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A review on nanoparticles in cancer therapeutics with its classification and synthesis

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Abstract

Cancer is a leading cause of death worldwide, with 7.9 million fatalities reported in 2007. The World Health Organization predicts that cancer-related deaths will increase to 12 million by 2030. Nanotechnology has emerged as a promising tool in cancer diagnosis, treatment, and prevention. Nanoparticles have been employed in drug delivery systems, imaging, and therapy due to their unique properties. This review aims to provide a comprehensive overview of nanoparticles, their classification, and applications in medicine. Nanoparticles can be classified based on their composition, size, and shape. Carbon-based nanoparticles, such as fullerenes, graphene, and carbon nanotubes, have been widely used in cancer therapy. Inorganic nanoparticles, including metal oxides and semiconductor nanoparticles, have also shown potential in cancer treatment. The review highlights the recent advances in nanoparticle-based cancer therapy, including targeted drug delivery, imaging, and therapy. The potential toxicity of nanoparticles is also discussed, and the need for further research to ensure their safe use in medicine is emphasized. Overall, this review provides a comprehensive overview of nanoparticles and their applications in cancer therapy.

Keywords: Cancer; Nanoparticles; Nanotechnology; Targeted therapy; Biomedical applications

1. Introduction

A group of disease collectively referred to as cancer are distinguished by their invasiveness and unchecked, random cell division. The identification of different cancer risk factors has been the subject of intense efforts over a number of years. Certain environmental (acquired) factors, such pollution and radiation, have been found to have major effects on the cause of certain malignancies [1]. The World Health Organization (WHO) reports that cancer was the leading cause of death worldwide in 2007 with 7.9 million fatalities. Globally, the number of cancer-related deaths is predicted to increase, reaching an estimated 12 million deaths by 2030 [2]**.** A poor diet, tobacco use, smoking, stress, and inactivity are all bad lifestyle choices that have a significant impact on determining one's chance of developing cancer. It has been difficult to determine the role of proto-oncogene mutations, tumour suppressor gene expression patterns, and DNA repair genes, even if several external factors have been identified as key causes of cancer. Hereditary variables are only implicated in 5–10% of cancer cases. Another important risk factor for cancer and many other types of cancer continues to rise older [1]. Precision medicine replaced conventional therapy with the introduction of cancer therapies. The novel therapeutic approaches made possible by nanoparticles' characteristics have expanded their use in cancer treatment beyond the realm of traditional medication administration. In cancer treatment, nanoparticles can be used to encapsulate active pharmaceutical substances and more effectively deliver them to the tumour location [3]. Among other metal nanoparticles (NPs), the production of silver (Ag) NP was projected to expand by hundreds of tonnes annually on a global scale. The commercial use of Ag NPs in electronics, optics, catalysis, home products, and a variety of medical applications is a prerequisite for the strong demand for Ag NPs. The broad-spectrum antibacterial and antiviral properties of Ag NPs are well-known [4]. The recent decades are characterised by the creation of new delivery systems for the best possible treatment results rather than the development of novel molecules to treat a variety of

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illnesses. Perhaps the largest factor contributing to this worry is nanomedicine [5]. Today, cancer is treated using conventional methods such as radiation, chemotherapy, and surgical excision, either separately or in combination. However, these methods typically have poor therapeutic efficacy and target or treat the tumour in an unspecific manner. In an effort to decrease side effects and increase therapeutic efficacy, several novel anticancer therapy formulations have recently been developed as a result of developments in nanotechnology. The Food and Drug Administration (FDA) approved some of the nanoformulations, namely Abraxane®, Onivyde®, Marqibo®, and Nanotherm®, which are used in clinical settings [6]. The goal of nanotoxicology's scope is to recognising possible risks that are helpful for assessing the safety of nanomedicines [7].

2. Definition of Nanoparticles

The European Snitions of nanomedicine. While the latter does not directly point to the nanoscale, the former does. "Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometres, where unique phenomena enable novel applications," according to the US National Nanotech Initiative [5]. NMs are "materials that have at least one dimension in the range of about 1 to 100 nm and show dimension-dependent behaviours," according to the US Food and Drug Administration (USFDA). Similarly, NMs have been described as "materials with any outward nanoscale dimension or possessing internal nanoscale surface structure" by the International Organisation for Standardization (ISO) [8]. The origins of nanotechnology and nanoscience concepts is usually linked to the famous lecture of Nobel laureate Richard Feynman at the 1959 meeting of the American Physical Society, “There’s Plenty of Room at the Bottom”. However, the use of nanotechnology and nanomaterials goes back in history long before that [9]. Numerous synthesis methods are either being developed or improved to enhance the properties and reduce the production costs. Several techniques are adjusted to achieve process particular nanoparticles to boost their optical, mechanical, physical and chemical capabilities. A vast development in the instrumentation has led to an improved nanoparticle characterization and subsequent application [10]. For example, imatinib has also been delivered using a NP system, which enhanced in a cancerous melanoma mouse model, tumour accumulation and regression in vivo enhanced the continued existence ratio to 40% after 60 days [11].

