

Advancing Cancer Treatment with Nuclear Nanomedicine and Nanoparticles

Basim A. Almayahi¹, Baneen Abdulkadhim Kamel²

¹Department of Physics, Faculty of Science, University of Kufa, Najaf, Iraq

²Department of Physics, Faculty of Science, Universiti Malaya, 50603 Kuala Lumpur, Malaysia

Malaysia

Faculty of Science, University of Kufa, Najaf, Iraq

Corresponding Author: basim.almayahi@uokufa.edu.iq

Abstract: Significant progress has been made in cancer treatment, yet the need for more precise and effective therapies persists. Nuclear nanomedicine and nanoparticles offer innovative solutions for enhancing cancer diagnosis and treatment. Due to their unique attributes, nanoparticles can target cancer cells selectively and deliver therapeutic agents directly to the tumor site. Integrating nuclear medicine with nanoparticles enables advanced approaches, such as using radioactive nanoparticles for localized radiation therapy or employing nanoparticles as carriers for imaging and therapeutic isotopes. While these methods show great promise, challenges like regulatory compliance and minimizing toxicity to healthy tissues must be addressed to ensure safe clinical application. This work explores the use of radioactive nanoparticles and functionalized nanocarriers for cancer therapy, focusing on their potential applications in drug delivery and theranostics. Ongoing research and development in this field could pave the way for highly targeted and effective cancer treatments, ultimately improving patient outcomes.

Keywords: Cancer treatment, nuclear nanomedicine, nanoparticles, radiation therapy, diagnostic imaging, drug delivery

Introduction

Cancer remains one of the leading causes of death worldwide, and despite significant advances in cancer treatment, there is still a need for more effective and targeted therapies. In recent years, the development of nuclear nanomedicine and nanoparticles has shown great promise in the diagnosis and treatment of cancer. Nuclear medicine involves the use of radioactive substances to diagnose and treat diseases, and it has been used for decades in cancer treatment. However, the traditional approach of using radioactive isotopes to deliver radiation to cancer cells has limitations, including non-specific targeting and toxicity to healthy cells. Nuclear nanomedicine is a rapidly evolving field that combines the principles of nuclear medicine and nanotechnology to develop new diagnostic and therapeutic tools for cancer treatment. One promising application of this approach is the use of nanoparticles to enhance cancer treatment [1]. Nanoparticles are tiny particles that can be engineered to carry drugs, imaging agents, or other therapeutic molecules. By targeting these nanoparticles to cancer cells, researchers hope to improve the effectiveness of cancer treatments while reducing side effects [2]. One example of this approach is the use of gold nanoparticles to enhance radiation therapy. Gold nanoparticles can be designed to absorb radiation and release energy, which can increase the amount of radiation delivered to cancer cells while sparing healthy tissues. This approach has shown promising results in preclinical studies, and clinical trials are underway to evaluate its safety and efficacy in humans [3]. Another example is the use of iron oxide nanoparticles for magnetic hyperthermia, a technique in which magnetic fields are used to heat and destroy cancer cells. Iron oxide nanoparticles can be targeted to cancer cells and then heated using an external magnetic field, which can kill the cancer cells while sparing nearby healthy tissues [4]. In addition to these approaches, researchers are exploring the use of other nanoparticles, such as liposomes and dendrimers, for targeted drug delivery and imaging. These technologies have the potential to revolutionize cancer treatment by improving the effectiveness of existing treatments and developing new therapies that are more targeted and less toxic [5]. However, it's important to note that nuclear nanomedicine is still a relatively new field, and much more research is needed to fully understand the potential benefits and risks of these approaches. As with any new medical technology, it will be important to conduct rigorous clinical trials to ensure that these treatments are safe and effective before they are widely adopted [6]. Nanoparticles, on the other hand, have emerged as a promising tool in cancer therapy due to their unique properties, including their small size, large surface area, and ability to be functionalized with targeting ligands. These properties allow nanoparticles to specifically target cancer cells and deliver therapeutic agents directly to the tumor site [7]. Combining nuclear medicine with nanoparticles can result in a powerful tool for cancer diagnosis and treatment. One approach is to use radioactive nanoparticles, which can be designed to accumulate in cancer cells and deliver radiation directly to the tumor site. This approach has been shown to be effective in preclinical studies, with increased tumor uptake and decreased toxicity to healthy tissues compared to traditional radiotherapy [8, 9]. Another approach is to use nanoparticles as carriers for radioactive isotopes, such as radionuclides or radioisotopes, which can be used for diagnostic imaging or targeted radiotherapy. These nanoparticles can be functionalized with targeting ligands, such as antibodies or peptides, to specifically bind to cancer cells and deliver the radioactive payload. This approach has the potential to increase the sensitivity and specificity of cancer imaging, as well as improve the efficacy of targeted radiotherapy [10, 11]. In addition to their potential in cancer diagnosis and treatment, nuclear nanomedicine and nanoparticles have also shown promise in other areas, such as drug delivery and

