nano-oncology [2, 3]. Advances in cancer nanotechnology will offer unique opportunities to simultaneously identify multiple molecular targets in small tumor samples for the application of appropriate therapeutic strategies. The use of nanoparticles in tumor imaging is advancing rapidly and will enable simultaneous identification and targeting of cancer-related antigens. Soon, nanoscience will make a big revolution not only in the field of cancer but at all stages of medical science [4]. This study aims to study and test the applications of nanotechnology in cancer diagnosis and treatment.

Materials and Methods

1/6

This article is written based on reviews of various articles in reputable journals and books on the use of nanotechnology in cancer treatment. The selection of sources is based on suitability to the topic, year of research, non-repetition, and comprehensiveness of the content. Different databases were used to collect and summarize information. Research and review articles were determined and analyzed using related keywords such as nanoscience, medical nanotechnology, cancer, drug carriers, cancer treatment, and diagnosis.

Nanoparticles are widely applied in cancer diagnosis and treatment

Nanotechnology has been developed to improve clinical diagnosis through increased sensitivity and early detection of cancer. Different types of nanomaterials are used in cancer diagnosis, such as quantum dots, polymer nanoparticles, carbon nanotubes, and dendrimers. To enhance the cancer detection capabilities of nanoparticles, they can be combined with aptamers, carbohydrates, antibodies, peptides, and other small molecules to specifically target molecules to reach the target site. pepper. For example, when breast carcinoma cells are detected, anti-cancer antibodies are conjugated to polyethylene glycol (PEG). This antibody-PEG complex is then attached to the surface of the nanoparticles via the sulfur group located at the distal end of the PEG linker [5].

Platinum nanoparticles

Studies have shown that platinum nanoparticles (PtNPs) have inherent antitumor activity due to their antioxidant capacity, resulting in inhibition of tumor growth. However, several recent studies have reported the toxic effects of platinum nanoparticles due to the size of the nanoparticles, as these nanoparticles were observed to accumulate in major organs and cells [6].

Gold nanoparticles

Gold nanoparticles (AuNPs) possess many unique properties for imaging techniques. In cancer imaging, gold nanoparticles provide a longer circulation time in the blood with the ability to better target tumors for higher-quality detection. AuNPs can be synthesized in many different sizes and shapes and have high flexibility. Furthermore, AuNPs have low cytotoxicity and better biocompatibility, making them promising candidates for clinical applications [7].

Magnetic nanoparticles

Magnetic nanoparticles are non-toxic and biocompatible. They are commonly used as biolabelled conjugates to identify cancer biomarkers. They also have high magnetic properties, whereby the movement of blood particles can be manipulated by an external magnetic field to reach particles near target cells and tissues. The magnetic properties of nanoparticles make them suitable for use in magnetic resonance imaging (MRI) [8]. For example, iron oxide nanoparticles are used in magnetically based cancer therapy, where magnetic spin is used to generate oxygen radicals for cancer detection. Furthermore, these nanoparticles can be remotely manipulated by an external electromagnetic field and induce local toxicity mediated by reactive oxygen and nitrogen species for tumor therapy. This type of treatment causes fewer side effects in normal healthy tissues [9, 10].

Polymer nanoparticles

Polymer nanoparticles (PNPs) have two types of structures, nanocapsules, and nanospheres, and have better mechanical strength, electrical conductivity as well as better optical and thermal

properties. Polymer nanoparticles are widely used in vaccines and tissue engineering. These nanoparticles can protect drug molecules during administration. PNP has been used in optical and magnetic resonance imaging to detect brain cancer. A dendrimer is a three-dimensional core-shell polymer that can cross the blood-brain barrier for better targeting. Polymer-based nanoparticles have disadvantages such as low stability, tendency to agglomeration, and difficult synthesis [11-13].

Metal oxide nanoparticles

Metal oxide nanoparticles including NiO, ZnO, MnO_2 , Fe2O3, TiO2, and Co3O4 are mixed metal oxides that have been recently used in electrochemical analysis to detect biomolecules. The use of metal oxides in the detection of biomolecules offers advantages such as better enzyme biocompatibility, which can improve detection accuracy. Another feature of metal oxide nanoparticles is that they can change their structure, which can affect the electrical and chemical conductive properties of the nanoparticles [14].

