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Nanomedicine Advancements in Cancer Therapy: A Scientific Review

Wael Abu Dayyih[1*¥], Mohammad Hailat[2¥], Shahd Albtoush[1], Eslam Albtoush[1], Alaa Abu Dayah[3], Ibrahim Alabbadi[4], Mohammed F.Hamad[5]

[1]Department of Pharmaceutical Chemistry, Faulty of Pharmacy, Mutah University, Al Karak. Jordan.
[2]Department of Pharmacy, Faculty of Pharmacy, Al-Zaytoonah University of Jordan, Amman. Jordan.
[3] Faculty of Pharmacy, Al-Ahliyya Amman University, Amman, Jordan.
[4] Department of Biopharmaceutics and Clinical Pharmacy, University of Jordan, Amman, Jordan.
[5] Department of Basic Medical Sciences, Faculty of Medicine, Al-Balqa Applied University, Al-Salt, Jordan.

ABSTRACT

Cancer nanomedicines, characterized by submicrometer-sized formulations, aim to optimize the biodistribution of anticancer drugs by minimizing off-target effects, reducing toxicity, enhancing target site accumulation, and improving overall efficacy. Numerous nanomedicines have been developed to improve the effectiveness and safety of traditional anticancer treatments. These include formulations with carbon nanotubes, nanodiamonds, enzyme-responsive nanoparticles for controlled drug release, dendrimers as nanoparticle drug carriers, quantum dot nanocarrier systems for precise drug delivery, solid lipid nanoparticles, and polymeric nanoparticles designed for targeted drug delivery. Additionally, nanotechnology has been explored in cancer treatment through gene therapy. Despite these advances, the complex nature of carrier materials and functional integration presents challenges in preparing these candidates for clinical translation. Nanotechnology, with its unique features at the nanoscale, offers novel possibilities for developing cancer therapies while increasing efficacy and safety. Although only a few nanotherapeutics have obtained clinical approval, exciting uses for nanotechnology are on the horizon. Nanoparticles possess unique transport, biological, optical, magnetic, electrical, and thermal capabilities due to their small size within the light wavelength spectrum. This results in high surface area-to-volume ratios, allowing for the incorporation of various supporting components in addition to active medicinal substances. These properties aid in solubilization, degradation protection, delayed release, immune response evasion, tissue penetration, imaging, targeted distribution, and triggered activation. In summary, the future of nanomedicine holds promise for introducing innovative platforms in cancer treatment. The research presented underscores the potential for nanoparticles to revolutionize anticancer therapies, enhancing the overall therapeutic approach.

Keywords: Nanoparticles; Anticancer therapy; Carbon-Based Nanomaterials; Metal-Based; Lipid-Based; Polymeric Nanoparticles.

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[*]***Corresponding author: Wael Abu Dayyih***
wabudayyih@mutah.edu.jo
[¥] Equal contributions
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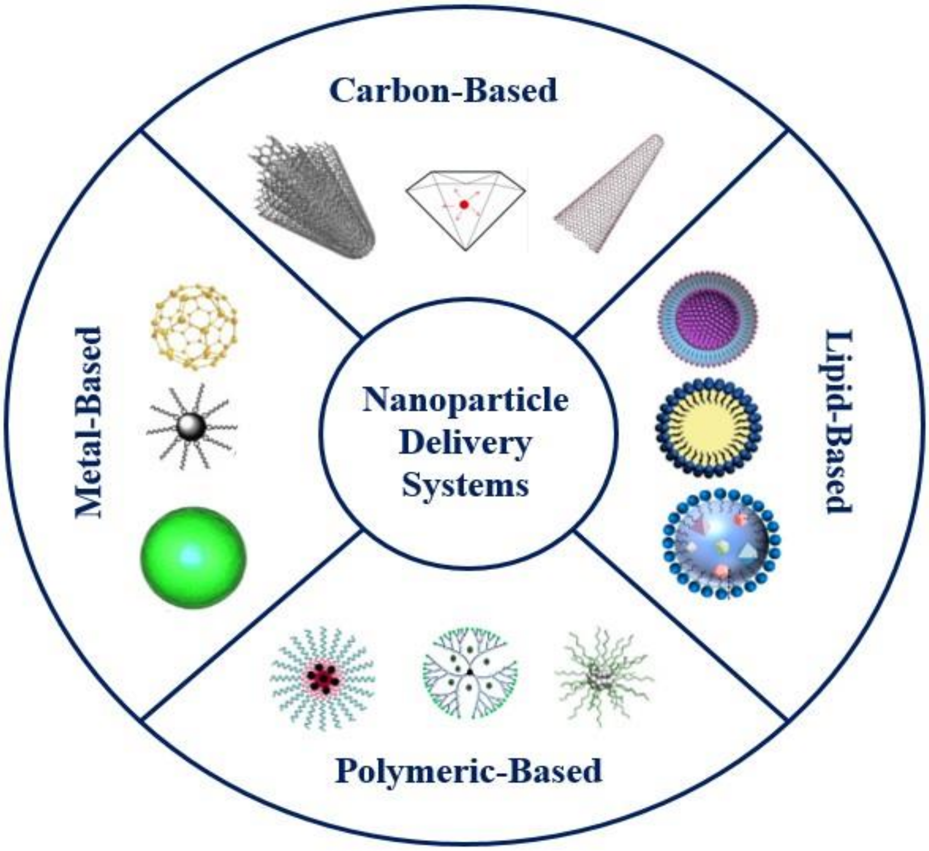

Graphical abstract

INTRODUCTION

In 2023, the United States was expected to have 1,958,310 new cancer cases and 609,820 cancer deaths [1]. Cancer treatment options include surgeries, radiation therapy, chemotherapy, immunotherapy, and targeted therapy. Surgical interventions remove cancerous tissue, radiation therapy eliminates cells, chemotherapy eradicates cells, immunotherapy boosts the immune system, and targeted therapy addresses genetic alterations. Chemotherapeutic agents are a crucial component of the diverse arsenal of cancer treatments [2,3].

Cancer treatment faces challenges such as severe side effects, drug resistance, and high economic burdens [4]. Nanotechnology, a multidisciplinary field combining chemistry, engineering, biology, and medicine, has emerged as a promising frontier in cancer research. Nanometer-sized nanoparticles interact with biomolecules on cell surfaces and inside cells, enabling effective and targeted medication delivery [5]. Several types of nanoparticles, including quantum dots, carbon nanotubes, liposomes, and gold nanoparticles, have shown promise in detecting and treating various cancers [6,7]. Recent advancements, such as bioaffinity nanoparticle probes and integrated nanodevices, hold significant potential for personalized oncology based on individual patients' molecular profiles [8] (Figure 1).