theranostics (combining diagnostic and therapeutic capabilities) [12, 13]. However, there are still challenges that need to be addressed in the development and translation of nuclear nanomedicine and nanoparticles for cancer therapy. These include optimizing the nanoparticle design for specific applications, improving targeting and retention in tumors, and addressing regulatory and safety concerns [14, 15].

Literature Reviews

Kostarelos K., Lacerda L., Pastorin G., Wu W., Wieckowski S., Luangsivilay J., Godefroy S., Pantarotto D., Briand J.P., Muller S. (2007). Cellular uptake of functionalized carbon nanotubes is independent of functional group and cell type. *Nature Nanotechnology*, 2(2), 108-113. doi: 10.1038/nano.2006.209. This literature review focuses on the cellular uptake of carbon nanotubes, including their mechanisms of uptake and potential toxicity. The authors discuss the implications of these findings for the development of carbon nanotube-based therapeutics and diagnostics [16].

Lee E.S., Gao Z. (2012). Cancer nanotechnology: promises and challenges. *Journal of Interdisciplinary Nanomedicine*, 1(1), 7-10. doi: 10.1002/jin2.5. This article provides an overview of the potential of nanotechnology in cancer therapy, including the use of nanoparticles for drug delivery, imaging, and radiation therapy. The authors also discuss the challenges that need to be addressed in the development and translation of these technologies to clinical practice [17].

"Nanoparticles for cancer therapy: progress, challenges and prospects" by H. Xie, H. Liu, and X. Luo in *Journal of Materials Chemistry B* (2016). This review article provides an overview of the use of nanoparticles in cancer therapy, including the potential of nuclear nanomedicine for targeted drug delivery and radiation therapy [18].

Shakeri-Zadeh A., Jalali F. (2018). Nanoparticles for cancer diagnosis and therapy. *Applied Physics Reviews*, 5(4), 041305. doi: 10.1063/1.5023445. This literature review focuses on the use of nanoparticles in cancer diagnosis and therapy. The authors discuss the various types of nanoparticles used in cancer therapy, including metallic, magnetic, and polymeric nanoparticles. They also highlight recent advances in the development of nanoparticle-based theranostic agents [19].

"Nuclear medicine and nanoparticles: towards a more targeted cancer therapy" by F. Grasset, L. Rbah-Vidal, and C. Roux in *Cancer Nanotechnology* (2019). This review article discusses the use of nuclear medicine and nanoparticles in cancer therapy, with a focus on the potential of radioactive nanoparticles and nanocarriers for targeted drug delivery and imaging [20].

Guo J., Rahme K., Li J., Holmes J.D., O'Driscoll C.M. (2019). Biomimetic and bioinspired nanoparticles for targeted drug delivery. *Biomaterials Science*, 7(10), 4086-4117. doi: 10.1039/c9bm00714j. This literature review explores the use of biomimetic and bioinspired nanoparticles for targeted drug delivery. The authors discuss the various approaches used to develop these nanoparticles, including surface functionalization, and highlight recent advances in the field [21].

"Advances in Nuclear Medicine for Cancer Diagnosis and Therapy" by N. Abdi and M. Gholamrezanezhad in *Seminars in Nuclear Medicine* (2020). This review article provides an overview of the latest advances in nuclear medicine for cancer diagnosis and therapy, including the use of nanoparticles for targeted drug delivery and imaging [22].

"Nuclear Medicine in Cancer Therapy: Present and Future" by A. H. Ali et al. in *Current Drug Targets* (2020). This review article provides an overview of the role of nuclear medicine in cancer therapy, including the use of nanoparticles for targeted drug delivery and imaging [23].