Quantum dots

Quantum dots (QDs) are nano-sized crystals capable of transporting electrons. Under UV light, QD can emit light of different colors with very high energy. QDs have an inactive site on their surface where specific antibodies can easily conjugate. Quantum dots are already used in drug delivery and treatment for lung cancer and can help clear up bacterial infections. In addition, conjugated QDs have been shown to inhibit P-glycoprotein gene expression in lung cancer cells by inducing miR-185 and miR-34b. miR-185 and miR-34b are potential targets for the treatment of lung cancer. Besides many benefits, QD also contains heavy metals such as cadmium, which are carcinogenic [15].

Graphene

Graphene is a lattice of regular hexagonal rings. It is very thin, transparent, light, and conducts heat and electricity well, making it an attractive material for imaging and oncology. Graphene also has a large specific surface area, which is useful for anticancer drug delivery due to the presence of π - π and hydrophobic interactions. Graphene oxide is an oxidized derivative of graphene and has been used in cancer therapy, drug delivery, and cellular imaging. In one study, a bright fluorescent probe based on graphene oxide was used to detect glutathione and cancer [16-18].

Fullerene

Fullerenes belong to the Buckminsterfullerene family, whose molecules contain carbon atoms connected by single or double bonds to form a lattice-like structure. Drug molecules can be trapped in the fullerene network for successful drug delivery. In a recent study, it was reported that fullerenes and metal nanomaterials can protect the human body against endogenous and exogenous reactive oxygen species by using their reducing properties. It has also been found that fullerenes and metal nanomaterials can selectively remove diseased cells from tissues and thereby prevent the development of chronic inflammatory diseases. Fullerenes and metal nanomaterials have great potential in the treatment of aging-related disorders [19, 20].

Carbon nanotubes

Carbon nanotubes are made from single-walled carbon. They are excellent materials and have many useful applications due to their electrical and thermal conductivity, strength, and lightweight

properties. In one study, carbon nanotubes functionalized with carboxyl groups were treated with a human T cell line, which induces caspase-2 gene expression in cells. The results showed that the survival rate of cancer cells treated with carbon nanotubes functionalized with the carboxyl group was slightly reduced. Furthermore, the results of molecular analysis showed that Cas2 mRNA was increased in cancer cells treated with carboxyl-functionalized carbon nanotubes [21, 22].

Liposomes

Liposomes are nanoparticles made up of lipids. They consist of a closed spherical lipid bilayer that forms an internal cavity and can accommodate aqueous solutions. Liposomal nanoparticles have had a significant impact on chemotherapy as they can improve selectivity, reduce cytotoxicity, and increase the solubility of hydrophobic drugs. In addition, magnetic liposomes have been used in cancer therapy, and liposomes IR-780, a very stable nanotherapeutic agent, have been used in the treatment of brain tumors [23, 24].

Dendrimers

Dendrimers are synthetic macromolecules with three-dimensional networks with a high number of functional groups. Dendrimer is used as a carrier of drugs and genes. They can also be used as antifungal, antibacterial, and anticancer agents. Dendrimer has three layers: molecular core, inner, and outer layers. Because of their structure, they possess multifunctional capabilities that make them useful in making next-generation nanodevices for imaging and diagnostics. In addition, because of their higher stability, water solubility, and reduced immunity, they have been used to deliver anticancer drugs. They can also cause hypervascularization, increased cancer cell permeability, and impaired lymphatic drainage, which is useful for passive targeting. The beneficial effects of dendrimers may lead to the selective accumulation of drug molecules in tumor tissues [16, 25].

Nanostructured lipid carriers (NLCs)

The use of lipid nanocarriers has shown promising results in cancer diagnosis and treatment. Polymer nanoparticles synthesized from a variety of lipid-based compounds or combined with carriers such as liposomes, autosomes, and transfersomes could help drugs overcome problems related to resistance to biofilm absorption. In one study, the combination therapy of irinotecan, a reactive oxygen species-sensitive prodrug, with conatumumab and a nanostructured lipid carrier with quercetin, was investigated for the treatment of colorectal cancer [5, 26, 27].

Nanorobots

Nanorobots are controlled devices consisting of nano-sized components. Because of their small size, they can interact with cell membranes and create a direct channel to the cell surface. Nanorobots can improve treatment efficiency by performing advanced biomedical treatments with minimally invasive operations [28].

mAb nanoparticles

In targeted therapies, monoclonal antibodies (mAb) are widely used due to their specific targeting abilities and anticancer effects. To further enhance the therapeutic effects of cancer drugs, mAbs are combined with cytotoxic drugs, known as antibody-drug conjugates (ADCs). By expressing

different specific antigens in the cancer cells and in the normal cells that drive the drug complex, less toxicity can be achieved. Trastuzumab (Herceptin) is a mAb used to treat human epidermal growth factor 2 (HER2)-positive breast cancer. Research has been conducted on the use of trastuzumab in the ADC system and results have shown an improved therapeutic effect compared with trastuzumab alone [29, 30].

