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Exploring the potential of nanoparticles as a drug delivery system for cancer therapy: A review

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ABSTRACT: In this review, we discuss the use of organic nanoparticles such as liposomes, polymeric nanoparticles, dendrimers, and inorganic nanoparticles such as gold nanoparticles and mesoporous silica nanoparticles in drug delivery in chemotherapy for cancer therapy. Another strategy is the use of nanoparticle vehicles for drug delivery through the natural openings on tumor vessels called fenestrations. Both of these can be functionalized to attach angiotensin to lymphocytes or any certain part of the cancer cell membrane, microenvironment, or cytoplasmic or nuclear receptor sites, and therefore a high concentration of drug delivery to targeted cancer cells is achieved, but with less or no toxicity to normal tissue. The potential advantages evident in this technology are useful approaches to established high-concentration drug treatment of cancer tissues without harming normal cells. Some features of a nanoparticle-based drug delivery system include the durability of the vehicle, biocompatibility, permeation, and ability to target specific types of cells. Organic and inorganic nanoparticles have developed this kind of drug-carrier system. Particulate systems are also still being explored for cancer drug resistance mechanisms, and their function in immunotherapy is expanding.

Keywords: Drug delivery, Cancer therapy, Polymeric nanoparticles, Gold nanoparticles

1. INTRODUCTION

Cancer can be described as an illness that results from the development of uncontrolled cells, usually through the process of proliferation, thus giving rise to uncontrolled growth and possibly also invasiveness. The main factors which are associated with its development are mutations or to contact with carcinogenic substances [1-3]. A subcategory of drug delivery is nanoparticles, small, and biocompatible materials that show interest for drug delivery because of their size, high surface area to volume ratio, and use in medicine and imaging. Due to the stability and the ability to control the size of the particles, gold nanoparticles are considered to be very worthwhile since may enhance the diagnose procedures, delivery of the drugs to target and the outcomes of the treatment [4-6]. Nanoparticles are considered as a promising tool for cancer theranostics concerning drug delivery and the improvement of the therapy's efficiency [7]. It has derived characteristics such as stability and biocompatibility which counter act situations that may lead to degradation of the drug and also prolong circulation of the drug in the body. Cancer vaccines can be made so specific for the cancer cells/tissues thereby reducing side effects and increasing the drug-dose on the tumor [8]. Drug delivery systems based on nanoparticles proven to reduce drug resistance mechanisms in cancer cells, compare to conventional chemotherapy and other treatments improving the efficacy of the procedure [9]. Nanoparticles of the higher generation can have multiple applications, and the functions of the drug delivery, imaging, and therapy can all occur simultaneously. Present research directions are aimed at creating new nanoparticle systems for application in cancer treatment problems similar to heterogeneity of tumors and resistance to therapy as well as various side effects. Thus, nanoparticles constitute a highly prospective area in the cancer treatment and drugs delivery with less side effects and higher efficiency [10,11]. The specific objectives of this review are therefore; To review the application of nanoparticles in cancer therapy in relation to their special characteristics, application and concerns. This exhibits their

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usefulness in increasing drug efficacy, decreasing the impact of drugs in the rest of the body, improving the rate and site of drug release for better treatment of cancer.

2. MECHANISM OF DRUG DELIVERY

Fundamentally, nanoparticles play many roles in cancer treatment through transportation by means of different actions. The EPR effect also increases nanoparticles' penetration into the tumor while, at the same time, decreasing the exposure of healthy tissues [12]. Stealth techniques such as ligands or antibodies further enhance the concentration of the drug to the desired cancer cells thereby enhancing the treatment outcomes and lessening the adverse effects [13]. Innovative types of polymeric drug delivery systems such as multistage drug delivery system (MSDDS) are responsive to the stimuli from the tumor microenvironment for a controlled drug release [14]. Cytotoxicity of nanoparticles is an important parameter as the particles can get inside the cells through direct transfer to the cytosol, changing the uptake mechanisms, or endocytosis. Knowledge of these uptake mechanisms is therefore quite essential especially in the delivery of drugs. They also include bypassing efflux, controlling release and metabolism of the drugs allowing the enhancement of the anticancer drug's effectiveness and reduction of the side effects [15,16].