"Recent advances in theranostic nanoparticles-based cancer treatment" by R. K. Dutta et al. in *Drug Discovery Today* (2020). This review article discusses recent advances in theranostic nanoparticles-based cancer treatment, including the use of nuclear nanomedicine for targeted drug delivery and imaging. This article reviews the use of nanotechnology in cancer therapy, including the use of nanoparticles for drug delivery and imaging. The authors also discuss the potential of nanotechnology in developing targeted therapies and the use of nanoparticles for imaging and diagnosis [24].

Advancements in Targeted Radionuclide Therapy for Cancer Treatment

Radionuclides are commonly used in targeted radionuclide therapy for cancer treatment. The therapeutic efficacy of radionuclides depends on their physical and biochemical properties, which determine their diagnostic or therapeutic nature. Radioisotopes that emit α - or β -particles, or Auger electrons, are the most effective in therapeutic radiopharmaceuticals. The choice of a radionuclide depends on several biomedical factors, including the type and size of the tumor, the density of the target, and its heterogeneity. Physical properties, such as half-life, decay mode, and radiation properties, are also crucial considerations. Biochemical properties, such as the need to preserve radioactivity in the tumor, as well as stability and toxicity in vivo, are equally important. Recent advances in cancer diagnosis and treatment have led to the development of new radiopharmaceuticals based on targeted delivery. Targeted radiopharmaceuticals selectively concentrate in the tumor area and destroy cancer cells with minimal radiation to healthy tissues, ensuring high therapeutic outcomes and minimal side effects. Moreover, theranostic radiopharmaceuticals that act as both diagnostic and therapeutic tools are gaining popularity, allowing for personalized medicine approaches in therapy planning. While promising results have been obtained using molecules such as antibodies and peptides to deliver radionuclides to the tumor, these molecules can typically carry only a few chelates linked to radionuclide atoms due to their small size. This necessitates the delivery of very high concentrations of radionuclide-carrying molecules to achieve significant therapeutic outcomes, potentially causing severe side effects. Additionally, the size of targeting agents falls within the range of renal filtration, leading to the rapid accumulation of radionuclides in the kidneys and causing renal failure and other problems. Furthermore, altered profiles of biodistribution and

pharmacodynamics must be taken into account when targeting molecules are used with radionuclides, as they can have potential immunogenic effects [25].

Nanoparticles as Radionuclide Delivery Systems for Cancer Therapy

Nanoparticles have emerged as promising carriers for radionuclides in cancer therapy due to their unique physical and biochemical properties. Their high surface-to-volume ratio and porous texture enable a higher loading of radionuclides, leading to improved therapeutic efficacy. Furthermore, when functionalized with appropriate polymers such as polyethylene glycol (PEG) or dextran, nanoparticles can have a prolonged circulation time in the bloodstream and accumulate selectively in tumors through the enhanced permeability and retention (EPR) effect [26].

Moreover, some nanoparticles possess unique properties that can be harnessed for additional imaging or therapeutic modalities, such as fluorescence, magnetic resonance imaging (MRI), photothermal therapy, and photodynamic therapy [27-29]. Several types of nanomaterials have been successfully used as carriers for diagnostic and therapeutic radionuclides in nuclear medicine, including organic nanoparticles like liposomes, solid-lipid and polymeric nanostructures, gold nanoparticles, magnetic nanoparticles such as Fe_3O_4 and $CoFe_2O_4$, carbon nanoparticles, and silica nanoparticles [30-33]. In some cases, the combination of radionuclides and nanoparticle-based imaging or therapeutic modalities has resulted in improved outcomes for cancer patients. For example, the use of nanoparticles in combination with radionuclides has enabled the integration of multiple imaging and therapeutic modalities into a single platform, improving the accuracy and efficacy of cancer diagnosis and treatment [34, 35].

