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Nanoparticles-based drug delivery system for cancer

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ABSTRACT: -

Nanoparticle-based drug delivery system (DDS)is considered promising for cancer treatment. Compared with traditional DDS, the nanoparticles- based DDS shows improved efficacy by; 1)increasing half-life of vulnerable drugs and proteins,2)improving the solubility of hydrophobic drugs, and 3)allowing controlled and targeted release of drugs in diseased site. Diagnosis and treatment of lung cancer have been characterized with a variety of challenges. the advancement in magnetic nanoparticles (MNP) technology, many challenges in the diagnosis and treatment of lung cancer are on the decline. Magnetic nanoparticles (MNPs) have demonstrated marked progress in the field of oncology. General nanoparticles are widely used in tumor targeting, and the intrinsic magnetic property of MNPs makes them the most promising nanomaterials to be used as contrast agents for magnetic resonance imaging (MRI) and induced magnetic hyperthermia.Nanoparticles (NPs) have the ability to incorporate multiple dugs and targeting agents and therefor lead to an improved bioavailability, sustained delivery, solubility, and intestinal absorption. Of the many possible core constituents ofnanoparticles (NPs), such as gold, silver, carbon nanotubes, fullerenes, manganese oxide, lipids, micelles, etc., iron oxide (or magnetite) based nanoparticles (NPs) have been extensively investigated due to their excellent superparamagnetic, biocompatible, and biodegradable properties. Finally, some views will be discussed concerning the toxicity and clinical translation of iron oxide nanoparticles (NPs) and the future outlook of nanoparticles (NPs) development to facility multiple therapies in a single formulation for cancer theragnostic.

KEY WORDS: -Inducedmagnetic hyperthermia, magnetic resonance imaging (MRI), magnetic nanoparticles (MNP), drug delivery, lung cancer

INTRODUCTION: -

Drug delivery system (DDS) has been used clinically and pre-clinically to deliver therapeutic substances for disease treatment. Conventional DDS is administrated by either oral intake or injection. Despite many advantages of the conventional DDS, such as ease of administration and widely accepted by patients, it has its major limitations and disadvantages:

- Limitedeffectiveness: - many drugs have variable absorption rate when taken orally, also the low pH environment combined with digestive enzymes can break down some of the drugs before the enter blood circulation.
- Lack of selectivity: - for drugs that need to target specific organs, oral drug delivery is not ideal due to its poor biodistribution. The drugs uptake in the detoxification organs such as liver or kidney could be high and can induce toxicity to those organs.

Controlled DDSs protect the drugs from degradation and clearance, helpful for delivery of proteins and new therapeutic agents such as gene therapy and RNA interference. They can help DNA and siRNA evade uptake by reticuloendothelial or other tissues and enzymatic degradation. Nanotechnology is shown to bridge the barrier the of biological and physical sciences by applying nanomedicine and nano based drugs delivery systems, where such particles are of major interest. Nanomaterials can be well-defined as a material with sizes ranged between 1 and 100nm, which influences the frontiers of nanomedicine starting from biosensors, microfluidics, drug delivery, and microarray tests to tissue engineering. Nanoscale sized particleexhibitunique structural, chemical,mechanical,magnetic,electrical, and biological properties.