3. ORGANIC NANOPARTICLES

3.1 LIPOSOMES NANOPARTICLES

Liposomal nanoparticles or LNPs are one of the most progressive drug delivery systems with characteristics that enable targeted delivery at diseased sites including tumors. These have a diameter of about 100 nm, small drug to lipid ratio, good drug input with high retention, and long circulation time. The size of LNPs could be regulated with Total Flow Rate and Flow Rate Ratio; the LNPs could be created to have the size of 60-70 nm, remain stable for 16 weeks and have 81 percent encapsulation efficiency [17-19]. Liposomal nanoparticles refer to some of the most recent drug delivery systems with the following benefits in cancer treatment [20]. These nanoparticles improve the drugs' uptake in tumor tissues; minimize drug side effects; and preserve drug integrity. They enhance the specificity of cancer chemotherapeutic agents, reduce the toxic effect on normal tissues, enhance solubility of the drug and deliver drugs in a controlled manner [21, 22]. Liposomes can be made in various size and composition to enhance delivery of drugs, some of the formulation are stable for a long time. They can incorporate different anti-cancer agents which in turn increases drug selectivity and decreased side effects [23]. Which can directly affect the cancer cells, an increase in drug selectivity and decrease the general side effects and toxicity of the therapy. As a result, they have the capacity to transport drugs in higher concentration to tissues that have tumours thus enhancing specific therapeutic action and minimizing toxic effects. Another application of liposomes is in drug delivery and imaging agents for assessment of the treatment progress. Nonetheless, due to their immunosuppressive and angiogenetic characteristics, therapy with nanoparticles is still important in cancer treatment Today, researchers are working to resolve issues, such as fragility, site-specific delivery and poor payload release prior to the required site [24-26]. Liposomes have shown a very good prospective in the treatment of hepatocellular carcinoma (HCC). They help to target the medications at the tumor tissues; an aspect that increases the effectiveness of the treatment. By functionalizing the liposomes with lactoferrin and peptides, more of the drug would be retained in the HCC cells. Liposomes can be made responsive to stimuli in the tumor micro environment and they are triage effective in delivering drugs. Till date, it has been evidenced that liposomal nanoparticles effectively inhibit liver cancer cell proliferation and increase apoptosis for the therapy of HCC [27-29]. Besides, it has a significant position in the treatment of triple-negative breast cancer (TNBC). These increase the effectiveness of method of drug delivery, decrease the side effects and overall improve the therapeutic efficacy. Liposomes can be modified with ligands to deliver the drugs with enhanced accumulation to TNBC cells hence a high cell apoptosis rate. Research shows liposomal formulation to reduce TNBC cell proliferation and increase the rate of tumor cell death; thus, the use of liposomal nanoparticles is considered a viable treatment for the said cancer [30,31].