Top-down vs bottom-up approaches to nanomaterial synthesis

Nanomaterial synthesis can be achieved through two main approaches: top-down and bottom-up. The top-down approach involves breaking down a larger material into smaller pieces until the desired size and shape of the nanomaterial is achieved [36]. On the other hand, the bottom-up approach involves building the nanomaterial from individual atoms or molecules, gradually assembling them into the desired structure. Both approaches have their advantages and disadvantages [37]. Top-down methods are generally faster and can produce large quantities of nanomaterials. However, the resulting particles may not have a uniform size or shape, and there is a limit to how small they can be made. Bottom-up methods, on the other hand, allow for precise control over the size, shape, and composition of the resulting nanomaterial [38]. However, they can be slower and more complex to carry out, and may not be as scalable for large-scale production [39, 40]. Overall, the choice between top-down and bottom-up approaches depends on the specific requirements of the application, as well as the desired properties of the nanomaterial.

Chemical synthesis of nanomaterials

Chemical synthesis of nanomaterials involves the use of chemical reactions to create nanoscale materials with specific shapes, sizes, and properties. This approach has the advantage of being highly controllable and scalable, allowing for the production of large quantities of nanomaterials with precise control over their characteristics [41]. One common chemical synthesis method is the sol-gel process, which involves the hydrolysis and condensation of metal alkoxides or other precursors to form a colloidal suspension or gel. The gel is then dried and heated to remove the solvent and organic residues, resulting in a solid material with a porous structure and high surface area [42]. Another popular method is the chemical reduction of metal salts, which involves the use of reducing agents to convert metal ions into metal nanoparticles. This approach is often used for the synthesis of noble metal nanoparticles, such as gold and silver, and can be carried out in aqueous or organic solvents [43]. Other chemical synthesis methods include the use of microemulsions, where the formation of nanomaterials occurs within surfactant-stabilized droplets of one phase dispersed in another, and the hydrothermal synthesis, which involves the use of high-temperature and high-pressure conditions to promote the formation of nanomaterials. Despite the advantages of chemical synthesis, there are also potential drawbacks, including the use of hazardous chemicals, the need for precise control over reaction conditions, and the difficulty in achieving uniform particle size and shape distributions [44]. These challenges require careful optimization and monitoring of the synthesis process to ensure reproducibility and minimize the risk of unintended outcomes [45]. Overall, chemical synthesis remains a powerful tool for the preparation of nanomaterials with tailored properties for a wide range of applications, including catalysis, electronics, energy, and biomedicine.

Physical methods for synthesizing nanomaterials (e.g. vapor deposition, laser ablation, electrodeposition)

Physical methods for synthesizing nanomaterials refer to techniques that use physical forces and energy sources to produce nanoparticles. Some of the commonly used physical methods for synthesizing nanomaterials include vapor deposition, laser ablation, and electrodeposition [46].

Vapor deposition is a technique that involves heating a solid material to its vaporization point and then condensing the vapor onto a substrate. This technique is commonly used for producing thin films and coatings [47]. In the context of nanomaterials synthesis, vapor deposition can be used to produce nanoparticles of metals, metal oxides, and other materials. Laser ablation involves using a high-energy laser to vaporize a target material, which then condenses to form nanoparticles. This technique is suitable for producing

nanoparticles of metals and metal oxides [48, 49]. Electrodeposition involves using an electric field to deposit metal ions onto a substrate, resulting in the formation of nanoparticles. This technique is commonly used for producing nanoparticles of metals such as copper, nickel, and gold. Other physical methods for synthesizing nanomaterials include plasma synthesis, sputtering, and ball milling. Each of these physical methods has its advantages and disadvantages [50, 51]. For example, vapor deposition and laser ablation can produce highly pure nanoparticles, but they may require expensive equipment and can be difficult to scale up for large-scale production. Electrodeposition is a relatively simple and low-cost technique, but it may produce nanoparticles with a wide size distribution [52].

Biological synthesis of nanomaterials (e.g. biosynthesis, biomaterialization)

Biological synthesis of nanomaterials refers to the use of biological systems such as microorganisms, plants, and animals to synthesize nanoparticles [53]. This approach has gained significant attention due to its eco-friendliness, low cost, and potential for large-scale production. Some of the commonly used biological methods for synthesizing nanomaterials include biosynthesis, biomaterialization, and green synthesis [54].

Self-assembly and template-assisted methods for nanomaterial synthesis

Self-assembly and template-assisted methods are important techniques for synthesizing nanomaterials with controlled size, shape, and composition. These methods rely on the spontaneous organization of building blocks, such as molecules or nanoparticles, into ordered structures [55].

