Applications and Research Status of Nanomaterials in Radiation Injury Treatment

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Abstract

With the development of nuclear technology applications in industry, medicine, and other fields, the likelihood of human exposure to radiation injury has increased accordingly. Although some small-molecule drugs for radiation injury treatment have been applied clinically or are in preclinical studies, their short blood circulation time and rapid metabolism greatly compromise their therapeutic efficacy. The application of nanomaterials in radiation injury treatment has garnered increasing attention from academic and medical communities. Compared with other small-molecule drugs, nanomaterials exhibit a series of advantages in radiation injury treatment research, including their remarkable bioactivity, chemical stability, exceptional histocompatibility, and targeted delivery capacity. Through rational design and development of nanodrugs, it holds promise for overcoming the limitations of existing small-molecule drugs for radiation injury treatment. Given the numerous advantages of nanomaterials, this review outlines the design strategies and classification of nanomaterials for radiation injury treatment, while also analyzing the pathogenic mechanisms of common radiation diseases and the current research status of utilizing nanomaterials for treatment, including nanomaterial-based decorporation therapy for internal radionuclide contamination. However, despite their broad application potential, the biosafety and clinical efficacy of these nanomaterials still require thorough investigation. Finally, the challenges and future prospects of using nanomaterials for radiation injury treatment are discussed.

Full Text

Application and Research Progress of Nanomaterials in the Treatment of Radiation Injury

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Abstract

With the expanding applications of nuclear technology in industrial and medical fields, the risk of radiation injury to humans has increased accordingly. Although several small-molecule drugs for radiation injury treatment have been applied clinically or are in preclinical research, their short circulation time and rapid metabolism significantly compromise therapeutic efficacy. The use of nanomaterials in radiation injury treatment has garnered increasing attention from academia and the medical community. Compared with small-molecule drugs, nanomaterials offer a series of advantages in radiation injury research, including superior bioactivity, chemical stability, excellent tissue compatibility, and targeted delivery capabilities. Through rational design and development of nanomedicines, it is hoped that the limitations of existing small-molecule radioprotective agents can be overcome. Given these numerous advantages, this review outlines the design strategies and classification of nanomaterials for radiation injury treatment, while analyzing the pathogenic mechanisms of common radiation-induced diseases and the current research status of nanomaterial-based therapies, including nanoparticle-based decorporation therapy for internal radionuclide contamination. However, despite their broad application potential, the biosafety and clinical efficacy of these nanomaterials require further investigation. Finally, we discuss the challenges and future prospects of using nanomaterials for radiation injury treatment.

Keywords: nanomaterials; radiation injury; radioactive diseases; decorporation enhancement

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The rapid development of nuclear technology represents a double-edged sword, bringing increasing benefits to humanity while simultaneously posing potential hazards. Radiotherapy, as a conventional cancer treatment, effectively kills tumor cells but inevitably damages surrounding healthy cells and tissues, triggering a series of radiation-induced diseases such as hematopoietic system injury, radiation enteropathy, radiation pneumonitis with pulmonary fibrosis, and radiation dermatitis [1]. Additionally, in scenarios including nuclear explosions, accidents, and dirty bomb attacks, ionizing radiation poses a serious threat to human health.

In this context, designing and developing radioprotective agents holds significant importance, with urgent demand for both nuclear accident rescue and radiological disease treatment. Considerable efforts have been made to identify effective protective agents, but most developed drugs remain organic small molecules with inherent limitations including low bioavailability, short circulation time, and rapid metabolism [2]. For instance, amifostine and similar drugs have short

half-lives and moderate toxicity, but excessive administration inevitably leads to clinical symptoms such as hypotension, nausea, vomiting, weakness, fatigue, and drowsiness [3]. Consequently, their general applicability in radiation medicine remains relatively limited.