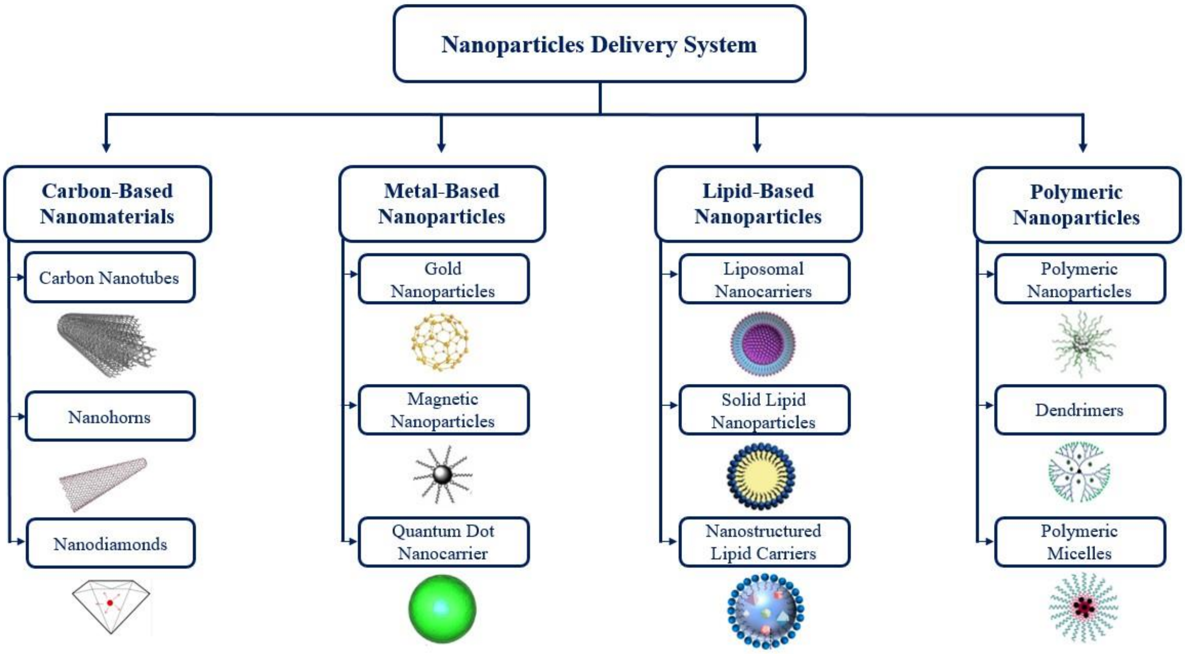

Figure 1: Comprehensive overview of nanotechnologies in cancer treatment.

While nanotechnology presents excellent prospects for cancer therapy, issues such as biocompatibility, in vivo dynamics, tumor-targeting efficiency, and cost-effectiveness must be resolved before broad clinical application [9]. Despite these challenges, the emergence of nanotechnology-based techniques offers promise for transforming cancer research by opening new paths for diagnostics and therapies [10,11]. This review traces the various nanotechnology-based cancer treatment options**Carbon-Based Nanomaterials**

Carbon-based nanostructured materials, such as nanotubes, nanohorns, and nanodiamonds, offer significant benefits in cancer treatment due to their small size and hybridized carbon atoms [12]. These materials facilitate easy functionalization, promote biocompatibility, and feature efficient drug transport, imaging, and controlled release mechanisms [12]. They also exhibit high in vivo stability, a large surface area for functionalization, and ease of penetration through biological barriers [13]. However, challenges like biocompatibility, toxicity evaluation, and regulatory hurdles remain [14]. Further research is needed to fully realize the potential of these nanoparticles in cancer care [15].

1. Nanotubes

Carbon nanotubes, with their unique optical properties, have gained popularity in cancer therapy due to their ability to convert light into heat [16]. This localized heat treatment enhances therapeutic effects and tumor specificity for nanoscale carbon catalysts [17]. The use of target-specific delivery systems in nanomedicine has redefined the field. Carbon nanotubes can be functionalized with various groups, allowing for more efficient delivery of medicines to cancerous cells [18]. They are classified into single-walled, double-walled, and multi-walled carbon nanotubes [19] (Figure 2).

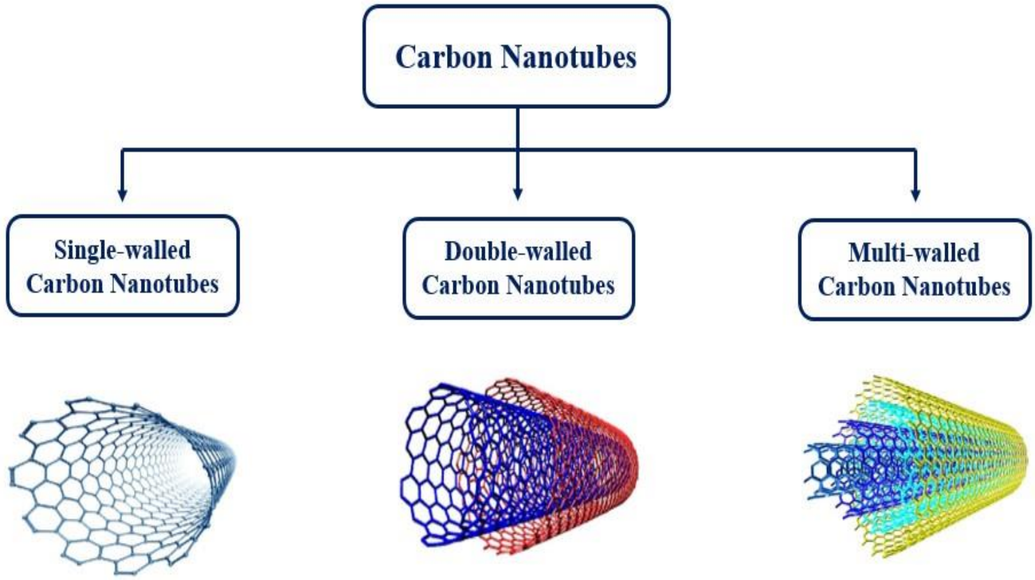

Figure 2: Classification of carbon nanotubes.

Carbon nanotubes possess various fascinating features due to their compact size and tubular form. Their electrical characteristics vary significantly between single-walled carbon nanotubes, which have a diameter of approximately 1 nm and a single graphene wall, and multi-walled carbon nanotubes, which have diameters ranging from 1 to 100 nm and multiple graphene walls [20]. These nanotubes exhibit physical and chemical characteristics such as a high aspect ratio, ultralight weight, exceptional mechanical strength, heightened electrical conductivity, and elevated thermal conductivity [21].

