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Cancer and nanotechnology: A mini review

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Abstrac

Cancer is a complex disease that is challenging globally. There are different types of this disease and many people suffer from it. According to global data, in 2020, about 19.3 million new cases and about 10 million deaths have been estimated. Therefore, timely diagnosis and appropriate treatment for any type of cancer is very important. Therapies include chemotherapy and radiotherapy; etc. existing treatments currently have many side effects. Therefore, scientists are looking for new ways to reduce these side effects. In recent years, nanotechnology has received much attention in the diagnosis, imaging and treatment of this disease. Nanoscience, especially nanoparticles in the field of drug delivery, imaging and treatment has helped a lot in the field of cancer, and in recent years, nanotranoscience has applied this science. nanotheranostics is a combination of treatment and diagnosis that allows doctors to make progress in treatment and Provide. appropriate dosing and timely intervention and provide chemotherapy for cancer by increasing efficacy and reducing toxicity. (2)

Keywords: Nanoparticle, Theranostics, Imaging

1 Introduction

This article discusses the application of nanoscience in the treatment and diagnosis of cancer. Many drug delivery systems have used nanoscience. The use of these nanoparticles is to enhance, stimulate or improve the effectiveness of drug treatment. (2-4) These substances can alter the binding to antibodies and target ligands to increase the effect of nanoparticles and make treatment more effective. Because of their small size, nanoparticles have the ability to cross pores, which is why they are effective in treating neurological diseases and brain cancer because they have the ability to cross the blood-brain barrier. (5, 6) Of course, it should be noted that their size will be troublesome for them. To solve this problem, it can be solved by Surface modification. (3, 4, 7) The nanoparticles were divided into different ways including shape, size, materials and preparation method, which makes each of them have different properties such as loading capacity, release and durability. (8, 9) Nanoparticles are divided into Dendrimers, Nanocapsules, Liposomes, Micelles, Nanospheres in terms of shape. (10, 11) In terms of ingredients, they are divided into two categories: organic and inorganic (12, 13), In terms of preparation method, they are classified into two types of nanospheres and nanocapsules.

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Polymers used as nanoparticles are associated with drugs that have a specific therapeutic purpose for a specific disease such as cancer, which are associated with nanocarriers in two ways, 1- The drug is encapsulated in the nanocarrier 2- The drug is conjugated on the surface of nanoparticles. (3, 9, 14) So far, many polymers such as: polyamide, polyaminoacid, polyalkyl-alpha-cyanoacrylate, polyester, etc. have been used. Professor Langer and Folkman were the first to demonstrate the controlled release of macromolecules through the polymer, which led to the development of an anti-inflammatory drug delivery system for cancer. Polymer-based nanoparticles are a good tool for conducting biomolecules of drugs, genes and vaccines. By encapsulating these drugs in these nanoparticles, the solubility and durability of drugs will be improved. Ultimately patient satisfaction. (15) Theranostic design studies are the same, for example, they use substances or drugs that are inherently imaging and have therapeutic properties, thus overcoming the heterogeneity and harsh conditions of the tumor environment and providing targeted treatment. The combination of separate agents with nanotraphic devices expands and enhances their effect, allowing tumor accumulation, effective drug delivery, and multiple imaging modalities. This system is a multi-component particle made of organic and mineral materials that is used to treat, detect and image it, Examples include drug / gene delivery, laser therapy (e.g., photodynamic therapy (PDT) and phototherapy (PTT)), and tomography (PET). (16) The relationship of separate agents with nanotransport nanocarriers improves treatment, drug release, diagnosis and treatment (17), Combining these separate

factors with nanotheranostics devices has made it possible for tumor aggregation, better diagnosis, and effective drug delivery. Often Nanosystems are often coated with a biocompatible polymer layer for better impact and combined with materials that can create contrast. Often external factors (pH, light and heat, etc.) are involved in the secretion of the drug and cause both the treatment and imaging goals to not be pursued.

