Journal of Clinical and Nursing Research, 2024, Volume 8, Issue 11
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

# Innovative Nanoparticle Synthesis and Multifaceted Applications in Medicine and Cancer Therapy

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**Abstract:** Nanotechnology has far-reaching implications and applications in multiple fields. The biomedical and health sectors can use nanotechnology concepts for medication delivery and treatment. Under controlled conditions, it can target and initiate administering drugs and several other therapeutic agents. Since cancer is the largest cause of death worldwide, prompt diagnosis and effective anticancer treatments are crucial. In this particular context, nanotechnology reduces side effects and directs drug delivery to specifically target cancer cells, providing unique benefits for cancer therapy. In the present thorough review, the most noteworthy new findings for 2010–2023 were compiled, which address the development and use of nanosystems for cancer treatment. Nanoparticles allow precise and controlled release of therapeutic substances at specific action locations, enabling targeted medication delivery. Size, shape, surface, charge, and loading methods impact its efficiency. Researchers have made advancements in encapsulating drugs into nanoliposomes and nanoemulsions, including paclitaxel and fisetin, and are currently testing their suitability in ongoing clinical trials. The purpose of this review is to serve as a continuous path toward recognizing the extraordinary potential of various nanoparticles in cancer therapies.

**Keywords:** Nanoparticles; Anticancer; Drug delivery; Therapeutics; Medicine

**Online publication:** November 26, 2024

## 1. Introduction

According to the 2022 cancer statistics, cancer is one of the major causes of death worldwide [1]. When treating

a cancer patient, chemotherapy, radiation, and surgery are the traditional therapeutic choices [2]. The disease damages the patient's fitness, which deteriorates with each therapy intervention over time, thereby determining the optimal course of action [3]. Other factors include the location and stage of the malignancy [3]. While there is a possibility of serious problems and an increased risk of dying from other diseases, these treatments can lower cancer mortality and recurrence rates. For a long time, radiotherapy has been a vital tool in the fight against cancer because it may be able to cure the disease, reduce symptoms, and increase survival [4]. However, radiation therapy also carries significant adverse consequences. Radiation therapy not only targets the tumour cells but also damages the surrounding normal tissue [5]. Chemotherapy is possible to treat cancer with a wide range of pharmacological classes, but doing so may have unfavorable side effects, including autoimmune-like conditions and potentially fatal adverse events brought on by the reactivation of cellular immunity [6].

Numerous scientific disciplines have made significant efforts to mitigate the aforementioned issues by investigating alternatives that avoid the toxicity and adverse effects of traditional medicines. Most of these novel strategies, like using inorganic nanoparticles with altered surfaces to combat cancer, are still undergoing extensive study [7]. However, research has demonstrated that they possess significant side effects. Radiation and chemotherapy have two primary drawbacks: their high toxicity to surrounding healthy cells, tissues, and organs, which can result in drug resistance during treatment, and their lack of specificity, which results in insufficient drug delivery at the targeted site [8]. To address these issues, the scientific community looks to nanotechnology, which has the potential to improve medicine delivery to target areas while also boosting efficacy and lowering adverse effects [9]. As a result, nanoparticles' large specific surface areas give them useful properties, such as the ability to become bio-functionalized and a useful interface that helps the nanoparticles interact with the tissues around them [10].

Scientists are creating many products that involve the manufacturing of nanoparticles or their use, and because of their potential efficacy and the need for fewer medications, nanomedicine is becoming a more popular study subject [11]. As a result, the application of nanoparticles in this situation may also help to augment, stimulate, or improve the efficacy of medication therapy at a lower cost. Nanoparticles have brought about a paradigm shift in the field of oncological therapy medication delivery [12]. Scientists have successfully solved problems related to drug solubility and systemic toxicity [13]. This has led to the development of several drug delivery systems based on nanoparticles that are now moving through different stages of clinical research. The intentional incorporation of nanoparticles has greatly enhanced the integration of imaging technologies into the fields of cancer diagnosis and treatment monitoring [14]. When sparingly loaded with imaging moieties like gold nanoparticles and quantum dots, these small structures can follow the spread of therapeutic agents in real time and instantly visualize neoplastic tumors [15].

The field of nanoparticle research has paid significant attention to the emerging field of "theranostics," an inventive idea that combines therapeutic and diagnostic functions [16]. Scientists have cleverly engineered some nanoparticles to fulfill two functions: they can carry drugs and provide useful imaging capabilities simultaneously. Clinical trials are currently thoroughly investigating this dual purpose to enhance the accuracy and effectiveness of cancer therapies [17]. Researchers have skillfully applied magnetics nanoparticles in hyperthermia therapy, using alternating magnetic fields to create controlled hyperthermic effects within cancer cells [18]. Researchers have conducted clinical trials for specific cancers to assess the therapeutic potential and viability of this approach [19].

In addition, nanoparticles have shown enormous promise in increasing the susceptibility of cancer cells

to radiation therapy [20]. Nanoparticles present the alluring possibility of delivering treatments with unmatched specificity in the field of precision oncology [21]. Adding ligands to nanoparticles that are specifically made to target cancer cells makes treatments much more effective overall and lowers the damage to healthy tissues [22]. This paper provides a brief overview of the use of nanoparticles. Nanoparticles typically have dimensions ranging from 1 to 100 nm and exhibit features that are highly dependent on surface area and size. Conversely, researchers have spent more time studying different polymeric nanoparticles and nanoliposomes [23], which are well-known drug carriers, about cancer treatments. On the other hand, researchers have studied different polymeric nanoparticles and nanoliposomes well-known drug carriers for cancer treatments for a longer period [24].

Despite numerous attempts, it is challenging to classify nanoparticles systematically due to their variety of forms. Therefore, nanoparticles can be categorized based on their form, average size, chemical makeup, and manufacturing method, among other factors [25]. Nanoparticles' high surface area-to-volume ratios are useful in a variety of applications mediated by surface phenomena [26]. When using nanoparticles for medication administration, for instance, specific surface area and surface functionalization are crucial factors to consider [27]. Their larger surface area allows for the attachment of more anticancer drugs, enhancing their effectiveness as drug delivery vectors. Due to their nanometric size, which allows them to pass across blood-brain barriers, nanoparticles can penetrate pores and aid in the development of more potent treatments for neurological diseases and brain tumours [28].