3. History of Nanoparticles

As history has shown, each period of civilization has its own name. For example, the Stone Age is the period from the first stone tools used by mankind, the Bronze Age is time when tools made of copper-tin alloy were used, and the Iron Age is the time when iron became the primary raw material used to make tools. This age might be referred to as the era of nanomaterials since nanotechnology is without a doubt one of the most popular buzzwords of the new century and has raised living standards to a considerable extent thus far. According to some researchers, nanotechnology will have such an important effect that it will be used to characterize a new era of global economic growth [12]. These days, nanomaterials are becoming crucial to human progress as a whole. For instance, employing green technology that primarily uses nanomaterials is the only way to lower the risk of global warming and climate change in the first place. since it has been established that technology utilizing nanomaterials is more efficient than those utilizing bulk materials. Second, technologies for diagnosing and managing the global epidemic of diseases are being developed using nanomaterials. For instance, in 2019, nanoparticles were used to identify and control COVID-19, a disease that was killing a lot of people worldwide [13]. Therefore, in order to study and apply the size-dependent properties of nanomaterials, it became crucial to develop advanced synthesis routes that not only offer control over the composition, which is usually necessary for traditional bulk synthesis, but also over particle size, size distribution, shape, and surface properties [14]. It wasn't until the 1980s that the miniaturization of instruments using microfabrication technology marked the start of the golden age of nanotechnology [12]. The Food and Drug Administration (FDA) in the United States has approved the usage and development of pharmaceuticals based on nanotechnology in a number of pharmaceutical businesses in recent years. The cost of this new technology is undoubtedly exceptionally high. Currently, $9 billion is spent annually on nanotechnology worldwide (Service, 2004). In fact, it is expected that the United States and Japan will invest $6.7 billion in this area's research and technical advancement through 2008. Due to the rapid growth of nanotechnology in many fields, even less developed nations have concluded that they cannot overlook this new technology as a potential investment in their future economic and social well-being [15]. Nowadays, nanoparticle technology is used in many different industries, especially in the fields of innovation, development, and production growth like Cancer treatment with tissue engineering biological assay using multi-colour optical treatment Cell and bio molecule manipulation Direction of proteins Exploration for commercial purposes [16].

Classification of Nanomaterials

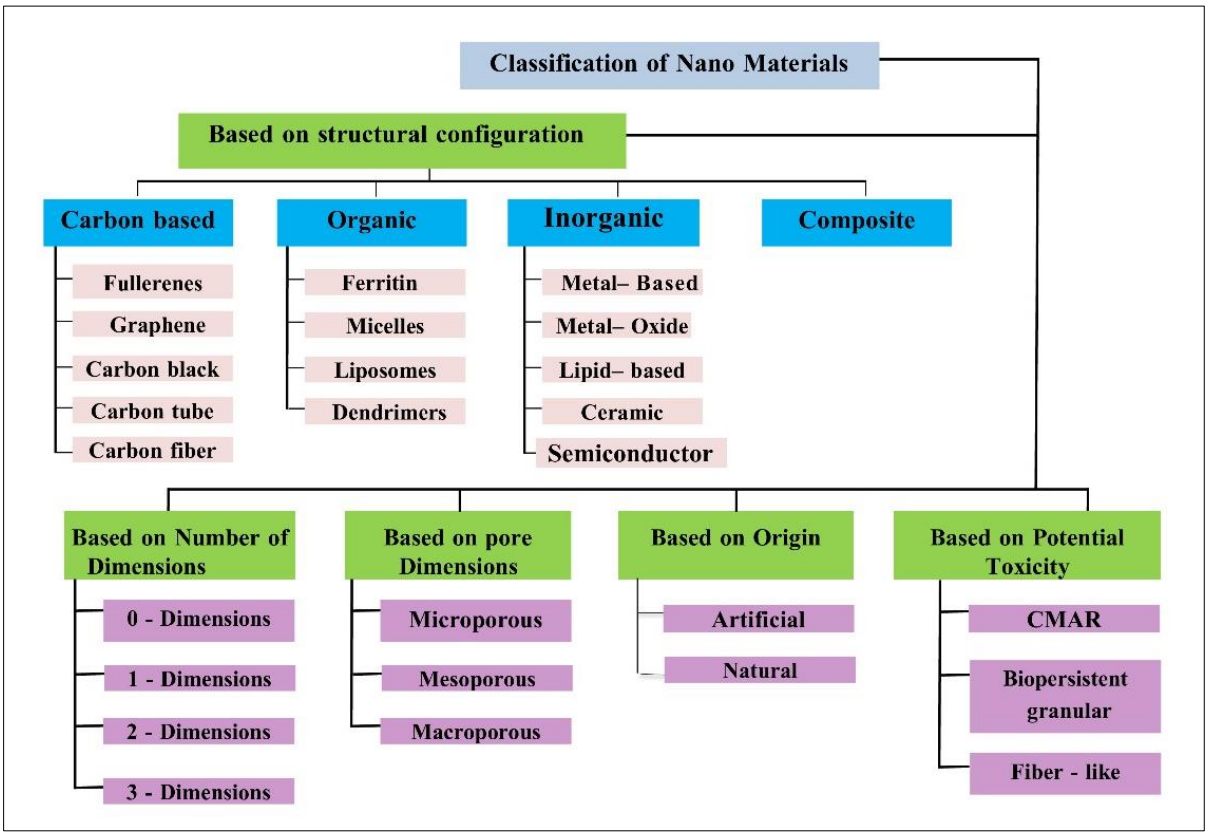

Figure 1 General classification of nanomaterials [13]

3.1. Classification of Nanoparticles based on structural composition

According to their structural composition, nanoparticles can be broadly divided into four groups: Carbon-based, Organic, Inorganic and Composite [13].

3.1.1. Carbon-based Nanoparticles:

These nanoparticles, which mimic hollow ellipsoids or tubes, are made completely of carbon. This family of materials includes carbon nanotubes, both single and multiwalled, graphene, fullerenes, nanofibers, fluorescent carbon quantum dots, and carbon dots. The materials mentioned above are widely used in many scientific fields due to their distinct mechanical, chemical, thermal, and physical properties [12].

Fullerenes, which are spherical or ellipsoidal structures composed of carbon nanomaterials, are what bucky balls are. With diameters of up to 8.2 nm for single layers and 4 to 36 nm for multi-layered fullerenes, fullerenes are spherical compounds that form from 28 to 1500 carbon atoms [13]. Buckminster fullerene (C60) is one of the most widely utilised and well-known fullerenes. Because of the cage-like configuration of its 60 carbon atoms, each of which possesses three separate bonds [17].