2 Advances in the design and integration of various nanotheranostics systems

Nanosystems between 5 and 200 nanometers in size are suitable for targeting tumors, However, the size of nanosystems depends on the type of tumor and their different characteristics. For example, the size of blood pressure is effective in choosing the size of nanoparticles and should be carefully considered. (18, 19) Also, different responses were observed in different applications of gold nanoparticles in dimensions between 20 and 200 nm. This is the result of the findings of Dreyfus et al**.** (19, 20) Various studies have shown that the amount that absorbs the most in tumors differs from the amount that gives the most contrast. (7) Resizing nanoparticles changes the properties associated with particle size. This statement is well observed for liposomes.Resizing of these nanoparticles affects the stability, interaction with the biological surface, bio-distribution of the encapsulated drugs. The small size of these particles increases their permeability and stability, and the larger size makes it possible to increase the drug loading and also makes it unstable. Becomes nanosystems. And are identified by RES and are cleansed of blood. (16, 17, 21) Therefore, a proper balance must be struck between increasing the drug load and optimal optometry. (22)

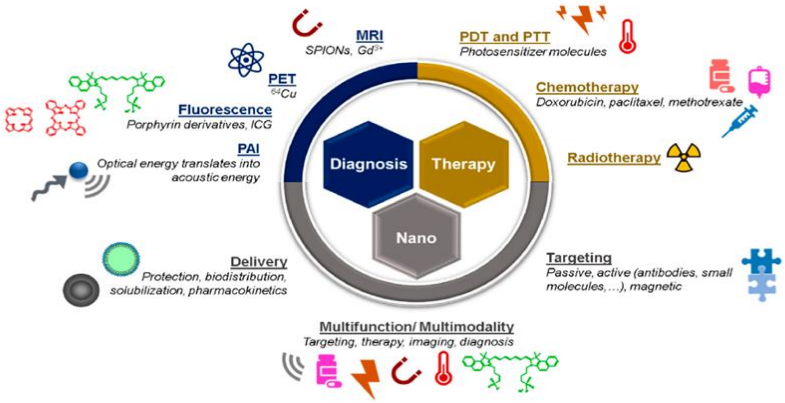

Figure 1. Schematic illustration of triple features in theranostic nanoplatforms, namely nano-sized particle, therapeutic, and diagnostic agents . (1)

Figure 1 (1)Dykman et al. (2016) are divided into three main categories, Composite nanoparticles (consisting of different nanomaterials including metals, biopolymers and lipids), multifunctional nanoparticles (with target groups and / or drugs) and multifunctional composite nanoparticles (which have the characteristics and applications of both groups). (23) The latter group offers promising approaches to theology. Modification of these nanosystems is done in order to combine with several composites and also provides surface performance of a combination of light-based methods (PDT, PTT) and active targeting of cancer(24) cells. In the design and construction of these platforms, attention should be paid to the stability of nanoparticles and their importance in manufacturing is very high because these nanoparticles are exposed to very different microenvironmental conditions of the tumor, For this reason, the use of these nanoparticles for drug delivery and imaging of the tumor is considered very important for biological purposes in cancer. Due to its optimal structure and formula, it is a multi-purpose nano-platform. This is why the signal is generated at the time of drug release and release at the tumor site and is generated, for example, by an external stimulus. Recent discoveries will create systems that allow double or triple action. (25) Kostevsek et al. Presented a one-step formulation by combining gold-iron oxide nanoparticles as a biocompatible polymer with the properties of photothermal heating and photoacoustic imaging (PAI) with a contrast agent. (26, 27) In the first approach, the set made it possible to evaluate the real-time pharmacokinetic distribution of anticancer therapy, in addition to comparing nanocarrier retention with free cisplatin. (16, 28) Willerding et al. By combining long-temperature liposomes (TSLs), the circulation of doxorubicin with a gadolinium-based contrast agent showed a significant improvement in drug delivery at the tumor site in MRI in vitro, and the use of this heating model was very useful. (29) The complexity of the interaction between nanoparticles with biomolecules, tissues, and organisms makes nanotheranostics systems one of the methods that measures this interaction. For example, real-time imaging, including the target of the tumor, is widely studied. Hyaluronic acid (HA), which is a polysaccharide, is widely used in many cancers. It is a natural ligand and has advantages. There are many, including low group toxicity, high compatibility, and low immunogenicity. (30-34) That is why HA is known as a factor used in all three diagnostic, imaging and treatment measures. (6, 31) Numerous cancer cells were tested (human pancreatic carcinoma, murine colon carcinoma, and both murine and human melanoma) Of these, only murine colon carcinoma (CT26 cell line) showed a significant difference between the conjugate and the drug. Absorption in these cancer cells is via the CDD4 receptor, which is dose- and time-dependent. It is likely that other significant mechanisms are also involved in this cases.(31, 35) One of the strengths of this experiment is the selection of conjugates with drugs and probes