3.2 POLYMERIC NANOPARTICLES

Polymeric nanoparticles with size between 1nm to 1000 nm are Colloidal particles utilized in therapeutics with an aim of delivering drugs specifically in cancer treatment. They can be modified and can be developed to have a specific pattern of drug release. They also have to be of a specific size to successfully be used in the delivery of these drugs. Polymeric nanoparticles are one of the effective systems to enhance the bioavailability along with target specific approach [32,33]. Conventional chemotherapy is facing a lot of limitations because of high rates of toxicity and multidrug resistance; therefore, polymeric nanoparticles are now the key of advanced cancer treatment and improvement of the therapy's efficiency [34]. This makes nanoparticles to exhibit required properties such as size, shape and the chemical makeup of the exterior surface to penetrate bio barriers, reach the tumor microenvironments and increase the solubility of drugs to improve the therapeutic effect of such drugs [35]. They can give targeted extended releasing property which can minimize the cytotoxicity and maximize the retention in tumor tissue. Polymeric nanocarriers can be conjugated or encapsulated with anticancer drugs so that it forms controlled prosperous drug delivery systems. Targeting ligands can help to increase the accumulation of the drug within the tumor tissues, therefore increasing the effectiveness of treatment. These nanoparticles also have the capability to recover the stimuli such as low pH or specific enzymes and would ensure the drug delivery to cancer cells, tumor blood vessels and immunes cells for anticancer immunotherapy. Due to their biodegradability and the capacity to overcome physiological and cellular barriers, NPs are considered an essential instrument to fight cancer [36-38]. Also, polymeric nanoparticles are also useful in the treatment plan of hepatocellular carcinoma (HCC) since it provides the drug with a route to the target site as well as boosts the results of the treatment. Recent research proved that the polymeric nanoparticles delivering anticancer agents, namely sorafenib, have better anti-cancer capabilities, do not allow the development of multidrug resistance, and promote apoptosis in HCC cells. This kind of nanoparticles can be functionalized for active targeting to enhance drug uptake in the tumor site. Furthermore, polymeric nanoparticles possess a high transfection efficiency in HCC cell lines which makes them suitable for gene transfer and target treatment of liver cancer cells [39-41]. Also, the polymeric nanoparticles find their application in the treatment of triple negative breast cancer and in general, it enhances the efficacy of the drugs through targeted delivery systems. These nanoparticles can be functionalized for targeted delivery so that enhanced concentration of drugs is achieved in the tumor sites and decreased concentration in the rest of the body. It has also been recognized in their ability to transport chemotherapeutics, genes, and Small-interfering RNA's, with improved effectiveness, solubility and less side effects. In regard to the treatment of TNBC, polymeric nanoparticles have also been reported to exhibit good therapeutic efficacy due to their ability to incorporate an enhanced and smart drug delivery system [42,43].

3.3 DENDRIMERS NANOPARTICLES

Dendrimers are the hyperbranched, monodispersed, and spherical nanosized macromolecules synthesized from peripheral Monomers, being currently explored in nanomedicine for its suitable applications in drug delivery systems, imaging and diagnostics. They can act as drug carriers, improve the solubility, stability and bioavailability of drug molecules and can be functionalized with targeting moieties or imaging agents. Dendrimers it has been utilized in functionalization of genes, antibacterial activity, as well as diagnostic and imaging properties that acts as a contrast agent for imaging techniques such as MRI, CT and optical imaging [44,45]. Dendrimers nanoparticles are helpful in developing the drug delivery systems in cancer treatment. These synthetic nanoparticles have a highly branched and spherical structure to enable the engineer of their specific features [46]. Compared with ordinary drug delivery systems, dendrimers exhibit the following benefits: The clear and unique structures of dendrimers are monodispersing, and drugs can be encapsulated in the interiors of these dendrimers [47]. Due to special features of their structure they are suitable for application in drug delivery; this increases therapeutic effectiveness and minimizes the side effects. Targeted drug delivery is critical in cancer therapy to avoid the potential of toxic outcomes of the administered drugs and enhance the therapeutic efficacy [48]. Dendrimers can be modifying at the surface by incorporation of targeting groups that allows for active/targeting or passive targeting of tumors. It has been observed that they engage with the drugs either physically via encapsulation or by electrostatic attraction or chemical coupling for a planned drug release at the tumor side. This is especially important in cancer treatment as it amplifies the selectivity and trolling of the drugs on cancer cells without affecting the normal ones [49]. Besides, dendrimers are capable of carrying a great deal of drugs to certain loci; thus, they valuable for the delivery of chemotherapeutic agents. They can also be employed when tracking the treatment outcomes and where they provide the theranostic aspect in cancer management [50]. Dendrimers have effectively delivered small interference RNA (siRNA) for gene silencing in Multidrug resistant cancer cells, and they have anti-tumor effects for stopping tumor cell migration and also inducing apoptosis [51,52].

