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# Cancer Treatment with Nanoparticles: An overview

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One of the greatest global causes of death is cancer. Chemotherapy, radiation therapy, and immunotherapy are all forms of cancer treatment, but they all have a number of drawbacks, including cytotoxicity, drug resistance, and other restrictions. The surface properties, ideal size, and shape of nanoparticles have revolutionised cancer treatment by enhancing biodistribution, pharmacokinetics, and biocompatibility. Additionally, the delivery of bioactive plant-based anticancer medicines such as vinca alkaloids, taxanes, podophyllotoxin, and others has been improved using phytonanotechnology. Novel silver nanoparticles are also used as a delivery mechanism for anticancer medications. In this overview, we'll look at silver nanoparticles for drug delivery in cancer disorders, phytonanotechnology, and important uses of nanotechnology.

Keywords: Cancer, Conventional chemotherapy, Mechanism, Nanotechnology, Silver nanoparticles

#### Introduction

One well-known and frequently used form of cancer treatment is chemotherapy. While chemotherapy utilises numerous, its primary function is to indiscriminately kill rapidly proliferating cells, including cancer and normal cells, which produces serious side effects, including bone marrow suppression, hair loss, and digestive issues. Despite the developments and in-depth study of new methods, the only available treatments at this time are surgery, radiation, chemotherapy, and immunotherapy. Nanotechnology has been used in medicine more and more over the past few decades, including applications for safer and more efficient tumour targeting, diagnosis, and therapy [1-4]. Due to their tiny size, biosafety, drug loading, and physical characteristics supporting physical therapy, nanoparticles are quickly exploited as carriers in novel cancer treatment regimens. Due to their special physical, chemical, and optical characteristics, silver nanoparticles are being explored more and more because they can be employed in a number of applications, such as the delivery of medication to specific bodily targets [5-8]. Liposomes, polymeric micelles, dendrimers, nanospheres, and nanocapsules are just a few examples of nanomaterials that are now used in drug delivery systems for cancer treatment that is being researched and evaluated. A novel chemotherapy-radiotherapy combination system based on chitosan nanoparticles has been presented as a treatment for breast cancer. Furthermore, because they act as platforms for medication combination therapy, NPs have shown advantages in the fight against antitumor multidrug resistance (MDR). Future cancer therapies using precision and individualisation could benefit from the use of nanoparticles. The basic principles of using the nano-carrier system in cancer therapy are covered in this article, along with current issues and potential directions for future research [9-11]. Based on their constituent materials, intended uses, and physical and

chemical properties, metal nanoparticles, non-metal nanoparticles, and composite nanoparticles are frequently used in medicine. Inorganic or organic compounds are used in chemical methods to decrease Ag+ ions chemically. The reducing agent (AgO) causes metallic silver to form, and as a result, colloidal metal silver particles are created. To reduce excessive agglomeration and hence aid in the regulation of the AgNPs amount, Stabilizers can be made from chitosan, cellulose, and a number of polymers such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), and polymethacrylic acid (PMAA). In order to coat AgNPs and give them a negative charge on their surface in order to achieve electrostatic stability, anionic species such as citrate, halides, carboxylates, and polyoxanions are some examples. The surface of polyethyleneimine, or PEI, is positively charged. To achieve steric stability, AgNPs interact with large chemical groups, such as organic compounds [12-16].

## PLGA-B u sed NPs Preparation

The most common method for creating PLGA NPs is called emulsification. It involves dissolving the medicine in a volatile organic solvent and adding it to an aqueous phase containing surfactants while stirring continuously. An oil/water (O/W) emulsion is then made using evaporation. The oil in water emulsion produced as a result of this process can be used to form a water/oil/water (W/O/W) emulsion by mixing it with another aqueous solution. Making solid/oil/water (S/O/W) or W/O1/O2 advanced emulsion techniques have been used to create PLGA-based microparticles [19-21]. Single-emulsion treatments have poor encapsulation efficiency for hydrophilic medications compared to double- or multiple-emulsion operations. The polymer concentration and evaporation stage affect the size of the NPs. The higher the polymer contents in the discontinuous phase, the larger the size of the resulting particles. Contrast compounds are employed in a variety of therapeutic procedures in a single formulation (iron oxides). Single emulsion strategy beat the other preparation methods in terms of encapsulation effectiveness, despite the low temozolomide loading in PLGA NPs. This widely used method has the problem of leaving surfactant residues on the NP's surface even after repeated washing operations [22-24].