that were previously used in the clinic and were administered at the same time. This and similar cases of this approach help to confirm the regulation of nanotheranostics Combinations that have both characteristics and can help patients be quickly approved and more accessible. (31) Today, significant advances have been made in the use of poly (lactic and glycolic acid) multi-purpose hybrid nanosystems. For example, both SPION and ICG have been converted to PLG and used in MR and NIFR imaging, and used in siRNA delivery. In a study, PLGA-dendrimer hybrid nano-platform was used for simultaneous delivery of doxorubicin and paclitaxel. (36) In addition, it consists of three layers, which are the central nucleus, which is PLGA, the middle layer, which is made of liposomes, and finally the outer layer, which is chitosan Used. (37) To enhance the effect, a targeted PLGA-based temperature-responsive nanosystem (PFH / DOX @ PLGA / Fe3O4-FA) can be combined with high-intensity focused ultrasound (HIFU) imaging and treatment with HIFU and doxorubicin. (38) PLGA copper oxide nanoparticles were used for simultaneous MR, ultrasound and PTT imaging. (39) Recently, the various features and applications of these light nanostructured nanosystems have been very effective in the treatment of cancer. (11) Multi-purpose hybrid nanotheranostics is expected to maintain the normal capabilities of nanoparticles such as drug delivery, increase penetration, maintain effect and easily modify the surface for coating and performance, as well as additional imaging capabilities and therapeutic properties. Among the nanoparticles described by light, hybrid multifunction systems, which are more complex than organic-organic materials, can offer a modified design and feature in imaging or therapeutic procedures. However, there are many obstacles and challenges in clinical translation. These points should be considered when extending drug delivery and other clinical measures for cancerous tumors.

3 Exploring Tumor Microenvironment for Improved Nanotheranostics Targeting

Knowing the characteristics of the tumor site is very effective in the effect of nanoparticles, because these factors will work to reduce or increase the effect of these nanoparticles. The effect of ERR is known as a factor that provides tumor entry and nanoparticle uptake based on size, charge and shape, but these factors have shown different diversity and complexity in different studies. Other factors that play a role in this distribution and make the distribution different include interstitial fluid pressure, blood flow, diffusion and stromal thickness. Also, the environmental conditions of the tumor should be considered (17, 40) , For example, we can refer to the pH and IFP of the environment. (41) These factors are widely used in the formulation of anti-cancer drugs and external factors can double the effect of these factors.

Several strategies are used to make better use of environmental conditions for better drug accumulation and increase the overall efficacy of treatment. These strategies show the superiority of nanotheranostics over monotherapy models.

4 Nanotheranostics is a highly functional alternative with high safety

Due to the fact that each of the diseases needs proper treatment with itself, nanomedicine and personal therapy are very popular today and have entered the field of treatment, and in the first place for diagnosis, we need appropriate and patient-related nanotheranostics, and multifunctional nanosystems offer us better capabilities than monotherapy nanoparticles.

Contrary to the positive results obtained in various studies of drug delivery systems, most of them have not yet been approved for use as an effective system. In the early stages of cancer diagnosis and treatment, nanotheranostics systems have been considered very effective and their use Are essential. On contrary to core-shell particles, multifunctional hybrid nanosystems which have more benefits such as real-time controlling of drug release, biodistribution and aggregation at the target site, raised therapeutic, effect and prediction of therapeutic function (consisting to disease progression and therapy outcome in exact time).in addition, in therapy planning, the prediction of therapeutic function and controlling personalized medicine, nanotheranostics might be helpful. Using these systems through imaging is another function of the pharmaceutical industry; for example in a preoperative situation or as optical guide during the resection pf breast cancer surgery and melanoma, eventually to improve the accuracy in the period of these cancers. According to our knowledge, no current nanotheranostic formulation has been allowed to use for clinical surgery, However if it applied to the right patients, will select by classification and subpopulation screening. For receiving the most appropriate therapy, Nanotheranositcs will anticipate the success of cancer therapy for the years ahead.