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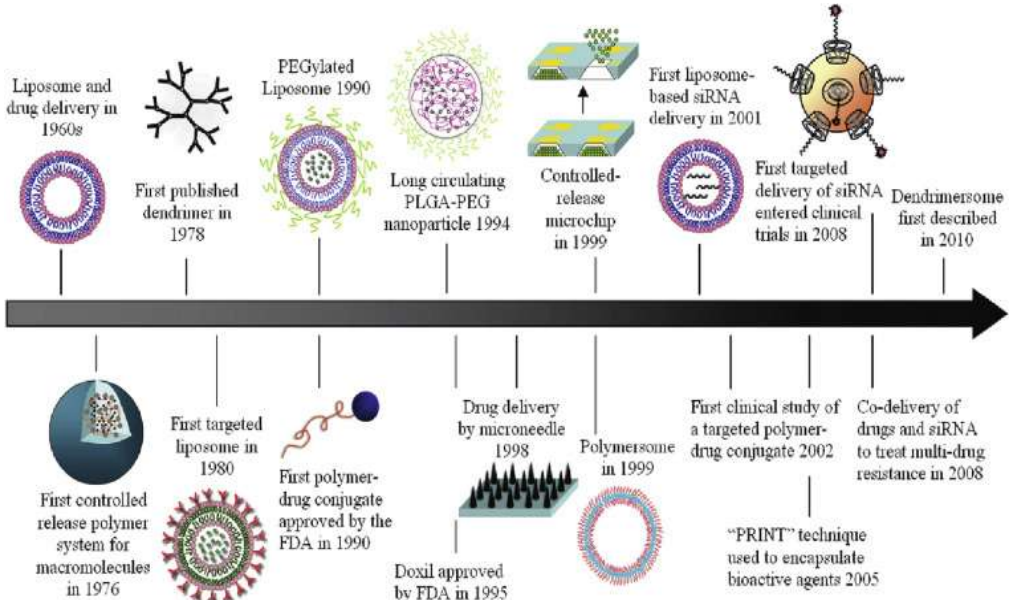

Cancer is still the main cause of death for patients worldwide with increasing incidence, and the research into cancer treatment is under the spotlight. Surgery, radiotherapy, chemotherapy and immunotherapy, as well as those combinational regimens are now the main clinical strategies. Since the first immune checkpoints blockade agent ipilimumab approved by the US Food and Drug Administration (FDA) in 2011, cancer immunotherapy has come of age and shown great clinical success. Chemotherapy is the vital weapon of cancer therapy. Chemoimmunotherapy, the combination of chemotherapy and immunotherapy, provides a superior synergistic effect for enhancing antitumor efficiency. Chemotherapy drugs kill tumor cell directly, while immunotherapy reactivates immune response to kill cancer cell. nano-based drug delivery system (NDDS) could improve the in vivo pharmacokinetic behaviors, increase the stability of drugs realize the targeted delivery and controlledreleaseof drugs, thus holding great promise for chemoimmunotherapy.Moreover, recent studies demonstrated that nanoparticle (NPs) could re-model immunosuppressive tumor microenvironment (TME). therefore, NDDS applied to chemoimmunotherapy is nowadays the hotspot in cancer treatment. The current applications of NDDS in chemoimmunotherapy were summarized.

Lung cancer is the most common cancer in men and women in developed countries. It is also the leading cause of cancer death worldwide, causing 18.4% of all cancer deaths. Approximately 70% of patients have advanced disease at the time of diagnosis, and only 15% of lungcancer patients are still alive 5 years after diagnosis: including physical exam, medical history, and imaging techniques such as X-ray, computed tomography (CT), bone scan, magnetic resonance imaging (MRI), positron emission tomography (PET), andcombined PET-CT scan. Nanoparticles (NPs) are synthetic particles with a diameter of <100 nm that are generally derived from diagnosis to cancer therapy. The size of these NPs is remarkably similar to most of biological structures and molecules. through this review, wewill discuss the potential use of NPs for the treatment of lung cancer.

Over the last few decades, nanotechnology has been increasingly used in medicine, including applications for diagnosis, treatment, and tumor targeting in s safer and more effective manner. Nanoparticles (NP)- based drug delivery systems have shown many advantages in cancer treatment, such as good pharmacokinetics, precise targeting of tumor cells, reduction of side effects, and drugs resistance (Dadwal et al.,2018; Palazzolo et al., 2018).