#### **Mechanical Methods**

The two most pertinent physical processes are laser ablation and evaporation-condensation. They require pricey, highly specialised equipment.

#### **Laser Ablation**

High-power laser pulses are used in this procedure to vaporise the material. The system consists of a laser beam, a high vacuum system with an inert gas introduction, and any substance that can be used to group materials into a solid target. A UV laser, such as an excimer laser, is required because some metal surfaces frequently reflect other wavelengths, such as IR or visible. A powerful laser beam evaporates the atoms from a solid source, colliding with inert gas atoms and cooling them to form clusters. They condense on the cooled substrate. The technical word for this process is laser ablation. The bulk of single-walled carbon nanotubes (SWNT) are produced using this method [28-30].

## **Biological method**

Biological methods don't employ chemical reagents. They depended on organisms like bacteria, fungi, algae, and plants with reducing agents in them that can reduce Ag+ ions. Some of the extracts used come from plants like *Azadirachta indica, Eucalyptus proceri, Calliandra haematocephala*, and *Madhuca longifolia* [31-33]. Others synthesise AgNPs from plants because it is easy, affordable, and environmentally friendly to do so. The therapeutic potential of AgNPs (anti-inflammatory, anti-cancer, antioxidant, etc.) is apparent. Agents that act as stabilising or capping agents are not necessary when using biological natural products as the starting ingredients to

synthesise AgNP [34-38].

# **Synthesis using Plant Extracts**

The use of plants in manufacturing nanoparticles is a relatively unexplored area compared to the usage of microorganisms. There are a few instances that indicate plant extracts might be used in the production of nanoparticles. The creation of gold nanoparticles using geranium plant extract is covered in this work [39-41]. An Erlenmeyer flask containing finely crushed leaves is heated in water for one minute. When leaves break, cells release compounds from within. After cooling, the solution is decanted. Within a minute of adding this solution to an aqueous  $HAuCl_4$  solution, gold nanoparticles start to form [42-44].

## **Emulsion-Solvent Evaporation Method**

The majority of nanoparticles are created using this method. The main components of this method are two phases. Emulsifying the polymer solution is necessary in the first aqueous phase. In the second step, the polymer mixture evaporates, and nanospheres are produced by causing polymer precipitation [45-47]. Nanoparticles are gathered via ultracentrifugation, and any unneeded or unwashed medication is removed before they are lyophilised for storage. Emulsifying the polymer solution and this method is also known as high-pressure emulsification and solvent evaporation. This process involves general stirring and homogenisation under high pressure to extract the organic solvent. The stirring rate, temperature, the kind and quantity of the dispersion agent, and the viscosity of the organic and aqueous phases can all be changed to adjust the size. This method can be applied to lipid-soluble medications, although there are restrictions due to scale-up issues. Among the polymers used in this method are PLA, Poly (- hydroxybutyrate) (PHB), Poly (caprolactone) (PCL), PLGA, Cellulose Acetate Phthalate, and EC.

# Methods of coacervation and ionic gelation

Gelatin, sodium alginate, and other biodegradable hydrophilic polymers like chitosan have all been used extensively in the production of nanoparticles. Ionic gelation is a technique created by Calvo and colleagues to produce hydrophilic chitosan nanoparticles. Chitosan, a polymer, and sodium tripolyphosphate, a polyanion, are both used in the procedure's two aqueous phases. In this process, the positively charged amino group of chitosan combines with the negatively charged tri polyphosphate to generate coacervates that range in size from nanometers to microns. The production of coacervates results from electrostatic interaction between two aqueous phases. In contrast, ionic interaction circumstances at room temperature allow the liquid to turn into a gel as a result of ionic gelation [56-59].

