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Chemical Characteristics of Nanoparticles: Cytotoxicity, Liposomal Modification, and Using of Nanoparticles in Cancer Therapy

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Abstract:
There is no indication that the phenomenal growth of nanotechnology during the last four decades will slow down. Nanotechnology and its ground breaking discoveries and products have permeated every industry, from healthcare to food production. The use of nanoparticles has considerably extended the shelf life of food items and enhanced the intracellular delivery of hydrophobic drugs. A critical evaluation of the risks associated with nanoparticles utilised in consumer items is urgently required due to the ever-increasing fascination with nanotechnology. The general public views nanotechnology as having many beneficial impacts on human health, which explains why this is the case. The composition is only one of several physicochemical variables that influence a nanomaterial's toxicity; these properties also differ from those of bulk materials. Size, area, chemistry, roughness, dispersion medium, and agglomeration ability are some of these characteristics. As new nanoparticle-based products hit store shelves daily, there is an urgent need to fill the knowledge gap on the relationship between physicochemical properties and the emergence of toxicological issues. Despite the potential of targeted drug delivery systems to improve cancer treatment, these methods are currently constrained by tumour heterogeneity and micro-environmental challenges. Improving the delivery of targeted therapies requires further study and innovation. Nanotechnology presents an exciting new direction for cancer treatment by allowing for the targeted destruction of cancer cells with minimal side effects on healthy tissues. The cancer microenvironment can be circumvented by using nanoparticles to transport therapeutic medicines straight to the tumour site. Nanoparticles can be made more effective by modifying their surfaces to increase their stability, circulation time, and cellular absorption. Challenges including drug resistance and limited drug penetration into solid tumours can be overcome with the use of nanoparticles in targeted therapy. To ensure long-lasting and successful treatment, these nanoparticles can be designed to release the therapeutic ingredients in a controlled way. In addition, the continuous progress in nanotechnology has the ability to enable personalised medicine techniques that are adapted to the specific demands of each patient, which might completely transform cancer treatment.
Keywords: Nanoparticles, Chemical Characteristics, Modification, Cancer Therapy

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Introduction

Researchers in the fields of biology, chemistry, and physics are looking to nanotechnology as the obvious next step in bringing together technology-based science and its sister disciplines. The term "nanoscience" refers to the study of phenomena and materials manipulation at atomic, molecular, and macromolecular scales, while "nanotechnology" describes the process of creating and using structures, devices, and systems by manipulating their size and shape at the nanometer scale. Modern nanotechnology has the ability to improve healthcare, ecology, energy, and space travel by creating devices on a minuscule or even molecular scale. Over the past several years [1, 2], the phrase "nanotechnology" has been used excessively and is now practically interchangeable with things that are highly promising and inventive. Nanotechnology, in a broader sense, could be defined as the manipulation of nanomaterials, which have at least one dimension ranging from 1 to 100 nanometers in size. Curiously, the positive attributes of these nanoparticles are bestowed by their unique physicochemical and biological properties, which set them apart from their conventional counterparts. Recent years have seen researchers devoting vast amounts of time and energy to studying various nanoparticles; as a result, engineered nanomaterials (ENMs) are proliferating in many areas of modern life, including cosmetics, food packaging, drug delivery, therapeutics, biosensors, and so on. This has led to the emergence of previously unseen pathways for the environmental and biological exposure of NPs. Considering the growing prevalence of nanomaterials in our environment, it is crucial to evaluate their potential toxicity. To further understand their impact, we must examine their physicochemical properties, such as their size, surface area, solubility, chemical composition, shape, agglomeration state, crystal structure, surface energy, surface charge, surface morphology, and coating. Additionally, we must determine the role of each characteristic property in causing toxic effects. This review aims to address these facts by analysing the association between the toxicity of manufactured nanomaterials and their physicochemical features. It is widely agreed that nanoparticles can cause a variety of harmful effects through various pathways, including allergic reactions, fibrosis, organ failure, nephron-toxicities, neurotoxicities, hepatological toxicities, splenic toxicities, and pulmonary toxicities. Nanotechnology involves purposefully modifying and engineering particles with a size between 1 nm and 100 nm so that they can be rearranged or assembled into nano-systems that perform better. Nanotechnology and its applications have propelled certain countries to the vanguard of scientific enquiry in the past ten years. One such country is Ireland. Technological manipulation of matter ultimately produces nanoparticles, which are, depending on their size, slightly larger than an atom as a result of molecular processing. When compared to traditional substances, they have superior qualities like auto-reactive stability and self-reassembly, making them very adaptable and allowing for easy modification to attain desired attributes like a large surface area [3-5]. Since its inception only twenty years ago, nanotechnology has grown in stature and is swiftly making its way out of universities and into the business world. Estimates indicate that nanotechnology will have a three trillion dollar effect on the world economy by 2020, thanks to the potential innovations it offers. This makes the field very attractive from an economic perspective. At the crossroads of chemistry, medicine, physics, and engineering, nanoparticles possess distinctive physicochemical characteristics, which may explain this. There have been tremendous advancements in many different areas of nanotechnology, which is why it is one of the most rapidly expanding scientific disciplines. At present, nanotechnology encompasses a vast array of fields, from electronics and energy to materials science and biology, among many others. Nanoscale transistors and other components are being investigated by electronics engineers as a means to fabricate smaller, quicker, and more energy-efficient gadgets. New materials and gadgets for energy storage, solar energy conversion, and other applications are being developed through the application of nanotechnology in the energy sector. Novel tissue engineering techniques, diagnostic instruments, and therapeutics are all emerging from the biomedical field's utilisation of nanotechnology. In sum, nanotechnology is a topic that is always changing and improving, and the current level of knowledge reflects that. There will be many fascinating new advancements and uses for nanotechnology in the future. Research into the possible medical uses of nanoparticles and nanomaterials is on the rise. The use of nanoparticles as carriers to transport medications to targeted cells or tissues in the body is an exciting new frontier in the field of drug delivery. Pharmaceuticals can be made more effective with fewer side effects by engineering nanoparticles with surface features that enable them to target sick cells while avoiding healthy ones. Sustained medication delivery over time is also possible with nanoparticles because of their ability to release their cargo in a regulated manner. Contrast agents in medical imaging and the identification of certain biomolecules in biological samples are two examples of the diagnostic applications of nanoparticles. To aid in tissue regeneration and repair, nanoparticles can either serve as scaffolds for the fabrication of new tissues or transport

signalling molecules such as growth factors. These and other possible uses of nanotechnology show enormous promise for enhancing the detection and treatment of numerous medical diseases [6, 7], even though nanomedicine is a growing discipline. With an emphasis on healthcare and the idea of drug delivery systems enabled by nanoparticles for the treatment of disease, this paper will provide a concise overview of the impact of nanotechnology in a number of biological domains. While nanoparticles are becoming increasingly popular in medicine, this article will examine both the potential negative consequences of their widespread use and the steps being taken to lessen such consequences through the creation of nanoparticle drug delivery systems (DSSs).