Graphene is a carbon allotrope. Graphene is a two-dimensional planar hexagonal network of honeycomb lattices composed of carbon atoms. The typical thickness of graphene sheets is 1 nm [18]. Carbon nanotubes (CNTs) are cylindrical tubes that are most conceived of as rolls of graphene. They were discovered in the late 1980s. They are separated into two types: single-walled and multi-walled carbon nanotubes. Because they are carbon-based, they can interact with immune cells to trigger an immunological response, which will stop the growth of tumours. They have historically been employed in thermal ablation therapy and as vectors for the transfer of DNA. To target colon cancer cells, for example, a fluorescent single-walled CNT containing doxorubicin enclosed in mAb is utilised. These CNTs combine to form a compound that the cancer cells effectively absorb, resulting in intracellular release of doxorubicin, whereas the CNTs are retained in the cytoplasm [1]. Carbon-based nanomaterials are used mainly for structural reinforcement as they are stronger than steel at times. Carbon based nanomaterials are thermally conductive along the length and non-conductive across the tube [13].

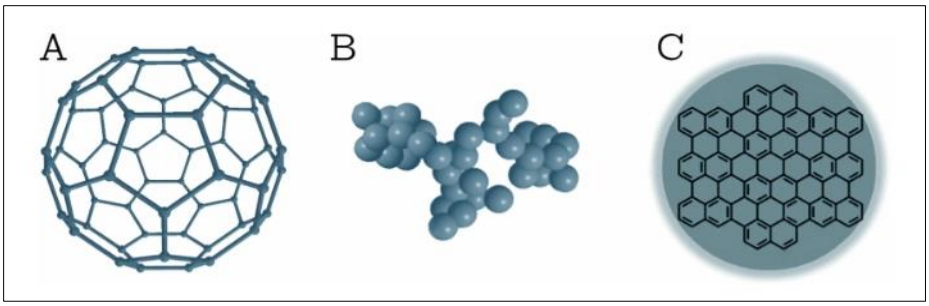

Figure 2 Different types of carbon-based Nanoparticles, A) C60 fullerenes; B) Carbon black NPs; and C) Carbon quantum dot [9]

3.1.2. Organic based Nanoparticles:

Organic molecules are converted into organic nanomaterials at the nanoscale. Liposomes, ferritin, dendrimers, and micelles are a few types of organic nanoparticles or polymers. Nanocapsule micelles and Liposomes are non-toxic biodegradable nanoparticles with hollow interiors that are light, heat, and electromagnetic radiation sensitive [13]. Another unique class of polymers that has been widely employed in cancer nanomedicine is dendrimers. They are branching, highly ordered polymeric macromolecules with consistent, recognisable sizes and forms. A central core, recurrent branching units, and terminal groups that provide adjustable surface features make up its basic structure [19]. Because dendrimers have a hydrophilic surface and a hydrophobic core, they can transport both hydrophilic and hydrophobic medications. The generation number, the chemical makeup of the core and branches, and the surface function group all affect the size, shape, and pharmacokinetics of dendrimers [5]. The size of the nanoparticle can vastly impact the delivery effectiveness in the excrescence towel. Decreasing the nanoparticle size can improve the nanoparticle penetration in excrescence towel but drop the nanoparticle retention effect. Thus, small nanoparticles with a high retention effect in excrescences are urgently demanded for effective glioblastoma multiform medicine delivery. Dendrimers are modified with spacers or liaison on the face to enhance drug release kinetics, half-life, softening capacity, and biocompatibility. Dendrimers could be effective medicine delivery vehicles for brain injury and neuroinflammation therapy similar as TBI, ischemic brain stroke and in brain excrescence. Beast models of ischemic grown-up and bambino strokes, ischemic optical neuropathy and brain injury related to cardiac arrest have shown accumulation of dendrimers in injured brain [20]. These nanoparticles offer outstanding pharmacokinetic control because they are highly amenable to surface modification by chemical methods. The most prominent of these nanoparticles are polymers composed of Chitosan, polylactic acid, gelatin, and poly (lactic and glycollic acid) copolymer. In addition, various kinds of nanoparticles can have these polymers coated on their surface [12].

Liposomes are tiny, spherical structures made of non-toxic phospholipids and cholesterol. Depending on the lipid used in the process of productiery vehicles that have a lengthy half-life in the bloodstream due to their natural composition. According to a recent review, Liposomes are being studied for the delivery of anticancer medications through a variety of encapsulating technologies [Hofheinz et al., 2005]. Anticancer drug-carrying Liposomes can target cancer cells for an extended period of time without harming healthy cells [21]. Liposomes can encapsulate drugs and deliver them to specific target tissues or cells, allowing for targeted therapy. This minimizes the exposure of healthy tissues to the drug, reducing side effects [22].

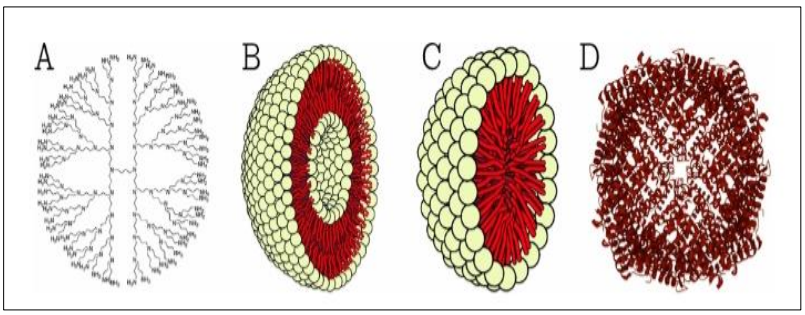

Figure 3 Diagrammatic Representation of organic Nanoparticles,1) Dendrimers, 2) Liposomes, 3) Micelles, 4) Ferritin [9]

3.1.3. Inorganic based Nanoparticles

Carbon is missing from inorganic nanoparticles. The benefits of inorganic nanoparticles include their hydrophilia, non-toxicity, and biocompatibility with living organisms. Inorganic nanoparticles are more stable compared to Organic nanoparticles [23]. Because of their low toxicity and biocompatibility, which allow for their use in environmental and biomedical applications, inorganic nanotubes, fullerenes, and 2D nanomaterials based on layered metal dichalcogenides like WS2 and MoS2 have emerged as highly promising nanostructures over their carbon counterparts in recent years [24]. Inorganic nonmetallic solids known as ceramic nanoparticles (NPs) are created by heating and then cooling. They come in thick, porous, hollow, amorphous, and polycrystalline forms. As a result, researchers are paying close attention to these NPs because of their uses in photocatalysis, dye photodegradation, catalysis, and imaging. (Thomas and others, 2015) [25]. Researchers are paying close attention to nanomaterials because of their use in applications like catalysis, photocatalysis, photodegradation of dyes, and imaging. Ceramic nanoparticles can be formulated in drug delivery systems, particularly in targeting tumours, glaucoma, and certain bacterial infections [13].