Nanoparticles(NPs) in cancer therapy: -

The NPs used in medical treatment usually have specific sizes, shapes, and surface characteristics as these three aspects have a major influence on the efficiency of the nano-drug delivery and thus control therapeutic efficiency (Bahrami et al., 2017). NPs with a diameter range of the 10 to 100nm are generally considered

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suitablefor cancer therapy, as they can effectively deliver drugs and achieve enhanced permeability and retention (EPR) effect. Smaller particles can easilybe filtered by kidneys (less than 1-2nm) (Venturoli and Rippe, 2005), whileparticles that are larger than 100nm are likely to be cleared from circulation by phagocytes (Decuzzi et al., 2009). , NPs are generally modified to become hydrophilic, which increases the time period of drugs in circulation and enhances their penetration and accumulation in tumour (Perrault et al., 2009; Wong et al., 2011; Yang et al., 2014)

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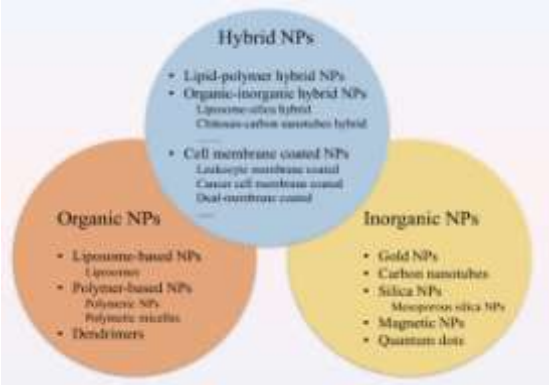

1. ORGANIC Nanoparticles (NPS): -

Organic NPs have been widely explored for decades and contain many types of materials. Liposome, the first nano-scale drug approved for clinical application (Zylberberg and Matosevic, 2016), consists of an outer lipid layer and a core entrapping either hydrophobic or hydrophilic drug. Liposomes can carry out many functions by modifying the lipid layer structure, including imitating the biophysical characteristics (e.g., mobility and deformation) of living cells (Hua and Wu, 2013; Lemière et al., 2015), which can help achieve the purpose of more effective therapeutic drug delivery. Additionally, dendrimers are another class of polymers that have been applied to nanomedicine. They are versatile and biocompatible macromolecules that are characterized by a three-dimensional branch structure (Nanjwade et al., 2009; Sherje et al., 2018). Their multiple functional groups on the surface enhance the capability of loading and delivering therapeutic agents. Furthermore, polymeric micelles, which are characterized by polymer self-assembly into nano-aggregates as they are composed of amphiphilic copolymers, constitute another kind of widely investigated polymer NPs (Zhou et al., 2018).Polymer-based NPs are another type of NP with specific structural arrangements for drug delivery formed by different monomers (Amreddy et al., 2018). Polylactic-co-glycolic acid (PLGA), a common polymeric NP, encompasses co-polymerization of glycolic acid and lactic acid. Given its better biocompatibility and biodegradation, as well as the EPR effect, PLGA is widely used as a carrier for drug delivery (Acharya and Sahoo, 2011; Saneja et al., 2019).The hydrophobic core enables the insoluble anticancer drugs to be absorbed and delivered smoothly, while the hydrophilic segment increases stability, thus reducing the uptake of the drug by the reticuloendothelial system and prolonging their time period in circulation (Cagel et al., 2017). Their multiple functional groups on the surface enhance the capability of loading and delivering therapeutic agents. Furthermore, polymeric micelles, which are characterized by polymer self-assembly into nano-aggregates as they are composed of amphiphilic copolymers, constitute another kind of widely investigated polymer NPs (Zhou et al., 2018).