Since the nanotechnology concept was proposed in the 1970s, nearly five decades of progress have yielded major breakthroughs in medical applications [4]. Nanomedicines possess multiple advantageous characteristics, including high solubility, biocompatibility, and stability, which establish the foundation for their medical applications [5]. First, some radioprotective drugs can be polymerized to achieve nanoscale formulations. Second, nanomaterials can serve as delivery vehicles for molecular radioprotective agents. Another well-studied category involves nanozymes, which, compared with conventional drugs, demonstrate higher antioxidant efficacy, greater stability, and enhanced tolerance in vivo. These antioxidant nanozymes have proven effective in eliminating various reactive oxygen species (ROS) and reactive nitrogen species (RNS), promoting DNA damage repair, and ameliorating oxidative damage in multiple radiation-induced disease models [6].

This review summarizes the design strategies and classification of nanomaterials for radiation injury treatment, focusing on the development status of various nanomedicines for radioprotection, including treatments for radiation-induced hematopoietic system injury, intestinal injury, brain injury, kidney injury, skin and reproductive system damage, radiation pneumonitis, pulmonary fibrosis, and nanomaterials for radionuclide decorporation. Finally, we discuss the challenges and future prospects of nanomedicine research. This review aims to help researchers better understand the progress in nanomaterial applications for radiation injury treatment and promote further advancement in this field.

Design Strategies of Nanomaterials for Radiation Injury Treatment

Nanomedicines can overcome the inherent limitations of conventional drugs, such as short circulation time and rapid metabolism. Additionally, nanomedicines offer advantages including strong catalytic activity, ease of mass production, long storage stability, low cost, and high stability under extreme conditions. Common nanomaterial design strategies include: (i) polymerization of small-molecule radioprotective drugs into nanomaterials, (ii) delivery of radioprotective drugs using nanocarriers, (iii) nanozymes with radioprotective effects, and (iv) stimuli-responsive nanomedicines.

2.1 Polymerization of Small-Molecule Radioprotective Drugs into Nanomaterials

Currently, multiple methods exist to polymerize radioprotective drugs into nanomaterials, including emulsification and high-pressure homogenization. For example, in emulsification studies, silymarin was successfully emulsified into 3-8

nm nanoemulsions using surfactants and co-surfactants. Compared with typical silymarin monomers, the nanosized formulation retained therapeutic efficacy while significantly improving bioavailability [7]. Using high-pressure homogenization, Chen synthesized nano GLSO@P188/PEG400 drugs (approximately 90 nm in size), which enhanced water solubility, further reduced excessive ROS production, and better protected mitochondria from X-ray damage [8]. This strategy offers a promising approach for addressing the poor water solubility of otherwise effective radioprotective drugs.

In some cases, nanomaterials can be assisted by other methods. For instance, lipoic acid (LA), a conventional radioprotective drug, has a very short plasma half-life, and its oral bioavailability drops to approximately 30% of the administered dose [9]. To address this limitation, researchers prepared 11 nm-sized lipoic acid nanocapsules (LANC) and demonstrated their therapeutic potential against 99mTc-MIBI-induced cardiovascular tissue damage [10].

2.2 Delivery of Radioprotective Drugs Using Nanocarriers

Beyond assembling drugs into nanoparticles, loading them onto low-toxicity nanocarriers represents another effective approach to enhance in vivo efficacy and overcome limitations such as low bioavailability. To achieve this goal, organic nanocarriers such as chitosan and poly(lactic-co-glycolic acid) (PLGA) are the most common non-toxic drug carriers of significant value [11]. In a study by Daoben Hua et al. [12], a novel oral nanomedicine PDA@Arg-CS(THA) (200 nm) was developed that effectively alleviated radiation-induced gastrointestinal syndrome.

Compared with organic nanocarriers, inorganic drug carriers offer advantages including stability, high loading capacity, and long circulation time. For example, Schweitzer et al. [13] utilized silica, a commonly used low-toxicity and biodegradable nanocarrier, to deliver melanin, thereby synthesizing melanin-coated nanoparticles that demonstrated protective effects against radiation-induced bone marrow damage.