5 Necessary measures for the use of nanoparticles in clinical conditions

The field of nanotheranostics Despite many advances in the clinical field, most applications of nanotheranostics in humans have not been fully studied and have not been studied in terms of safety. To use them, we need to pay attention to many features such as biocompatibility, indestructibility and how these nanoparticles interact with the immune system, On the other hand, there is a need for a close relationship between different disciplines. Observance of these cases leads to increasing the quality of application of these nanoparticles in different sectors

6 Problems of nanocarriers in increasing patient survival

Distinctive biological properties of tumor structures such as physically damaged arteries (42), abnormal extracellular matrix, and high interstitial fluid pressure can reduce the impact of nanocarriers. (15, 43) And some of them disappear and this problem is also problematic in external obstacles and has faced many problems for researchers (44). One of the challenges that affects the effective release of nanocarriers and chemotherapy nutrients is the increase in interstitial fluid pressure, which is caused by abnormal blood flow and impaired venous and lymphatic drainage. (45) Liposomes and polymers are very useful because of the useful properties of the researchers, but because the relationship between these nanoparticles and cells is very complex and has adverse effects that reduce their survival and longevity (Table I).

TableI. Nanomaterials as drug carriers: advantages and disadvantages.

Nanomaterials	Advantages	Disadvantages

Liposomes	Controlled release, reduced toxicity, improved stability	Distribution and removal mechanism, breakage *in vivo*	
Polymers	Variety, controllable molecular weight	Inflammatory response, degradation pathway	Dendrimers
Nanosized cavity, controlled release, self-assembly		Immunoreaction, hematological toxicity	
Micellar nanoparticles	Simple prescription, passive targeting	Scale-up production, cytotoxicity	
Inorganic Nanomaterials	Multifunctional, modifiable, ability to combine diagnosis and treatment	Metal toxicity, stability, storage	

The instructions for liposomal formulation initially focused on reducing the toxicity of nanoparticles, and this measure reduced the effectiveness, and for effectiveness we will need more time for the nanoparticles to release drugs. The challenge is to achieve the right balance between reducing toxicity, increasing the effectiveness and stability of nanoparticles. (46) There is disagreement about the safety of biopolymers, and some of these biopolymers themselves cause cytotoxicity. (47, 48) For example, PEI activates caspase-3 and destabilizes the plasma membrane. This function causes it to be termed propaoptosis , However , inflammatory and immune responses have been reported in several trials. (7, 49, 50) And PLGA, the acidic product that triggers the inflammatory response, showed the lowest levels of toxicity and biocompatibility in both in vitro and in vivo environments (51), Because of this, progress has led to the recognition of polymers with high therapeutic efficacy and few side effects.

Due to their unique surface, Dendrimers have made a huge contribution to the design of nanosystems, and the toxicity of these nanocarriers is related to the final groups of areas around them. (52) And cation Dendrimers with high charge density and weight have more stability (PAMAM, PPI, and PLL) This stability causes them to be more toxic, which is due to their additional positive charge, but the neutral and anionic groups are less toxic. (53-56) One thing that can be done in this regard is to correct the surface of Dendrimers with reagents with minimal toxicity. Cytotoxicity and immune response and chronic inflammation are among the challenges in using other nanoparticles such as inorganic nanoparticles and materials. (57)For targeted treatment, minerals and nano-minerals can be stimulated with external factors such as pH, but the problem with this method is the limitation of penetration into the target tissue. (57, 58) Research seeks to eliminate the activity of these nanoparticles in order to purposefully use these substances to increase patient survival and the carrier nanoparticles can penetrate and destroy the tumor nucleus. Today's research will be to increase the use and construction of nanoplatforms in the future, which has attracted the attention of pharmaceutical companies.

7 Conclusion

In this study, nanoparticles and their benefits and applications in diagnosis, imaging and treatment are discussed. Nanoparticles can be used in medicine in the fields of diagnosis and treatment of diseases, drug delivery and imaging. Today's research will be to increase the use and construction of successful nanoplatforms in the future, which is the focus of pharmaceutical companies. Despite the many challenges and limitations in the use of nanoparticles in medicine, it is hoped that in the not too distant future we will see much progress not only in the field of cancer but also in most fields of medicine.

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