Consumption Sector

Researchers have been hard at work developing methods to extend the shelf life of food and enhance its absorption of nutrients in response to the rising demand for nutritious food products. In order to accomplish these objectives, nanotechnology has been utilised extensively in the delivery of nutraceuticals and preservation of food in recent years. Nanoparticles have shown a lot of potential when applied to packaging materials as barrier molecules or antibacterial agents. Because of its inherent antibacterial qualities, silver nanoparticles (AgNP) are one of the most commonly used nanoparticle additions for this purpose. The addition of AgNP to food products is possible in two ways: first, as an edible biodegradable coating for foods including meat, poultry, and fruits; and second, as an active element in the polymeric matrix of the packaging material. Actually, research has looked into how AgNP-containing packaging can extend the shelf life of asparagus, chicken, orange juice, and strawberries by preventing the growth of harmful microbes like E. coli, S. streptococcus, fungi, and yeasts. Zinc oxide (ZnO2) and titanium dioxide (TiO2) are two more substances that are effective against a wide range of food pathogens, including S., in addition to AgNP. pneumoniae, Salmonella typhi, and Staphylococcus aureus. It is known that they are employed to preserve foods like strawberry puree, orange juice, and liquid egg albumen. The whitening effects of TiO2 and the UV protection of ZnO2 have led to their use as food additives, respectively. Nano-encapsulation is a tried-and-true method for improving the release of taste and functional nutrients from food products. Modified starch, cellulose, chitosan, and dextrin are common components of carbohydrate-based delivery systems used for encapsulation. As an example, liposomes based on phosphatidylcholine have been used to deliver vitamin C [8-10]. This encapsulation is believed to keep the nutrient's bioavailability higher than free oral supplements, probably because of controlled release of the content. Bioactive substances in food, such curcumin and resveratrol, can be better preserved and absorbed when encased in chitosan nanoparticles. Research into the potential of polymer-based nanoparticles like chitosan and poly-(lactic-co-glycolic acid) (PLGA) to encapsulate and transport bioactive substances like vitamins and antioxidants in food items is ongoing. Because of its large surface area and lack of toxicity, silica nanoparticles have been investigated for their use as bioactive chemical carriers and food additives. One example is the use of silica nanoparticles to enhance the sensory qualities of drinks and sauces while also delivering minerals like iron. Generally speaking, the use of nanotechnology in the food sector has allowed for the practical and cost-effective extension of the shelf life of fresh food goods. Packaging nanoparticles [11, 12], like AgNP, may occasionally leach into the primary food product, posing toxicity concerns; however, nanoparticles utilised to enhance nutraceutical delivery may be comparatively non-toxic. The harmful effects of ingesting AgNPs are poorly understood, despite the fact that it is possible to eat up to 80 g of AgNPs each day. Some studies have found that ingesting AgNPs has no negative health impacts, while others have found that doing so is extremely harmful.

Cosmetics Market

Many cosmetics brands now incorporate nanomaterials into their wares, attesting to the widespread use of nanotechnology in this sector. Nanoparticles of zinc oxide and titanium dioxide are commonly added to sunscreen in the sunscreen industry. These tiny particles are effective at filtering out UV rays and pose no major health risks. Additionally, since the particles are smaller, an aesthetically undesirable "white streaking" may appear when the cream is applied. Various liposome formulations, including ethosomes and transferosomes, are utilised in cosmetics to enhance the transdermal administration of active substances. These liposomes can be made from either synthetic or natural lipids. Because liposomal lipid bilayers can fuse with cell membranes and change the fluidity of the membranes to facilitate the entry and delivery of liposomal content, they are mostly used in cosmetics to improve the transdermal delivery of cosmetic chemicals. Although nanotechnology is prevalent in the cosmetic industry [13, 14],

as it is in all industries, there are safety concerns regarding the use of nanoparticles in cosmetics owing to the frequent and extensive use of many cosmetics. This is especially true when it comes to bathing products, where AgNPs are active antibacterial ingredients. Similarly, dental products, such as mouthwash and toothpaste, contain AgNPs due to their activity against various yeast strains.

The field of nanomedicine

Molecular mechanical robots that can perform surgery or implant themselves in the body to aid malfunctioning organs in their functional recovery were detailed by him. The use of sophisticated drug delivery systems based on both synthetic and naturally occurring chemicals is one area where nanotechnology has had a profound impact on medical practice. Scientists at Harvard University's Wyss Institute, for example, created a "nano-robot" that can deliver anticancer medications to cancer cells with pinpoint accuracy. Nano-robots have potential in the field of cardiovascular medicine, such as those that can mend damaged blood vessels by emulating the functions of artificial platelets or assist people whose coronary arteries have been blocked. is likewise a work in progress. The development of more efficient methods of transporting medications is one of the primary medical uses for nanotechnology. Many classical medications are undergoing intense research to find ways to make them more effective [15, 16], as the prevailing thinking is that their low bioavailability and aqueous solubility limit their absorption and retention in biological systems. It is believed that the physical features and smaller size of many nanoparticles provide them enhanced pharmacokinetic capabilities; depending on the type of nanoparticle, they can target certain cells for selective action. Nanoparticles have the potential to alter cellular processes by penetrating target cells and accumulating in subcellular structures; this has led the FDA to approve several of these particles for clinical use, which could improve the treatment of chronic diseases like diabetes, cancer, and kidney disease. Encapsulated messenger RNA (siRNA) or DNA (in gene therapy), inorganic metals and metal complexes, and chemotherapeutic drugs with pharmacologic properties are among the most common nanoparticles utilised in therapeutic research. But because the cell barrier is so impenetrable to certain of these nanoparticles, delivery mechanisms are necessary to overcome this obstacle [17, 18]. Liposomes, micelles, chitosan, and synthetic dendrimers are just a few of the nanoparticle delivery systems that have been developed as a result. It is feasible to evade the toxicity of anticancer medications by entrapping hydrophobic and hydrophilic chemicals into liposomes. For example, the use of nanoparticles in liposomes has a long history of success in the treatment of disease; for example, the FDA has authorised DoxilTM (liposomal doxorubicin) for the treatment of ovarian cancer and Kaposi sarcoma. Therefore, liposomal encapsulation is a viable option for increasing the medicinal efficacy of drugs. Furthermore, liposome alteration enables active or passive tumour targeting. As a result, the therapeutic payload is more effectively delivered to the cancer cells in the tumour, with little effect on the healthy cells. By enclosing doxorubicin in DPPC-based liposomes, the drug's cytotoxicity is increased while its toxic side effects are reduced. This improves the antitumoural therapeutic efficacy compared to conventional doxorubicin. Nanoparticles, which can have their size, shape, optical, magnetic, and electronic properties adjusted, are also useful for medical and diagnostic imaging of internal organs and tissues. In order to address the radiation concerns associated with current imaging methods, researchers have developed multifunctional imaging platforms utilising nanoparticles derived from silica and iron oxide. One such platform is MRI/optical dual-modal imaging. Because of its biodegradability, iron oxide is both biocompatible and a magnetoresponsive metal. What makes it an ideal MRI imaging material is this, together with its optical characteristics. As MRI contrast agents, iron oxide nanoparticles have seen extensive use. Because of their superparamagnetic properties, they can change the tissue's magnetic relaxation times, which in turn increases the contrast in magnetic resonance imaging (MRI). Cancer detection, inflammatory imaging, and atherosclerosis imaging are just a few of the clinical imaging applications that have made advantage of this characteristic. Nanoparticles derived from silica have a similar history of use as CT imaging X-ray contrast agents. Due to their high X-ray attenuation, silica nanoparticles can be utilised to improve the contrast in computed tomography (CT) pictures. This can aid in the detection and monitoring of various diseases and ailments, including inflammation and cancer. A nanoparticle made of silica that has a luminous core and a paramagnetic shell was described by Kim et al. With the combination of the MRI's magnetic field and the nanoparticle's optical properties, this one-of-a-kind nanoparticle opens the door to the prospect of multimodal imaging. Functionalizing the paramagnetic shell with target peptides or moieties is another option. With this, it may be possible to zero in on cancer cells in particular. Combining the MRI's

magnetic field with the nanoparticles' magnetic and optical characteristics, this method eliminates the requirement for radioactive tracers often employed in PET and CT scans to identify and track changes in live tissues for diagnostic purposes. On top of all that, medical implants [19-22], wound dressings, medical apparel, and antimicrobial devices all make use of nanoparticles, especially AgNPs, as coating materials. Traditional disinfection methods merely kill bacteria, which might not be enough to prevent subsequent infections. Instead, as long as the nanoparticle stays on the surface of the material, medical equipment and clothing materials coated with AgNP continue to be effective against a broad variety of bacterial strains. From its potential as a bactericidal medicinal agent to its imaging and diagnostic applications, nanotechnology appears to be playing an important role in the medical field. Enhanced nanotechnology research in the medical domain is not slowing down, and these advancements are conceivable because of the characteristics that are unique to nanoparticles. To enable nanoparticles to target particular cells or tissues, their surfaces can be functionalized with a variety of moieties, including small chemicals, antibodies, or polymers. When developing the nanoplatform, keep these functionalizations' stability, specificity, and efficiency in mind. The iron oxide core of the nanoparticles must be stable so that it does not break down or clump together in biological systems; this is especially crucial because some of these nanoparticles are known to be quite reactive. To be considered biocompatible, a nanoplatform must not cause any kind of unwanted reaction in living organisms, including swelling, toxicity [23, 24], or an immunological response. Consideration of the payload's release kinetics from the nanoplatform is crucial for therapeutic applications. For the payload's safe and effective delivery, the release rate has to be precisely managed. Consideration of targeting and accumulation in the target tissue or organ is especially crucial for therapeutic applications including nanoplatforms. To achieve its full therapeutic potential, the nanoplatform has to be able to accumulate just in the intended target area and target only those areas.