Self-assembly refers to the process by which molecules or nanoparticles arrange themselves into an ordered structure without external direction. This can occur through a variety of mechanisms, such as hydrogen bonding, van der Waals interactions, and electrostatic interactions. Self-assembly can be used to create a wide range of nanostructures, including spheres, rods, tubes, and vesicles [56]. Template-assisted methods involve using a pre-formed template to direct the assembly of building blocks into a specific structure. Templates can be either hard (e.g. a porous membrane) or soft (e.g. a self-assembled monolayer). By controlling the size and shape of the template, as well as the properties of the building blocks, it is possible to create a wide range of nanostructures with high precision [57].

Some examples of self-assembly and template-assisted methods for nanomaterial synthesis include [58]:

1. Self-assembled monolayers (SAMs): This technique involves the spontaneous assembly of molecules onto a substrate to form a monolayer. SAMs can be used as templates for the growth of nanoparticles, as well as for the functionalization of surfaces with specific chemical groups.

2. Block copolymer self-assembly: Block copolymers are polymers consisting of two or more chemically distinct blocks. When dissolved in a solvent, the blocks can separate and form ordered structures, such as spheres or cylinders. These structures can then be used as templates for the synthesis of nanomaterials.

3. Nanoparticle self-assembly: Nanoparticles can spontaneously assemble into ordered structures, such as arrays, superlattices, and nanocrystal clusters. This can be controlled by varying the size, shape, and surface chemistry of the nanoparticles.

4. Electrodeposition: This technique involves the electrodeposition of metal ions onto a substrate in the presence of a template, such as a self-assembled monolayer. The resulting metal structure can then be used as a template for the synthesis of nanomaterials.

5. Vapor-phase deposition: This technique involves the deposition of atoms or molecules onto a substrate in the gas phase. By controlling the deposition conditions, it is possible to create a wide range of nanostructures, such as nanotubes and nanowires.

Overall, self-assembly and template-assisted methods offer a powerful approach to the synthesis of nanomaterials with controlled size, shape, and composition. These techniques have broad applications in fields such as catalysis, sensing, and electronics.

Post-synthesis functionalization of nanomaterials

Post-synthesis functionalization of nanomaterials refers to the process of modifying the surface of already synthesized nanomaterials with various functional groups, molecules, or polymers in order to tailor their properties and functionality for specific applications [59]. This process is often critical for maximizing the potential of nanomaterials in various fields, such as drug delivery, imaging, and sensing. Some commonly used post-synthesis functionalization methods include chemical modification, surface adsorption, electrostatic adsorption, and encapsulation. The choice of method depends on the specific properties of the nanomaterial, the functional group to be attached, and the intended application [60]. For example, in drug delivery, post-synthesis functionalization can improve the biocompatibility and specificity of the nanomaterial to target specific cells or tissues. In sensing, functionalization can improve the selectivity and sensitivity of the nanomaterial to detect specific analytes.

Scale-up and commercial production of nanomaterials

The scale-up and commercial production of nanomaterials require a systematic and efficient approach to ensure the quality and reproducibility of the product. Some of the important considerations in scaling up the production of nanomaterials include process optimization, equipment design, and quality control [61]. There are several methods for scaling up the production of nanomaterials, including:

Continuous flow synthesis: This involves the use of continuous flow reactors to produce a large quantity of nanomaterials in a continuous manner. This approach offers several advantages, including improved product quality, reproducibility, and reduced production costs.

Batch synthesis: This involves the production of nanomaterials in large batches using traditional batch reactors. While this approach is more familiar and easier to implement, it may result in batch-to-batch variability and may not be as cost-effective as continuous flow synthesis.

Microfluidic synthesis: This approach involves the use of microfluidic devices to produce nanomaterials. Microfluidic synthesis offers several advantages, including precise control over reaction parameters and the ability to produce highly uniform nanomaterials.

Upscaling of laboratory processes: This involves the modification of laboratory-scale processes to allow for the production of larger quantities of nanomaterials. This approach is often used when a new process or material is being developed and needs to be scaled up for commercial production. Several companies specialize in the commercial production of nanomaterials, including Nanosys, Nanocomposix, and NanoMaterials Technology. These companies use various approaches to scale up the production of nanomaterials, depending on the specific material and application. They also employ rigorous quality control measures to ensure the consistency and purity of their products [62].