2.INORGANICNanoparticles(NPs): -

Inorganic NPs have the advantages of a higher surface area to volume ratio. They have a wide and easily modified surface conjugation chemistry and facile preparation, although this usually occurs at the expense of poorer biocompatibility and biodegradability (Jiang et al., 2016). The inorganic NPs that have been studied include gold NPs (AuNPs), carbon nanotubes (CNTs), quantum dots, magnetic NPs (MNPs), and silica NPs (SNPs). AuNPs are the most widely studied inorganic NPs, and mixed monolayer-protected clusters based on the gold core are considered to be a promising candidate in the drug

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delivery system (Han et al., 2007). The gold core is inert and non-toxic, and surface-functionalized AuNPs have been proven to enhance drug accumulation in tumours as well as to overcome the drug resistance (Cheng et al., 2013). Moreover, AuNPs are thought to be involved in multimodal cancer treatment including gene therapy, photothermal therapy and immunotherapy (Han et al., 2007; Jiang et al., 2016; Riley and Day, 2017). They have been shown to demonstrate high efficacy in chemotherapy and gene therapy for cancer treatment (Basoglu et al., 2018; Mandriota et al., 2019). Furthermore, magnetic hyperthermia using MNPs can achieve thermal ablation of tumours, which offers alternative cancer treatment (Hoopes et al., 2017; Legge et al., 2019).

carbon nanotubes are a type of tubular material that have been shown to have broad potential in the drug delivery field due to their unique biological, physical, and chemical properties. As a result, they have been used to deliver anticancer agents including doxorubicin, paclitaxel, and methotrexate siRNA for a variety of cancers (Madani et al., 2011). Meanwhile, CNTs produce heat when they are exposed to near-infrared radiation, which could be applied to thermal ablation for cancer therapy (Luo et al., 2013).The large internal pore volume enables them to encapsulate the maximum amount of anticancer drugs, and the supramolecular components act as a cap, allowing capture and release of drugs (Cheng et al., 2019; Lei et al., 2019).

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3.HYBRID Nanoparticle (NPs): -

Lipid-polymer hybrid NPs, which consist of an inner polymeric core and a lipid shell, have been demonstrated to be a promising drug delivery platform in the treatment of pancreatic cancer (Hu et al., 2010; Zhao et al., 2015), breast cancer (Gao et al., 2017; Li et al., 2019), and metastatic prostate cancer (Wang Q. et al., 2017). This type of hybrid NPs combines the high biocompatibility of lipids with the structural integrity provided by polymer NPs, and are therefore capable of encapsulating both hydrophilic and hydrophobic drugs in order to achieve a better therapeutic effect (Cheow and Hadinoto, 2011; Zhang R.X. et al., 2017). The combination of organic and inorganic hybrid nano-materials is a common method of NP design. For example, a liposome-silica hybrid (LSH) nanoparticle consists of a silica core and a surrounding lipid bilayer and has been synthesized and shown to be valid in delivering drugs to kill prostate and breast cancer cells (Colapicchioni et al., 2015).

The LSH nanoparticle has also been reported to offer a platform for the synergistic delivery of gemcitabine and paclitaxel to pancreatic cancer in a mouse model of the disease (Meng et al., 2015). Kong et al. (2015) created an advanced nano-in-micro platform by assembling the porous silicon NPs and giant liposomes onto a microfluidic chip, and co-delivery of synthesized DNA nanostructures and drugs in this platform was proven to significantly enhance cell death of doxorubicin-resistant breast cancer cells. Furthermore, (Wong et al., 2011) proposed a multistage NP delivery system to achieve deep penetration into tumours by changing the size and characteristics of NPs at different stages. In their study, the size change of NPs was achieved by protease degradation of the cores of 100-nm gelatine NPs within the tumour microenvironment in order to release 10-nm quantum dot NPs.

The coatings include cell membranes derived from leukocytes, red blood cells, platelets, cancer cells, and even bacteria.(Parodi et al. 2013) have shown that coating nano porous silicon particles with a cell membrane which is purified from leukocytes can prevent the nano-carrier from clearance by phagocytes, and the characteristics of this hybrid particle allow the drug to have extended time period in circulation, leading to increased accumulation in the tumour.