One of the most promising NPs for use in medicine is quantum dots. However, due to their various toxic effects in both in vitro and in vivo tests, they may be harmful to human health [26]. Both metallic and non-metallic characteristics can be found in semiconductor nanoparticles. By altering it, they display unique characteristics and huge band gaps. Electronic gadgets and photocatalysis both make extensive use of them. For instance, ZnS, ZnO, CdS, CdSe, and CdTe are group II–VI semiconductor materials. GaN, GaP, InP, and InAs are included in Groups III–V. Recently, researchers have been interested in semiconductor graphene nanocomposites. The semiconductor's chemical and physical characteristics can be enhanced by graphene. Piezoelectric graphene composite materials can be used for gas sensing sensitivity [27]. For a variety of reasons, gold nanoparticles (AuNP) are the most popular and have been the go-to choice in many investigations. The most significant ones are their physicochemical properties, low cytotoxicity, enzymatic stability, and chemical resistivity (for additional details on gold nanoparticles and their properties) [28].

3.1.4. Composite Nanoparticles

Composites Nanomaterials are formed through the combination nanoparticles with other nanoparticles, nanoparticles with larger-scale materials, and nanomaterials with bulk-type materials. Nanomaterials are already being employed to improve mechanical, thermal, and flame-retardant characteristics in a wide range of items, including automotive components and packaging materials [13].

3.2. Classification based on Dimensions of Nanoparticles

Nanomaterials are divided in our types based on their size: 0D, 1D, 2D, and 3D [13].

- **Zero-dimensional (0D):** 0D with length, width, and height. Corresponding Author is fixed at a single place, example- Nano dots [29]. Nanoparticles with a single dimension: For decades, electronics, chemistry, and engineering have used one-dimensional systems such as thin films or fabricated surfaces [30].
- **One-dimensional nanomaterials (1D):** It include nanofibers, nanotubes, nanohorns, nanorods, thin films, and nanowires [13].
- **Two-dimensional nanoparticles (2D):** Materials belong to this class have two dimensions beyond the nanoscale. Nanosheets, nanofilms, and nanolayers are three examples [9].
- **Three-dimensional nanoparticles (3D):** 3D nanoparticles also known as bulk nanomaterials. These nanoparticles are not inherently small in any dimension. In other words, they are larger than 100 nm in three dimensions. These consist of bundles of nanowires, bundles of nanotubes, core shells, multiple nanolayers, and nanocomposites [21].

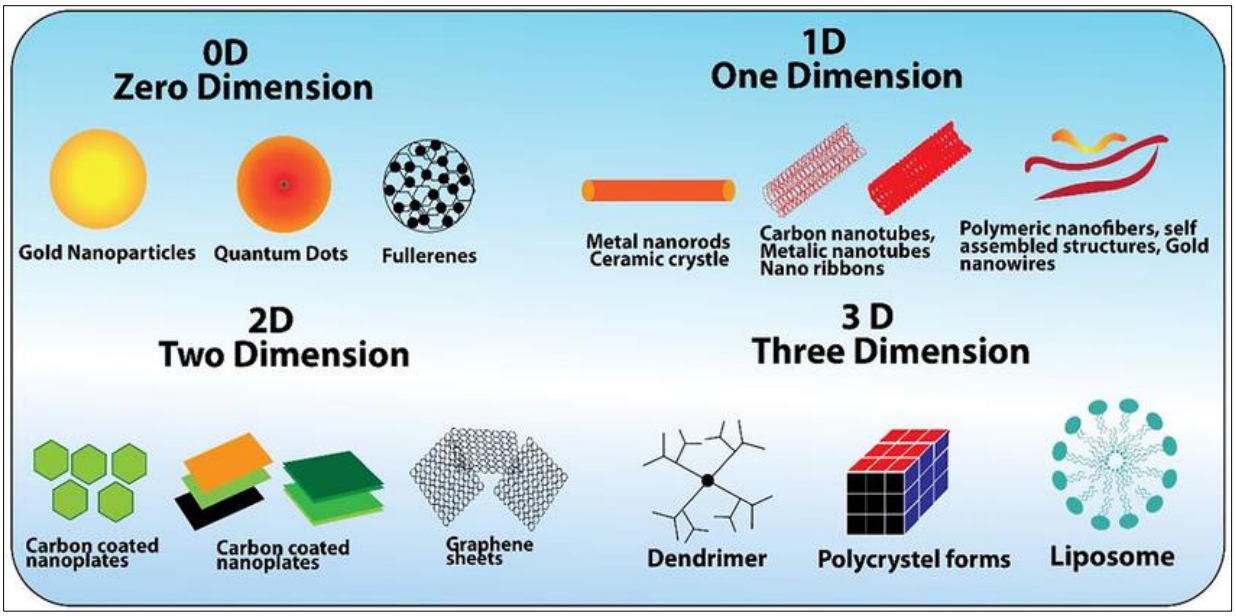

Figure 4 Dimensions Of Nanoparticles [31]

3.3. Classification of Nanoparticles based on pore dimensions

Nanomaterials are classified into three groups based on the length of their diameter dimensions, which are:

- **Micro porous Materials:** NMs have pores < 2 nm in diameter and are commonly defined as nanopores (e.g., zeolites and metal-organic frameworks). Microporous materials are widely used for air filtration and gas separation to provide a contaminant-free gas exchange [32].
- **Meso porous Materials:** Mesoporous materials have pores with a diameter large enough to hold some large molecules larger than 2 nm but smaller than 50 nm.
- **Macro porous Materials:** Macro porous materials are materials with pores with enough diameters (greater than 50 nm) to host very large molecules, such as polyaromatic systems or small biological molecules [13].