2.3 Nanozymes for Radiation Injury Treatment

The design and synthesis of nanozymes mimic antioxidant enzymes to scavenge various ROS or RNS induced by radiation. Compared with conventional radioprotective drugs, antioxidant nanozymes exhibit higher antioxidant efficacy, stronger stability, and greater tolerance to harsh in vivo microenvironments, and have proven effective in ameliorating oxidative damage in different radiation disease models. The following sections summarize five common types of antioxidant nanozymes: (i) cerium oxide-based nanozymes, (ii) transition metal dichalcogenide nanozymes, (iii) noble metal nanozymes, (iv) carbon-based nanozymes, and (v) MXene nanozymes.

2.3.1 Cerium Oxide-Based Nanozymes The mechanism of cerium oxide nanoparticles (CNPs) primarily involves their facile redox reactions in biological systems, with rapid transitions between Ce^{4+} and Ce^{3+} oxidation states (induced by oxygen vacancies). Researchers have noted that CNPs allow hydrogen precipitation to neutralize toxic free radicals, ensuring their utility in effective radiation injury treatment [14][15].

2.3.2 Transition Metal Dichalcogenide Nanozymes Unlike cerium oxide, which relies primarily on cerium valence state changes, transition metal elements have attracted attention due to their inherent active redox reactivity. Transition metal dichalcogenides (TMDCs) containing transition metal elements possess unique layered structures with the MX_2 formula, where M represents transition metals (Mo, W, Re, Ti, Hf, Nb, Ta) and X represents chalcogen elements (S, Se, Te). Essentially, this layered structure forms a sandwich-shaped X-M-X layer with covalent bonds within layers and weak van der Waals forces between adjacent layers, enabling flexibility and tunability for multiple configurations. These characteristics confer TMDCs with special advantages including strong free radical scavenging ability, good biocompatibility, and low biological toxicity [16].

2.3.3 Noble Metal Nanozymes Platinum (Pt) is an important material for developing noble metal nanomedicines. Takeki Hamasaki [17] discovered that Pt nanoparticles can scavenge $\bullet O_2^-$ and $\bullet OH$ radicals. Wang et al. [18] synthesized hollow platinum-palladium-rhodium (PtPdRh) nanocubes that demonstrated catalase-, peroxidase-, and superoxide dismutase (SOD)-like activities, effectively removing ROS. Wei et al. [19] further incorporated molybdenum (Mo) to synthesize PtPdMo, which inhibited intestinal epithelial cell apoptosis, reduced multi-organ oxidative stress responses, and increased bone marrow and peripheral blood cell counts by eliminating ROS accumulation and enhancing DNA repair capacity.

2.3.4 Carbon-Based Nanozymes Carbon-based nanomaterials have attracted widespread attention in radiation medicine due to their ability to strongly react with and scavenge free radicals through unsaturated bonds. Currently reported carbon-based nanomaterials include zero-dimensional fullerenes, one-dimensional carbon nanotubes, and two-dimensional graphene.

Fullerenes are typical zero-dimensional allotropes of graphitic carbon, known as C_{60}. Sergey V. Gudkov et al. [20] investigated unmodified hydrated C_{60} fullerene molecules (C_{60}UHFM) and found they could reduce ROS generation in irradiated water, alleviate leukocyte and platelet loss by reducing DNA damage, promote small intestine tissue regeneration, and mitigate radiation injury in treated mice. Another team synthesized water-soluble fullerenol@nano-montmorillonite (NMMT) through mechanochemical synthesis, which exhibited high chemical stability and broad free radical scavenging capacity, effectively reducing ROS-induced mitochondrial and DNA damage. Notably, NMMT as a drug carrier

demonstrated strong intestinal adhesion capability, prolonging fullerenol retention in the duodenum and thereby alleviating radiation-induced diarrhea, weight loss, and duodenal histopathological damage in mice [21].