Carbon nanotubes play a crucial role in cancer research due to their cylindrical shapes, which are similar to rolled graphene sheets, and their excellent mechanical strength, strong electrical conductivity, and considerable thermal conductivity [20]. They serve as carriers for targeted drug delivery and imaging agents for diagnostics. Recently, carbon nanotubes have been extensively researched in various cancer treatment techniques, including drug administration, lymphatic-targeted chemotherapy, thermal therapy, photodynamic therapy, and gene therapy [21].

Despite their promising attributes, rigorous investigation into toxicity and biocompatibility is imperative before their widespread clinical use. Regulatory challenges must be addressed to ensure the safe and practical application of nanotubes in cancer therapeutics [6]. Carbon nanotubes have recently emerged as intriguing medical agents, indicating potential advancements [22]. In vitro studies have shown that multi-walled carbon nanotubes can facilitate the enzymatic cleavage-based release of the anticancer medication methotrexate in breast cells, and dendrimer-modified multi-walled carbon nanotubes can effectively deliver doxorubicin [23]. Single-walled carbon nanotubes have demonstrated efficacy as low-toxicity carriers for drug delivery in lung cancer treatment [6].

2. Nanohorns

Carbon nanohorns are a family of carbon nanomaterials with a unique ability to adsorb various molecules, making them promising candidates for controlled drug release applications [24]. They have a distinctive hexagonal stacking structure, resulting in microporosity and mesoporosity. Structural modifications, achieved through oxidation, introduce nanoscale windows on the walls of single-walled carbon nanohorns, controlling size and concentration while enhancing microporosity and inducing mesopores [25]. The conical structure influences the electronic properties of single-walled carbon nanohorns, demonstrating semiconductor behavior depending on oxidation status and gas adsorption [26]. Carbon nanohorns exhibit unique magnetic characteristics, including temperature-activated paramagnetic susceptibility and antiferromagnetic correlations between localized electrons [26]. They can be functionalized through covalent bonding, π-π stacking, and metal nanoparticle decoration, enhancing their compatibility and enabling a wide range of applications [26].

Single-walled carbon nanohorns are versatile in cancer therapy, acting as potent anticancer nanoparticles that induce apoptosis [27]. They serve as effective drug delivery systems for chemotherapeutics, allowing controlled release and minimizing dosage. They can also be used in photothermal, photodynamic, and gene therapies, contributing to cancer diagnosis through immunosensing that targets specific biomarkers [27]. A water-dispersible nanohybrid, created by integrating carbon nanohorns with polyglycerol-gold, has been developed to release doxorubicin, enhancing cell apoptosis and tumor observation [28].

3. Nanodiamonds

Nanodiamonds are a promising platform for theranostic applications due to their ease of synthesis, small size, inertness, surface functional groups, biocompatibility, stable fluorescence, and long fluorescent lifetime [29]. These properties have accelerated their use in cancer therapy and imaging, emphasizing the rational tailoring of particle surfaces to deliver bioactive chemicals, resist aggregation, and form composite materials [30]. Nanodiamonds can be artificially manufactured using detonation, chemical vapor deposition, or high-temperature, high-pressure techniques [31]. They exhibit strong fluorescence with minimal toxicity, making them promising for drug delivery systems, fluorescent bio-labels, and multimodal theranostic systems [32]. Additionally, they are cost-effective and can be sourced from mining waste, making them economically viable for diverse biomedical applications. Nanodiamonds can traverse the blood-brain barrier, making them potential carriers for brain-targeted drug delivery [33]. They also exhibit enhanced absorption when administered from the basolateral side of cells, which is particularly beneficial for specific cell types [34].

Table 1 provides a comprehensive overview of carbon-based nanomaterials and their applications in cancer therapy.

Table 1 presents a list of carbon-based nanomaterials used in cancer therapy, including nanotubes, nanohorns, and nanodiamonds. Nanotubes, including single-walled, double-walled, and multi-walled carbon nanotubes, have unique cylindrical structures with exceptional mechanical strength, electrical, and thermal conductivity. They are utilized in drug delivery, thermal therapy, photodynamic therapy, and gene therapy. Nanohorns, conical horn-shaped nanostructures with controlled size, increased porosity, semiconductor behavior, and temperature-activated magnetic features, are used in anticancer drug delivery, targeted chemotherapy, photothermal and photodynamic cancer therapy, as well as cancer gene therapy and immunosensing. Nanodiamonds, including those produced by detonation and fluorescent nanodiamonds, are chemically stable, biocompatible, extremely hard, transparent, and highly thermally conductive. They are applied in various cancer treatments.

Table 1: A comprehensive summary of carbon-based nanomaterials and their applications in cancer therapy

Carbon-based nanomaterials	Type	Size	Structure	Characteristics	Preparation Method	Applications in Cancer	References
Nanotubes	▪ Single-walled carbon nanotubes	▪ < 1 nm in diameter	▪ Single cylindrical layer of carbon atoms arranged hexagonally.	▪ Exceptional mechanical strength. ▪ High electrical conductivity. ▪ Significant thermal conductivity.	▪ Arc discharge method ▪ Laser ablation method ▪ Chemical vapor deposition method ▪ Gas-phase catalytic method	▪ Anticancer drug delivery ▪ Lymphatic targeting chemotherapy ▪ Thermal therapy ▪ Photodynamic therapy ▪ Gene therapy	[35–39]
	▪ Double-walled carbon nanotubes	▪ 1-50 nm in diameter	▪ Two layers of graphene sheets rolled into cylindrical structures.	▪ Enhanced structural stability compared to SWCNTs. ▪ Combined properties of both inner and outer walls.			
	▪ Multi-walled carbon nanotubes	▪ 1-100 nm in diameter	▪ Multiple layers of graphene sheets arranged concentrically.	▪ Increased mechanical strength compared to SWCNTs. ▪ Enhanced thermal and electrical conductivity.			
Nanohorns	Single-walled carbon nanohorns	▪ 2–5 nm in diameter	▪ Conical horn-shaped nanostructures.	▪ Have unique internal and external pores. ▪ Controlled size and increasing porosity. ▪ Show semiconductor behavior based on their conical structure. ▪ Display temperature-activated magnetic features.	▪ CO_2 laser ablation method ▪ Arc discharge method	▪ Anticancer drug delivery ▪ Targeted chemotherapy ▪ Photothermal and Photodynamic Cancer Therapy ▪ Cancer Gene Therapy and Immunosensing	[40–42]
Nanodiamonds	▪ Detonation nanodiamonds ▪ Fluorescent nanodiamonds	1-100 nm in diameter	▪ Diamond-like crystalline structure on a nanoscale, which consists of carbon atoms arranged in a tetrahedral lattice.	▪ Chemically stable and resist reactions. ▪ Biocompatible. ▪ Extremely hard, ideal for industrial tools. ▪ Transparent. ▪ High thermal conductivity.	▪ High-pressure, high-temperature method ▪ Detonation method	▪ Anticancer drug delivery ▪ Targeted chemotherapy ▪ Photothermal and Photodynamic Cancer Therapy ▪ Cancer Gene Therapy and Immunosensing	[35,43–46]

