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Nanostructured boron compounds for biomedical applications: Drug delivery, imaging, and cancer therapy

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Abstract

Nanostructured boron compounds have arisen as multifunctional materials with considerable potential in biological applications, especially in drug administration, imaging, and cancer treatment. Their distinctive physicochemical characteristics, such as elevated surface area, adjustable shape, chemical stability, and biocompatibility, render them appropriate for the development of improved nanocarriers and therapeutic medicines. Diverse synthesis methodologies, encompassing top-down and bottom-up procedures, permit meticulous regulation of size, shape, and functioning. These compounds exhibit effective functionality in targeted drug delivery, contrast enhancement for multimodal imaging, and tumor-selective therapies, including boron neutron capture therapy (BNCT). Furthermore, their capacity to amalgamate several therapeutic and diagnostic activities within a singular platform renders them exemplary candidates for combination and theranostic strategies. Notwithstanding existing hurdles concerning toxicity, regulatory frameworks, and scalable production, ongoing interdisciplinary research is anticipated to facilitate their clinical translation and enhance their application in customized medicine. This review aims to comprehensively examine the properties, synthesis methods, biomedical applications, and current challenges of nanostructured boron compounds, highlighting their potential role in the future of personalized therapy.

Keywords: Nanostructured boron; Drug delivery; Biocompatibility; Nanocarriers; Theranostics

1. Introduction

Nanostructured boron compounds have emerged as potential candidates in biological research owing to their multifunctionality. These materials hold significant value in three primary domains: medication delivery, imaging, and cancer therapy. Their structural diversity, spanning inorganic boron clusters, polyhedral boranes, boron nitride, and boronic acid-linked organics, facilitates extensive tunability in size, shape, and function [1], [2], [3].

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Importantly, recent studies have reported concrete biomedical outcomes that highlight their translational potential. For example, laser-synthesized elemental boron nanoparticles demonstrated high tumor selectivity and significant inhibition of glioblastoma growth through BNCT [18,28]. Boron nitride nanospheres functionalized with folate achieved a 2–3-fold increase in cellular uptake compared with non-functionalized systems, improving targeted chemotherapy delivery [36]. Hydroxylated boron nitride nanocarriers have also shown exceptional drug-loading efficiency, enabling dual therapeutic and diagnostic performance [4], [5], [6].

This review aims to explore the types, synthesis methods, properties, biomedical applications, and existing challenges of nanostructured boron compounds, while highlighting their potential for future clinical translation.

2. Overview of nanostructured boron compounds

Nanostructured boron materials comprise a diverse array of morphologies, each presenting distinct chemical and physical properties. This encompasses elemental boron nanoparticles, boron nanotubes, and nanoribbons, each produced by techniques that enable regulation of size, shape, and crystallinity. Principal synthesis techniques encompass chemical processing, physical procedures including laser ablation and plasma deposition, and thermodynamic treatments. Their multifunctionality, stability, and aptitude for surface modification make them especially appropriate for biomedical applications, including targeted drug delivery and precision imaging [7], [8], [9], as summarized in Table 1.

Table 1 summarizes the major types of nanostructured boron architectures, highlighting their morphology, key features, and potential applications. This summary serves as a foundational reference for Section 2, offering a structural framework for understanding how morphology influences biomedical and technological functions. Nanostructured boron materials display diverse topologies that significantly affect their chemical reactivity, mechanical properties, and biological applications.

Table 1: Varieties of Nanostructured Boron architecture: forms, attributes, and functional insights.

Nanostructure Type	Description	Key Characteristics
Boron Nanoparticles	Spherical or quasi-spherical particles composed of pure boron, typically ranging from 1–100 nm in size.	- High surface area - Enhanced chemical reactivity - Tunable particle size - Excellent for drug loading and catalytic use
Boron Nanotubes	Cylindrical hollow structures made from boron atoms arranged in a tubular form at the nanoscale.	- Outstanding mechanical strength - Electrical conductivity - High thermal stability- Promising for sensors and drug carriers
Boron Nanoribbons	Flat, ultra-thin ribbon-like 2D structures of boron with high aspect ratios and edge reactivity.	- Anisotropic electronic properties - Surface functionalization potential - Useful in nanoelectronics and biointerfaces

2.1 Types of Boron compounds

Various kinds of boron compounds are amenable to nano-formulation, including elemental boron, borides, carboranes, and boronic acid derivatives. The synthesis of these materials can be achieved using four primary methodologies: top-down procedures such as high-pressure treatment and sonication; chemical reduction utilizing boron precursors; direct deposition via thermal or laser methods; and bottom-up synthesis from atomic or molecular precursors. Each technique affects the ultimate characteristics, facilitating the meticulous design of boron nanostructures for particular biomedical applications [10], [11], [12], [13], as summarized in Table 2.