One of the many benefits of developing therapeutics at the nanoscale is that nanoparticles can solve anticancer medication solubility and stability issues [29]. Putting a drug that does not dissolve well in a hydrophilic nanocarrier can help it get to where it needs to go and be used [30]. This is because water solubility limits bioavailability and slows down the development of new drugs. Nanocarriers or synthetic chemicals must encapsulate antineoplastic medicines to prevent the excretion or breakdown of anticancer compounds [31]. Additionally, nanotechnology can selectively reroute chemicals to cancer cells or enhance drug penetration and redirection because of its physicochemical characteristics [32]. Anticancer medicines employ both active and passive targeting strategies in their rerouting [33]. Furthermore, the quick cargo release of nanocarriers makes nanomedicine treatment stimuli-sensitive. A pH-independent medication can be catenated like doxorubicin into pH-sensitive nanoparticles to enhance cellular absorption and intracellular release. Ultimately, directed nanomedicine treatments decrease the tumor's resistance to anticancer medications [34]. Targeted input and multidrug-resistant adenosine triphosphate outflow pump-driven excretion generally reduce non-specificity [35]. Nanomedicine can slow down the rate at which a drug moves through the body, making it easier for stimulus-responsive drugs to get into the body and block the drug's endocytic input [36].

## 2. Synthesis of nanoparticle

A variety of techniques can synthesize nanoparticles (NPs), broadly categorized into two classes: the bottom-up approach and the top-down approach.

### 2.1. Bottom-up synthesis

Bigger molecules undergo a destructive process to break down into smaller components, which then transform into the appropriate nanoparticles [25]. Various decomposition techniques, such as chemical vapour deposition (CVD), physical vapour deposition (PVD), and grinding and milling, are examples of this

method. For instance, a study employed the milling process to synthesize coconut shell (CS) nanoparticles. Ceramic balls and a planetary mill were used to finely grind raw CS particles for varying durations. Through a variety of characterization methods, the study examined ways the milling duration affected the total size of the nanoparticles. The Scherer equation revealed that the nanoparticles' crystallite size decreased as the milling duration increased [37]. Furthermore, the brownish colour diminished with every hour because of the nanoparticles' decreasing size. SEM data supported the X-ray pattern, indicating a reduction in particle size over time [38]. Another work used a top-down destructive method to create spherical magnetite nanoparticles from natural iron oxide (Fe2O3) ore. When organic oleic acid was present, the particles produced ranged in size from approximately 20 to 50 nm [39].

A straightforward top-down method synthesizes colloidal carbon into spherical particles with a controllable size [40]. This method was based on the steady chemical adsorption of Polyoxometalates (POM) on the carbon interfacial surface [41]. This made the carbon black stick together into smaller, spherical particles that were evenly distributed in size and could spread out easily [42]. Micrographs showed that as the sonication period increased, the size of the carbon particles shrank. Transition-metal dichalcogenide nanodots (TMD-NDs) were synthesized from their bulk crystals using a top-down mix of grinding and sonication procedures [43]. Nearly all TMD-NDs found with diameters less than 10 nm exhibit excellent dispersion due to their limited size range.

## 2.2. Top-down synthesis

This method, often known as the "building up" method, entails creating nanoparticles from comparatively simpler materials. This strategy includes techniques for sedimentation and reduction, as well as sol-gel, green synthesis, spinning, and biological synthesis, to synthesize TiO2 anatase nanoparticles containing graphene domains [44]. They used precursors for titanium isopropoxide and alizarin to create a photoactive composite, which catalyzed the breakdown of methylene blue [45]. Alizarin was selected because of its potent ability to bind TiO2 via its axial hydroxyl terminal groups. According to the SEM results, the size of the nanoparticles increases as the temperature rises. A top-down laser irradiation method to successfully make well-uniform spherical Au nanosheets with monocrystalline structures. Recently, the solvent-exchange approach produced limit-sized low-density lipoprotein (LDL) nanoparticles for medical cancer medication administration [46]. Nucleation represents the bottom-up approach in this strategy, whereas growth represents the top-up method [47].

Researchers have synthesized monodispersed and spherical bismuth (Bi) nanoparticles using both top-down and bottom-up methods, with outstanding colloidal characteristics [48]. The top-down approach transformed bismuth into a molten form and then emulsified it within cooked diethylene glycol to make the nanoparticles, while the bottom-up approach boiled bismuth acetate within ethylene glycol [48]. The nanoparticles produced by the two techniques ranged in size from 100 nm to 500 nm. Numerous researchers are drawing attention to the feasibility and less harmful nature of green and biogenic bottom-up synthesis methods [49]. These procedures are both economical and environmentally benign, as they create nanoparticles using biological systems such as plant extracts, bacteria, yeast, fungi, aloe vera, tamarind, and even human cells. Researchers have synthesized gold nanoparticles from the biomass of wheat and oat, using microorganisms and plant extracts as reducing agents.