Mechanism of targeting: -

Targeting of cancer cells specifically is a vital characteristic of nano-carriers for drug delivery, as it enhances the therapeutic efficacy while protecting normal cells from cytotoxicity. In order to better address the challenges of tumor targeting and the nano-carrier system design, it is crucial to first understand tumor biology and the interaction between nano-carriers and tumor cells.

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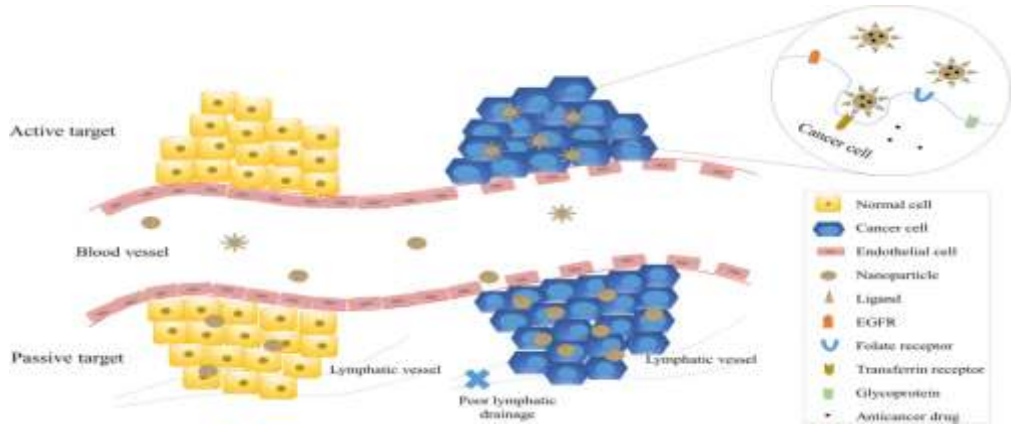

1.Passive targeting: -

In passive targeting, the drugs are successfully delivered to the target site in order to play a therapeutic role. High proliferation of cancer cells induces neovascularization, and large pores in the vascular wall lead to a worsening perm selectivity of tumor vessels compared to normal vessels (Carmelite and Jain, 2000). the poor lymphatic drainage associated with cancer increases the retention of NPs, allowing the nano-carriers to release their contents to tumor cells. The EPR effect is influenced by the size of NPs, as many studies have demonstrated that smaller NPs have better penetrability but do not leak into normal vessels (Torchilin, 2005; Carita et al., 2018). On the other hand, larger particles are more likely to be cleared by the immune system (Sykes et al., 2014).

Glycolysis yields an acidic environment and reduces the pH of the tumor microenvironment. Subsequently, some pH-sensitive NPs are triggered by the low pH level and are able to release drugs within the vicinity of cancer cells (Lim et al., 2018).However, there are some limitations with regards to passive targeting, including non-specific drug distribution, non-universal existence of the EPR effect and different permeability of blood vessels across various tumors (Jain, 1994).

2.Active targeting: -

Active targeting specifically targets cancer cells through direct interactions between ligands and receptors. The ligands on the surface of NPs are selected to target the molecules that are overexpressed on the surface of cancer cells, which allows them to distinguish targeted cells from healthy cells (Shi et al., 2011; Kamaly et al., 2012).

The types of targeting moieties include monoclonal antibodies, peptides, amino acids, vitamins, and carbohydrates (Danhier et al., 2010). These ligands specifically bind to receptors on targeted cells, and the widely investigated receptors include transferrin receptor, folate receptor, glycoproteins, and the epidermal growth factor receptor (EGFR).

Mechanisms of NPs in Overcoming Drug Resistance: -

The mechanisms of tumor drug resistance include cellular and physiological factors, such as overexpression of ATP binding cassette (ABC) transporters (e.g., efflux transporter) (Litman et al., 2000), defective apoptotic machineries, interstitial fluid pressure, and acidic and hypoxic tumor microenvironment.