3.4. Classification of Nanoparticles based on its origin

There are two types of Nanoparticles based on its Origin:

- **Natural nanomaterials:** these nanoparticles and nanostructured materials are created through natural (bio)geochemical or mechanical processes that have no connection to human activities or processes. Examples include foraminifera (primarily chalk) and virus (capsid, protein) structures, wax crystals that coat lotus or nasturtium leaves, spider and silk spider mites, blue tarantula hues, gecko foot spatulas, some butterfly wing scales, natural colloids (milk, blood), horny materials (claws, skin, feathers, hair), nacre, corals, and the human bone matrix [33].
- **Synthetic (Artificial) nanomaterials:** These are generated through mechanical grinding, engine exhaust and smoke, or by physical, chemical, biological, or hybrid synthesis. The issue of risk assessment methodologies has arisen in recent times since there has been an increase in the production and subsequent release of engineered NMs, as well as their use in consumer goods and industrial applications [34].

3.5. Classification of Nanoparticle based on its Potential Toxicity

Nanomaterials are divided into three categories according to their potential toxicity.

- **Fiber nanoparticles:** Fiber-like nanoparticles are comparable to hard, bio-permanent carbon nanotubes, fiber-like metal oxides, and carbon nanotubes, however they lack the asbestos-like characteristics.
- **Bio-resistant granular nanoparticles:** The proposed exposure limits for bio persistent granular nanoparticles are 2 × 107 particles/m3, comparable to gold, silver, cobalt, lanthanum, lead, iron, iron oxide, cerium oxide, antimony oxide, and tin oxide.

- **CMAR nanoparticles:** CMAR stands for carcinogenic, mutagenic, asthamagenic, and reproductive poisons. Nickel, cadmium-containing QDs, chromium VI, beryllium, arsenic, and zinc chromate are some examples of CMAR nanoparticles. The proposed work exposure limits for this are 2 × 107 - 4 × 107 particles/m3. For insoluble nanoparticles with no work exposure limit, 0.003 mg m−3 is proposed. The proposed value is for soluble nanoparticles with no [13].

4. Synthesis of Nanoparticles

The production of electronic devices and the synthesis of materials are being drastically changed by nanotechnology. A vital part of nanotechnology and nanoscience is the synthesis of nanomaterials. Numerous regulating elements have a role in the nucleation and subsequent formation of stabilised nanoparticles during the synthesis of nanomaterials. Temperature, reactant concentrations, reaction duration, and pH are some of these variables. Studies show that altering the Variations in the size and shape of synthesised nanoparticles are often caused by the pH of the reaction solution. In particular, smaller particles are typically produced by higher pH values, while larger particles are likely to be produced by lower acidic pH values [35]. The required size, suitable surface characteristics, and the kind of material-metals, semiconductors, ceramics, polymers, etc. All have an essential part in choosing the synthesis technique to produce the necessary NPs [36]. There are two primary groups of techniques used to synthesise nanomaterials: top-down and bottom-up methods [13].

4.1. Bottom-Up Method

The buildup of material from atoms to clusters of nanoparticles is known as the bottom-up or constructive technique [9]. Typically, this method uses the reduction and sedimentation techniques. Because it may result in less waste, this method is thought to be more cost-effective. Sol-gel, spinning, green synthesis, chemical vapour deposition (CVD), pyrolysis, and biosynthesis are the most widely utilised examples of this technique [37]. The possibility to generate metallic nanoparticles with a more uniform chemical composition and a significantly lower number of flaws is an obvious advantage of the bottom-up method [12].

4.2. Top up Method

The reduction of a bulk substance to nanometric scale particles is known as the top-down or destructive method [9]. NPs are created when a bigger molecule decomposes or breaks down into smaller pieces. Mechanical milling, chemical etching, laser ablation, sputtering, electroexplosion, thermal decomposition, and nanolithography are among its methods [1]. Large amount of material can be divided into smaller, nanoscale particles with this technique [38]. The ultimate flaw in the surface structure is the main drawback of the top-down method. Because of their high aspect ratio, these surface structural flaws can have a significant effect on the final physical properties and surface chemistry of metallic nanoparticles [12].

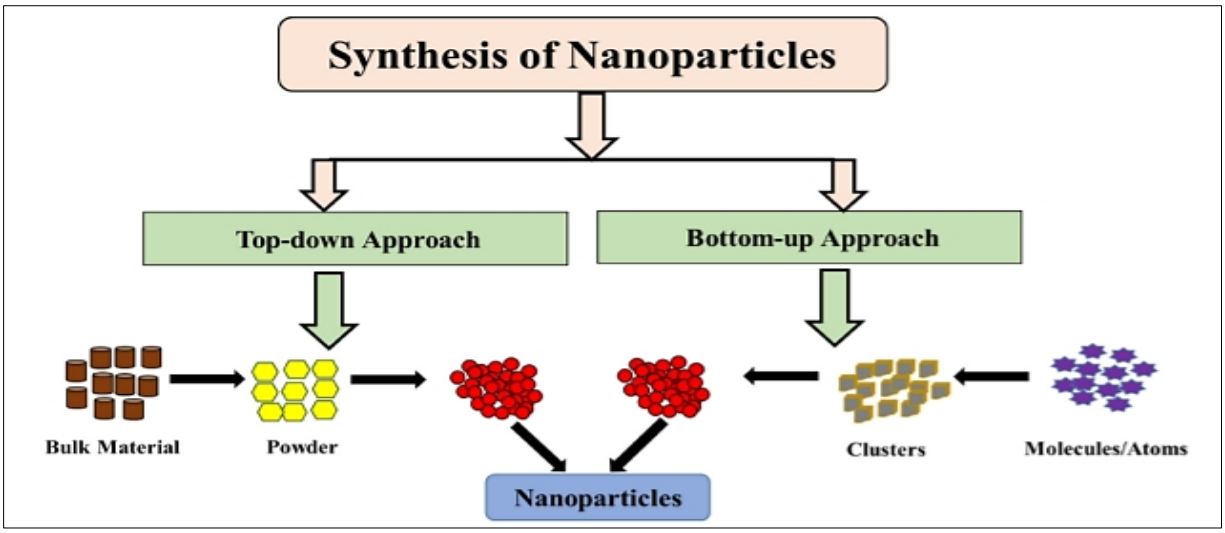

Figure 5 Schematic representation of 'top-down approach' and 'bottom-up approach' for synthesis of nanoparticle review [35]

5. Methods for producing Nanoparticles

There are currently several physical, chemical and biological methods possible to produce multiple types of nanoparticles.