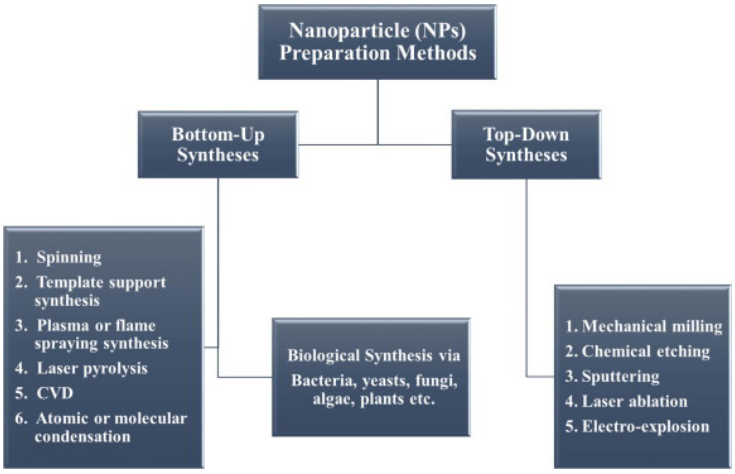


**Figure 1.** Nanoparticles synthesis approaches, bottom-up and top-down approaches.

**Table 1.** Bottom-up and top-down approaches merits and demerits

| Top–down method | Merits | Demerits |
|---|---|---|
| Optical lithography | A trustworthy, well-established micro- or nanofabrication instrument, especially for chip manufacturing, with a high throughput and adequate resolution. | The trade-off between sensitivity and resolution in the resist process necessitates sophisticated, costly, clean room-based procedures. |
| E-beam lithography | This highly precise technique, often used in research settings, is a useful tool for nanofabrication, enabling the creation of desired-shaped nanostructures as small as 20 nm. | It is expensive, slow (serial writing method), low-throughput, and challenging for nanofabrication below 5 nm. |
| Scanning probe lithography | Chemicals with high molecular and mechanical resolution Nanopatterning abilities that are precisely regulated. The resists contain nanopatterns for silicon transfer, as well as the ability to manipulate both large molecules and single atoms. | High-throughput applications and production are restricted, and the procedure can be costly, particularly when using ultra-high vacuum scanning probe lithography. |
| Atomic layer deposition | It achieves atomic-level precision in digital thickness control by creating pinhole-free nanostructured films over vast regions, one atomic layer at a time. | According to the use of many components, this procedure is typically sluggish and costly because it uses many components. |
| **Bottom-up method** | **Merits** | **Demerits** |
| Atomic layer deposition | Enables precise atomic-level digital thickness control by depositing single atomic layers at a time; large-scale, pin-hole-free nanostructured films; The films exhibit excellent repeatability and adhesion due to the establishment of chemical bonds at the first atomic layer. | It is typically a laborious and costly procedure because vacuum components are involved. It might be challenging to economically deposit some metals, multicomponent oxides, and crucial semiconductors for technology. |
| Sol gel nanofabrication | Chemical synthesis is a low-cost technique that fabricates a wide range of nanomaterials, including materials with multiple components such as glass, ceramic, film, fiber, and composite materials. | Not readily scalable, it is typically challenging to regulate the synthesis process and the ensuing drying stages. |
| DNA-scaffolding | The system allows for the highly accurate assembly of nanoscale parts into programmable configurations with far smaller dimensions (less than 10 nm in half-pitch). | A wide range of topics need to be investigated, such as throughput, cost, line edge roughness, compatibility with CMOS fabrication, and innovative unit and integration procedures. |
| Molecular self-assembly | Nanosystems that are accurate down to the atomic level can be synthesized by stretching patterns very large and letting deep molecular nonpatterns with a width of less than 20 nm form. | Nanosystems are more difficult to design and create than mechanically directed assemblies. |

# 3. Application of nanoparticles

## 3.1. Application of nanoparticles in medicine

Simple or complex, nano-sized inorganic particles have special physical and chemical characteristics that make them essential building blocks for the creation of innovative nano devices with uses in the physical, biological, biomedical, and pharmaceutical domains [50]. Nanoparticles (NPs) are becoming more valuable in medicine because of their capacity to provide medications in the right quantities, increase therapeutic efficacy, lessen adverse effects, and increase patient compliance [12]. Biomedical applications frequently employ iron oxide particles such as maghemite ($Fe_2O_3$) and magnetite ($Fe_3O_4$) [51]. Mie theory and the discrete dipole approximation approach frequently determine their optical characteristics, leading to the use of NPs for biological and cell imaging, as well as photothermal therapy [52]. Polyethylene oxide (PEO) and polylactic acid (PLA) nanoparticles (NPs), which are hydrophilic, have shown promise as ways to deliver drugs [53]. The use of superparamagnetic iron oxide nanoparticles (NPs) with specific surface chemistry in medication administration, tissue regeneration, immunoassays, hyperthermia, MRI contrast enhancement, and cell separation [54]. Antigen-antibody interactions, using labeled antibodies, can detect analyses in tissue slices.

Biodegradable NPs are gaining attention for drug delivery because they can efficiently transport medications while minimizing negative effects. Liposomes are a promising drug carrier, although they have drawbacks such as low stability and low encapsulation efficiency [55]. Compared to liposomes, polymeric NPs have improved drug stability and controlled release characteristics. The surface plasmon resonance (SPR) characteristics of semiconductors and metallic nanoparticles make them promising for cancer treatment and detection [56]. Multi-hydroxylated NPs have demonstrated antineoplastic action with decreased toxicity, whereas gold nanoparticles can convert absorbed light into localized heat for laser photothermal therapy. Silver nanoparticles are being used more often in home items and wound dressings due to their antibacterial properties [57]. Functionalized $TiO_2$, ZnO, $BiVO_4$, Cu-, and Ni-based NPs specifically target microbial species in textiles, medicine, water disinfection, and food packaging.

## 3.2. Application of nanoparticles in anticancer activity

The current difficulties in treating cancer with traditional medicines have led to further advancements in nanotechnology. The exponential growth of nanoscience has led to the development of therapeutically active nanomaterials (NMs) [58]. They have great potential in cancer treatment because NMs alter the profile of medication toxicity. Improved surface properties enable nanoparticles (NPs) to diffuse more readily within tumor cells, minimizing toxicity and delivering the right medication dosage to the tumor site [59]. Using NMs with tumor-specific components, it overcomes the challenges of the anticancer agent's indiscriminate biodistribution and excessive dosage administration by targeting cancer cells [28]. This article focuses on the most recent developments in the application of different nanomaterials to cancer treatment, including their ability to target organelles, tumor microenvironment (TME), and cancer cell surfaces [59]. Nano routes are transforming the paradigm of cancer management through the distribution of anticancer drugs.

## 3.3. Application of nanoparticles in drug delivery

Nanoparticles, typically in the size range of 1–100 nanometers, are minuscule particles that can encapsulate therapeutic agents such as small molecules, proteins, peptides, or nucleic acids [60]. Protein and polysaccharides are used as nanomaterials for the formation of composite scaffolds that have favorable properties to use [61].

They represent a state-of-the-art technology in drug delivery, carrying many advantages over traditional drug formulations. Nanoparticles can functionalize targeting ligands like aptamers, peptides, or antibodies to identify and attach to specific cells or tissues. This precise delivery of medications to the intended site of action minimizes side effects and enhances therapeutic efficiency [62].

Although initially developed to serve as vaccination and chemotherapy agent carriers, nanoparticles are stable, solid particles composed of degradable polymers that range in size from 10 to 1000 nm. Medicinal substances can become enmeshed in the particle matrix, adhere to the particle surface, and become trapped in the polymer [63]. Oncology is the primary field of study for most of the research on using nanoparticles as a medicine delivery mechanism [64]. In addition to enhancing retention and permeability, nanoparticles can concentrate in tumour masses, inflammatory areas, and infection sites. While it is also feasible to produce multiple unique medications and selectively administer that particular medication to the cancerous tissue, a colloidal shell encases a cancer-fighting medication, which breaks down over time, while a lipid layer encases an antiangiogenics medication [65]. When injected intravenously, the cancer cells absorb this nanoparticle. The first action of the antiangiogenesis medication is to inhibit the intermediaries involved in blood vessel formation. The release of the anti-cancer medication subsequently leads to the effective elimination of cancer cells [66]. A nanoscale, an effective vehicle for the anticancer medication to reach the neoplastic location, enables all of that.