Research on one-dimensional carbon nanotubes remains limited, though they have shown excellent cellular permeability and other properties suitable for drug delivery systems [22]. Two-dimensional carbon-based nanomaterials are represented by graphene and graphdiyne, among which graphene oxide is a water-soluble, non-toxic, biodegradable, and modifiable nanomaterial. All its carbon atoms are exposed, with edge carbon atoms being more reactive than planar atoms, and its open structure enables effective capture of oxygen radicals [23].

2.3.5 MXene Nanozymes Based on comprehensive understanding of two-dimensional (2D) nanomaterials represented by graphene, many 2D nanosheets have been applied in radiation medicine due to their large surface area ratio and high cargo-loading structures. Typically, 2D-structured nanomaterials such as titanium carbide and niobium carbide, also known as MXenes with the chemical formula $M_{n+1}X_nT_x$ (n=1~3), where M and X represent early transition metals and C or N elements respectively, and T denotes surface functional groups [24].

2.4 Stimuli-Responsive Nanomedicines

Stimuli-responsive nanoparticles, also known as smart nanomaterials, have limited applications in radiation medicine, with most research focusing on ROS and radiation responses. ROS-responsive nanomedicines can degrade and release drugs that react with ROS, serving as a targeted radiation injury treatment approach. For example, utilizing the ROS-responsive linker thioketone, which induces cascade activation under ROS stimulation, drug-loaded nanoparticles (PCEC/WR-1065NPs) were prepared to deliver WR-1065 to cells. Results showed that PCEC/WR-1065NPs could prevent drug destruction by gastric fluid and intelligently release WR-1065 at ROS lesion sites, thereby improving survival benefits and alleviating hematopoietic injury [25]. Although this direction holds great potential, developing efficient ROS-responsive nanomedicines remains a significant challenge.

Applications of Nanomedicines in Radiation Injury Treatment

Based on the aforementioned design strategies, numerous nanomedicines for radiation injury treatment have been reported, demonstrating promising application prospects. The following sections summarize nanomaterial-mediated radiation injury treatment from the perspective of different tissues/organs .

3.1.1 Treatment of Hematopoietic System Injury

The human hematopoietic system exhibits suppressed blood cell production and pancytopenia following ionizing radiation exposure, with varying radiosen-

sitivity among different hematopoietic cells. Severe cases can lead to infectious complications and hemorrhagic syndrome, with some organisms requiring hematopoietic reconstruction due to failure of self-repair mechanisms. Experimental studies have shown that TiO_2 nanomedicines provide protective effects against radiation damage, gradually restoring hematopoietic system function as validated through in vivo plasma stability experiments and radiation biological effects in lethally irradiated mice [26]. Another approach using ultrasound microbubbles combined with hydrogen and cerium oxide nanoparticles also demonstrates radioprotective effects [27]. Ultrasmall Au-MoS_2 nanoclusters formed by hybridizing MoS_2 with gold exhibit enhanced catalytic H_2O_2 decomposition capacity, protecting bone marrow hematopoietic systems from high-energy radiation damage [28]. Xia [29] compared conventional salidroside (SE) with nano-liposome-encapsulated salidroside (SNL) for subacute radiation injury protection, finding that the nanoscale formulation provided more significant improvement in hematopoietic function. Ren [30] developed ultrathin two-dimensional niobium carbide (Nb_2C) MXene nanomedicines, which were shown to reverse radiation-induced hematopoietic system damage and significantly improve survival rates in irradiated mice, expanding applications for internal radiation nanomedicines. Lee [31] reported a γ-tocotrienol (GT3) nanomedicine (GT3-Nano) that effectively mitigated sublethal and lethal myelosuppression from total body irradiation in mice, promoting rapid hematopoietic recovery. Wang [32] developed a 4-pentylbenzeneboronic acid (PBA)-modified crocin-I nanomedicine that demonstrated effective ROS targeting and scavenging activity, good in vitro biocompatibility, and significant prevention of radiation-induced peripheral blood cell damage.