# **Nanoparticles for Medical Imaging**

Numerous nanoparticles, including iron oxide nanoparticles (NPs), exhibit optical, magnetic, acoustic, and electromagnetic capabilities in addition to other characteristics that can be useful for imaging. Studies have shown that injecting NPs into target tissues enhances image contrast and offers better image guidance for cancer surgery and diagnostics [4, 60-63]. For instance, in cryosurgery, NPs can improve the image quality of the edges of the ice ball and the tumour, enabling more accurate ice ball coverage and a greater therapeutic effect. In addition, the vast majority of the nanoparticles used in imaging are made of metal. Depending on the variations in imaging principles, different metal materials will be used to make nanoparticles [64-67].

## **Mechanisms of Targeting**

Targeting cancer cells is a crucial component of nano-carriers for medication delivery since it increases therapeutic effectiveness while protecting healthy cells from harm. The targeted design

of NP-based medications has been the subject of numerous studies [21, 68-70]. To correctly manage the difficulties of tumour-targeted therapy and nano-carrier system design, it is crucial first to understand tumour biology and the interaction between nano-carriers and tumour cells. The two fundamental types of targeting systems are passive targeting and active targeting [28, 71, 72].

## **Active Targeting**

By directly interacting with receptors and ligands to target cancer cells, the ligands on the surface of NPs are chosen to target molecules that are overexpressed on the surfaces of cancer cell surfaces, enabling them to distinguish between cancer cells and healthy cells [73-75]. Internalised NPs can successfully release therapeutic drugs because receptor-mediated endocytosis takes place when ligands on NPs interact with receptors on the surface of cancer cells. Active targeting is, therefore, perfect for delivering macromolecular drugs like proteins and siRNAs. Some examples of targeting moieties include monoclonal antibodies, peptides, amino acids, vitamins, and carbohydrates. Among the most studied ligands that connect to receptors on targeted cells (EGFR) are the transferrin receptor, folate receptor, glycoproteins, and epidermal growth factor receptor [23, 76-82].

# **Passive Targeting**

Passive targeting is used to benefit from the differences between cancer and healthy tissue. With passive targeting, the medications are delivered to the desired area and begin their therapeutic effects. Neovascularisation brought on by high cancer cell proliferation results in tumour vessels having lower perm selectivity than healthy arteries because of many holes in the vascular wall and macromolecules that supply cancer and accumulate in tumour tissue, such as NPs brought on by faulty angiogenesis [83-85]. NPs are retained in cancer patients due to insufficient lymphatic outflow, which allows the Nanocarriers to be employed to convey their contents to cancer cells [86-88]. The EPR effect, which results from these processes, is one factor that propels passive targeting. The EPR effect is impacted by NP size in a number of ways. Smaller NPs offer higher penetrability yet do not leak into typical capillaries, according to a study. On the other hand, larger particles are more likely to be destroyed by the immune system [89-92]. In addition to the EPR effect, the tumour microenvironment is an important factor in the passive delivery of nanomedicines. One of the metabolic characteristics of cancer cells is glycolysis, which serves as the main fuel source for the growth of these cells. The acidic environment created by glycolysis lowers the pH of the cancer microenvironment. The low pH triggers some pH-sensitive NPs and can release drugs close to cancer cells as a result. The non-universal occurrence of the EPR effect, nonspecific medication distribution, and variable blood vascular permeability across tumours are all serious drawbacks of passive targeting [93-98].