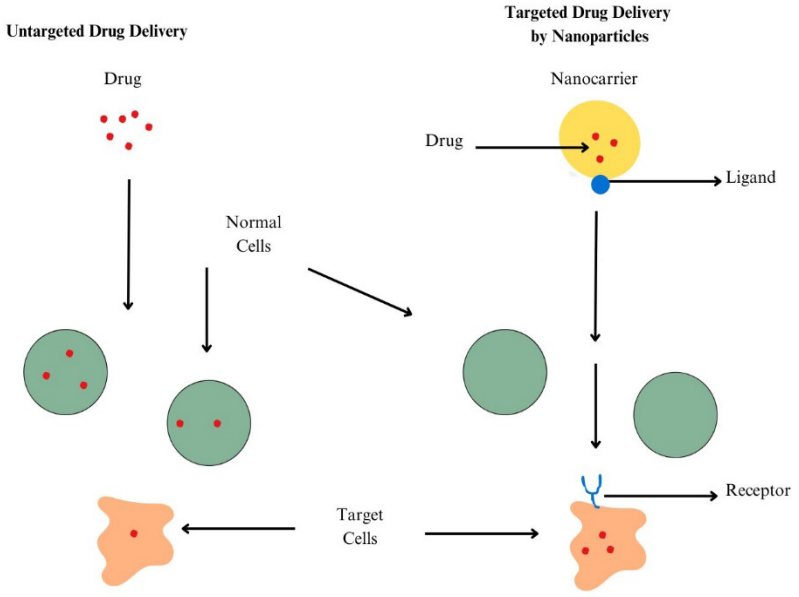


**Figure 2.** Untargeted drug delivery (left) and targeted drug delivery by nanoparticles (right)

Nanoparticles can release medications in a regulated manner, either continuously for an extended period or in response to specific stimuli such as pH, temperature, enzymes, or light [67]. This controlled release profile allows for the maintenance of therapeutic medication levels within the intended range, thereby maximizing effectiveness and minimizing side effects [68]. The poor solubility and bioavailability of many medications, particularly hydrophobic chemicals, limit their therapeutic effectiveness. Nanoparticles can encapsulate these medications, protecting them from deterioration, and enhancing their solubility and durability in physiological settings [69]. Due to this increased bioavailability, better drug absorption and distribution translate into greater therapeutic results. The protective shell that nanoparticles provide shields the encapsulated medicine from

enzyme breakdown and adverse environmental conditions [70]. This defense strengthens the medication's stability throughout the body's circulation, extending its half-life and enabling prolonged release at the intended location. By delivering many medications at once that have distinct physicochemical characteristics, nanoparticles can overcome drug resistance and produce synergistic benefits [71]. This strategy is especially helpful for treating complicated illnesses like cancer, as combination therapies that target several pathways can increase efficacy and lower the chance of tumor recurrence. By delivering pharmaceuticals directly to the target site and minimizing systemic exposure, nanoparticles can lessen the toxicity associated with traditional therapeutic formulations [72]. This targeted delivery enhances the therapeutic intervention's safety profile by reducing the likelihood of off-target effects on healthy tissues. Nanoparticles offer the possibility of personalized medical techniques by enabling customized drug delivery plans based on unique patient features [73]. This personalization can result in therapeutic interventions that are more patient-centered and effective, maximizing therapy efficacy while minimizing side effects.

**Table 2.** List of different types of nanoparticles with their composition and applications [66]

| Types of nanoparticles | Composition | Applications |
|---|---|---|
| Solid lipid nanoparticles | Melted lipid diffused in aqueous surfactant | A less toxic and extra firm colloidal carrier as substitute substance to polymer |
| Polymeric nanoparticles | Decomposable polymer | regulated and targeted delivery of drugs |
| Polymeric micelles | Amphiphilic block copolymer | regulated and organized delivery of hydrophobic drugs |
| Magnetic nanoparticles | Magnetite $Fe_2O_3$, Meghe mite covered with dextran | Drug for targeting diagnostics in medication |
| Carbon nanoparticles | Metals, semiconductors or carbon | Regulated transfer of drug to DNA and gene |
| Liposomes | Phospholipid vesicles | Regulated delivery of drug |
| Nanoshells | Dielectric core and metal shell | Targeted drug delivery to tumor |
| Ceramic nanoparticles | Silica, alumina, titania | Delivery of drugs and biomolecules |
| Nanopores | Aerogel, which is created by cell gel chemistry | Carriers for focused drug release |
| Nanowires | Silicon, cobalt, gold or copper-based nanowires | Carries electrons in nanoelectronics |

## 3.4. Applications of nanoparticles as therapeutic agents

Nanoparticles themselves can serve as therapeutic agents due to their unique qualities and abilities [74]. This makes them excellent options for a range of medical applications. Copper, zinc oxide, and silver nanoparticles possess intrinsic antibacterial qualities [74]. They can damage microbial membranes, stop enzyme function, and produce reactive oxygen species, which can effectively kill or stop the growth of viruses, fungi, and bacteria [57]. These antimicrobial nanoparticles have potential uses in medical implants, wound dressings, and anti-infection surface coatings. It is possible to create nanoparticles so that they reduce the body's inflammatory reactions. As an example, gold nanoparticles that are coated with peptides or anti-inflammatory drugs can target tissues that are inflamed and stop the pathways that cause inflammation [75]. This could help treat asthma, inflammatory bowel disease, and rheumatoid arthritis. Researchers are thoroughly studying the potential of nanoparticles in cancer therapy. Functions can be added to different kinds of nanoparticles, like liposomes, polymeric nanoparticles, and inorganic nanoparticles, so they can only reach tumor cells and deliver photothermal agents, nucleic acids, or chemotherapeutic medicines [76]. These nanoparticles can improve the effectiveness of anticancer drugs and reduce side effects by breaking down multidrug resistance, making it easier for drugs

to build up at the site of the tumor, and making combination therapy more possible. For neurodegenerative illnesses like Alzheimer's, Parkinson's, and stroke, nanoparticles exhibit promise in neuroprotection and neurodegeneration treatments [77]. Putting nanoparticles into the central nervous system that contain growth factors, neuroprotective drugs, or stem cells can help neurons survive, heal damaged tissue, and improve functional recovery. Researchers are exploring the use of cardiovascular nanoparticles in the treatment of various cardiovascular illnesses such as atherosclerosis [78], myocardial infarction, and thrombosis. Nanoparticles functionalized with antioxidants, thrombolytic medications, or anti-inflammatory medicines can target plaque deposits, reduce inflammation, and dissolve blood clots, thereby treating or preventing cardiovascular events. These useful instruments for immunotherapy applications have the ability to alter the body's immunological responses [75]. Nanoparticles can be engineered to carry adjuvants, immune checkpoint inhibitors, or antigens that can activate or deactivate specific immune pathways. This could lead to new treatments for autoimmune diseases, allergies, and cancer immunotherapy [79].