Nuclear nanomedicine with a focus on safety

This topic pertains to the use of nuclear technology in the field of nanomedicine with a particular emphasis on ensuring safety for patients and healthcare professionals involved in the treatment process. The integration of nuclear technology in nanomedicine has shown significant promise in the diagnosis and treatment of various diseases, but it is essential to ensure that such applications are safe for all involved parties. Advancements in this field require careful consideration and evaluation of potential risks and safety protocols to minimize adverse effects and maximize the benefits of this technology. Nuclear nanomedicine is a rapidly growing field that utilizes the properties of nanomaterials and radioisotopes for medical diagnosis and therapy. Despite the potential benefits of nuclear nanomedicine, it is important to consider the safety aspects of using radioactive materials [63].

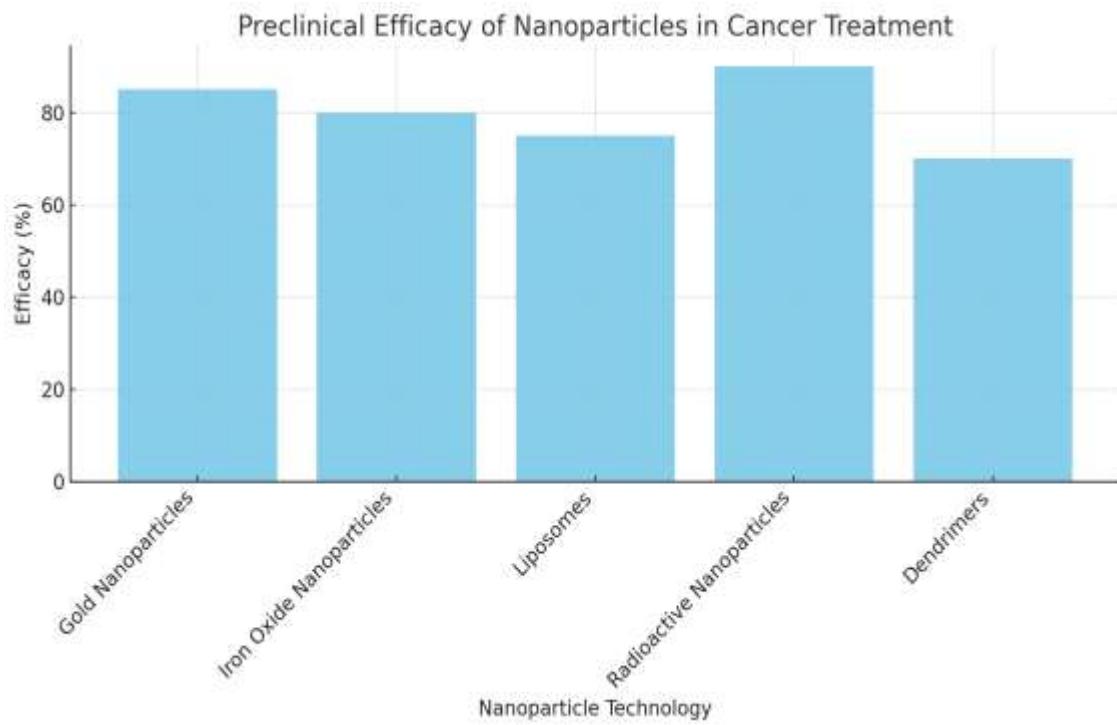
Several studies have focused on developing safe nuclear nanomedicine techniques. One approach is to develop targeted delivery systems that specifically target cancer cells, minimizing the exposure of healthy cells to radiation. This can be achieved through the use of specific ligands that bind to receptors on the cancer cells, such as antibodies or peptides. Another approach is to use radioisotopes with shorter half-lives, reducing the risk of radiation exposure to healthy tissue. In addition, careful consideration of the biodistribution and pharmacokinetics of the radiolabeled nanomaterials can help to minimize potential side effects. It is also important to consider the potential risks associated with the production and disposal of radioactive nanomaterials. Proper handling and disposal methods must be implemented to ensure the safety of workers and the environment. Overall, while nuclear nanomedicine has great potential for medical applications, it is important to prioritize safety in the development and implementation of these technologies.