Properties of Nanoparticles in Physiology and Chemistry

In the medical field, nanoparticles exhibit improved pharmacologic behaviour in comparison to bigger molecules due to their unique combination of characteristics. So, a lot of work is going into studies to figure out how to optimise the size, shape, surface area, and surface chemistry of nanoparticles so they may be used most effectively in medicine. A variety of methods exist for synthesising nanoparticles; for example, gold nanoshells, liposomes, and micelles can all have their sizes and forms modulated throughout the synthesis process according to their intended uses. During production, nanoparticles have the potential to clump together into larger particles, which, depending on their composition, could either increase or decrease their cytotoxicity. In targeted drug delivery systems [25, 26], reactive groups or molecules, like antibodies, can be attached to nanoparticle surfaces to alter their surface chemistry. Nanoparticles can be managed to achieve precise sizes and shapes by a variety of physicochemical features, such as charged surfaces, agglomeration, and the capacity to conjugate other groups to surfaces. Nanoparticles are able to be more reactive in the biological environment than regular particles because of these characteristics.

Dimensions and Extent

Because of their extremely small size—anywhere from 1 nm to 100 nm—nanoparticles have an exceptionally high surface area to volume ratio. Some normally inert particles, like gold, become reactive in the nanoscale range due to this feature of nanoparticles, which has a high surface area of contact per mass unit compared with larger particles. Nanoparticles are able to penetrate bodily tissues and fluids more easily than their bulk counterparts because of their tiny, controlled size. The rate of endocytosis, distribution, retention, and elimination of nanoparticles inside biological systems is essentially affected by their size and surface area. Nanoparticles are not able to passively pass through cell membranes; rather, they are internalised by endocytosis in a size-dependent manner, according to the vast body of literature on nanoparticle transport into normal and cancer cell lines. Internalisation of nanoparticles less than 200 nm is facilitated by clathrin-coated vesicles, although endocytosis by caveolae is known to occur for bigger nanoparticles, typically 500 nm. However, nanoparticles are susceptible to phagocytosis in immune cells like macrophages. Microparticles (less than 500 nm) enter immune cells via the phagocytotic pathway, whereas particles with larger sizes (between 2 and 3 m, about the size of bacterial cells) show the greatest phagocytotic uptake. Nanoparticles, like liposomes, can now be designed to be as small as possible so that they can be taken in by mammals cells as efficiently as possible.

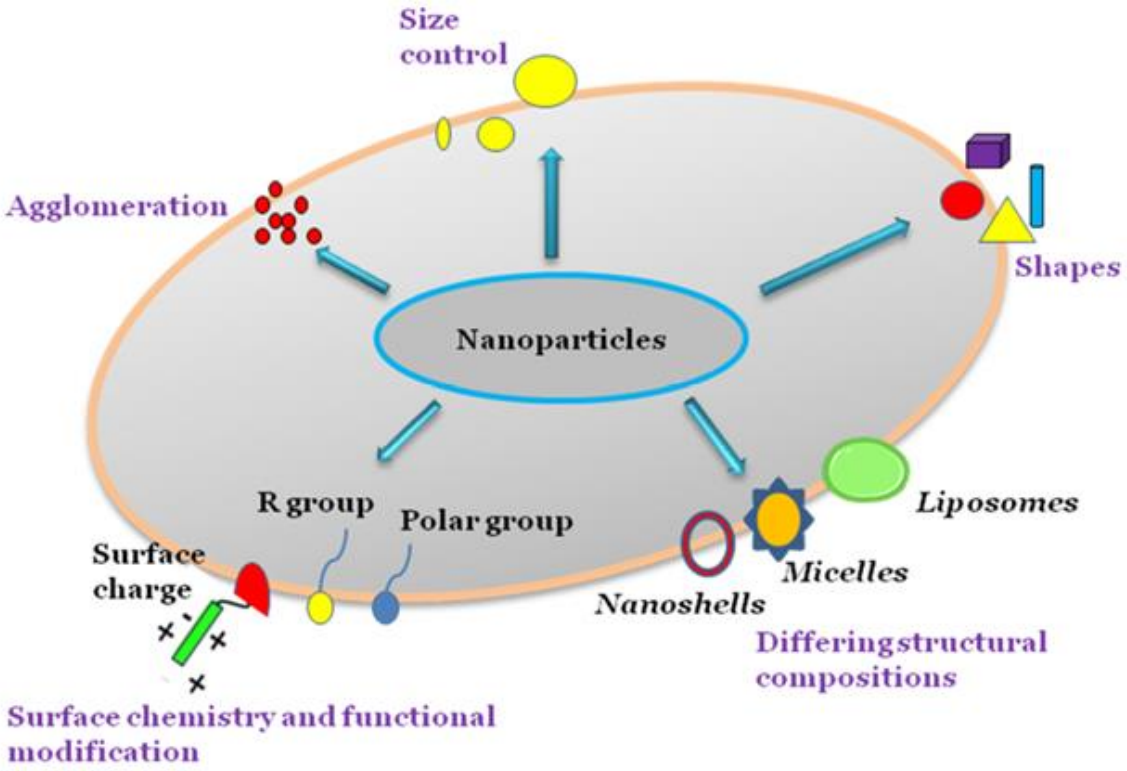

Figure 1. Physicochemical properties of nanoparticles.

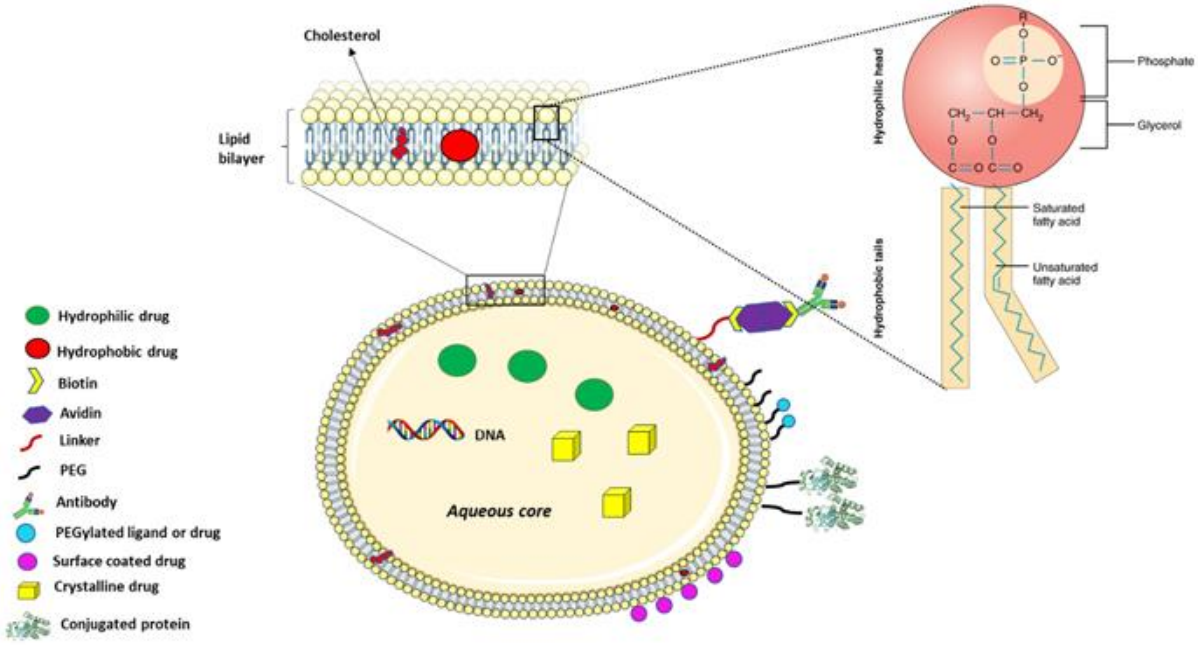

Figure 2. Liposomal modification for drug delivery.