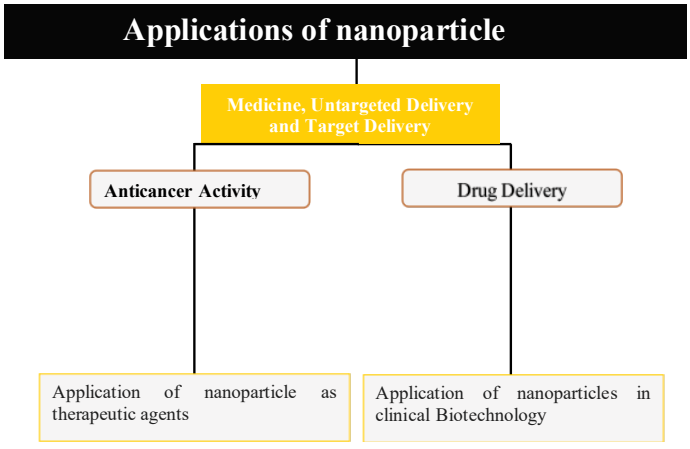


**Figure 3.** Schematic representation of applications of nanoparticles in anticancer activity and drug delivery.

## 4. Usage in clinical settings

Researchers have thoroughly studied NPs for their potentially beneficial anticancer effects in a variety of human cancer cell lines, including MDA-MB-231 breast cancer cells, IMR-90 lung fibroblasts, endothelial cells, and U251 glioblastoma cells [80]. NPs demonstrated considerable potential as efficient drug delivery methods against tumors. Traditional cancer therapies like radiotherapy, chemotherapy, and surgery have established drawbacks such as drug toxicity, erratic side effects, issues with drug resistance, and a lack of specificity [81]. NPs overcome these drawbacks by reducing side effects and improving cancer therapy effectiveness. One of their unique selling points is their ability to administer medications with precision and traverse various biologic barriers. The combination of targeted delivery of anticancer medications to tumor tissues and green manufacturing of NPs is a novel strategy for enhancing cancer treatment [82]. One of the most intriguing and difficult methods available today for efficient, tailored cancer treatment is theranostics, which combines diagnostics and therapy [83]. NPs can create scattering lights for imaging when they selectively absorb into malignant cells [84]. Despite their proven effectiveness in dental treatment, NPs continue to be a contentious candidate because of their inconsistent toxicity in biological systems. It is interesting to note that NPs have shown encouraging action against the malaria pathogen *Plasmodium falciparum* as well as its associated vector,

the female Anopheles mosquito. In oral, cutaneous, and inhalational exposures, NP bioavailability is low; nevertheless, it varies according to the particle size, dosage, surface coating, and soluble fraction [85].

**Table 3.** List of nanoparticles with their neurotoxic effects [66]

| Nanoparticles | Neurotoxic effects |
|---|---|
| Carbon nanotubes | It initiates the synthesis of reactive oxygen species, escalate oxidative stress, restrain cell growth, and cause apoptosis. |
| Silver nanoparticles | It causes a decline in the anti-oxidation capability of anti-oxidative enzymes and escalate oxidative stress. |
| Titanium oxide nanoparticles | It initiates oxidative stress, causes inflammation of neurons, cause genotoxicity, imbalance neurotransmitters, and suppress signaling pathways. |
| Iron oxide nanoparticles | It causes inflammation of neurons, apoptosis, and the infiltration of immune cells. |
| Silica | It causes intellectual disruption, synapse alterations, and increases oxidative stress. |
| Organic nanoparticles | It causes oxidative stress, inflammation and appoptosis in nerve cells. |

## 5. Future and challenges

Even with all of the recent improvements in cancer care, it is still one of the leading causes of death worldwide. Past research revealed that traditional therapy approaches can have a plethora of unintended consequences. As a result, researchers are trying to come up with new approaches to cancer diagnosis and therapy. The pharmaceutical industry has recently given a lot of attention to the green synthesis of NPs [86]. Although green chemistry is, non-toxic, inexpensive, and ecologically benign, biologic approaches have certain drawbacks. NPs' high levels of biodegradability and clearance are also essential for preventing any potential long-term toxicity [87]. When it came to treatments based on nanomedicine, NPs demonstrated enormous promise.

However, clinical trials are necessary to determine the future use of NPs-based nanomedicine. Clinical studies need to resolve the main issues of biodegradability, dosage, and mode of administration. Additionally, NPs can be a crucial imaging and detection tool for cancer cells in the early phases of cancer diagnosis [88]. It has already been demonstrated that the green production of NPs aids *in vivo* fluorescent tumor imaging. The use of green-synthesized NPs will be anticipated as a potential cancer treatment and diagnostic tool in the future era of cancer treatment.

## 6. Conclusion

This paper provides an extensive overview of nanoparticles (NPs), including information on their types, synthesis techniques, characterizations, physicochemical characteristics, and applications. Several characterization methods, including SEM, TEM, and XRD, have demonstrated that NPs have a shape that can be controlled and range in size from a few nanometers to 500 nm. Their small size and large surface area allow for a variety of applications. Their optical characteristics also become more significant at the nanoscale, increasing their importance in photocatalytic applications. Synthetic approaches can achieve the controllable morphology, size, and magnetic properties of nanoparticles (NPs), thereby enabling their adaptability in diverse sectors. Nevertheless, concerns about the health risks associated with the careless use and release of NPs into the environment persist, despite their benefits. Resolving these issues is imperative to ensure the safe and

ecologically responsible use of NPs.

## Author contribution

Conceptualization: Zartasha Aftab
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Writing – original draft: Zartasha Aftab, Syed Muhammad Ahmad Bukhari, Hafiz Muhammad Sultan, Muhammad Zubair
Writing – review & editing: all authors
Visualization: Maysoon Ahmed Abou El Niaaj

## Disclosure statement

The authors declare no conflict of interest.

## References


[1] Bray F, Laversanne M, Sung H, et al., 2024, Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians, 74(3): 229–263.

[2] Feria A, Times M, 2024, Effectiveness of Standard Treatment for Stage 4 Colorectal Cancer: Traditional Management with Surgery, Radiation, and Chemotherapy. Clinics in Colon and Rectal Surgery, 37(2): 62–65.