In conclusion, effective cancer treatment with few side effects is one of the challenges of medical science and medicine. Nanotechnology has the potential to revolutionize cancer treatment and diagnosis. Nanoparticles can deliver drugs very precisely to tumors and bypass healthy tissue; They can also significantly reduce the amount of drugs needed to treat cancer. On the one hand, the idea of the human body as a system of complex molecular networks, and on the other hand, the advancement related to the targeting of this system by nanoscale technologies can revolutionize understanding and treatment, and can prevent disease. Nanoparticles designed to carry a drug are decorated with proteins that can penetrate tumor cells like a key. In this article, several nanostructures and their capabilities have been briefly discussed. It should be noted that the effectiveness of each synthesized nanostructure in the therapeutic field depends primarily on the biocompatibility of this structure; After ensuring biocompatibility, designing the right nanostructure will be the key to successful cancer treatment. Diagnosis plays an important role in cancer treatment, therefore, in recent years, with the expansion of nanotechnology and the application of nanoparticles in the field of medical science, efficacy, and risk lower, more effective methods currently studied in this area. field. In the short term, nanotechnology could enable early detection of cancer and the simultaneous delivery of anticancer agents to identified tumors. This technology plays a decisive role in cancer treatment and may offer the potential to prevent further cancer growth.

References

References

- 1. Fitzmaurice C, Abate D, Abbasi N, Abbastabar H, Abd-Allah F, Abdel-Rahman O, Abdelalim A, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017: A Systematic Analysis for the Global Burden of Disease Study. *JAMA oncology*. 2019; 5(12)DOI
- 2. Ferrari M. Cancer nanotechnology: opportunities and challenges. *Nature Reviews. Cancer*. 2005; 5(3)DOI
- 3. Jain KK. Nanotechnology in clinical laboratory diagnostics. *Clinica Chimica Acta; International Journal of Clinical Chemistry*. 2005; 358(1-2)DOI
- 4. Salehzadeh M, Norouzian P, Abbasalipourkabir R. The use of nanoparticles in diagnosis and treatment of breast cancer: A review. *Pajouhan Scientific Journal*. 2015; 13(2)
- 5. Pavitra El, Dariya B, Srivani G, Kang S, Alam A, Sudhir P, Kamal MA, et al. Engineered nanoparticles for imaging and drug delivery in colorectal cancer. *Seminars in Cancer Biology*. 2021; 69DOI
- 6. Wang J, Cao F, He S, Xia Y, Liu X, Jiang W, Yu Y, Zhang H, Chen W. FRET on lateral flow test strip to enhance sensitivity for detecting cancer biomarker. *Talanta*. 2018; 176DOI
- 7. Aygun A, Gülbagca F, Ozer, Ustaoglu B, Altunoglu YC, Baloglu MC, Atalar MN, Alma MH, Sen F. Biogenic platinum nanoparticles using black cumin seed and their potential usage as antimicrobial and anticancer agent. *Journal of Pharmaceutical and Biomedical Analysis*. 2020; 179DOI
- 8. Yang Y, Yan Q, Liu Q, Li Y, Liu H, Wang P, Chen L, Zhang D, Li Y, Dong Y. An ultrasensitive sandwich-type electrochemical immunosensor based on the signal amplification strategy of echinoidea-shaped Au@Ag-Cu2O nanoparticles for prostate specific antigen detection. *Biosensors & Bioelectronics*. 2018; 99DOI