Examples of Nanoparticles used for Chemotherapeutic Drug Delivery: -

In cancer chemotherapy, nanomedicine has special significance. In this review, we will discuss the applications, advantages, and limitations of different types of NPs used to deliver chemotherapy drugs.

Liposomes: -

Liposomes are mainly composed of natural or synthetic phospholipids, have good biocompatibility, are biodegradable, and do not cause immune reactions. Liposomes can deliver both lipophilic and hydrophilic compounds, fat-soluble drugs, and amphiphilic drugs that can be inserted into the liposome bilayer phospholipid membrane, and water-soluble drugs are stored in the aqueous compartment. Liposomes are also regarded as a universal drug carrier that can deliver

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many different types of drugs.(1) increase the solubility of hydrophobic drugs; (2) improve the biological distribution of chemotherapeutic drugs and the selectivity of therapeutic agents; (3) reduce the cytotoxicity of chemotherapeutic drugs to normal tissues, thereby reducing its toxic side effects; and (4) extend the cycle time of chemotherapeutic drugs and control the release. In the past few years, many liposomes chemotherapeutic agents have observed positive results in the clinic, and some of them have been approved by the European Medicines Agency and the US Food and Drug Administration (FDA) for the treatment of various Kind of cancer.

Protein-Based Nanocarriers: -

Protein is formed by one or more polypeptide chains with a certain spatial conformation and biological activity. Protein-based NPs have the following advantages for the delivery of tumor chemotherapy drugs: (1) Proteins are endogenous and have excellent biocompatibility. (2) Proteins have biological activity. Protein-based nanoplatforms can inherit this effect without further surface modification, which will greatly simplify the synthesis process. (3) Amino acid residues constituting the basic unit of protein have various functional groups (such as -COOH and -SH) that can be used in combination with chemotherapeutic drugs, which imparts function expansibility to protein. Human serum albumin is the main component in serum, consisting of 585 amino acid residues, with a molecular weight of 66.5 kDa. Paclitaxel (PTX) preparation (Abraxane) based on human serum albumin (HSA) obtained FDA approval in 2005, HSA has been widely studied as a chemotherapeutic drug carrier. Paclitaxel is a hydrophobic chemotherapeutic drug, and toxic-solubilizing agents such as polyoxymethylene castor oil/PEG-35 castor oil/ethanol are often used to administer the drug. In order to minimize the risk of hypersensitivity, clinical use of corticosteroids such as dexamethasone is often used to pretreat patients. Even so, 40% of all patients still have mild hypersensitivity reactions, with adverse reactions such as bronchospasm, urticaria, abdominal and limb pain, and so on.

Targeting to Cancer Cells: -

Transferrin receptors are overexpressed in most solid tumor cells and are expressed at low levels in normal cells. Thus, transferrin-conjugated NPs are used as an active targeting method to deliver drugs for cancer treatment (Amreddy et al., 2015; Liu et al., 2015; Santi et al., 2017). Epidermal growth factor receptor is a member of the ERBB family of tyrosine kinase receptors. EGFR, which is overexpressed in varieties of cancers, is involved in several processes of tumor growth and progression and has already been utilized as a target for cancer treatment (Nicholson et al., 2001; Sigismund et al., 2018). For example, targeting human epidermal receptor-2 (HER-2) is a common therapy for HER-2 positive breast and gastric cancer. Hence, NPs that have been designed to incorporate modified ligands that bind to EGFR in order to target EGFR-overexpressed cancer cells is a promising method of drug delivery (Alexis et al., 2008). cancer cells usually express various types of glycoproteins, including lectins, which are non-immunological proteins that recognize and specifically bind to certain carbohydrates (Minko, 2004). Targeting cancer cell-surface carbohydrates by lectins conjugated to NPs constitutes the direct lectin targeting pathway, while inversely targeting lectins on cancer cells using carbohydrates moieties that are incorporated into NPs is referred to as the reverse lectin targeting pathway (Minko, 2004; Obaid et al., 2015).