[3] Engelhardt M, Ihorst G, Duque-Afonso J, et al., 2020, Structured Assessment of Frailty in Multiple Myeloma as a Paradigm of Individualized Treatment Algorithms in Cancer Patients at Advanced Age. Haematologica, 105(5): 1183.

[4] Olivares-Urbano MA, Griñán-Lisón C, Marchal JA, et al., 2020, CSC Radioresistance: A Therapeutic Challenge to Improve Radiotherapy Effectiveness in Cancer. Cells, 9(7): 1651.

[5] Dilalla V, Chaput G, Williams T, et al., 2020, Radiotherapy Side Effects: Integrating a Survivorship Clinical Lens to Better Serve Patients. Current Oncology, 27(2): 107–112.

[6] Anand U, Dey A, Chandel AKS, et al., 2023, Cancer Chemotherapy and Beyond: Current Status, Drug Candidates, Associated Risks and Progress in Targeted Therapeutics. Genes & Diseases, 10(4): 1367–1401.

[7] Magro M, Venerando A, Macone A, et al., 2020, Nanotechnology-Based Strategies to Develop New Anticancer Therapies. Biomedicine, 10(5): 735.

[8] De Ruysscher D, Niedermann G, Burnet NG, et al., 2019, Radiotherapy Toxicity. Nature Reviews Disease Primers, 5(1): 13.

[9] Haleem A, Javaid M, Singh RP, et al., 2023, Applications of Nanotechnology in the Medical Field: A Brief Review. Global Health Journal, 7(2): 70–77.

[10] Sanità G, Carrese B, Lamberti A, 2020, Nanoparticle Surface Functionalization: How to Improve Biocompatibility and Cellular Internalization. Frontiers in Molecular Biosciences, 7: 587012.

[11] Farjadian F, Ghasemi A, Gohari O, et al., 2019, Nanopharmaceuticals and Nanomedicines Currently on the Market: Challenges and Opportunities. Nanomedicine, 14(1): 93–126.

[12] Joseph TM, Mahapatra DK, Esmaeili A, et al., 2023, Nanoparticles: Taking a Unique Position in Medicine. Nanomedicine, 13(3): 574.

[13] Neal JM, Barrington MJ, Fettiplace MR, et al., 2018, The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity: Executive Summary 2017. Regional Anesthesia and Pain Medicine, 43(2): 113–123.

[14] Wang C, Fan W, Zhang Z, et al., 2019, Advanced Nanotechnology Leading the Way to Multimodal Imaging-Guided Precision Surgical Therapy. Advanced Materials, 31(49): 1904329.

[15] Siddique S, Chow JC, 2020, Gold Nanoparticles for Drug Delivery and Cancer Therapy. Applied Sciences, 10(11): 3824.

[16] Alshehri S, Imam SS, Rizwanullah M, et al., 2020, Progress of Cancer Nanotechnology as Diagnostics, Therapeutics, and Theranostics Nanomedicine: Preclinical Promise and Translational Challenges. Pharmaceutics, 13(1): 24.

[17] Booth CM, Karim S, Mackillop WJ, 2019, Real-World Data: Towards Achieving the Achievable in Cancer Care. Nature Reviews Clinical Oncology, 16(5): 312–325.

[18] Joshi R, Perala RS, Srivastava M, et al., 2019, Heat Generation from Magnetic Fluids Under Alternating Current Magnetic Field or Induction Coil for Hyperthermia-Based Cancer Therapy: Basic Principle. Journal of Research and Cancer, 10(4): 156–164.

[19] Golovin YI, Zhigachev A, Efremova M, et al., 2018, Ways and Methods for Controlling Biomolecular Structures Using Magnetic Nanoparticles Activated by an Alternating Magnetic Field. Nanotechnology in Research, 13: 295–304.

[20] Shen H, Huang H, Jiang Z, 2023, Nanoparticle-Based Radiosensitization Strategies for Improving Radiation Therapy. Frontiers in Physics, 14: 1145551.

[21] Kuncic Z, Lacombe S, 2018, Nanoparticle Radio-Enhancement: Principles, Progress and Application to Cancer Treatment. Physics in Medicine and Biology, 63(2): 02TR01.

[22] Tian H, Zhang T, Qin S, et al., 2022, Enhancing the Therapeutic Efficacy of Nanoparticles for Cancer Treatment Using Versatile Targeted Strategies. Oncology, 15(1): 132.

[23] Bilal M, Qindeel M, Raza A, et al., 2021, Stimuli-Responsive Nanoliposomes as Prospective Nanocarriers for Targeted Drug Delivery. Journal of Drug Delivery Science and Technology, 66: 102916.

[24] Silva CO, Pinho JO, Lopes JM, et al., 2019, Current Trends in Cancer Nanotheranostics: Metallic, Polymeric, and Lipid-Based Systems. Pharmaceutics, 11(1): 22.

[25] Khan Y, Sadia H, Ali Shah SZ, et al., 2022, Classification, Synthetic, and Characterization Approaches to Nanoparticles, and Their Applications in Various Fields of Nanotechnology: A Review. Cancers, 12(11): 1386.

[26] Joudeh N, Linke D, 2022, Nanoparticle Classification, Physicochemical Properties, Characterization, and Applications: A Comprehensive Review for Biologists. Journal of Nanobiotechnology, 20(1): 262.

[27] Ijaz I, Gilani E, Nazir A, et al., 2020, Detailed Review on Chemical, Physical and Green Synthesis, Classification, Characterizations and Applications of Nanoparticles. Green Chemistry Letters and Reviews, 13(3): 223–245.

[28] Tao Y, Lan X, Zhang Y, et al., 2022, Navigations of the Targeting Pathway of Nanomedicines Toward Tumor. Expert Opinion on Drug Delivery, 19(8): 985–996.

[29] Halwani AA, 2022, Development of Pharmaceutical Nanomedicines: From the Bench to the Market. Pharmaceuticals, 14(1): 106.

[30] Qi J, Hu X, Dong X, et al., 2019, Towards More Accurate Bioimaging of Drug Nanocarriers: Turning Aggregation-Caused Quenching into a Useful Tool. Advanced Drug Delivery Reviews, 143: 206–225.

[31] Alqosaibi AI, 2022, Nanocarriers for Anticancer Drugs: Challenges and Perspectives. Saudi Journal of Biological Sciences, 29(6): 103298.

[32] Gao S, Yang X, Xu J, et al., 2021, Nanotechnology for Boosting Cancer Immunotherapy and Remodeling Tumor

Microenvironment: The Horizons in Cancer Treatment. ACS Nano, 15(8): 12567–12603.