#### **Targeting Cancer Cells**

Transferrin, a type of serum glycoprotein, transports iron into cells. While normal cells only moderately express transferrin receptors, the majority of solid tumour cells do. Transferrinconjugated NPs are therefore employed as an active targeting method for the administration of cancer medications [99-102]. When compared to unmodified NPs, transferrin-modified NPs have been reported to have higher cellular absorption efficiency and enhanced intracellular drug delivery. Furthermore, research indicates that transferrin-conjugated NPs play a crucial role in limiting chemotherapy that is resistant to drugs. The folic acid vitamin is required for the production of nucleotides. It is taken up by a folate receptor that is only present a few kinds of healthy cells [103-105]. The alpha isoform of the folate receptor (FR-), which is found on the surface of haematological tumours, is overexpressed in about 40% of human malignancies. As a result, targeting folate receptors with folate-conjugated nanoparticles has gained popularity as a cancer treatment strategy. Furthermore, lectins—nonimmunological proteins that recognise and bind to certain carbohydrates—as well as other glycoproteins, are commonly expressed by cancer

cells. While the reverse lectin targeting technique uses carbohydrates moieties incorporated into NPs to target lectins on cancer cells, the targeting lectins directly strategy uses lectins coupled to NPs to target cancer cell-surface carbohydrates. The ErbB family of tyrosine kinase receptors includes the epidermal growth factor receptor [106, 108, 109]. Most tumour growth and progression processes involve EGFR, which is overexpressed in several malignancies and has previously been employed as a cancer therapy target. Blocking the human epidermal receptor (HER-2) is a common treatment, for example, for breast and stomach cancer that is HER-2 positive. Therefore, EGFR-overexpressed cancer cells can be specifically targeted using nanoparticles that contain modified EGFR ligands. Another active targeting method that can help increase target specificity is the combination of two cancer-specific ligands into a single NP.

#### **Dendrimers**

Since they differ from linear polymers in their systematic structure and special characteristics, they are of interest as an intracellular drug delivery mechanism for cancer therapy. It is possible to isolate the active site, which is similar to active sites in biomaterials because functional molecules are encapsulated within dendritic structures. In addition, dendrimers differ from other polymers in that their outer shells can be functionalised to make them water-soluble using charged species or other hydrophilic groups. One researcher created dendrosomal CAP nanoformulations via an esterification process, and they were then examined for anticancer effects in vitro using the VERO, Hep 2, and MCF-7 cell lines. According to earlier research, these dendrimers exhibited significant cytotoxicity on the VERO cell line with an IC50 of 1.25 g/mL and MCF7 and HEp2 cell lines with an IC50 of 0.62 g/mL. Scientists produced gallic acid dendrimers with polyamidoamine (PAMAM) and tested them on MCF-7 breast cancer cells using Tomalia's divergent growth technique. When it comes to drug loading, these dendrimers have a lot of surface functionality and versatility. The IC50 values of the gallic acid-loaded PAMAM dendrimers were much higher than those of free gallic acid, indicating the potential for dendrimers to be used as a nanotechnology platform for enhanced cytotoxicity in MCF-7 breast cancer cells.

#### **Carbon Nanotubes**

Long, thin carbon cylinders are known as carbon nanotubes. These are synthetic rod-based half-width DNA strands. These enormous macromolecules are unique in size, shape, and physical characteristics. Carbon nanotubes are made from graphene. Patterns resembling honeycombs appear since the carbon atoms in graphemes are arranged in a sp2-bonded structure. The two types are single-wall carbon nanotubes (SWCNTs), which include one layer of graphene, and multi-wall carbon nanotubes (MWCNTs), which contain numerous graphene wells. Concentric cylinders with a hollow centre and regular periodic interlayer spacing make up the MWCNTs.

#### Characteristics of nanoparticles

Nanoparticle size, charge, shape, and surface characteristics, as well as their physicochemical characteristics Additionally, the cellular absorption and in vivo biodistribution of these drug carriers. The main traits that affect the lifetime and delivery of nanoparticles will be covered in this section. Size Particle size is one of the most crucial factors affecting the nanoparticle circulation time. Following systemic administration, mechanical filtration causes nanoparticles to collect in the spleen, where they are removed by the reticuloendothelial system (RES). For instance, Kupffer cells, the main element of RES, serve a crucial role in the clearance of particles that have been collected in the liver. 100-200 nm is currently regarded as the best size for drug delivery systems since nanocarriers took advantage of the EPR effect in tumours and escaped filtration in the spleen while being large enough to avoid absorption in the liver. Through renal clearance or extravasation, particles having a diameter of less than 5 nanometers are quickly expelled from the bloodstream. Furthermore, the liver, spleen, and bone marrow all develop an accumulation of particles larger than 15 micrometres. Additionally, phagocytosis, macropinocytosis, caveolar-mediated endocytosis,