Targeting to Endothelium: -

The interaction between vascular endothelial growth factor (VEGF) and VEGF receptors (VEGFRs) plays an essential role in vascularization (Apte et al., 2019). Additionally, targeting VEGFR-2 and VEGFR-3, two major VEGF receptors, simultaneously by liposomes has been shown to enhance therapeutic efficacy (Orleth et al., 2016). The interaction between vascular endothelial growth factor (VEGF) and VEGF receptors (VEGFRs) plays an essential role in vascularization (Apte et al., 2019). Additionally, targeting VEGFR-2 and VEGFR-3, two major VEGF receptors, simultaneously by liposomes has been shown to enhance therapeutic efficacy (Orleth et al., 2016). Vascular cell adhesion molecule-1 (VCAM-1) is an immunoglobulin-like glycoprotein that is also expressed on the surface of the tumor endothelium and is involved in angiogenesis by interacting with vascular endothelial cells. Overexpression of VCAM-1 can be observed in various cancers (Dienst et al., 2005), indicating its potential role in the active targeting of NPs for drug delivery. Integrins are cell surface receptors for extracellular matrix proteins that play an important role in tumor cell migration and invasion (Desgrosellier and Cheresh, 2010). Integrins are

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cell surface receptors for extracellular matrix proteins that play an important role in tumor cell migration and invasion (Desgrosellier and Cheresh, 2010).

Targeting Efflux Transporters: -

Efflux transporters reduce intercellular drug concentration by pumping the drug out of the cell, leading to a failure of treatment. Among them, P-glycoprotein (P-gp), one of the most widely investigated efflux transporters, is overexpressed in several drug-resistant tumors (Schneider and Hunke, 1998; Allen et al., 2000). The nanoparticle-based drug delivery system can modify the control of drug release. For example, several researches have utilized low pH level and redox as triggers for drug release in NPs (Yu et al., 2018; Kundu et al., 2019). Furthermore, NPs, such as polymers, also act as MDR modulators (Qin et al., 2018). For instance, micelles based on amphiphilic deblock polymer of N-(2-hydroxypropyl) methacrylamide (HPMA) and poly (propylene oxide) block (PPO) are able to inhibit P-gp (Braunová et al., 2017). Efflux transporters belong to a family of ABC transporters that have been proven to play essential roles in drug resistance. Combination therapy is another strategy to treat drug-resistant cancers. To this end, NP-based combination therapy has been able to overcome the problem of pharmacokinetic differences between different drugs by assembling multiple therapeutic agents within a single drug carrier, thereby fighting drug resistance and improving the therapeutic effect of cancer therapy (Cuvier et al., 1992; Schneider and Hunke, 1998; Allen et al., 2000; Susa et al., 2009). This system showed a more effective anti-tumor function when compared to chemotherapeutic and P-gp inhibitor combination therapy. This system showed a more effective anti-tumor function when compared to chemotherapeutic and P-gp inhibitor combination therapy.