5.1. Physical method for Nanoparticles Synthesis

To produce the desired product, physical methods for the synthesis of metallic nanoparticles rely on the use of microwaves, ultrasound, irradiation, or mechanical grinding, among other techniques. These methods require a significant amount of energy because they require the maintenance of high pressures and temperatures in most of them [12]. When it comes to the homogeneity of nanoparticle distribution and the lack of solvent contamination in thin films, physical techniques dominate chemical ones [35]. AgNPs are created via a variety of physical methods, including transformation, spark release, and evaporation–condensation. Metal nanoparticles (NPs) with an average size of 9.5 nm are also produced using the thermal breaking process [39].

5.2. Chemical Method for Nanoparticles Synthesis

In essence, reducing agents, stabilizing/capping agents, and metallic precursors are needed for chemical processes. Nucleation and NP growth are the methods involved in the reduction of silver salt [39]. chemical approach, which synthesises nanoparticles using both organic and inorganic reducing agents. Ions are reduced by reducing chemicals, which causes metals to form and cluster into oligomeric clusters. These clusters result in the formation of metallic colloidal particles [35]. These techniques don't require complicated machinery and are said to be quick, simple, convenient, and cheap (for large-scale production). Furthermore, there is no discernible loss of stability when the finished nanoparticles are held for a long period of time [12]. Although there are several benefits to producing nanoparticles chemically, it is noted that using solvents and hazardous chemicals to stabilise the particles is not environmentally friendly [12]. The chemo-reduction process is the most efficient way for creating stable nanoparticles. Elemental hydrogen, ascorbate, citrate and borohydride thio-glycerol, and 2-mercaptoethanol are among hazardous substances employed in the manufacture of AgNPs [39].

5.3. Biological Method for Nanoparticles Synthesis

The most practical way to get around the drawbacks of synthetic chemical processes is to use biological green synthetic approaches. The greener approach is a simple, cost-effective, trustworthy, and environmentally responsible way for creating AgNPs; a further advantage is the simplicity of choosing the solvent medium [39]. Bio molecules are complex nanostructures that have evolved and been programmed by sequence information. Proteins, viruses, diatoms, DNA, and RNA are all useful assets that serve as template or blueprint for the creation of nanoparticles [35]. The ability of microorganisms to remove or accumulate metal has already been used in numerous biotechnological processes, including bioleaching and bioremediation, and interactions between microbes and metals have been widely described. The synthesis of nanoparticles using biological methods is simple, cost-effective, and energy-efficient (the majority of bioprocesses take place at room temperature and under normal pressure), uses natural resources, and is environmentally friendly because it lacks the use of harsh, costly, and toxic chemicals [12].

6. Mode of action of Nanoparticle

The growth or engineering of a medication or gene delivery system that has a superior ability to target tumour cells while sparing normal healthy cells is crucial for effective cancer therapy [1]. It is widely acknowledged that insufficient tumour penetration of therapeutic nanoparticles and unsatisfactory drug release rate (NP) are the main barriers to improving the effectiveness of anticancer treatment [40]. An ideal cancer therapy nanodevice must still release the payload quickly after it reaches the intended site of action in order to kill tumour cells. Currently, there is increasing interest in designing functional polymers that are responsive to the tumour microenvironment in order to boost intracellular drug release [41]. In most cases, nanoparticles cause cancer cells to undergo apoptosis by a many processes, the most researched of which is apoptosis mediated by reactive oxygen species (ROS). Further modes of action of nanoparticles in inducing apoptosis in cancer cells include immunological interventions, site-specific cytotoxicity, transcription inhibition, and up-and-down-regulation of proteins. The final effect is apo reticuloendothelial, however it is essential to note that many of these processes include a sequence of cross-talk [3]. Nanoparticles are breaks down, excreted, and/or retained in different body compartments after entering the human circulation. The size, shape, and surface characteristics of various nanoparticles, as well as their clearly unique physiochemical characteristics, impact how they are absorbed, distributed, metabolized, and removed from the human body and within cells. The absorption, distribution, metabolism, and elimination receptors are the names given to these mechanisms [42].Therefore, developing nanomaterials that precisely target the desired cells or tissues and have no

adverse effects is crucial and of interest to researchers. Anticancer activity in both in vitro and in vivo model systems has been reported. Quan et al. shown in their study that the concentration of AgNPs affects the mortality of cancer cells [39].

6.1. Targeted Drug Delivery System

In order for anticancer medications to be effective in treating cancer, they should ideally be able to reach bodily barriers and reach the targeted tumour tissues after delivery with low volume or blood circulation activity loss. Second, medications with a regulated release mechanism of the active form should be able to kill tumour cells only, without affecting healthy cells, once they have reached the tumour tissue. By concurrently raising the intracellular concentration of medications and minimising dose-limiting toxicities, these two fundamental strategies are also linked to increases in patient survival and quality of life [43]. The technology used to administer drugs has recently been improved. It considers a number of factors, including time, pharmacokinetic processes, drug absorption processes, and bioavailability for optimal drug delivery [44]. NPs which has diameter between 10 and 100 nm are typically thought to be appropriate to treat cancer. The targeting mechanisms must be addressed in order to comprehend the process of contact and crosstalk between NP carriers and cancer cells as well as tumour biology. Passive targeting and active targeting are the two basic categories into which the targeting techniques can be divided [1]. There are fewer side effects, better pharmacokinetics, and a greater EPR affect linked to this increased therapeutic efficacy. In addition, enhanced tumour selection and drug distribution in cancer cells are caused by the target ligands' superior binding efficacy on the nanoparticle surface. It was discovered that the negatively charged hyaluronic acid-based nanoparticle shown site-specific cytotoxicity to tumour cells that expressed CD44. Additionally, as proven by the multifunctional titanium phosphate nanoparticle's tailored delivery of chemotherapeutic medicines, the therapeutic efficacy may be tracked in real-time. Since the nanoparticles had a high drug loading capacity and enhanced cell uptake mediated by the folate receptor, these were intended for both cellular uptake and cytotoxicity [3].