These diverse nanomedicine construction strategies demonstrate tremendous clinical potential and practical significance for designing and developing more hematopoietic system-targeted nanomaterials with preventive and therapeutic effects, good biocompatibility, bioavailability, and biosafety. Unfortunately, most newly developed nanomedicines remain in preclinical stages. While their efficacy has been confirmed in animal models, further validation is needed for human radiation injury treatment applications, including assessment of toxicity, tolerability, absorption, and excretion.

3.1.2 Treatment of Radiation-Induced Intestinal Injury

The small intestine is the second most radiation-sensitive organ in the human body, and X-ray irradiation-induced gastrointestinal damage represents a serious clinical problem in radiotherapy, limiting radiation doses and causing radiation enteritis and other adverse reactions post-treatment. Crypt damage is central to radiation-induced intestinal injury, as small intestinal crypt epithelial cells are highly radiosensitive, though crypt proliferative cells possess substantial sublethal damage repair capacity, making them primary therapeutic targets. However, the broad application of many conventional molecular drugs in gastrointestinal treatment is limited by their lack of oral activity. Many nanomate-

rials exhibit good chemical stability, maintaining drug activity in the complex gastric acid environment [33].

Zhang [34] developed polydopamine-coated oral nanomedicines that effectively alleviate radiation-induced gastrointestinal syndrome, primarily targeting free radicals with superior scavenging effects compared to conventional antioxidants. Xie [35] developed graphdiyne nanoparticles (GDY NPs) as novel nanomedicines with unique physicochemical properties for effective gastrointestinal treatment. Graphdiyne possesses strong delocalized π-conjugated structures and highly reactive diacetylene bonds, enabling efficient, multi-type free radical scavenging activity. Additionally, due to their nanoscale size, GDY NPs can remain in the gastrointestinal tract for relatively extended periods. These characteristics allow GDY NPs to effectively scavenge ROS through oral administration, protecting the gastrointestinal tract from radiation damage while enabling rapid excretion and low toxicity post-treatment. Zhang [36] constructed an oral microalgae-nano integrated system combining natural spirulina (SP) and astaxanthin nanoparticles (ASXnano) to improve intestinal symptoms following radiation injury by leveraging combined microalgae and nanoparticle properties.

Therapeutic agents targeting intestinal crypt damage are the most direct and effective approach. Wei [39] provided compelling evidence that intestinal stem cells (ISCs) residing in crypts are essential for maintaining intestinal epithelial homeostasis and promoting regeneration post-injury, with the miRNA-200 family closely associated with radiation damage. miRNA-200-loaded lipid nanomedicines were shown to promote intestinal epithelium regeneration in canonical microRNA-deficient mice. Additionally, carbonized polymer dots possess ROS scavenging capacity that can reduce cellular and tissue oxidative stress damage. One team [37] prepared novel carbonized polymer dot nanomicrospheres (S-rCPDs@MPs) that were experimentally confirmed to reduce intestinal crypt cell apoptosis, alleviate mesenteric vascular endothelial damage, inhibit TGF-$ $1 mRNA expression in intestinal tissue, protect intestinal flora diversity, and provide positive effects for radiation-induced intestinal injury treatment. Other intestinal-targeted nano-injection formulations based on Prussian blue also demonstrate therapeutic efficacy [38].

In summary, multiple entry points exist for gastrointestinal radiation injury treatment, and related nanomedicine design can be optimized through various aspects including size, administration route, and targeting of important therapeutic targets to improve treatment effectiveness.

3.1.3 Treatment of Radiation-Induced Pneumonia and Pulmonary Fibrosis

The lung is one of the most severely affected organs by radiation-induced injury, with up to 20% of patients developing radiation-induced lung injury post-radiotherapy. Currently recognized radiation-induced lung injury progresses through three stages: latent phase, pneumonitis phase, and late fibrosis phase.