and clathrin-mediated endocytosis are all influenced by particle size when it comes to cellular internalisation. As already mentioned, the size range significantly affects cellular internalisation and biodistribution. Furthermore, according to recent studies, particle shape, along with size range, has a substantial impact on cellular internalisation and biodistribution. Additionally, Gratton and colleagues looked at how particle size and shape affected the frequency of internalisation in HeLa cells. They discovered that particles with the same volume but different forms internalised at radically different rates. Godin and colleagues discovered that discoidal particles accumulated five times more in breast tumours than spherical particles while having equal diameters. Thus, despite size being a key design criterion for nanocarriers for many years, mounting data suggests that size is no longer a significant consideration. The longevity of nanoparticles in blood circulation after systemic distribution depends on their surface properties. Following delivery, opsonins, such as complement proteins and immunoglobulins, may be attached to nanoparticles to aid macrophage recognition. Because of this, opsonisation plays a crucial role in defining how nanoparticles behave in systemic circulation. Rats' blood circulation was improved by the surface modification of PEGylated liposomes with rat serum albumin (RAS) in contrast to unmodified PEGylated liposomes. In order to conduct further research, total serum protein concentrations were measured in both the absence and presence of RAS coating. As a result, RAS-modified liposomes significantly decreased the overall quantity of serum proteins that can cause opsonisation in serum. The releasing properties of nanoparticles determine release characteristics and the effectiveness of treatment in target locations. Conventional medications used in clinics have a short therapeutic window due to the fast rise and fall of plasma drug levels after systemic injection, which leads to borderline dosages and adverse effects. Additionally, medication delivery systems make an effort to provide the appropriate drug concentration at the target site within the therapeutic range, reducing side effects and patient discomfort. Osmotic pressure, mechanical pumping, and electrokinetic transportation are all methods that can be used to provide zero-order release kinetics, which can maintain constant plasma drug levels over time. Furthermore, biocompatible polymeric nanoparticles are used to extend the time of drug release due to their lengthy biodegradation times, which can range from days to months. A polymer's biodegradation rate greatly depends on its molecular weight. Both poly lactide-co-glycolide (PLGA) and polylactic acid (PLA) were employed to assess the sustained release of docetaxel following intravenous administration. There is evidence that the molecular weight of the polymer and the drug's release rate are closely related. A polymer with a low molecular weight produced a prolonged payload release, while a polymer with a high molecular weight caused the material to decay very slowly. A multistage delivery system is another option for promoting extended payload release, with mesoporous silicon particles (MSP) showing very strong potential for drug delivery. One of the qualities of MSPs that can be tailored for particular applications and objectives is their physical characteristics. We used MSPs that contained nanoliposomes contained (siRNA) to cause target mRNA degradation.

#### Conclusion

A new era in cancer treatment has begun with the use of nanotechnology in cancer therapy. When compared to conventional pharmaceuticals, NP-based drug delivery systems have improved pharmacokinetics, biocompatibility, tumour targeting, and stability. They also have lower systemic toxicity and can overcome drug resistance. These benefits make NP-based drugs useful in chemotherapeutics, targeted therapy, radiation, hyperthermia, and gene therapy. These novel active or passive targeting techniques can considerably increase survival rates by reducing the harmful effects of conventional chemotherapies. Due to the fact that it is an easy and environmentally benign process that does not involve the use of chemical reagents, the biosynthesis of AgNPs is becoming more and more popular. Since cancer is one of the most lethal diseases, nanotechnology's contribution to precision medicine while avoiding potentially deadly side effects may help to encourage a shift in clinical practice in favour of a life-saving approach.

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