The surface chemistry of nanoparticles can be influenced by the pH of their delivery environment; this feature has been used to stimulate medication release in the acidic tumour microenvironment. Recent research has demonstrated, for instance, that carrageenan oligosaccharide-capped AuNP release epirubicin at an acidic pH, leading to cell death in HCT-116 colorectal cancer cells. Nanoparticles' surfaces influence their mobility in biological systems that contain water, which in turn influences their reactivity and delivery. Their versatile surface qualities make them ideal for use in biomedical sensor applications, implant coatings, and medication delivery systems, among others. To avoid postoperative infection caused by resistant strains of Staphylococcus epidermidis and Staphylococcus aureus, for instance, researchers created a titanium implant surface functionalized with AgNPs, which have antimicrobial

characteristics [27-29]. A lipid bilayer encased in an outer watery core forms liposomes, which have medicinal applications due to their ability to transport drugs. Just like the plasma membrane, the liposomes are made with cholesterol to limit the phospholipid's fluidity. To make them compatible with the mammalian cell membrane and improve their intracellular transport, nanoparticles like AuNPs and even traditional medications are frequently coated with lipid layers, similar to liposomes. The liposome's active phospholipid heads allow for the targeted administration of a wide range of substances, among its other functional advantages. One way to increase liposome bioavailability is to conjugate PEG to their surface. This makes the liposomes invisible to phagocytes, who then flush them out of the body. To further enhance the liposomal surface's ability to target specific cells, active groups like folate and monoclonal antibodies can be added by PEGylation or other linkers. Cancer cells bind folate within the body to fuel their unchecked proliferation, which is why folate is commonly used. On cancer cell surfaces, folate receptors are highly expressed. In contrast, the sheer variety of receptors and surface antigens that may be engineered into monoclonal antibodies makes them a more versatile tool for targeted delivery. Nanoparticles or medications can be more efficiently delivered to tumour cells for targeted cancer cell eradication when these active surface agents are conjugated to their surfaces.

Shape

Nanomaterials can be synthesised in a variety of shapes and sizes, as mentioned above. The final step of synthesis, which usually entails nucleation of the nanoparticles from seed, allows for the modification of their morphologies. Nucleation is the process by which nanoparticle crystals are grown by first fusing together their nuclei, which are called seeds. A nanoparticle's form is as important as its size when it comes to its biological activity and responsiveness. Endocytosis is more common for nanoparticles with a spherical or rounded form than for those with a rod or tube shape. This occurs due to the fact that the shape influences endocytosis, which in turn disrupts the manner in which the membrane envelops the nano-construct when coming into touch with it [30-34]. Thus, the cell's failure to activate the actin-dependent membrane dynamics essential for endocytosis is likely to blame for the lower endocytosis of nano-rods or other forms. This could be the explanation for why the majority of pharmacologic nanoparticles have a spherical shape. Contrarily, new research on nanoparticles of various forms has revealed promising uses for these particles in medication delivery. According to Zhao et al., long-rod nanoparticles outperform spherical and short-rod nanoparticles in terms of bioavailability and particle encapsulation capacity. Nanorods and nanospheres are the most active forms of nanostructures, however other shapes like nanoflowers and nanoprisms do exist. This is likely because to the distinctive morphologies of these other structures. Nanoparticle endocytosis is strongly influenced by their form. Both clathrin-mediated and clathrin-independent mechanisms can lead to endocytosis. The endocytic pathway that a nanoparticle follows, and thus its internalisation by the cell, can be influenced by its form. Highly selective clathrin-mediated endocytosis is responsible for the uptake of spherical or spherical-like nanoparticles. In order for clathrin to encase the nanoparticle and start the internalisation process, the particle must meet certain size and shape requirements. On the other hand, clathrin-independent routes are frequently utilised for the internalisation of nanoparticles with complicated or irregular geometries. Particle size and charge are two of several variables that might affect this less selective process.

Nanoparticles' Physicochemical Characteristics and How They Influence Their Toxic Effects

While nanoparticles might offer certain desirable traits due to their unusual qualities compared to their bulk counterparts, it's paradoxical that these same attributes could also provide them some unusual harmful processes. As we will see in the parts that follow, the conventional wisdom holds that nanomaterials' toxicity stems from their size, surface area, composition, morphologies, etc. Particle Dimensions and Surface Area The interaction between materials and biological systems is greatly influenced by particle size and surface area. Nanomaterial surfaces appear to be more reactive both with themselves and with their surrounding environment as a result of the apparent exponential growth in surface area relative to volume brought about by shrinking material sizes. It is important to mention that the system's response [35-37], distribution, and elimination of materials are determined by particle size and surface area. Size is known to play a role in a number of biological processes, such as endocytosis, cellular uptake, and the efficiency of particle processing in the endocytic pathway. Researchers have used different cell types, culture conditions, and exposure times to assess the cytotoxicity of NPs of varying sizes in vitro. However, assessing their

toxicity in living organisms is challenging because of the particles' complexity and the need for a more thorough understanding of biological systems. Despite this, several authors have used different in vivo models to assess the toxicity of NPs in biological systems. Nanoparticles' capacity to penetrate biological systems is generally responsible for their size-dependent toxicity. and alter the molecular blueprints of several macromolecules, disrupting essential biological processes in the process. Size plays a crucial effect in the development of oxidative reactions and the formation of free radicals, which is one of the main ways in which ENMs cause toxicity in living organisms. Several writers have pointed out that smaller particles are better able to generate ROS. Free radicals pose risks to biological systems primarily by damaging DNA, oxidising lipids, and triggering inflammatory reactions. In addition, multiple investigations using various types of nanoparticles demonstrated that surface area is an important component in the development of harmful effects in rats, specifically inflammation of the lungs and other tissues generated by epithelial cells. The oxidation and DNA damaging properties of nanomaterials increase in a dose-dependent manner as their size decreases due to an increase in surface area. much more than that of bigger particles having the same mass. The pharmacological behaviours of nanoparticles are also determined by their size. When injected intravenously, NPs smaller than 50 nm rapidly reach almost all tissues and may cause toxic effects in some of them. Conversely, RES readily absorb NPs larger than 50 nm, especially positively charged particles between 100 and 200 nm in size, preventing them from reaching other tissues. The reticuloendothelial system (RES) protects other tissues through clearance, but oxidative stress mostly affects RES organs including the liver and spleen [38, 39]. Numerous toxicological investigations have proven that nanoparticles with reduced sizes of dimensions This finding suggests that the inherent toxicity of nanoparticles may be influenced by factors other than size and surface area, such as the chemical composition of their contents.

How Particle Form and Aspect Ratio Influence

In order to create more effective nanomaterial based targeted delivery systems, there has been a flurry of recent significant progress in understanding the interaction between particle size and shape; nevertheless, this also reinforces the need to investigate their adverse effects. Fibres, rings, tubes, spheres, and planes are just a few of the many shapes that nanomaterials can take, as seen in Figure 1. Carbon nanotubes, silica, allotropies, nickel, gold, and titanium nanomaterials are just a few of the countless nanoparticles that have been found to exhibit shape-dependent toxicity. In vivo membrane wrapping mechanisms during endocytosis or phagocytosis are impacted by shape dependent nanotoxicity. Research has shown that spherical nanoparticles, as opposed to rod-shaped or fiber-like ones, undergo endocytosis more rapidly and with less effort. It has also been noted that when the aspect ratio increases. Asbestosis, mesothelioma, and lung carcinoma were all caused by asbestos fibres longer than 10 microns, 5 microns, and 2 microns, respectively. This is because macrophages are unable to properly clear the respiratory tract of longer fibres, thus they cause asbestosis. In their study, Hamilton et al. demonstrated that alveolar macrophages in mice mount an inflammatory response in response to TiO2 fibres that are 15 mm in length, which is significantly more hazardous than fibres that are 5 mm in length. The plasma shelf life is inversely proportional to the toxicity of long-aspect fibres. It may only take a few months for the soluble fibres to dissolve in the lung fluid, but the insoluble fibres will most likely stay there forever. Also, in comparison to spherical particles, long-aspect ratio-particles (SWCNTs) cause far more lung damage. In addition, after intra-abdominal instillation, long MWCNTs elicit inflammation of the abdominal wall, but short MWCNTs did not. Therefore, these phenomena would undoubtedly contribute to the development of safer nanotechnology-based systems as their complexities are better understood. The Influence of Surface Charge. Nanoparticle toxicity is largely defined by their surface charge, which determines how they interact with biological systems. Nanoparticle surface charge largely regulates several properties of nanomaterials, including transmembrane permeability, plasma protein binding, colloidal behaviour, and selective adsorption. Note that due to their improved opsonization by the plasma proteins, positively charged nanoparticles exhibit far higher cellular absorption than neutral or negatively charged nanoparticles. They can also cause platelet aggregation and hemolysis [40, 41], according to the research. because of which the body becomes extremely poisoned. When exposed to nanoparticles, surface charge changes their size and structure via aggregate or agglomeration development, which in turn affects the organism's reaction. In general, 50 nm NPs are able to pass through the skin because of their tiny size and high specific surface area, whereas 500 nm particles are able to bypass the skin's barrier due to their high charge concentration, which is the result of their high density and number of charged groups. The research fraternities have

used various amendments to shield or modulate the surface characteristics of NPs to reduce their toxic manifestations. Since the surface charge largely influences their interactions with biological systems, a glimpse of these efforts is provided in the later part of the paper. Crystalline Structure and Composition Influence.