Radiation pneumonitis is an acute inflammatory process characterized by recruitment of various immune cells to tissues, expression of multiple cytokines, chemokines, and adhesion molecules, resulting in interstitial and alveolar space edema. Radiation fibrosis (RF) is primarily driven by accumulation of fibroblasts and myofibroblasts that extensively produce collagen and extracellular matrix (ECM) proteins, leading to impaired tissue and organ function [40]. Nanomedicine treatment principles primarily target related immune cells and ECM.

Anna [41] demonstrated that hyaluronic acid nanomedicine application induces significant changes in radiation-induced lung injury-related molecules and cells, reducing harmful radiation-induced responses in lung tissue and decreasing ECM degradation that leads to RF. Li [42] synthesized mannosylated polydopamine nanomedicines to address the inability of current RF drugs to effectively target the lungs and the difficulty of inhalation therapy to penetrate airway mucus. By targeting M2 macrophages and inhibiting the TGF-$ $1/Smad3 signaling pathway, this approach alleviates radiation-induced RF, providing a novel nanomedicine for treatment and mitigation. Zhou [43] employed antioxidant liposome-anchored mesenchymal stem cells (MSCs) by modifying drug-loaded nanocarriers on MSC membranes, promoting changes in immune cell numbers and activity (primarily neutrophils, macrophages, and regulatory T cells) to enhance therapeutic effects against radiation-induced lung injury, reduce inflammation, and ultimately prevent RF formation.

3.1.4 Treatment of Radiation-Induced Brain Injury

Up to 90% of brain cancer survivors experience radiation-induced cognitive dysfunction following radiotherapy, resulting from damaged neurovascular endothelial cells and increased blood-brain barrier permeability that leads to cognitive decline. The key to developing therapeutic agents lies in protecting cells and the blood-brain barrier to mitigate cognitive impairment caused by radiation-induced brain injury [44]. Leavitt [45] validated that nanoinjection drugs derived from human neural stem cell extracellular vesicles could alleviate radiation-induced cognitive dysfunction and neuroinflammation. Abdelkader [46] evaluated the neuroprotective effects of gold nanoparticles and α-lipoic acid mixtures against radiation-induced brain injury in rats, demonstrating that the combination produced synergistic effects that reduced oxidative stress, DNA damage, and histopathological injury more effectively than either agent alone. These research paradigms provide valuable insights for designing and developing treatments for radiation-induced brain and nervous system diseases.

3.1.5 Treatment of Radiation-Induced Kidney Injury

The hypothalamic-pituitary-adrenocortical system represents an important defensive and adaptive function in response to ionizing radiation exposure. It is widely accepted that activation of adrenocortical function during the initial phase of radiation injury constitutes a crucial anti-damage response, and

the structural and functional integrity of this system is an important factor in maintaining organismal radiation resistance. Therefore, developing drugs that protect and improve adrenocortical function post-irradiation is key to enhancing treatment efficacy. In a joint publication by Ni and Christopher [47], molybdenum-based polyoxometalate nanomedicines (POM) were reported to possess strong ROS scavenging capacity for treating radiation-induced kidney injury. Zhang [48] designed highly catalytic cysteine-protected MoS_2 nanomedicines and conducted preclinical animal studies, demonstrating that MoS_2 application improved survival rates in irradiated mice. Adhikari [7] prepared nanosized silymarin formulations (3-8 nm) and evaluated their cytotoxicity on human embryonic kidney (HEK) cells using MTT assays, analyzing cell mortality post-irradiation. The study demonstrated that nanosized silymarin provides kidney protection, particularly against γ-radiation-induced oxidative stress. These findings indicate that nanomaterials have potential for preventing and treating radiation-induced kidney diseases.

3.1.6 Treatment of Other Radiation Injuries

Radiation can cause severe damage to the reproductive system, inducing apoptosis in radiosensitive spermatogenic cells and testicular damage. In females, although ovarian radiosensitivity is lower than testicular tissue, the ovaries remain sensitive organs, with severe cases potentially leading to infertility. The novel nanomedicine MgH_2 for reproductive function damage has been evaluated in biochemical and cytotoxicity assays, showing protective effects on male Sertoli cells, spermatogonia, and round spermatozoa to preserve spermatogenesis. MgH_2 can improve radiation-induced male reproductive system damage by inhibiting mitochondria-mediated testicular germ cell apoptosis, blocking the G2/M phase, and exerting anti-inflammatory and anti-apoptotic effects. MgH_2 also demonstrates some reparative effects on ovarian radiation injury, though this was not the focus of the study [49].