[33] Mahmoudian M, Salatin S, Khosroushahi AY, 2018, Natural Low-and High-Density Lipoproteins as Mighty Bio-Nanocarriers for Anticancer Drug Delivery. Current Cancer Drug Targets, 82: 371–382.

[34] Haider M, Elsherbeny A, Pittalà V, et al., 2022, Nanomedicine Strategies for Management of Drug Resistance in Lung Cancer. International Journal of Molecular Sciences, 23(3): 1853.

[35] Gote V, Nookala AR, Bolla PK, et al., 2021, Drug Resistance in Metastatic Breast Cancer: Tumor Targeted Nanomedicine to the Rescue. International Journal of Molecular Sciences, 22(9): 4673.

[36] Meel RVD, Sulheim E, Shi Y, et al., 2019, Smart Cancer Nanomedicine. Nature Nanotechnology, 14(11): 1007–1017.

[37] Singh J, Sharma S, Soni S, et al., 2019, Influence of Different Milling Media on Structural, Morphological and Optical Properties of the ZnO Nanoparticles Synthesized by Ball Milling Process. Materials Science in Semiconductor Processing, 98: 29–38.

[38] Nath D, Singh F, Das R, et al., 2020, X-Ray Diffraction Analysis by Williamson-Hall, Halder-Wagner and Size-Strain Plot Methods of CdSe Nanoparticles: A Comparative Study. Materials Chemistry and Physics, 239: 122021.

[39] Ansari SM, Sinha BB, Phase D, et al., 2019, Particle Size, Morphology, and Chemical Composition Controlled CoFe2O4 Nanoparticles with Tunable Magnetic Properties via Oleic Acid Based Solvothermal Synthesis for Application in Electronic Devices. Applied Applied Nanomaterials, 2(4): 1828–1843.

[40] Bhosale SR, Bhosale RR, Jagadhane KS, et al., 2023, Recent Trends in Synthetic Top-Down Approach for Mesoporous Carbon: A Seminal Review. Journal of Mesoporous Nanomaterials, 10(1): 601–601.

[41] D'Cruz B, Amin MO, Al-Hetlani E, 2021, Polyoxometalate-Based Materials for the Removal of Contaminants from Wastewater: A Review. Industrial and Engineering Chemistry Research, 60(30): 10960–10977.

[42] Khodabakhshi S, Fulvio PF, Andreoli E, 2020, Carbon Black Reborn: Structure and Chemistry for Renewable Energy Harnessing. Carbon, 162: 604–649.

[43] Azam A, Yang J, Li W, et al., 2023, Tungsten Diselenides (WSe2) Quantum Dots: Fundamental, Properties, Synthesis, and Applications. Progress in Materials Science, 132: 101042.

[44] Shoyiga HO, Martincigh BS, Nyamori VO, 2021, Hydrothermal Synthesis of Reduced Graphene Oxide-Anatase Titania Nanocomposites for Dual Application in Organic Solar Cells. International Journal of Energy Research, 45(5): 7293–7314.

[45] Padmanabhan NT, Thomas N, Louis J, et al., 2021, Graphene Coupled TiO2 Photocatalysts for Environmental Applications: A Review. Catalysis, 271: 129506.

[46] Rajeshkumar S, Lakshmi T, 2021, Green Synthesis of Gold Nanoparticles using Kalanchoe pinnata and its Free Radical Scavenging Activity. International Journal of Dentistry and Oral Science, 8(7): 2981–2984.

[47] Samal R, Rout CS, 2020, Recent Developments on Emerging Properties, Growth Approaches, and Advanced Applications of Metallic 2D Layered Vanadium Dichalcogenides. Advanced Materials Interfaces, 7(8): 1901682.

[48] Mourdikoudis S, Sofer Z, 2021, Colloidal Chemical Bottom-Up Synthesis Routes of Pnictogen (As, Sb, Bi) Nanostructures with Tailored Properties and Applications: A Summary of the State of the Art and Main Insights. Chemistry, 23(45): 7876–7898.

[49] Tripathy S, Rodrigues J, Shimpi NG, 2023, Top-Down and Bottom-Up Approaches for Synthesis of Nanoparticles. Nanoparticle Formation Mechanisms and Its Targeted Diseases, 145: 92–130.

[50] Palit S, Hussain CM, 2020, Nanodevices Applications and Recent Advancements in Nanotechnology and the Global Pharmaceutical Industry. Nanomaterials in Diagnostic Tools and Devices, Elsevier, Amsterdam, 395–415.

[51] Yusefi M, Shameli K, Jumaat AF, 2020, Preparation and Properties of Magnetic Iron Oxide Nanoparticles for

Biomedical Applications: A Brief Review. Journal of Advanced Research in Materials Science, 75(1): 10–18.

[52] Ansari K, Ahmad R, Tanweer MS, et al., 2024, Magnetic Iron Oxide Nanoparticles as a Tool for the Advancement of Biomedical and Environmental Application: A Review. Biomaterials and Devices, 2(1): 139–157.

[53] Liu S, Qin S, He M, et al., 2020, Current Applications of Poly (Lactic Acid) Composites in Tissue Engineering and Drug Delivery. Chemical Physics and Biophysical Engineering, 199: 108238.

[54] Montiel Schneider MG, Martín MJ, Otarola J, et al., 2022, Biomedical Applications of Iron Oxide Nanoparticles: Current Insights, Progress, and Perspectives. Pharmaceuticals, 14(1): 204.

[55] Guimarães D, Cavaco-Paulo A, Nogueira E, 2021, Design of Liposomes as Drug Delivery System for Therapeutic Applications. International Journal of Pharmaceutics, 601: 120571.

[56] Gonzalez Gomez A, Hosseinidoust Z, 2020, Liposomes for Antibiotic Encapsulation and Delivery. Advances in Drug Delivery, 6(5): 896–908.

[57] Hamad A, Khashan KS, Hadi A, 2020, Silver Nanoparticles and Silver Ions as Potential Antibacterial Agents. Journal of Inorganic Polymers and Materials, 30(12): 4811–4828.

[58] Samuel MS, Ravikumar M, John JA, et al., 2022, A Review on Green Synthesis of Nanoparticles and Their Diverse Biomedical and Environmental Applications. Chemistry, 12(5): 459.

[59] Yousaf A, Tasneem N, Mustafa A, et al., 2021, Gastric Cancer Associated Risk Factors and Prevalence in Pakistan. ASEAN Journal of Science and Engineering, 1(2): 73–78.