Metal-Based Nanoparticles

Metallic nanoparticles, derived from noble metals such as gold, silver, and platinum, are increasingly studied for their potential applications in fields such as catalysis, polymer composites, disease diagnosis, sensor technology, and optoelectronic media labeling [47]. These nanoparticles are produced and stabilized using various techniques, which impact their morphology, stability, and physicochemical characteristics [48]. Metal-based nanoparticles, made of elements like gold, silver, iron, and platinum, exhibit unique physical and chemical properties due to their small size and enhanced surface area [49]. Besides their use in medicine, they are also utilized in electronics, catalysis, and environmental remediation. Metal-based nanoparticles offer targeted drug delivery, early cancer detection, and medicinal properties [50]. However, challenges include potential toxicity, biodistribution issues, uncertain immunological responses, production cost concerns, and regulatory approvals [51]. Table 2 comprehensively summarizes metal-based nanomaterials and their applications in cancer therapy.

Table 2: A comprehensive summary of metal-based nanomaterials and their applications in cancer therapy.

Metal-based nanomaterials	Size	Structure	Characteristics	Preparation Method	Applications in Cancer	References
Gold nanoparticles	▪ 5-100 nm	▪ Diverse structures, such as spheres, rods, cages, and tubes.	▪ Precise control over size and shape. ▪ Color and optical features. ▪ Fluorescence modulation. ▪ Electromagnetic field. ▪ Surface plasmon resonance and high surface area.	▪ The sol-gel micro reactors method ▪ Physical vapor deposition method ▪ Reduction method ▪ γ-Irradiation v ▪ Biosynthesis method	▪ Anticancer drug delivery ▪ Targeted chemotherapy ▪ Tumor imaging ▪ Tumor radio sensitization ▪ Tumor hyperthermia ▪ Tumor gene therapy	[52–55]
Magnetic nanoparticles	1-100 nm	▪ Diverse such as core-shell, monodisperse, composite, hollow, and clustered.	▪ Can be composed of pure metals. ▪ Offer versatile and safe theranostic properties. ▪ Easy synthesis and modification. ▪ Possess intrinsic magnetic features.	▪ Co-precipitation method ▪ Microemulsion method ▪ High-temperature method ▪ Hydrothermal method ▪ Sonochemical method	▪ Anticancer drug delivery ▪ Targeted chemotherapy ▪ Tumor imaging ▪ Tumor biosensors ▪ Tumor hyperthermia	[56–59]
Quantum dot nanocarrier	2-10 nm	▪ Core-shell design.	▪ Resist degradation for extended cellular tracking. ▪ 10–20x brighter and more stable than organic dyes. ▪ Stable fluorophore. ▪ High drug loading ▪ Chemically inert imaging ▪ Dual drug encapsulation	▪ Microemulsion method ▪ Sol-gel method ▪ Hotsolution decomposition method ▪ Hot-arrangement decay method ▪ Molecular beam epitaxy method ▪ Physical vapor deposition method ▪ Chemical vapor deposition method ▪ Physical vapor deposition method ▪ Chemical vapor deposition method ▪ Green method	▪ Anticancer drug delivery ▪ Tumor imaging ▪ Tumor diagnosis	[60–65]

Table 2 presents a summary of metal-based nanomaterials and their applications in cancer therapy. Gold nanoparticles, sized between 5-100 nm, offer precise control over size and shape, color and optical features, fluorescence modulation, electromagnetic fields, surface plasmon resonance, and high surface area. They are utilized in anticancer drug delivery, targeted chemotherapy, tumor imaging, radiosensitization, tumor hyperthermia, and tumor gene therapy. Magnetic nanoparticles, ranging from 1-100 nm, exhibit diverse structures and offer versatile and safe theranostic properties. Composed of pure metals, they are easy to synthesize and modify. Quantum dot nanocarriers, sized between 2-10 nm, feature a core-shell design, resist degradation, and are 10-20 times brighter and more stable than organic dyes. They possess stable fluorophores, high drug-loading capacity, chemically inert imaging properties, and dual drug encapsulation capabilities. These are used in anticancer drug delivery, tumor imaging, and tumor diagnosis.

1. Gold Nanoparticles

Gold nanoparticles are emerging as potent tools in cancer therapy, offering a multifaceted approach to anticancer treatment [66]. They are gaining popularity in cancer management due to their advantageous properties, including cytotoxicity against specific cancer cells, size-dependent inhibition, and tunable optical properties [67]. Due to their controlled synthesis, gold nanoparticles are also valuable in bioimaging, theranostics, and cancer treatment. Their unique physical and chemical characteristics, influenced by their diverse shapes and sizes, contribute to their versatility [68]. Recent studies highlight the impact of size, surface charge, and functional groups on cytotoxicity, making careful consideration essential for their safe and effective use in biomedical applications, particularly in cancer management [69]. Malaikolundhan et al. synthesized gold nanoparticles using Albizia lebbeck aqueous leaf extract, demonstrating promising therapeutic effects against colon cancer cells [70]. Wang et al. developed paclitaxel-conjugated gold nanoparticles, focusing on the positioning of small molecular drugs within nanoparticles [71]. This two-step drug release process emphasizes the promise of paclitaxel-gold nanoparticles as a novel method of cancer therapy [72].

2. Magnetic Nanoparticles

Magnetic nanoparticles, composed of materials like iron, cobalt, or nickel, are tiny particles with unique physical and chemical characteristics [73]. They have gained attention in fields like medicine, electronics, and environmental science due to their versatile applications [74]. They are used in biomedical applications such as Magnetic Resonance Imaging (MRI), drug delivery, data storage, sensors, and information storage, as well as in antiferromagnetic and paramagnetic nanoparticles [75]. Their magnetic manipulation through an external field provides a key advantage, and their chemical composition, size, shape, morphology, and magnetic behavior are pivotal in determining their biomedical applications [76]. Magnetic nanoparticles are a promising basis for a multimodal theranostic platform in biomedical applications. Ursachi et al. synthesized nanocomposites with a magnetic core for precise targeting, a polymeric surface shell for stability and multifunctionality, and the chemotherapeutic agent paclitaxel [77].