Targeting Apoptotic Pathway: -

Defective apoptotic machineries enable cancer cells to evade apoptosis and increase survival, thereby contributing to drug resistance in cancer (Viktorsson et al., 2005). The defective apoptotic pathway is often triggered by deregulating Bcl-2 and nuclear factor kappa B (NF-κB). Bcl-2 is a widely investigated anti-apoptotic protein, is highly expressed in many cancers, and is a key player in drug resistance, suggesting its potential as a target for reversing drug resistance. In addition to suppressing anti-apoptotic moieties, the activation of pro-apoptotic compounds can also be used to combat apoptotic pathway-mediated drug resistance. For example, combining ceramide with the chemotherapeutic drug paclitaxel augments the therapeutic efficacy of various drug-resistant tumor models (Devalapally et al., 2007; van Vlerken et al., 2010). In addition to suppressing anti-apoptotic moieties, the activation of pro-apoptotic compounds can also be used to combat apoptotic pathway-mediated drug resistance. For example, combining ceramide with the chemotherapeutic drug paclitaxel augments the therapeutic efficacy of various drug-resistant tumor models (Devalapally et al., 2007; van Vlerken et al., 2010). As p53 plays a significant role in apoptosis, reinstating p53 function or other tumor suppressors is considered a potential way to overcome drug resistance in cancer. Therefore, p53 gene therapy utilizing a nanoparticle-based delivery system has been further researched. Transfecting the p53 gene by cationic solid lipid NPs and PLGA has been reported in lung (Choi et al., 2008) and breast cancer cells (Prabha and Labhasetwar, 2004), respectively. Targeting to mitochondria led to a reduction in ATP production, which is required by ABC transporters. Additionally, paclitaxel-loaded TPP-Pluronic F127-hyaluronic acid nano micelles caused mitochondrial outer membrane permeabilization (MOMP), which resulted in the release of cytochrome Cand activation of caspase-3 and caspase-9, leading to apoptosis of drug-resistant lung cancer cells (Wang et al., 2020).

The Role of NPs in Cancer Immunotherapy: -

Cancer immunotherapy is mainly achieved by activating the anti-tumor immune response (Zang et al., 2017). NP-associated immunotherapy includes nano vaccines, artificial antigen-presenting cells (aAPCs), and targeting of the immunosuppressed tumor microenvironment (TME) (Zang et al., 2017). Nano vaccines deliver tumor-associated antigens (TAAs) and adjuvants to APCs, such as dendritic cells (DCs) (Paulis et al., 2013). NPs, such as liposomes, gold NPs, PLGA NPs, micelles, and dendrimers all have the capability of cytoplasmic delivery of TAAs into DCs, thus enhancing the immune response against tumor cells (Guo et al., 2015). Targeting the immunosuppressive TME is mainly achieved by targeting tumor-associated macrophages (TAMs), myeloid derived suppressor cells (MDSCs), and regulatory T cells (Tregs), all of which are important cell types in the TME (Shao et al., 2015). furthermore, in order to minimize interactions with

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the reticuloendothelial system, NPs are usually modified with PEG (Zang et al., 2017).Alternative approaches of combined chemo-immunotherapy include co-delivery of chemotherapeutics and monoclonal antibodies into porous silicon NPs, which have been effective in stimulating complement activation, antibody-dependent cell cytotoxicity (ADCC), and immune response against cancer cells (Li et al., 2018).

CONCLUSION AND FUTURE PERSPECTIVES: -

Nanotechnology applied to cancer therapy has led to a new era of cancer treatment. Various types of NPs, including organic and inorganic NPs, have already been widely used in the clinical treatment of several cancer types.Compared to traditional drugs, NP-based drug delivery systems are associated with improved pharmacokinetics, biocompatibility, tumor targeting, and stability, while simultaneously playing a significant role in reducing systemic toxicity and overcoming drug resistance. These advantages enable NP-based drugs to be widely applied to chemotherapy, targeted therapy, radiotherapy, hyperthermia, and gene therapy. According to different mechanisms of MDR, NPs that are loaded with varieties of targeting agents combined with cytotoxic agents can achieve the reversal of drug resistance. The NP size, shape, composition, and surface are all the factors that affect the interactions of NPs with the immune system. Although nano vaccines and artificial APCs have demonstrated increased efficacy compared to traditional immunotherapy, the clinical efficacy of this treatment remains unsatisfactory, and the safety and tolerance of these new approaches need to be further investigated. Furthermore, designing hybrid NPs that are more suitable for cancer therapy and engineering NPs that target cancer cells more specifically using targeting moieties merits further exploration.