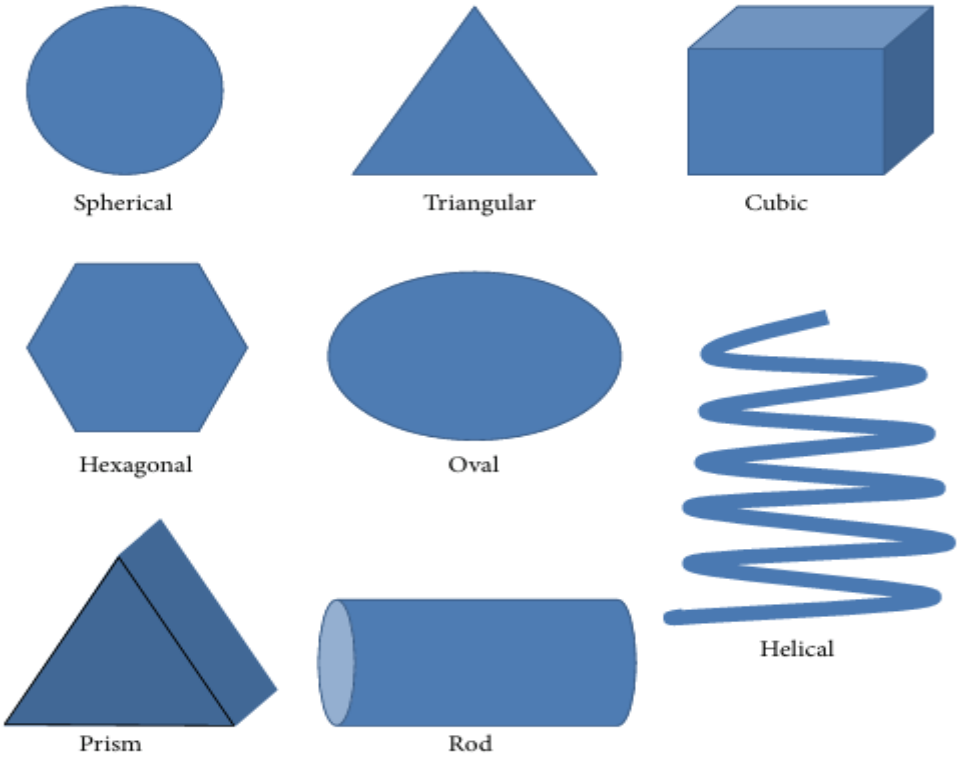

Figure1: Variousshapesofnanoparticles.

The Impact of Density and Accumulation.

Nanoparticle toxicity is affected by their aggregation states as well. A number of factors, including size, surface charge, and composition, determine the aggregation states of NPs. The buildup of aggregates of carbon nanotubes over extended periods of time causes cytotoxic consequences, whereas the individual nanotubes themselves do not cause acute toxicity when found in the liver, spleen, and lungs. Pneumothorax interstitial fibrosis is worsened by agglomerated carbon nanotubes, which have more negative consequences overall. In addition, it has been noted that the toxicity of nanoparticles diminishes as their concentration increases.

The Impact of Media and Solvents. It has been observed that the toxicity of nanoparticles can be influenced by changes in their size, which in turn are affected by changes in their dispersion and agglomeration states, which are in turn affected by changes in the conditions of their medium or solvent. The size of TiO2, ZnO, or carbon black particles is found to be much larger in PBS compared to water. Additionally, it is well agreed that NPs exhibit variable diameters in biological environments. As a result, nanoparticle toxicity varies with the nature of the suspension medium; conversely, the same nanoparticles can display diverse hazardous effects when dissolved in various media. Nanomaterial formulations may have improved physicochemical and solution properties thanks to the dispersion agent, but the toxicity of the nanoparticles may have been negatively impacted.

The Cytotoxicity of Nanoparticles

Worries about potential risks from increased human exposure have arisen in tandem with the development of nanotechnology and its widespread use in modern life. Research into the harmful effects of nanoparticle exposure sparked the development of nanotoxicology. Recent work in this area has shown that nanoparticles' hazardous effects stem from the same characteristics that make them pharmacologically useful. A number of studies have used various cell lines and experimental settings to examine the toxicity of various nanoparticles. For example, research has demonstrated that carbon nanotube toxicity impacts soil bacterial diversity, stunts the growth of Daphnia magna, Chlorella vulgaris, and Oryziaslatipes, and causes oxidative stress, membrane damage, and inflammation in the human

A549 lung cancer cell line. Nanoparticles can infiltrate tissues and cells, where they alter vital cellular functions such as rupturing the membrane of subcellular structures and inducing an overproduction of reactive oxygen species (ROS), according to various studies. Cell death, DNA damage, and deregulation of cell signalling are all outcomes of oxidative stress, which is itself caused by high quantities of reactive oxygen species (ROS). Surface modification of nanoparticles is a common method for improving their functionalities. Because the toxicity of nanoparticles is affected by their surface chemistry, this could unintentionally make them more lethal. By interacting with various intracellular or extracellular biomolecules, nanoparticles with reactive surface moieties can disrupt the normal processes required to maintain tissue or cellular homeostasis, depending on their location within the biological system. One example is that charged AuNPs are more likely to generate oxidative stress, which in turn decreases mitochondrial function and increases the expression of genes related to DNA damage, making them more cytotoxic than neutral AuNPs. It has been observed that anionic cyanoacrylic nanoparticles are more lethal to macrophages than their cationic counterparts. The phagocytotic attraction of macrophages for bacterial cell membranes, which exhibit an overall negative charge owing to the Lipid A molecule of the LPS component, may explain these variations. In contrast, a Chinese Hamster Ovary (CHO-K1) cell line demonstrated that aminated iron oxide nanoparticles with an overall positive charge were more efficiently internalised and caused greater cytotoxicity than a PEGylated version. In order to prolong their action in vivo and boost their absorption, nanoparticles are often PEGylated. This also decreases their immunogenicity [42]. The delayed uptake by cells leading to a large reduction in their cytotoxicity may explain why PEGylated particles retain their stability and also why they are retained. Nanoparticles' harmful effects in vivo are dependent on several factors, including their size, shape, and aspect ratio. Nanoparticles having a larger aspect ratio may be more bioavailable and have a lower clearance rate, both of which contribute to their higher cytotoxicity. It is not uncommon for nanoparticles to have cytotoxicity characteristics comparable to asbestos. Similar to asbestos fibres, these particles can cause macrophage cell death during phagocytosis and may even encourage cancer formation. To back this claim, Wozniak et al. demonstrated that compared to their larger 200 nm-sized counterparts, the 50 nm and under gold nano spheres and rods were more cytotoxic to HeLa and HEK293T cell lines. One possible explanation is that the nanoparticles have an optimal surface area for interacting with chemicals inside cells, which allows them to be internalised by cells more efficiently.