- 9. Chakraborty D, Viveka TS, Arvind K, Shyamsundar V, Kanchan M, Alex SA, Chandrasekaran N, Vijayalakshmi R, Mukherjee A. A facile gold nanoparticle-based ELISA system for detection of osteopontin in saliva: Towards oral cancer diagnostics. *Clinica Chimica Acta; International Journal of Clinical Chemistry.* 2018; 477DOI
- 10. Zeng Y, Bao J, Zhao Y, Huo D, Chen M, Yang M, Fa H, Hou C. A sensitive label-free electrochemical immunosensor for detection of cytokeratin 19 fragment antigen 21-1 based on 3D graphene with gold nanopaticle modified electrode. *Talanta*. 2018; 178DOI
- 11. Orel VE, Tselepi M, Mitrelias T, Rykhalskyi A, Romanov A, Orel VB, Shevchenko A, et al. Nanomagnetic Modulation of Tumor Redox State. *Nanomedicine: Nanotechnology, Biology, and Medicine.* 2018; 14(4)DOI
- 12. Vilímová I, Chourpa I, David S, Soucé M, Hervé-Aubert K. Two-step formulation of magnetic nanoprobes for microRNA capture. *RSC advances*. 2022; 12(12)DOI
- 13. Zhou J, Meli VS, Yu-Tin Chen E, Kapre R, Nagalla R, Xiao W, Borowsky AD, et al. Magnetic resonance imaging of tumor-associated-macrophages (TAMs) with a nanoparticle contrast agent. *RSC advances*. 2022; 12(13)DOI
- 14. Sharma M. Transdermal and intravenous nano drug delivery systems: present and future, in Applications of targeted nano drugs and delivery systems. *Elsevier*. 2019;p. 499-550.
- 15. Ren L, Wang L, Rehberg M, Stoeger T, Zhang J, Chen S. Applications and Immunological Effects of Quantum Dots on Respiratory System. *Frontiers in Immunology*. 2022; 12DOI
- 16. Abbasi E, Akbarzadeh A, Kouhi M, Milani M. Graphene: Synthesis, bio-applications, and properties. *Artificial Cells, Nanomedicine, and Biotechnology.* 2016; 44(1)DOI
- 17. Lee XJ, et al. Functionalization of graphene for nanodelivery of drugs, in Synthesis, Technology and Applications of Carbon Nanomaterials.. 2019, Elsevier.157-176.
- 18. Zou Y, et al. Isotopic graphene-isolated-Au-nanocrystals with cellular Raman-silent signals for cancer cell pattern recognition. *Chemical Science*. 2018; 9(10):2842-2849. DOI
- 19. Kroto, H.W.W, D.R.M. fullerene. 2022 23 January 2023]; Available from: https://www.britannica.com/science/fullerene.
- 20. Mao C, Cai X. Nanomaterials and Aging. *Current Stem Cell Research & Therapy.* 2021; 16(1)DOI
- 21. Amreddy N, Ahmed RA, Munshi A, Ramesh R. Tumor-Targeted Dendrimer Nanoparticles for Combinatorial Delivery of siRNA and Chemotherapy for Cancer Treatment. *Methods in Molecular Biology (Clifton, N.J.).* 2020; 2059DOI
- 22. Lotfipanah S, Zeinali M, Yaghmaei P. Induction of caspase-2 gene expression in carboxyl-functionalized carbon nanotube-treated human T-cell leukemia (Jurkat) cell line. *Drug and Chemical Toxicology*. 2021; 44(4)DOI
- 23. Dong Y, Tchung E, Nowell C, Kaga S, Leong N, Mehta D, Kaminskas LM, Boyd BJ. Microfluidic preparation of drug-loaded PEGylated liposomes, and the impact of liposome size on tumour retention and penetration. *Journal of Liposome Research*. 2019; 29(1)DOI
- 24. Samson AAS, Park S, Kim S, Min D, Jeon NL, Song JM. Liposomal co-delivery-based quantitative evaluation of chemosensitivity enhancement in breast cancer stem cells by knockdown of GRP78/CLU. *Journal of Liposome Research*. 2019; 29(1)DOI
- 25. Dendrimers. 1 January 2023]; Available from: https://www.cd-bioparticles.net/biodegradable-polymers/dendrimers?page=2.
- 26. Cho H, Hossain MK, Lee J, Han J, Lee HJ, Kim K, Kim J, Lee K, Choi J. Selective isolation and noninvasive analysis of circulating cancer stem cells through Raman imaging. *Biosensors & Bioelectronics*. 2018: 102DOI
- 27. Duarte M, Subedi P, Yilmaz E, Marcus K, Laurell T, Ekström S. Molecularly imprinted polymers synthesized via template immobilization on fumed silica nanoparticles for the enrichment of phosphopeptides. *Journal of molecular recognition: JMR*. 2018; 31(3)DOI
- 28. De Jong WH, Borm PJA. Drug delivery and nanoparticles:applications and hazards. *International Journal of Nanomedicine*. 2008; 3(2)DOI
- 29. Nieto C, Vega MA, Martín Del Valle EM. Trastuzumab: More than a Guide in HER2-Positive Cancer Nanomedicine. *Nanomaterials (Basel, Switzerland)*. 2020; 10(9)DOI
- 30. Sievers EL, Senter PD. Antibody-drug conjugates in cancer therapy. *Annual Review of Medicine*. 2013; 64DOI