3. Quantum Dot Nanocarrier

Quantum dots, highly fluorescent nanocrystals, show potential in biomedical applications, particularly in cancer screening, tumor classification, and imaging, with advancements in technology enabling multifunctional probes [60]. Quantum dot nanocarriers, utilizing semiconductor nanoparticles' electronic and optical properties, offer precise drug delivery through a core-shell architecture, using various synthesis methods for design flexibility [61]. They offer high drug loading capacity, efficient surface area, targeted delivery, real-time imaging, biocompatibility, precise control, simultaneous drug delivery, and reduced side effects [64]. Challenges in quantum dot materials include potential toxicity risks, biocompatibility studies, hazardous handling, and long-term stability concerns, necessitating careful handling and consideration of potential degradation over time [62].

Quantum dot nanocarriers offer targeted cancer treatment, real-time monitoring, and combination therapy, enhancing efficacy and utilizing quantum dots' unique properties for personalized therapeutic strategies [63]. Li et al. developed nanocarriers for precise nucleus-targeted anticancer drug delivery and real-time imaging. These nanocarriers combine an enzyme-activatable peptide with mesoporous silica-coated quantum dots, enhancing antitumor activity and demonstrating superior efficacy [78]. Rezaei et al. developed a pseudohomogeneous carbon-based vehicle, chitosan-citric acid-arginine-carbon quantum dots, for efficient gene transfer into cells. This carboplex, resistant to enzyme destruction, outperforms chitosan and enables more efficient gene transfection [79].

Lipid-Based Nanoparticles

Lipid-based nanoparticles are advanced drug delivery systems for targeted therapeutic agent encapsulation, offering versatile, biocompatible platforms in various forms such as liposomes, solid nanoparticles, and nanostructured carriers [80,81]. Prepared using techniques like solvent evaporation, homogenization, and microemulsion, these nanoparticles provide high drug encapsulation efficiency, controlled release, and biocompatibility for therapeutic applications [82,83]. They show promise in cancer treatment, enhancing targeted drug delivery and minimizing systemic toxicity, thus contributing to personalized cancer therapies and advancements in oncology [84,85]. Table 3 comprehensively summarizes lipid-based nanoparticles and their applications in cancer therapy.

Table 3 presents lipid-based nanomaterials and their applications in cancer therapy. Liposomal nanocarriers, ranging from 50 to 1000 nm in size, offer high drug loading capacity, stability, and biocompatibility, mimicking natural lipid membrane structures. They can be prepared using various methods, including thin-film hydration, detergent removal, solvent injection, ethanol injection, ether injection, reverse-phase evaporation, sonication, extrusion, high-pressure homogenization, freeze-drying, supercritical reverse, microfluidic methods, and membrane contactor methods. Solid-lipid nanoparticles, sized between 50 and 1000 nm, offer controlled release and targeting capabilities with low toxicity and protection for labile drugs. They are formulated without organic solvents, allowing for flexible sterilization and versatile encapsulation. Nanostructured lipid carriers, ranging from 10 to 1000 nm in size, offer controlled release and targeting with excellent biocompatibility. They are easy to scale up and sterilize, can be formulated without organic solvents, and offer versatile encapsulation.

1.Liposomal Nanocarriers

Liposomal nanocarriers are advanced drug delivery systems with spherical structures, a hydrophilic core, and a bilayer of phospholipids, forming spontaneously when lipids are hydrated in aqueous environments [45]. Liposomes, composed of synthetic or natural phospholipids, arise spontaneously from water molecules and hydrophobic phosphate groups and are loaded with pharmaceuticals through various techniques [86]. Liposomal nanoformulations, ranging from 50-500 nm, are crucial for drug delivery in biomedical applications, with tiny, giant, and multilamellar types facilitating efficient cell uptake and tissue penetration [88]. Liposomes, with their stable, biocompatible, and degradable structure, play a crucial role in encapsulating hydrophilic drugs and influencing their pharmacokinetics and biodistribution [87, 95]. With cancer treatment approvals, liposomes offer efficient drug delivery, protection, improved bioavailability, and reduced side effects. Challenges include rapid clearance and stimulus-sensitive structures [83]. Zarrabi et al. developed intelligent biocompatible stealth nanoliposomes for targeted curcumin delivery, showing high drug entrapment efficiency and controlled release patterns. These liposomes hold promise for cancer therapy but require further validation and clinical trials [96]. Ghafari et al. developed nanoliposomes containing cisplatin, enhancing its efficacy and mitigating side effects. The modified formulations showed improved cellular absorption and cytotoxicity, offering the potential for improved therapeutic efficacy [97].

Table 3: A comprehensive summary of lipid-based nanomaterials and their applications in cancer therapy.

Lipid-based nanomaterials	Size	Structure	Characteristics	Preparation Method	Applications in Cancer	References
Liposomal nanocarriers	▪50-1000 nm	▪Spherical	▪High drug loading ▪Stability and biocompatibility ▪Mimics natural lipid membrane structure ▪Avoids immune system ▪Amphipathicproperties liposomes can encapsulate hydrophilic and hydrophobic drugs.	▪Thin-film hydration method ▪Detergent removal method ▪Solvent injection method ▪Ethanol injection method ▪Ether injection method ▪Reverse-phase evaporation method ▪Sonication method ▪Extrusion method ▪High-pressure homogenization method ▪Freeze-drying method ▪Supercritical reverse method ▪Microfluidic methods ▪Membrane contactor method	▪Anticancer drug delivery ▪Targeted chemotherapy ▪Tumor diagnosis	[45,86–88]
Solid-lipid nanoparticles	▪50-1000 nm	▪Spherical	▪Controlled release and targeting ▪Low toxicity ▪Labile drug protection ▪Flexible sterilization ▪Formulated without organic solvents. ▪Versatile encapsulation ▪Reduced side effects	▪High shear homogenization ▪Hot homogenization ▪Cold homogenization ▪Ultrasonication method ▪Microemulsion method ▪Supercritical fluid method ▪Solvent evaporation method ▪Double emulsion method ▪Spray drying method	▪Anticancer drug delivery ▪Targeted chemotherapy ▪Tumor diagnosis	[89–91]
Nanostructured lipid carriers	▪ 10-1000 nm	▪Spherical	▪Controlled release and targeting Excellent biocompatibility ▪Easy to scaleup and sterilize ▪Formulated without organic solvents. ▪Versatile encapsulation	▪Hot homogenization ▪Cold homogenization ▪Microemulsion method ▪High-pressure homogenization ▪Solvent evaporation method ▪Phase inversion method ▪Ultrasonication method ▪Membrane contractor method	▪Anticancer drug delivery ▪Targeted chemotherapy ▪Tumor diagnosis	[92–94]