Radiation dermatitis (RD) is the most common complication of radiotherapy, affecting up to 95% of cancer patients during treatment. In nuclear accidents, radiation skin injury often becomes the most common radiation disease due to inadequate timely protection. Acute RD clinical manifestations begin with edema, warmth, and typical erythema, followed by dryness, and in severe cases, skin hemorrhage and necrosis [50]. Although many existing drugs and dressings can prevent and treat RD, including trolamine, SOD-containing ointments or sprays, corticosteroids, and hyaluronic acid, they suffer from poor stability and easy inactivation during long-term storage. Yin [51] demonstrated that topically applied fullerenol nanomedicines reduced intracellular ROS production, alleviated DNA damage and apoptosis in human fibroblasts (HFF-1), and mitigated RD in mice more effectively than typical RD drugs. Zhou [52] designed multifunctional silica-cerium oxide nanomedicines targeting miRNA-129 to achieve high-quality healing of radiation-induced skin injury.

Oral mucositis is one of the most common complications in head and neck can-

cer patients receiving radiotherapy. Morsy [53] demonstrated through randomized clinical trials that topical Omega-3 nanoemulgel drugs are beneficial for improving radiation-induced oral mucositis and may potentially modulate oral microbiome dysbiosis.

Developing nanomedicines for radiation disease treatment holds significant scientific and practical value. Although nanomaterials offer numerous beneficial properties for treatment, this research remains in early stages, requiring further validation of in vivo safety and determination of the most effective administration methods to meet clinical demands.

3.2 Nanomaterials for Radionuclide Decorporation

Current drugs for promoting radionuclide excretion from the body (decorporation agents) are primarily chelating agents that form stable, non-metabolizable soluble compounds with radionuclides, facilitating excretion through natural metabolic pathways (urine and feces). For example, FDA-approved DTPA (diethylenetriaminepentaacetic acid) can be used for plutonium, americium, and curium decorporation [54]. However, conventional decontamination or decorporation drugs are sometimes inefficient or even lacking for elements such as uranium or thorium. Although existing chelators can effectively complex radionuclides in vitro, they may lack affinity and specificity in biological tissues or exhibit unfavorable pharmacokinetics, leading to inadequate dispersion efficacy or toxic side effects. Recent discoveries show that nanomedicines can be prepared to improve chelator absorption, distribution, and excretion, enhancing bioavailability and decorporation effectiveness.

3.2.1 Uranium Decorporation Hexavalent uranyl ions (UO_2^{2+}) can enter the human body through skin and mucous membranes, respiratory inhalation, and food chains, depositing in kidneys and bones where they are difficult to metabolize and excrete. The chemical and radiological toxicity of uranium causes irreversible damage to kidney function, urinary systems, DNA, and biomolecules. To date, chelator-based decorporation is considered the most effective treatment for internal uranium contamination. Since uranyl has an extremely short residence time in blood, it must be captured in the bloodstream as quickly as possible to reduce bodily deposition. For instance, metal-organic framework (MOF)-based nanomedicines can improve capture efficiency through better kinetics [55]. Hu [56] prepared water-soluble low-molecular-weight chitosan-diethylenetriaminepentaacetic acid (WSC-DTPA) nanomedicines that demonstrated good decorporation effects for internal uranium contamination, with 92.7% of the WSC-DTPA nanomedicine showing both decorporation and radioprotective effects on liver and kidney tissues in uranium-contaminated rats. Shi [57] reported novel bifunctional uranium chelators including 3,2-HOPO-modified chitosan nanomedicines (COS-HOPO), PEG-modified melanin nanomedicines (PEG-MNPs), and tri-lacunary polyoxometalates ($Na_9[A\text{-}PW_9O_{34}] \cdot 7H_2O$, PW9), achieving dual "decorporation + protection" effects.