Cancer therapy efficacy of medication delivery methods based on nanoparticles

There is hope that nanoparticles can improve the delivery of anticancer agents, lessen systemic toxicity, and boost therapeutic efficacy. Clinical trials and preclinical investigations have demonstrated encouraging outcomes. To improve clinical translation, however, problems including unstable drug loading capacities, possible side effects, and other obstacles must be overcome. Modifying the surfaces of nanoparticles or creating new drug encapsulation techniques are two examples of the ways being investigated by researchers to increase the drug loading capacity. Improving these systems' therapeutic efficacy is as simple as increasing drug loading. Another obstacle in clinical translation is stability concerns. Scientists are looking for ways to make nanoparticles more stable, like applying protective coatings or tweaking the composition, in order to solve stability problems. To further reduce the likelihood of adverse effects, researchers are taking great care to synthesise nanoparticles from biocompatible materials and are performing extensive toxicity tests prior to beginning clinical trials [43]. Targeted drug delivery methods for many diseases, including cancer cells, are being developed in the promising area of nanomedicine. Because cancer cells proliferate so rapidly and evade conventional treatment approaches, scientists are concentrating their efforts on developing lipid-based drug delivery systems that employ nanoparticles to encapsulate and transport medications to certain cells or regions. Extensive research and optimisation efforts are being undertaken to fine-tune the size, surface charge, and composition of these nanoparticles to assure their effectiveness and safety. To make sure they are safe for use in clinical settings, researchers are also looking into their biocompatibility and possible toxicity. Creating drug delivery systems that target specific areas with therapeutic substances while reducing unwanted side effects and increasing treatment efficacy is our top priority. To optimise the design of lipid-based nanoparticles and understand biological interactions, interdisciplinary collaborations among chemists, biologists, and doctors are essential. To improve stability and biocompatibility, chemists can design and synthesise different lipid compositions, while biologists research cellular uptake and intracellular trafficking. In preclinical models or clinical trials, clinicians can assess the therapeutic efficacy and possible toxicity of the nanoparticles, giving important feedback for further

optimisation of the design. Problems with long-term stability and possible accumulation in specific organs remain, nevertheless, for nanoparticles derived from lipids. Their effectiveness and safety in living organisms can be greatly affected by the intricate relationship between several biological components, including immune response and nanoparticle clearance processes. Cancer treatments make use of a variety of nanoparticles. By targeting cancer cells specifically, nanoparticles can increase the efficacy of chemotherapy while decreasing its negative effects. They can also induce hyperthermia, which kills cancer cells. Nanoparticles also have the potential to improve medical imaging methods, which would lead to more accurate cancer monitoring and localisation. When it comes to cancer treatment [44], nanoparticles have a lot of promise for better patient outcomes and new developments. Thus, prior to moving on with human trials, it is essential to conduct comprehensive investigations into these parameters and comprehend how they impact the behaviour of nanoparticles. To ensure a smooth transition into clinical use, it is crucial to find ways to make nanoparticles more stable and reduce their buildup in organs. Our review focuses on the cancer therapy's nanodrug delivery system.

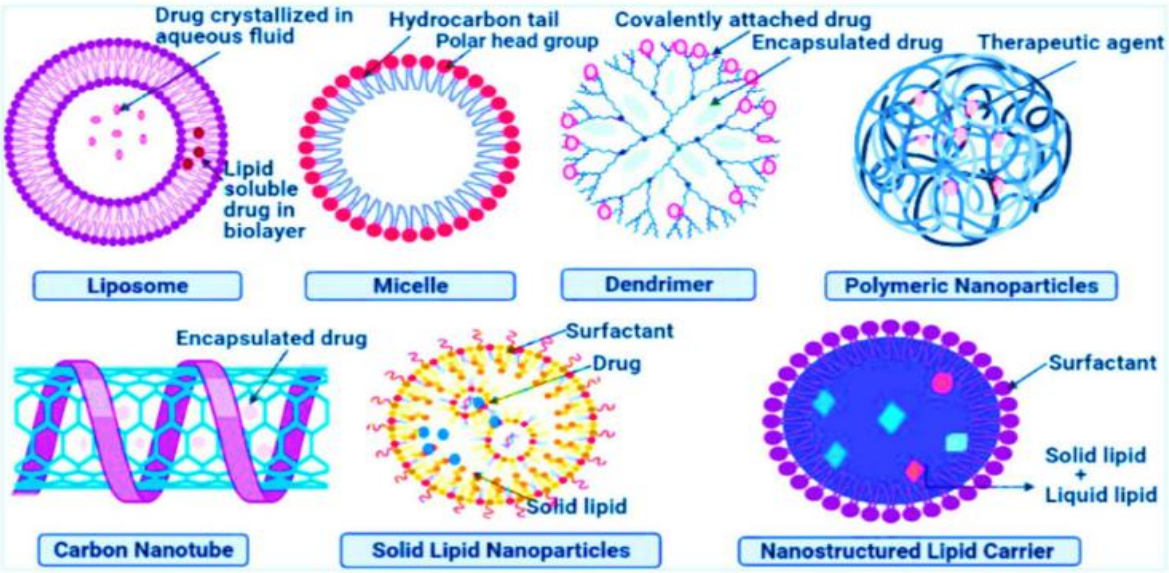

Fig. 1. Different types of nanoparticles are used in cancer treatment

Why medicine delivery is so important

Nanoparticles' potential for enhancing drug delivery systems through targeted and controlled release of drugs is a promising area of research in nanomedicine. As a result, this may make pharmacological treatments more effective while decreasing their negative effects. To maximise therapeutic effects, encapsulating medications within nanoparticles shields them from degradation, transports them straight to the site of action, and allows for regulated release. This breakthrough in nanomedicine has the ability to significantly improve patient outcomes by reshaping drug distribution. Healthcare providers now have the ability to precisely manage the quantity and time of medication release using drug delivery systems based on nanoparticles. This allows for more tailored and successful treatment strategies. Also, for neurological illnesses, for example, the use of nanotechnology in drug administration has opened up new avenues for drug delivery to hitherto unreachable parts of the body. This innovative technology could revolutionise the medical industry and greatly enhance patient care. By customising medicines to each patient's own genetic composition and illness features, personalised medicine also paves the way for novel nanoparticle-based therapies. The use of this tailored method results in treatments that are more effective and accurate, which in turn reduces the likelihood of unpleasant responses and maximises the effectiveness of therapy. Traditional pharmacological therapy may be thwarted by biological barriers, however nanoparticles have demonstrated potential in bypassing these obstacles. Chemotherapy nanoparticles can selectively target tumour cells while avoiding healthy cells, resulting in fewer harmful side effects. Nanoparticles also have the ability to cross the blood-brain barrier, which opens up new possibilities for the treatment of neurological diseases like Alzheimer's by facilitating the direct delivery of therapeutic medications to the brain. If this customised drug delivery system can make chemotherapy more effective while reducing its side effects, it might completely change the way cancer is treated. In addition,

nanoparticles have the potential to be created with controlled drug release mechanisms, guaranteeing a therapeutic impact that lasts for an extended period of time. An issue that could arise with using nanoparticles for targeted drug administration is the possibility of cancer cells developing resistance to the drugs. Nanoparticle chemotherapy becomes less effective as tumour cells develop resistance to the medications delivered by the particles. The development of drug resistance in tumour cells can greatly diminish the efficacy of nanoparticles in cancer treatment, notwithstanding their potential advantages in focused drug delivery. The problem of drug resistance emphasises the importance of continuously researching and developing targeted drug delivery methods. Researchers are putting a lot of effort into finding ways to combat drug resistance, such as exploring new delivery systems or mixing different kinds of nanoparticles. By resolving this issue, we can maximise the use of nanoparticles in targeted medication delivery, which could improve cancer patients' therapies.