4. INORGANIC NANOPARTICLES

4.1 GOLD NANOPARTICLES

Gold Nanoparticles (AuNPs) are nanoscale gold atoms that are of interest due to their physical and chemical properties that are different from that of coarse gold. It is possible to have them synthesized and altered with comparative ease and they are bio compatible and have low toxicity. AuNPs are utilized in cancer theranostics, photothermal therapy, biosensing, and imaging purposes [53,54]. AuNPs can be applied in cancer therapy because they have the following features: size and shape changeability, high S/V, optically-active properties owing to surface plasmon polaritons. Such nanoparticles can increase the effectiveness of the anticancer medications and minimize their toxicity, which in turn may facilitate the targeted delivery of the drugs to the tumor cells. They can also penetrate MDRI which helps in increasing the toxicity of anticancer drugs and overcoming drug resistance in cancer cells. AuNPs can not only entrap a single drug but also can be used for delivering several drugs in combination to the diseased site [32] [55]. Again, AuNPs have the ability to provide controlled release of the drugs. It can be controlled so that large concentration of the drugs can be released when certain signals are detected, thus the drug reaches the tumor site in the correct proportions. By having a controlled release mechanism, the formulation of the drug increases its therapeutic value while at the same time decreases the systemic toxicity. AuNPs are also applied in cancer imaging for diagnostic purposes as image contrast in computed tomography (CT), magnetic resonance imaging (MRI) and optical imaging [56,57]. AuNPs have been found to have potential therapeutic application for several types of cancer such as hepatocellular carcinoma. Medullary thyroid cancer (MTC) which is gold core nanoparticle conjugated with DM1 was quite effective in both mechanical thrombectomy (MT) and medical adverse events epidemiology MAE-murine xenograft models and was even superior to free DM1 and sorafenib. AuNPs also facilitated radiosensitivity of the HCC cells, thus resulting to better treatment. The results indicated that the mice treated with polysaccharide-coated AuNPs had immunoregulatory activity and anticancer effects on HCCC. This process should be continued for other types of cancer [58,59].

4.2 MESOPOROUS SILICA NANOPARTICLES

Mesoporous silica nanoparticles (MSN) holds potentials for drug delivery since they are biocompatibility, pronounced drug release and effectiveness to hinder tumor growth. They are multipurpose for bio imaging, drug delivery systems, biosensors and tissue engineering applications. Yet, there are requirements for precise control of their structure and surface in order to create materials to be applied. [60,61]. Mesoporous silica nanoparticles are believed to have potential as a drug delivery system for cancer therapy because of their excellent property such as large surface area and pore volume of MSNs. They are characterized by the ability to control the pore size and pore volume that dictates the rate and area of drug release in the body. MSNs also maintain a stable structure and do not undergo a degradative process; they also increase the solubility of the compounds. These PPs can be readily tailored to enhance biocompatibility and to achieve desired drug release profiles and increased selectivity to cancer cells [62,63]. MSNs can also be utilized for avoiding the requirement of multiple delivery systems by serving as a vehicle of multiple therapeutic agents at a time. Here it is crucial to note that the main advantage of MSNs lies in the fact that they are capable to avoid the drawbacks of conventional chemotherapy ways by offering a controlled drug delivery platform. More studies and innovations are required in the field of MSNs to optimize the usage of such platforms in the progress of cancer treatment [64,65].

5. CONCLUSIONS

Nanoparticles in cancer treatment have prompted the use of many types of nanoparticles, such as organic and inorganic NPs, to advance clinical treatment of many types of cancer. These nanoparticles have enhanced features such as better pharmacokinetics, toxicity profile, tumor specificity, and steadiness, and better pharmacokinetics, better biodistribution, and better efficacy also overcome the problem of drug resistance. They are commonly applied in chemotherapy, targeted therapy, radiotherapy, hyperthermia, and gene therapy. Nanocarrier delivery systems mean better delivery of the combinatorial therapy and might help to address the drug efflux pump, defective apoptotic pathway, and hypoxia tumor environment. These targeting agents, when used in conjugation with cytotoxic agents when encapsulated in NPs, can reverse drug resistance. The studies on the effective targeting of new nanoparticles for cancer therapy have been highly active in the last few years due to the identification of new nanoparticle carrier systems and anti-cancer drugs. The diagnosis of the cancer through the use of nanoparticles and the application of a gene therapy technique have been reviewed in detail in the literature, and some of the innovative treatment strategies have been taken through a clinical trial. For early intervention or cure of the advanced cancer, better detection and targeting strategies are mandatory. In nanotechnology researche, provisions towards early detection, treatments, and prevention of cancer shall be realized to enhance the span and quality of life of the victims.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

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