2. Solid Lipid Nanoparticles

Solid lipid nanoparticles (SLNs) are a submicron-sized drug delivery system composed of a solid lipid matrix, surfactants, and cosurfactants, ensuring controlled drug release and stability [89,90,98]. SLNs offer biocompatibility, biodegradability, and regulated medication release, making them promising for large-scale drug delivery systems and versatile for various routes [89,90]. SLNs show potential in cancer therapy by improving drug efficacy and overcoming the challenges of traditional chemotherapy [99]. They enhance cellular uptake, prolong drug circulation, and increase apoptosis induction [90]. Qureshi et al. developed docetaxel-incorporated lipid nanoparticles to improve their pharmacokinetic profile and solubility [100]. The nanotechnology template engineering technique demonstrated 96% incorporation efficiency and sustained release characteristics. The nanoparticles exhibited increased anticancer activity and improved therapeutic outcomes in breast cancer treatment [100]. Smith et al. developed solid lipid nanoparticles to enhance the therapeutic effectiveness of 5-fluorouracil (5-FU) in colorectal cancer therapy [101]. The nanoparticles, loaded with unique PEGylated lipids and a surfactant mixture, showed lower IC50 values and increased tumor efficacy in HCT-116 cancer cells. This underscores the need for intelligent nano-delivery systems [101].

3. Nanostructured Lipid Carriers

Nanostructured lipid carriers, combining solid and liquid lipids, offer improved drug delivery and controlled release through high-pressure homogenization, solvent emulsification/evaporation, and microemulsion techniques [92]. Nanostructured lipid carriers are effective due to their biocompatibility, solvent-free preparation, cost-effectiveness, and controlled drug release, making them eco-friendly and cost-effective for mass production and sterilization [92]. They offer efficient drug delivery, versatility in transporting lipophilic and hydrophilic drugs, and biodegradability, making them a promising choice for environmental sustainability [93,102]. Nanostructured lipid carriers provide enhanced drug delivery, controlled release, and efficient transport in cancer treatment, outperforming complex formulation optimization and limited long-term stability for specific drugs [92,93]. Sun et al. developed biocompatible, biodegradable quercetin-nanostructured lipid carriers to improve water solubility, stability, and cellular bioavailability [103]. These carriers demonstrated increased cytotoxicity and apoptosis in breast cancer cells, indicating potential for chemoprevention [103]. Ferreira et al. optimized nanostructured lipid carriers as methotrexate carriers using hot ultrasonication [104]. The carriers exhibited robustness, a spherical shape, and 87% entrapment efficiency. They released methotrexate quickly and persistently without harming fibroblasts [104].

Polymeric Nanoparticles

Polymeric nanoparticles, composed of synthetic or natural polymers (Figure 3), offer customizable features in medication delivery systems and biocompatibility, making them safe and efficient for drug administration, as summarized in Table 4-A [105,106].

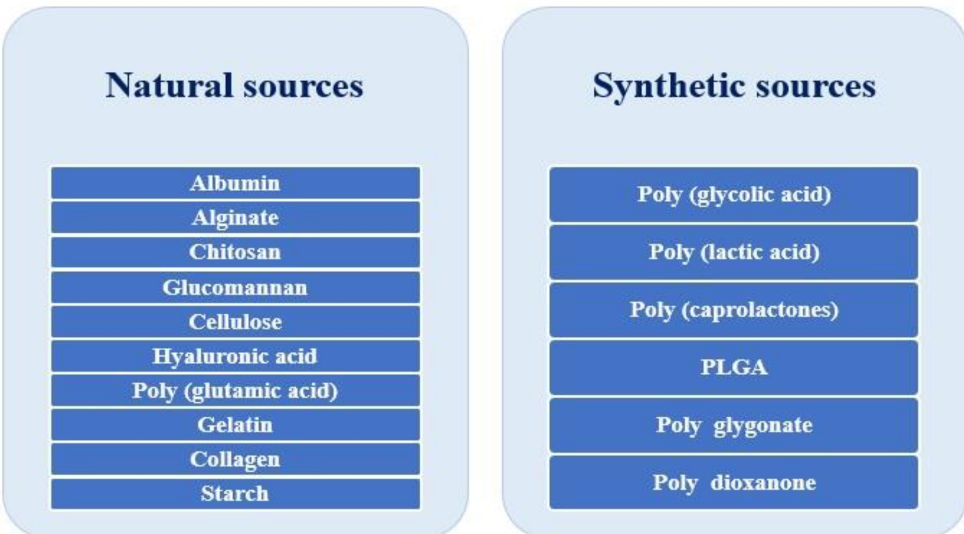

Figure 3: Commonly used polymers for cancer drug delivery.

Table 4-A: Comprehensive summary of polymeric-based nanoparticles and their applications in cancer therapy [105,106].

Table 4- B: A comprehensive summary of polymeric-based nanomaterials and their applications in cancer therapy.

Polymeric-based nanomaterials	Size	Structure	Characteristics	Preparation Method	Applications in Cancer	References
Polymeric nanoparticles	▪ 10-1000 nm	▪ Spherical, Rod-shaped, polyhedral, filamentous, star-shaped, and core-shell.	▪ Ease of surface modification ▪ Biocompatibility ▪ Versatility with natural and synthetic polymers. ▪ Enable controlled and targeted drug release ▪ High encapsulation efficiency ▪ Good stability ▪ Biodegradability ▪ The ease of surface modification ▪ Precise particle size control	▪ Solvent evaporation method ▪ Double emulsification method ▪ Emulsion diffusion method ▪ Nanoprecipitation method ▪ Coacervation method ▪ Salting out method ▪ Dialysis method ▪ Supercritical fluid method	▪ Anticancer drug delivery ▪ Targeted chemotherapy ▪ Cancer diagnosis and imaging	[107–109]
Dendrimers	1-100 nm	▪ Compact and globular structure.	▪ Hyperbranched subunits. ▪ High structural control. ▪ Well-defined architecture. ▪ Monodisperse with precise molecular weight, shape, and size. ▪ Surface functional groups for drug conjugation and inner cavities for drug entrapment. ▪ Lower glass temperatures.	▪ Divergent synthesis ▪ Convergent synthesis ▪ Hypercores and branched monomer growth ▪ Double exponential growth ▪ Lego chemistry ▪ Click chemistry	▪ Anticancer drug delivery ▪ Targeted chemotherapy ▪ Cancer diagnosis and imaging	[110–113]
Polymeric micelles	1-100 nm	▪ Spherical or globular shape, characterized by a core-shell structure	▪ Amphiphilic properties ▪ Hydrophobic core ▪ Size and shape control ▪ Enhanced drug solubility ▪ Extended blood circulation ▪ Biodistribution control ▪ Low toxicity and fast clearance ▪ No drug modification is needed	▪ Direct dissolution ▪ Solvent evaporation ▪ Dialysis	▪ Anticancer drug delivery ▪ Targeted chemotherapy ▪ Cancer diagnosis and imaging	[114–118]