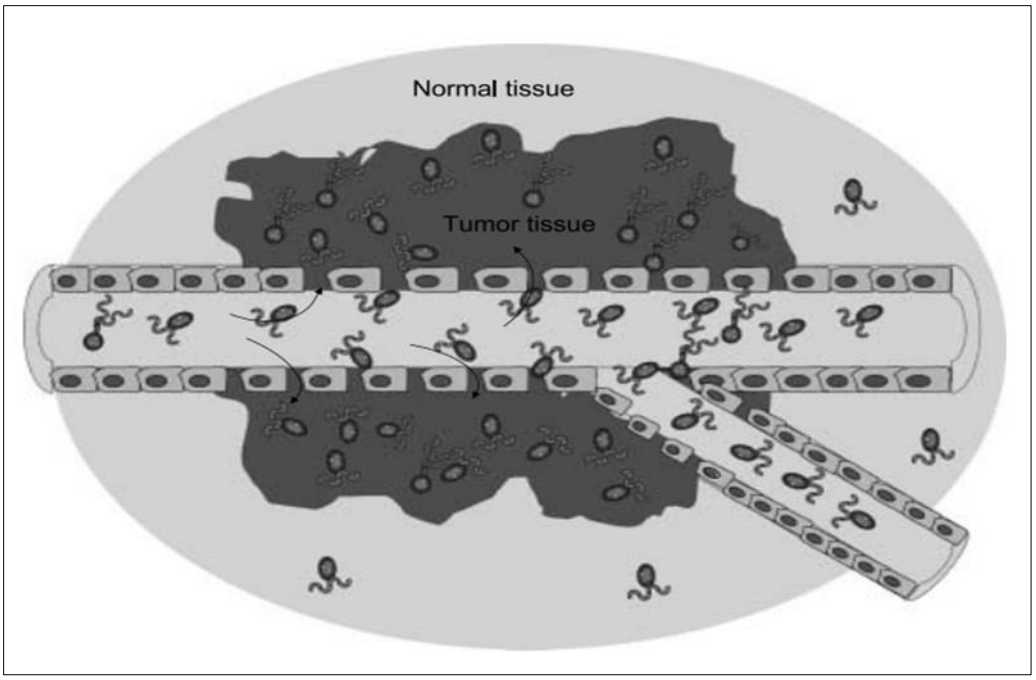

Figure 6 Tumor targeting of nanoparticles passively by enhanced permeability and retention. Long-circulating therapeutic nanoparticles accumulate passively in solid tumor tissue by the enhanced permeability and retention effect. Angiogenic tumor vessels are disorganized and leaky. Hyperpermeable angiogenic tumor vasculature allows preferential extravasation of circulating nanoparticles [43].

6.2. Passive Targeting by Nanoparticles

Longer blood circulation and a higher likelihood of reaching the targeted tumour tissues are two benefits of nanoparticles that meet the size and surface features requirements outlined above for avoiding reticuloendothelial system capture. Macrophages, including nanoparticles, can selectively aggregate in tumours due to the distinct pathophysiology features of tumour vasculature [43]. For instance, a nanoparticle's propensity to extravasate from discontinuous blood arteries, including those in the liver and spleen, can be altered by varying its size [45].

6.3. Active Targeting

Active targeting is defined as a particular ligand receptor interaction for intracellular localization that happens only after blood circulation and extravasation. Active targeting is classified into three types: first order (organ targeting), second order (cell targeting), and third-order (intracellular targeting). When coupled with nanoparticles, ligands such as antibodies, peptides, and nucleic acid aptamers can enable active targeting [46].