[60] Yetisgin AA, Cetinel S, Zuvin M, et al., 2020, Therapeutic Nanoparticles and Their Targeted Delivery Applications. Molecules, 25(9): 2193.

[61] Sultan H, 2021, Protein and Polysaccharide Base Biomaterial for the Formation of Composite Bone Scaffold. AlQalam Journal of Medical and Applied Sciences, 4(2): 80–88.

[62] Fu Z, Xiang J, 2020, Aptamer-functionalized Nanoparticles in Targeted Delivery and Cancer Therapy. International Journal of Molecular Sciences, 21(23): 9123.

[63] Marques A, Costa P, Velho S, et al., 2020, Functionalizing Nanoparticles with Cancer-targeting Antibodies: A Comparison of Strategies. Journal of Controlled Release, 320: 180–200.

[64] Gavas S, Quazi S, Karpinski TM, 2021, Nanoparticles for Cancer Therapy: Current Progress and Challenges. Nanomedicine Reviews Letters, 16(1): 173.

[65] Hari SK, Gauba A, Shrivastava N, et al., 2023, Polymeric Micelles and Cancer Therapy: An Ingenious Multimodal Tumor-targeted Drug Delivery System. Drug Delivery and Translational Research, 13(1): 135–163.

[66] Riaz M, Zubair M, Iqbal MK, et al., 2024, Exploring the Platelet and Cancer Cell Interaction in Metastasis Targeting: Platelets and Cancer Cell Interaction. Journal of Clinical Oncology and Medical Sciences, 4: 834–844.

[67] Lavrador P, Esteves MR, Gaspar VM, et al., 2021, Stimuli-responsive Nanocomposite Hydrogels for Biomedical Applications. Advanced Functional Materials, 31(8): 2005941.

[68] Adepu S, Ramakrishna S, 2021, Controlled Drug Delivery Systems: Current Status and Future Directions. Materials, 26(19): 5905.

[69] Sánchez A, Mejía SP, Orozco J, 2020, Recent Advances in Polymeric Nanoparticle-encapsulated Drugs Against Intracellular Infections. Materials, 25(16): 3760.

[70] Ahmed U, Abubakar M, Khan SS, et al., 2024, Long Non-coding RNA and Progression of Breast Cancer. Oncology Treatment Discovery, 2(3): 38–64.

[71] Yao Y, Zhou Y, Liu L, et al., 2020, Nanoparticle-based Drug Delivery in Cancer Therapy and Its Role in Overcoming Drug Resistance. Frontiers in Molecular Biology, 7: 193.

[72] Alghamdi MA, Fallica AN, Virzì N, et al., 2022, The Promise of Nanotechnology in Personalized Medicine. Journal of Personalized Medicine, 12(5): 673.

[73] Mitchell MJ, Billingsley MM, Haley RM, et al., 2021, Engineering Precision Nanoparticles for Drug Delivery. Nature Reviews Drug Discovery, 20(2): 101–124.

[74] Ullah MW, Manan S, Khattak WA, et al., 2020, Biotemplate-mediated Green Synthesis and Applications of Nanomaterials. Current Pharmaceutical Design, 26(45): 5819–5836.

[75] Abubakar M, Bukhari SMA, Mustfa W, et al., 2024, Skin Cancer and Human Papillomavirus. Journal of Pharmacology, 31(2): 790–816.

[76] Rehman B, Abubakar M, Kiani MN, et al., 2024, Analysis of Genetic Alterations in TP53 Gene in Breast Cancer: A Secondary Publication. Proceedings of Anticancer Research, 8(3): 25–35.

[77] Riaz MA, Abubakar M, Ayyoub R, et al., 2024, Expression Analysis of Caspase-3 (CASP3) Gene in Leukemia Patients Using Quantitative Polymerase Chain Reaction (qPCR) and Western Blot Techniques. Journal of Cancer Biomoleculars and Therapeutics, 1(2): 10–16.

[78] Pala R, Anju V, Dyavaiah M, et al., 2020, Nanoparticle-mediated Drug Delivery for the Treatment of Cardiovascular Diseases. International Journal of Nanomedicine, 15: 3741–3769.

[79] Yousaf A, Tasneem N, Mustafa A, et al., 2021, Gastric Cancer Associated Risk Factors and Prevalence in Pakistan. Engineering, 1(2): 73–78.

[80] Gurunathan S, Park JH, Han JW, et al., 2015, Comparative Assessment of the Apoptotic Potential of Silver Nanoparticles Synthesized by Bacillus tequilensis and Calocybe indica in MDA-MB-231 Human Breast Cancer Cells: Targeting p53 for Anticancer Therapy. International Journal of Nanomedicine, 10(1): 4203–4223.

[81] Kang Y, Datta P, Shanmughapriya S, et al., 2020, 3D Bioprinting of Tumor Models for Cancer Research. Applied Adhesion and Biomechanics, 3(9): 5552–5573.

[82] Ma Z, Fan Y, Wu Y, et al., 2019, Traditional Chinese Medicine-Combination Therapies Utilizing Nanotechnology-Based Targeted Delivery Systems: A New Strategy for Antitumor Treatment. International Journal of Nanomedicine, 22(14): 2029–2053.

[83] Tabish TA, Dey P, Mosca S, et al., 2020, Smart Gold Nanostructures for Light-Mediated Cancer Theranostics: Combining Optical Diagnostics with Photothermal Therapy. Advanced Science, 7(15): 1903441.

[84] Wang Y, Xu S, Shi L, et al., 2021, Cancer-cell-Activated In Situ Synthesis of Mitochondria-Targeting AIE Photosensitizer for Precise Photodynamic Therapy. Angewandte Chemie International Edition, 60(27): 14945–14953.

[85] Ferdous Z, Nemmar A, 2020, Health Impact of Silver Nanoparticles: A Review of the Biodistribution and Toxicity Following Various Routes of Exposure. International Journal of Molecular Sciences, 21(7): 2375.

[86] Gour A, Jain NK, 2019, Advances in Green Synthesis of Nanoparticles, Advanced Chemistry. Nanomedicine, and Biotechnology, 47(1): 844–851.

[87] Ying S, Guan Z, Ofoegbu PC, et al., 2022, Green Synthesis of Nanoparticles: Current Developments and Limitations. Innovation, 26: 102336.

[88] Wen H, Jung H, Li X, 2015, Drug Delivery Approaches in Addressing Clinical Pharmacology-Related Issues: Opportunities and Challenges. Therapeutic Advances Journal, 17: 1327–1340.