Table 4-B presents a comprehensive overview of polymeric-based nanomaterials and their applications in cancer therapy. Polymeric nanoparticles, ranging from 10 to 1000 nm, have various structures and offer ease of surface modification, biocompatibility, and versatility. They enable controlled drug release with high encapsulation efficiency, stability, biodegradability, and precise particle size control. Preparation methods include solvent evaporation, double emulsification, emulsion diffusion, nanoprecipitation, coacervation, salting out, dialysis, and supercritical fluid methods. Dendrimers, sized between 1 and 100 nm, have a compact and globular structure with hyperbranched subunits. They offer high structural control, well-defined architecture, monodispersity, surface functional groups for drug conjugation, inner cavities for drug entrapment, and lower glass transition temperatures. They are used in anticancer drug delivery, targeted chemotherapy, and cancer diagnosis and imaging. Polymeric micelles, ranging from 1 to 100 nm, have a spherical or globular shape with a core-

shell structure. They possess amphiphilic properties, enabling enhanced drug solubility, extended blood circulation, biodistribution control, low toxicity, and fast clearance without drug modification.

Polymeric nanoparticles offer flexibility in medication delivery systems, allowing controlled release and targeted distribution, potentially improving the effectiveness and safety of medicinal applications in various medical contexts [119].

1. Polymeric Nanoparticles

Polymeric nanoparticles offer advanced drug delivery in cancer treatment, featuring a core-shell design for stability and controlled release facilitated by advanced techniques like nanoprecipitation and solvent evaporation [120]. They are ideal for cancer therapy due to their versatility in encapsulating various payloads, including drugs, genes, and imaging agents [121]. They enhance drug stability, improve pharmacokinetics, and reduce side effects [122]. However, challenges include complex formulations, potential toxicity, and size constraints [123]. Research has shown promising results in ovarian cancer treatment, with paclitaxel-loaded nanoparticles showing potential [124]. Additionally, PLGA-based polymeric nanoparticles are efficient delivery vehicles for various drugs [125].

2. Dendrimers

Dendrimers, highly branched macromolecules with tree-like structures, are valuable in cancer research due to their precision in design and functionality, achieved through controlled synthetic processes [111]. Made of polyamidoamine (PAMAM), dendrimers are a versatile tool in cancer treatment due to their uniform size, precise molecular weight, and ability to carry multiple functional groups [126]. They offer controlled release capabilities, enhanced solubility of drugs, and targeted delivery to specific cells. However, challenges like complex synthesis and potential toxicity at higher concentrations are drawbacks [127]. Dendrimers excel in targeted drug delivery, minimizing side effects, and aiding in cancer imaging, visualization, and combined diagnostics and therapy [128]. They also show promise in gene delivery, photodynamic therapy, and immunotherapy support. Guanglan et al. used PLA and hyaluronic acid-modified half-generation PAMAM G4.5 dendrimers as intelligent carriers for administering paclitaxel and sorafenib in liver cancer treatment [129]. Torres-Pérez et al. developed a unique one-step PAMAM dendrimer formulation loaded with methotrexate and D-glucose for triple-negative breast cancer cell lines, demonstrating that dendrimers containing methotrexate and D-glucose significantly decreased cell viability, outperforming free methotrexate [130].

3. Polymeric Micelles

Polymeric micelles, formed by self-assembling amphiphilic block copolymers, have a hydrophobic core and shell, facilitating drug solubilization in aqueous solutions, as summarized in Table 4-B [114]. With a size range of 10-100 nm, polymeric micelles offer advantages such as improved drug solubility, circulation time, and targeted drug delivery [131]. However, they also present challenges like complex synthesis and limited drug loading capacity. Polymeric micelles are extensively explored for cancer applications, including drug delivery and imaging [132]. Studies have shown their efficacy against cancer stem cells and gastrointestinal cancers [133]. Electron-stabilized polymeric micelles loaded with docetaxel show promise as a therapeutic option for advanced-stage gastrointestinal malignancies [134].

Table 4-B presents a comprehensive overview of polymeric-based nanomaterials and their applications in cancer therapy. Polymeric nanoparticles, ranging from 10 to 1000 nm, are versatile and easy to modify. They enable controlled drug release with high efficiency, stability, and biodegradability. These nanoparticles are used in anticancer drug delivery, targeted chemotherapy, and cancer diagnosis and imaging. Dendrimers, sized between 1 and 100 nm, have a compact and globular structure with hyperbranched subunits. They offer high structural control, monodispersity, and lower glass transition temperatures. Polymeric micelles, ranging from 1 to 100

nm, have a spherical or globular shape with a core-shell structure. They possess amphiphilic properties, enabling enhanced drug solubility, extended blood circulation, biodistribution control, low toxicity, and fast clearance without drug modification. Preparation methods include direct dissolution, solvent evaporation, and dialysis.

Table 4- B: A comprehensive summary of polymeric-based nanomaterials and their applications in cancer therapy.

Polymeric-based nanomaterials	Size	Structure	Characteristics	Preparation Method	Applications in Cancer	References
Polymeric nanoparticles	▪10-1000 nm	▪Spherical, Rod-shaped, polyhedral, filamentous, star-shaped, and core-shell.	▪Ease of surface modification ▪Biocompatibility ▪Versatility with natural and synthetic polymers. ▪Enable controlled and targeted drug release ▪High encapsulation efficiency ▪Good stability ▪Biodegradability ▪The ease of surface modification ▪Precise particle size control	▪Solvent evaporation method ▪Double emulsification method ▪Emulsion diffusion method ▪Nanoprecipitation method ▪Coacervation method ▪Salting out method ▪Dialysis method ▪Supercritical fluid method	▪Anticancer drug delivery ▪Targeted chemotherapy ▪Cancer diagnosis and imaging	[107–109]
Dendrimers	1-100 nm	▪Compact and globular structure.	▪Hyperbranched subunits. ▪High structural control. ▪Well-defined architecture. ▪Monodisperse with precise molecular weight, shape, and size. ▪Surface functional groups for drug conjugation and inner cavities for drug entrapment. ▪Lower glass temperatures.	▪Divergent synthesis ▪Convergent synthesis ▪Hypercores and branched monomer growth ▪Double exponential growth ▪Lego chemistry ▪Click chemistry	▪Anticancer drug delivery ▪Targeted chemotherapy ▪Cancer diagnosis and imaging	[110–113]
Polymeric micelles	1-100 nm	▪Spherical or globular shape, characterized by a core-shell structure	▪Amphiphilic properties ▪Hydrophobic core ▪Size and shape control ▪Enhanced drug solubility ▪Extended blood circulation ▪Biodistribution control ▪Low toxicity and fast clearance ▪No drug modification is needed	▪Direct dissolution ▪Solvent evaporation ▪Dialysis	▪Anticancer drug delivery ▪Targeted chemotherapy ▪Cancer diagnosis and imaging	[114–118]