Medications delivered by means of nanoparticles

By targeting cancer cells specifically and reducing collateral harm to healthy tissues, medication delivery methods based on nanoparticles hold great potential for enhancing cancer treatment. Nevertheless, in order to properly utilise these systems, the issue of drug resistance must be resolved. Researchers are looking on methods to make these systems more successful and to find a technique to beat drug resistance. To combat drug resistance in its various forms, combination treatments use nanoparticle-based methods to provide numerous medications all at once. Cancer cells have built-in systems that prevent medications from reaching their targets, yet nanoparticles can actively circumvent these processes. Controlled drug release from designed nanoparticles ensures sustained medication levels with minimal side effects. To go a step further, scientists are constantly working to make nanoparticle-based systems more precise, so they can attack cancer cells while avoiding healthy ones. This bodes well for the future of cancer treatment, as it could lead to more targeted and efficient therapies. Research on gene therapy compounds that can counteract or prevent cancer cells from developing a resistance to drugs is also ongoing. Chemotherapy medications encapsulated in nanoparticles can reach cancer cells precisely while avoiding their resistance mechanisms. Nanoparticles like these have the potential to increase the efficacy of cancer treatments by bypassing drug resistance and going straight to cancer cells. Nevertheless, due to mutations or genetic variances, some cancer cells may not react well to treatments based on nanoparticles. It is possible for some cancer cells to find ways to actively repel or neutralise nanoparticles, rendering them useless for therapeutic delivery to specific cells. Nanoparticles have the ability to engage intricately with cancer cells, which raises the risk of toxicities and unintended side effects that could damage healthy tissues and organs. Treatments based on nanoparticles may or may not be efficient in killing cancer cells, and this fact must be carefully considered. Nanoparticle treatments may not work as well on some cancer cells because of their specific traits. It is important to thoroughly evaluate the potential for off-target effects and unexpected outcomes prior to the widespread usage of medicines based on nanoparticles in clinical settings. Furthermore, it is essential to think about how nanoparticles will be delivered to cancer cells. The efficacy of nanoparticles is highly dependent on how well they can access and enter the tumour location. In order to guarantee patient safety and minimise any unanticipated dangers, it is crucial to comprehend the possible long-term consequences and safety profile of treatments based on nanoparticles.

Benefits and drawbacks of medication delivery methods based on nanoparticles

One of the many benefits of drug delivery systems based on nanoparticles is their ability to increase therapeutic efficacy by better targeting and penetrating drugs into tumour cells, which is particularly useful in the treatment of cancer. The systems do have certain limitations, though, including the fact that they may be poisonous and that there is a chance that they may not be recognised or cleared by the immune system. Optimising and addressing the limits of these systems for safe and effective therapeutic applications requires extensive research. Coating nanoparticles with biocompatible materials, surface-targeting ligands, and generating stimulus-responsive nanoparticles that release their cargo in response to specific cues within the tumour microenvironment are all ways to modify the surface features of nanoparticles. To increase their circulation time in the body and their capacity to enter cancer tissues, another method is to design nanoparticles with controlled size and form. Researchers are also looking into the possibility of using multifunctional nanoparticles to enhance the overall effectiveness of cancer treatment by delivering therapeutic medicines, imaging agents, and targeting molecules all at once. More precise and effective cancer treatments may

soon be available, thanks to advancements in nanomedicine. In order to decrease systemic dosages and harm to healthy organs, nanoparticles have been created to transport chemotherapy medications straight to tumour cells. The results of these preclinical investigations are encouraging, suggesting that this strategy may one day be used in clinical practise to better the outcomes for patients. Drug resistance is still an issue because tumour cells can evolve to withstand these treatments by mutating or activating other signalling pathways. Combination medicines that attack numerous pathways at once are being considered as a potential solution to the problem of drug resistance. Nanoparticles with improved targeting capabilities are also under development with the goal of delivering medications directly to cancer cells that have developed resistance. These approaches show a lot of promise for enhancing the efficacy of cancer treatments and overcoming the problem of drug resistance. Researchers are also looking at immunotherapies as a potential way to boost the immune system's ability to fight off cancer cells that have developed resistance. Through the utilisation of the immune system, these treatments have demonstrated encouraging benefits in terms of improving patient outcomes and overcoming medication resistance. The identification of biomarkers that can foretell medication resistance is an area of active investigation since it holds the key to developing more individualised treatment plans for patients.

Therapeutic nanoparticles derived from lipids

Nanoparticles derived from lipids have the potential to improve medication stability, solubility, and targeting while also being biocompatible, making them an attractive option for drug delivery. Nanoparticles have the potential to enhance the efficacy of cancer treatments by interacting with tumour cells that have developed resistance to many drugs. In order to bypass efflux pumps on MDR cancer cells, lipid nanoparticles can be used. The accumulation of medicines inside the cells is then able to kill them. Preclinical trials have demonstrated that this tailored drug delivery system can improve chemotherapy's efficacy in treating tumours that have developed resistance to the treatment. Unfortunately, these nanoparticles failed to effectively target MDR cancer cells in a human clinical trial, leading to minimal cell impact and subpar therapy results. This poses a problem for improving cancer treatment results and creating new cancer medicines. The poor efficiency of these nanoparticles in targeting MDR cancer cells requires further research to understand the underlying causes. Patients with resistant tumours may have better treatment results if researchers look into other drug delivery mechanisms that can get around this problem. Looking into combination therapy is one way to get around nanoparticles' lack of effectiveness in targeting MDR tumour cells. Nanoparticles may be more successful and lead to better patient outcomes if used in conjunction with other treatment techniques like immunotherapy or gene therapy. Furthermore, in order to create more personalised and efficient cancer treatments, it is necessary to comprehend the particular biological processes that contribute to multidrug resistance. Only then can we hope to discover new therapeutic targets.

Clinical application of polymer-based nanoparticles for medication delivery

Liposomes are biocompatible spherical vesicles that can encapsulate a variety of medicinal substances. They have the ability to improve patient outcomes by increasing drug stability and bioavailability, and they are biocompatible. Additional polymer-based nanoparticles under investigation for potential therapeutic application include dendrimers and polymeric micelles. The enormous surface area and controlled release of drugs are both made possible by dendrimers' highly branched structure. To tailor their interactions with certain biological targets, they can be functionalized in a variety of ways. A core-shell configuration with a hydrophobic core and a hydrophilic shell is formed when amphiphilic block copolymers self-assemble. This process results in the formation of polymeric micelles. Due to the hydrophobic core's ability to encapsulate and preserve the drug from degradation, polymeric micelles have demonstrated promise in transporting hydrophobic medicines to tumour locations. The hydrophilic coating also increases the medication delivery efficiency by allowing it to circulate in the bloodstream for a longer period of time. Polymeric micelles have the ability to improve targeted medicine delivery and patient outcomes due to their unique characteristics. Because of their unusual shape, they can encapsulate hydrophobic medications inside their core and remain stable in water. Adding ligands or antibodies that identify cancer cell markers to the surface of dendrimers allows them to be tailored to target cancer cells. Drugs are delivered more efficiently and with fewer side effects with this customised delivery system. On the other hand, tumour delivery systems have the risk of off-target binding, which means they might attach to healthy cells that have markers similar to tumour cells. This can cause

harm to healthy tissues and render the delivery system ineffective because it lacks the intended selectivity. Researchers are looking into several ways to make targeted delivery systems more selective in order to overcome this difficulty. The use of sophisticated imaging methods for cancer cell identification and characteriszation is one strategy that could lead to the creation of more targeted ligands or antibodies that can detect tumour markers with greater precision. To further reduce off-target binding and any side effects, researchers are using nanotechnology to create multifunctional dendrimers that can selectively target cancer cells while avoiding healthy organs.

Nanoparticles made of polymers: pros and cons for medication delivery

Nanoparticles made of polymers can encapsulate a wide range of therapeutic agents, including small molecules, proteins, and nucleic acids, making them particularly versatile in drug delivery. These nanoparticles are ideal for targeted drug administration because their size, surface characteristics, and release kinetics may be precisely tuned by simple chemical manipulation. But, there are constraints to think about, including the difficulty in precisely controlling drug release kinetics and the possibility of toxicity and immunogenicity. Factors such as pH, temperature, and enzyme activity can affect how polymers degrade, which further complicates the kinetics of drug release. To circumvent these restrictions and improve the efficacy of polymer-based medication delivery systems, researchers are continually investigating new tactics and technology. The creation of pH-responsive polymer nanoparticles for specific medication delivery is one such example. Upon encountering fluctuations in pH levels within the body, such those present in tumour microenvironments, these nanoparticles release the medication payload. Researchers can control the pace of drug release and ensure therapeutic doses reach the place of need by adding pH-sensitive polymers to the nanoparticle mix. By taking this route, we can increase the drug's effectiveness while decreasing the likelihood of harmful effects on healthy cells. Consistent and targeted drug release is hard due to the fact that pH levels in tumour microenvironments can vary greatly among cancer types and even within the same tumour. Researchers have been looking into new ways to make pH-sensitive polymers more responsive because they can be ineffective when it comes to responding to small changes in pH, which can cause drugs to be released too early or in the wrong places. Including "stimulus-responsive moieties" into the polymer's structure is one approach that shows promise. This allows for a more targeted release of the medication in reaction to individual variations in pH. To further enhance the accuracy and efficiency of drug delivery, another method is to combine pH-sensitive polymers with other targeting mechanisms. These mechanisms could include ligand-receptor interactions or magnetic targeting. These developments could greatly enhance the efficacy of medication delivery systems based on pH-sensitive polymers.