Neutron Activation Method for the Synthesis of Nanoformulations Labeled with Radioisotopes

The preparation of nanoformulations labeled with a radioisotope using the neutron activation method is an important area of research in nuclear nanomedicine. This technique involves the use of a neutron source to activate stable isotopes and produce radioisotopes that can be incorporated into nanomaterials. The resulting radioisotope-labeled nanomaterials have potential applications in various fields, including biomedical imaging and targeted therapy [64]. One advantage of the neutron activation method is that it allows for the production of a wide range of radioisotopes, including those that are not easily accessible through other methods. Additionally, this method is relatively simple and does not require expensive equipment. However, it is important to ensure that the resulting nanoformulations are safe for use in vivo and do not pose a risk to human health or the environment [65]. Several studies have investigated the safety of radioisotope-labeled nanomaterials prepared via the neutron activation method. These studies have shown that the toxicity of the nanomaterials depends on various factors, including the chemical composition of the material, the radioisotope used, and the size and surface charge of the nanoparticles. To ensure the safe use of these materials, it is important to carefully consider these factors and to conduct rigorous toxicity testing [66]. Pie chart, and bar chart summarizing the advancements in cancer treatment using nuclear nanomedicine and nanoparticles (Table 1 and Figs. 1, 2).

Table 1 comparison for some literature reviews

Technology	Applications	Efficacy (Preclinical Success %)	Challenges
Gold Nanoparticles	Enhance radiation therapy	85%	Toxicity concerns in healthy tissues



Iron Oxide Nanoparticles	Magnetic hyperthermia	80%	Limited clinical trials, potential for overheating
Liposomes	Targeted drug delivery	75%	Drug loading capacity limitations
Radioactive Nanoparticles	Tumor-specific radiation	90%	Regulatory and safety issues
Dendrimers	Theragnostic	70%	Complex synthesis and cost

Preclinical Success Rates of Nanoparticles in Cancer Treatment

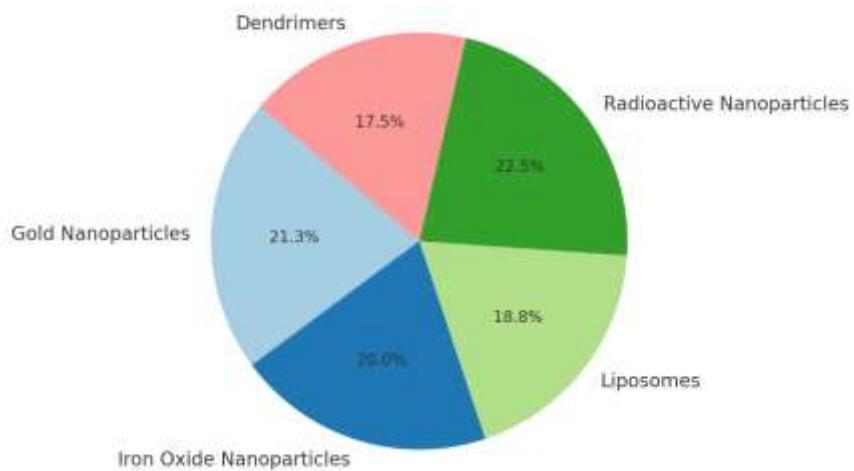


Figure 1. The rates of different technologies in cancer

preclinical success nanoparticle treatment

Figure 2. Highlights the efficacy percentages of each nanoparticle technology

Conclusions

The integration of nuclear medicine with nanoparticles represents a significant leap forward in cancer diagnosis and treatment, paving the way for more targeted and efficient therapies. Techniques like neutron activation for creating radioisotope-labeled nano formulations hold great potential but require rigorous safety measures for practical biomedical use. These advancements promise personalized cancer treatment approaches that reduce harm to healthy tissues. Progress in nanotechnology, imaging agents, and radiopharmaceuticals has opened new doors for innovative cancer solutions. However, key challenges such as ensuring safety, enhancing effectiveness, and scaling production for clinical applications must be addressed. Collaborative research across disciplines will be vital to fully harness the potential of these technologies, ultimately aiming to improve patient care and quality of life while offering new avenues for combating cancer.

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