CONCLUSIONS

In 2023, the United States is expected to have 1,958,310 new cancer cases and 609,820 cancer deaths. Nanotechnology, a multidisciplinary field combining chemistry, engineering, biology, and medicine, has emerged as a promising frontier in cancer research. Nanoparticles, including carbon-based nanomaterials, nanohorns, nanodiamonds, metal-based nanoparticles, gold nanoparticles, magnetic nanoparticles, quantum dot nanocarriers, lipid-based nanoparticles, solid lipid nanoparticles (SLNs), polymeric nanoparticles, dendrimers, and polymeric micelles, have shown promise in detecting and treating various cancers. However, challenges such as biocompatibility, toxicity evaluation, and regulatory hurdles remain. Carbon nanotubes, nanohorns, and nanodiamonds offer benefits in cancer treatment due to their small size and hybridized carbon atoms. Metal-based nanoparticles, derived from noble metals like gold, silver, and platinum, provide targeted drug delivery, early cancer detection, and medicinal properties. Gold nanoparticles are emerging as potent tools in cancer therapy due to their advantageous properties, including cytotoxicity against specific cancer cells, size-dependent inhibition, and tunable optical properties. Magnetic nanoparticles have gained attention in fields such as medicine, electronics, and environmental science due to their versatile applications.

This comprehensive review combines existing knowledge on nanomaterials in cancer therapy and highlights their various applications and potential benefits in improving cancer treatment outcomes. It advances scientific knowledge by providing a thorough overview of nanomaterial properties, preparation methods, and applications, making it an invaluable resource for cancer researchers and clinicians. Furthermore, it emphasizes the importance of ongoing research and development using nanomaterials to address cancer treatment challenges, leading to advances in personalized and effective cancer therapy strategies.

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التطورات في مجال العلاج باستخدام الأدوية المحضرة باستخدام العلاج النانوي في علاج مرض السرطان: مراجعة علمية

وائل أبو دية*[1]، محمد هيلات[2]، شهد البطوش[1]، إسلام البطوش[1]، ألاء أبو دية[3]، إبراهيم العبادي[4]، محمد فايز حمد[5]

[1] قسم الكيمياء الصيدلانية، كلية الصيدلة، جامعة مؤتة، الكرك، الأردن.

[2] قسم الصيدلة، كلية الصيدلة، جامعة الزيتونة الأردنية، عمان، الأردن.

[3] قسم الصيدلة، جامعة عمان الأهلية، الأردن.

[4] قسم الصيدلة الحيوية والصيدلة السريرية، الجامعة الأردنية، عمان، الأردن.

[5] قسم العلوم الطبية الأساسية، كلية الطب، جامعة البلقاء التطبيقية، السلط، الأردن.

ملخص

العلاجات النانوية للسرطان، والمميزة بتكوينات حجمها النانومترية، تهدف إلى تحسين توزيع الأدوية المضادة للسرطان في الجسم، وتقليل التأثيرات الجانبية (والغير مرغوبة نتيجة استهداف انسجة غير سرطانية)، وتقليل السمية، وزيادة تراكم هذه العلاجات في المواقع الهدف، وتحسين الكفاءة العامة للعلاجات. لقد تم تطوير العديد من العلاجات النانوية لتحسين فعالية وسلامة العلاجات المضادة للسرطان التقليدية. تشمل هذه التطورات تكوينات تحتوي على أنابيب نانوية من الكربون، وجزيئات من الألماس نانوية الحجم، وجسيمات نانوية تستجيب للإنزيمات بالتزويد المنتظم من الدواء، و"الديندرايمرات" كحاملات للدواء على شكل جسيمات نانوية، وأنظمة حمل الدواء بجسيمات النانو النقطية لتوصيل الدواء بدقة متناهية، وجسيمات الدهون الصلبة النانوية، وجسيمات البوليمر المصممة لتوصيل الدواء بشكل مستهدف. وعلاوة على ذلك، تمت مناقشة التكنولوجيا النانوية في علاج السرطان باستخدام العلاج الجيني. على الرغم من هذه التقدمات، فإن الطبيعة المعقدة لمواد الحمل والتكامل الوظيفي تحمل العديد من الصعوبات في تحضير أنظمة ايصال السالفة الذكرهذه للتطبيق السريري. التكنولوجيا النانوية، بميزاتها الفريدة على مستوى النانو، تقدم إمكانيات جديدة لتطوير علاجات السرطان مع زيادة الكفاءة والسلامة. وبالرغم من أن عددًا قليلاً من العلاجات النانوية حصلت على الموافقة السريرية، إلا أن هناك استخدامات مثيرة للدهشة للتكنولوجيا النانوية في المستقبل. تتمتع الجسيمات النانوية بقدرات فريدة في قدراتها على النقل، والخصائص البيولوجية، والبصرية، والمغناطيسية، والكهربائية، والحرارية الخاصة بها بسبب صغر حجمها. وهذا يؤدي إلى نسب سطح كبيرة مقارنة بالحجم، مما يسمح بدمجها مع مكونات داعمة مختلفة بالإضافة إلى المواد الدوائية الفعالة. تساعد هذه الخصائص الجزيئات النانوية في عمليات التحلل، والحماية من التحلل، وتأخير إطلاق العلاجات المقصود، وتجنب الاستجابة المناعية، وتعزيز اختراق الأنسجة، والتصوير، والتوزيع المستهدف، والتفعيل المستند. وخلاصة القول، فان مستقبل العلاجات النانوية يعد واعدًا بإدخال منصات مبتكرة في علاجات السرطان المختلفة. تؤكد الأبحاث التي تم عرضها وتلخيصها على إمكانية أن تحدث الجسيمات النانوية ثورة في علاجات مكافحة السرطان، مع تعزيز النهج العلاجي العام.

الكلمات الدالة: الجسيمات النانوية؛ العلاج المضاد للسرطان؛ المواد النانوية القائمة على الكربون؛ الجسيمات النانوية القائمة على المعادن، القائمة على الدهون، البوليمرية.

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* ***المؤلف المراسل: وائل أبو دية***

wabudayyih@mutah.edu.jo

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