7. Role of Nanoparticles to treat cancers

- Chemicals that are proven to effectively destroy cancer cells are used in conventional chemotherapy. However, in addition to killing tumour cells, these cytotoxic medications can cause adverse reactions include fatigue, hair loss, nausea, neuropathy, and weakened immune systems. Chemotherapeutics can be administered directly to the tumour using NPs as drug carriers, protecting healthy tissue in the process. Comparing to traditional chemotherapy, nanocarriers offer several benefits [5].
- Brain cancer is the most dangerous sickness in terms of treatment. Brain malignancies are the most difficult to cure because to the limitations imposed by the blood-brain barrier. The brain microvascular endothelium, which produces barriers separating blood from the brain's neuronal tissues, is found in the blood-brain barrier (BBB). The blood-brain barrier (BBB) prevents harmful poisons, xenobiotics, and other metabolites from entering the brain. The majority of brain cancers are gliomas and brain cancers. Among the most lethal tumors are these two varieties of brain cancer. Nanoparticles have a lot of promise for treating brain cancer because of their small size (in nm), tissue-specific targeting abilities, and ease of transit across the blood-brain barrier [47].
- One of the main issues with cancer treatment and management is drug resistance. It is effective against every kind of cancer and every kind of treatment. When illnesses develop resistance to medicinal treatments, a phenomenon known as drug resistance arises. There are two categories of drug resistance: 1) intrinsic and 2) acquired. Pre-existing mutations in genes related to cell proliferation or death are typically the cause of innate resistance. The term "acquired resistance" refers to the kind of resistance that arises following a specific anti-tumor treatment and can be caused by changes in the TME during treatment or by the development of additional mutations. Nanoparticles can also be employed to overcome treatment resistance associated with cancer because of their incredible ability to co-encapsulate several therapeutic substances [1].
- Hypoxia is yet another factor supporting MDR. Some tumour cells are frequently in a hypoxic state because of aberrant blood arteries near the tumour and the increased oxygen demand from the quickly expanding tumour. Chemotherapy medications frequently fail to reach the hypoxic portion of the tumour. An oxygen ramp produced by hypoxia inside the tumour exacerbates tumour heterogeneity and promotes a more aggressive phenotype. Furthermore, it has been shown that the low oxygen levels promotes the overexpression of efflux proteins. Hypoxia-inducible factor 1α (HIF-1α), the main protein, plays a crucial part. Therefore, one strategy to combat drug resistance is to target or silence the HIF-1α gene. NPs containing HIF-1α siRNA can be used to reduce hypoxia-mediated drug resistance [1].
- DNA nanotechnology is a relatively new process in which self-assembling DNA strands hybridise with one another to form a functional nanostructure with a very high degree of spatial programmability. The DNA strands were modified to integrate inorganic nanomaterials (such as fluorescent nanomaterials and two-dimensional nanosheets) for use in cancer treatment and detection. In order to create distinctively shaped nanostructures, several linear DNA strands with predetermined sequences were successfully hybridised to self-assembled DNA tiles.These DNA tiles can be programmed to form 2D and 3D nanoribbon lattices by joining with other tiles.In order to connect with receptors on the surfaces of cancer cells and initiate signal transduction or other biological mechanisms, they can be further modified with additional nanoparticles like gold, graphene, or graphene oxide [3].
- Theragnostic, it is a nuclear medicine and personalised medicine technique based on radioactive drugs. It uses one radioactive drug to identify tumours and another chemical to cure them. Diagnostics and treatment are combined in the synergistic field of therapeutics. The realisation that using particles at the nanoscale offers several benefits in diagnosis and treatment has led to the development of nanosensors and nanomedicine. The discipline of applying and refining nanomedicine techniques for advanced theragnostic goals is known as "nanotheranostics." Polymer conjugations, gold-based and silica-based nanomaterials, dendrimers, micelles, liposomes, metal and inorganic nanoparticles, carbon nanotubes, and nanoparticles of biodegradable polymers are examples of nanocarriers that are used and improved in this process. In order to achieve better theragnostic effects, these carriers are used to deliver therapeutic and diagnostic substances precisely while minimizing potential side Resistance [48].
- Because of the enhanced permeability and retention (EPR) effect, the capacity of nano-carriers to target tumours is also crucial in PDT employing nanoparticles [49].

- Nanoparticles have been used more and more as carriers in novel tumour treatment techniques because of their small size, biosafety, drug loading, and physical characteristics, which can support physical therapy. The advantages of these nanoparticle-mediated treatments include their multifunctionality, less toxicity, and improved therapeutic outcome. Furthermore, a number of nanoparticle-mediated medical imaging technologies are more accurate and clearer, which aids in precise tumour identification [50].
- Using nanoparticles in clinical diagnostics, nanodiagnostics improves sensitivity and transforms early cancer diagnosis. The diagnosis of cancer uses a variety of nanomaterials, including dendrimers, carbon nanotubes, quantum dots, and polymeric nanoparticles. Combining nanoparticles with specific small molecules, such as aptamers, polysaccharides, antibodies, and peptides, improves their detection capabilities [51].
- Circulating tumour DNA (ctDNA) is made up of cancer-derived DNA fragments that are about 100 and 200 base pairs long and move through the bloodstream. ctDNA, which is released from primary tumours or circulating tumour cells (CTCs), can be used to identify genetic defects unique to cancer. Finding genetic anomalies Even before any symptoms show up, ctDNA can help diagnose cancer. Highly selective hybridisation with nucleic acid probes that have complimentary sequences can be used to identify genetic defects linked to cancer. A DNA silver nanocluster (NC) fluorescent probe was created to identify a single exon in the BRCA1 gene in breast cancer. Under ideal circumstances, this probe greatly increased the limit of detection (LOD). Nanocluster fluorescence generated via recognition hybridisation was used to identify large deletion mutations in BRCA1 [52].
- The development of imaging probes with enhanced contrast enhancement, heightened sensitivity, regulated biodistribution, improved spatial and temporal information, multifunctionality, and multimodal imaging across MRI, PET, SPECT, and ultrasound is made possible by the distinct optical, magnetic, and chemical characteristics of materials at the nanoscale. These characteristics may eventually result in clinical benefits including personalized medication, real-time illness progression evaluation, and earlier discovery [53].
- In order to provide concentrated local medication delivery with the potential for sustained release, NPs can be safely loaded with therapeutic chemicals when accompanied by biodegradable carriers. These characteristics allow them to access bodily cavities and the bloodstream for therapeutic purposes with less invasion and enhanced absorption [54].
- Nanoparticles also have a high avidity as they can be coated with multiple copies of ligands, which will allow multiple bond interactions with cellular target moieties, thereby increasing their association constant by 4 to 5 orders of magnitude. This is advantageous as it will allow more nanoparticles to accumulate at the site of the tumor, thereby increasing the signal-to-noise ratio, which allows cancerous tissue to be better highlighted relative to adjacent normal tissue [55].

8. Conclusion

Millions of people die every year from cancer, making it a big public health problem around the world. Even though cancer treatment has come a long way, traditional methods often don't work very well and have serious side effects. Nanotechnology has become an interesting way to try to make cancer detection and treatment better. Nanoparticles can be made to target specific cancer cells while doing less damage to healthy organs. Nanoparticles of different types, such as carbon-based, organic, inorganic, and hybrid nanoparticles, have been created to help treat cancer. These nanoparticles have shown potential in enhancing drug delivery, imaging, and therapy. However, further research is needed to fully understand the potential risks and benefits of nanoparticles in cancer therapy. With continued advances in nanotechnology, nanoparticles are likely to play an increasingly important role in the fight against cancer.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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