Nanoparticles have drugs embedded into them.

Encapsulation, adsorption, and drug conjugation are three ways that drugs can be loaded into nanoparticles during their manufacture. Adsorption entails the binding of pharmaceuticals to the surface of pre-formed nanoparticles, whereas encapsulation permits controlled release of drugs. Coacervation, co-precipitation, and self-assembly are methods that can be used to achieve encapsulation. In co-precipitation, the drug and polymer are precipitated at the same time, whereas in co-acervation, a polymer-rich phase is formed to encapsulate the drug. Nanoparticles encasing the medicine are created via self-assembly by taking advantage of the characteristics of specific polymers. However, nanoparticles can have drugs chemically attached to their surfaces through a process called drug conjugation, which enables controlled release and targeted distribution. There is promise for optimising therapeutic efficacy through the use of these diverse approaches, which enable flexibility in drug loading into nanoparticles. Drug conjugation, self-assembly, and co-precipitation allow researchers to modify the drug-loading procedure according to the medications and the release characteristics they want. This adaptability is vital for getting the drug to the target site of action as efficiently as possible and for the nanoparticles to load drugs efficiently. In addition, these techniques make it possible to attach targeting ligands to the surface of the nanoparticles, which allows for targeted distribution to cells or tissues that are sick. Improving drug loading methods will play a crucial role in pushing nanomedicine forward as more and more drugs are being delivered by nanoparticles. Encapsulation not only increases the stability of the medicine but also protects it against degradation. To increase the efficacy of therapy, nanoparticles can be engineered to have a better interface with biological systems, allowing cells to absorb them more easily. For the purpose of cancer treatment, scientists have created lipid-based nanoparticles that improve the stability of the medicine, make it water-soluble, and allow for targeted delivery to tumour cells with minimal side effects to healthy tissues. To further

improve drug delivery precision and decrease adverse effects, nanoparticles can be designed to target specific cells or tissues. This specific method has demonstrated encouraging outcomes in enhancing the effectiveness of many treatments, such as gene therapy and chemotherapy. New developments in nanomedicine have the potential to dramatically alter the way many diseases are treated and greatly enhance the results for patients. The tailored delivery technique has the potential to revolutionise cancer treatment in the long run, but it faces a serious threat from the emergence of drug-resistant tumour cells. Potentially preventing their broad use in clinical settings are the high costs and complexity of producing these nanoparticles on a massive scale.

Nanoparticle zeroes in on malignancy

The design and content of nanoparticles determine their ability to target tumours. Attaching targeted compounds that bind to receptors on cancer cells to the surface of the nanoparticle is one typical strategy. This enhances the nanoparticle's efficiency while limiting damage to healthy cells, allowing it to selectively accumulate in the cancer. On top of that, certain nanoparticles can be programmed to release their medicinal cargo in reaction to certain environmental cues, such changes in temperature or pH. To make the nanoparticles more targeted and ensure the therapeutic payload is released at the right area, these qualities might vary in response to a stimulus. Both the efficacy of cancer treatment and the risk of adverse effects from non-specific drug distribution are enhanced by this method. Stimulation-responsive nanoparticles are engineered to secrete their medicinal cargo in reaction to predetermined stimuli, including variations in temperature or pH. This opens the door for scientists to develop a method of drug delivery that targets tumours specifically, enhancing its effectiveness while reducing its impact on healthy cells. There is significant hope that this strategy will enhance cancer treatments while simultaneously decreasing patient burden. With stimulation-responsive nanoparticles, the medication can be delivered only to the cancer site, reducing collateral harm to surrounding healthy cells and tissues. This not only makes cancer therapies more effective, but it also improves patients' quality of life by lowering the side effects of traditional chemotherapy. The therapeutic payload is released when the nanoparticles encounter acidic conditions in tumours, which allows them to effectively target and kill cancer cells while sparing healthy tissues. This mechanism is based on variations in pH inside the tumour microenvironment. Patients taking chemotherapy will have fewer negative side effects and the treatment will be more effective as a result. When nanoparticles come into contact with acidic environments outside of the tumour, they may damage healthy tissues as well, which could compromise the aim of limiting side effects in patients and cause unintended injury. Because of this, creating tailored delivery systems that limit nanoparticle activation to the tumor's acidic environment is of the utmost importance. The selectivity of these nanoparticles is another area of active investigation for the purpose of minimising damage to healthy tissues.

How nanoparticles selectively target cancer cells

Among the many current uses for nanotechnology are diagnostic instruments, cancer imaging, and targeted delivery systems. These methods target cancer cells using ligands or antibodies that attach to receptors that are overexpressed. As a result, nanoparticles can only accumulate in tumour tissue and stay away from healthy cells. Furthermore, pH-responsive nanoparticles have the ability to detect the acidic conditions within tumours and selectively release their payload, enhancing the efficacy and safety of cancer treatments. Biosensors and lab-on-a-chip devices are examples of nanotechnology-based diagnostic instruments that are currently in development for the purpose of detecting cancer biomarkers in bodily fluids. This will enable early identification and the development of customised treatment regimens. Nanosensors can detect minute amounts of a particular cancer biomarker in a patient's blood, which could greatly improve patient outcomes and the likelihood of a successful therapy, thus reshaping the cancer diagnostic and treatment landscape. Additionally, drug delivery systems that specifically target cancer cells are now under development, with the goal of avoiding side effects and enhancing the efficacy of chemotherapeutic drugs. The problem is that false positives and misinterpretation might happen since not all cancer biomarkers are specific to only one kind of cancer. There has to be extensive research on the potential hazards and problems associated with using nanotechnology in drug delivery systems before it is widely used. These include toxicity and immune response.

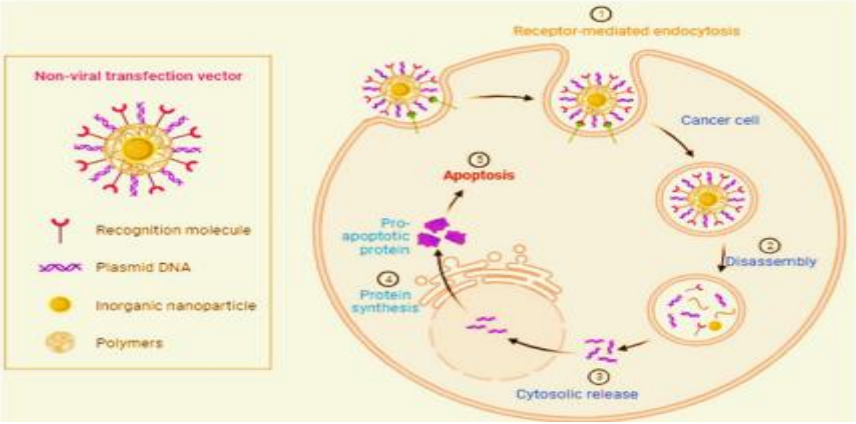

Fig. 5. Nano system in death induced gene therapy for cancer.

Conclusion

Despite the potential of targeted drug delivery systems to improve cancer treatment, these methods are currently constrained by tumour heterogeneity and microenvironmental challenges. Improving the delivery of targeted therapies requires further study and innovation. Nanotechnology presents an exciting new direction for cancer treatment by allowing for the targeted destruction of cancer cells with minimal side effects on healthy tissues. The cancer microenvironment can be circumvented by using nanoparticles to transport therapeutic medicines straight to the tumour site. Nanoparticles can be made more effective by modifying their surfaces to increase their stability, circulation time, and cellular absorption. Challenges including drug resistance and limited drug penetration into solid tumours can be overcome with the use of nanoparticles in targeted therapy. To ensure long-lasting and successful treatment, these nanoparticles can be designed to release the therapeutic ingredients in a controlled way. In addition, the continuous progress in nanotechnology has the ability to enable personalised medicine techniques that are adapted to the specific demands of each patient, which might completely transform cancer treatment.

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