Further research by Shi [59] confirmed that COS-HOPO is a low-toxicity nanodecorporation agent, with its tetradentate ligand COS-HOPO-4 showing better decorporation effects due to stronger uranium complexation ability. Miao [58] prepared PEG-modified melanin nanomedicines (MNPs-PEG) that demonstrated significant uranium decorporation effects in vitro and in cellular and mouse models. Bai [60] synthesized novel covalent organic nanomedicines (CON-AO) with toxicity comparable to traditional actinide chelators but superior decorporation efficacy. While these studies have achieved preliminary success in animal decorporation models, market approval and application require solving challenges in large-scale synthesis, clinical efficacy, and safety.

3.2.2 Strontium Decorporation Among Sr's 21 isotopes, 17 are radioactive. ^{85}Sr and ^{87} Sr were previously used for bone scan imaging, while ^{89}Sr is now used medically to treat bone metastases. Strontium shares similar chemical properties with calcium, and 99% of strontium entering the human body accumulates in bone, where radioactive strontium metabolizes slowly and produces continuous irradiation with serious consequences. Current strontium decorporation approaches abroad involve bone metabolism influence methods combined with chelators. Non-nano chelators with relatively high strontium decorporation efficacy include S106, S186, and traditional Chinese medicine chicken gizzard lining, while nanomedicine research for strontium decorporation remains scarce. The team led by Xu Yujie [61][62] prepared novel nanodecorporation drug chitosan-ethylenediaminetetraacetic acid (CTS-EDTA) and evaluated its decorporation effects on radioactive strontium through animal experiments. While conventional EDTA decorporation drugs primarily distribute in extracellular fluid and cannot effectively decorporate intracellular radioactive strontium, the new nanodecorporation drug can easily cross biological membrane barriers due to its biological properties, enabling decorporation of both extracellular and intracellular radioactive strontium. Studies demonstrated that the novel nanomedicine CEC-Nano showed significantly better ^{89}Sr decorporation effects than conventional drugs, with prophylactic administration showing superior efficacy. This research also provides experimental basis for further development of broad-spectrum radionuclide decorporation drugs.

To date, synthesis and preparation of nanodecorporation drugs require multifaceted optimization, and their binding affinity to radionuclides in vivo and systemic toxicity require clinical validation.

Summary and Outlook

Using common design strategies for radiation injury treatment nanomaterials, rational design of nanomedicines for various radiation injuries is achievable. However, research on nanomaterials for radiation injury treatment remains in early stages. Despite numerous beneficial properties, their development and clinical application face many challenges requiring further consideration and innovation:

(1) Designers must recognize from the outset that nanomedicines exhibit certain toxicity to humans under specific conditions. Nanomedicine particle size, shape, and surface charge are primary factors affecting toxicity and should be considered during research. Some studies have found that nanomaterials can cause cellular damage during or after uptake by elevating ROS levels, inducing oxidative stress and autophagy effects [63], which requires researchers' attention.

(2) Current research depth on nanomedicines remains relatively limited, and research strategies need updating. The radiation damage process involves multi-level complex interactions spanning subatomic, free radical, molecular, biomolecular, organelle, cellular, and even tissue levels. While free radicals and ROS occupy relatively upstream positions in the damage event chain, they are not the only important targets. The exact mechanisms of nanomedicine treatment require further elucidation, and future research must consider many important factors including immune mechanisms and the in vivo microenvironment associated with injury.

(3) Although increasing cellular and animal experiments have demonstrated the tremendous potential of nanomaterials in radiation injury treatment, large-scale application remains distant. First, nanomaterial selection and synthesis methods require optimization. Second, translation from laboratory to clinic must be advanced, including improving drug safety evaluation methods and promoting clinical trials.

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