Table 2 delineates a comprehensive classification of four primary categories of boron compounds amenable to nanostructure engineering, emphasizing critical distinctions in composition, synthesis techniques, and prospective medicinal uses. This table serves as a concise sum ary of Section 2.1, providing a structured overview of the types of boron compounds suitable for nanoformulation.

Table 2: Boron compounds suitable for nanoformulation synthesis methods and biomedical relevance.

Type of Boron Compound	Description	Applicable Synthesis Methods	Effect on Nanostructure Properties	Potential Biomedical Applications
Elemental Boron	Pure boron used in nanoparticle or nanotube form.	- Top-down (e.g., sonication, high-pressure milling) - Thermal laser ablation	- Particle size and shape controllability - High chemical purity - Surface reactivity	- Drug delivery carriers - Imaging agents
Borides	Compounds of boron with metals (e.g., TiB_2, FeB).	- Chemical reduction - High-temperature bottom-up synthesis	- High hardness - Electrical conductivity - Chemical stability	- Antibacterial coatings - Bioelectronics
Carboranes	Cage-like boron-carbon clusters, often highly stable.	- Bottom-up molecular assembly - Chemical synthesis from precursors	- Exceptional thermal and chemical stability - Biocompatibility	- Boron neutron capture therapy (BNCT) - Cancer treatment vectors
Boronic Acid Derivatives	Boron compounds with $B(OH)_2$ functional groups; reactive toward diols and sugars	- Wet chemical synthesis - Functionalization on nanoparticles via post -synthetic modification	- High binding specificity to biological molecules - Excellent for surface modification	- Biosensors - Targeted drug delivery

2.2 Synthesis methods

The production of nanostructured boron materials is essential for assessing their appropriateness for biomedical applications. Boron-derived compounds, including borides, boron carbides, boron nitride, and elemental boron, can be manufactured using hydroboration, sol-gel processes, chemical vapor deposition, laser ablation, and electrochemical methods. These compounds present unique benefits: borides demonstrate elevated conductivity and catalytic efficacy, whereas boron carbide and boron nitride are recognized for their durability and stability. Functionalized variants such as boron nitride nanotubes adorned with drug delivery moieties or mesoporous architectures engineered for tumor targeting exemplify the therapeutic capabilities of these materials [8], [10], [14], [15], [16], [17], as summarized in Table 3.

Table 3 delineates the principal synthetic techniques utilized in the fabrication of nanostructured boron materials. It outlines the categories of boron-based compounds that can be synthesized via each method, along with the distinctive material characteristics relevant to biomedical applications. These include borides, boron carbide, boron nitride, and elemental boron. Select structures, such as functionalized boron nitride nanotubes and mesoporous boron frameworks, highlight the therapeutic promise of these nanomaterials in drug delivery and tumor targeting. Accordingly, Table 3 serves as a structured summary of Section 2.2, correlating each synthesis method with compound types and their biomedical utility.

Table 3: Synthesis techniques for nanostructured Boron compounds: methods, products, and biomedical significance.

Synthesis Method	Resulting Compounds	Acquired Properties	Examples of Biomedical Applications
Hydroboration	Boron nitride, boron carbide, borides	- Formation of B–H bonds - Potential for chemical surface modification	Fabrication of functionalized boron nitride nanotubes for drug delivery

Sol-Gel Process	Nano boron oxides, boron-based gels	- Formation of mesoporous structures - High uniformity - Suitable for biomolecule loading	Development of tumour-targeted drug delivery systems
Chemical Vapor Deposition (CVD)	Boron carbide, boron nitride	- High crystalline - Precise control over shape and thickness	Formation of functional nanoscale coatings on biomedical surfaces
Laser Ablation	Elemental nanoboron, boron carbide	- High-purity particles - Tunable size and dispersion	Preparation of nanoscale imaging agents
Electrochemical Methods	Metallic borides (nanostructured)	- Precise surface structuring - Potential for electrochemical modification	Development of conductive bioelectrodes for therapy or stimulation

3. Properties of nanostructured Boron

Nanostructured boron compounds exhibit various chemical, physical, and biological properties that render them appropriate for medical applications. Their elevated surface area, reduced density, and robust mechanical and thermal stability establish a basis for multifunctionality. They demonstrate stable bonding and reactive capability for drug conjugation at the chemical level. They exhibit excellent dispersibility, configurable dimensions, and compatibility with imaging and delivery agents from a physicochemical perspective. Toxicological assessments indicate minimal cytotoxicity and advantageous clearance characteristics, bolstering their suitability for improved treatment [5], [18], [19], [20], [21], as summarized in Table 4.

Table 4 presents a systematic summary of the fundamental characteristics of nanostructured boron and their direct relevance to biomedical applications, focusing on targeted drug administration, diagnostic imaging, and theranostic integration. It serves as a summary of Section 3, highlighting the core properties and their biomedical implications.

Table 4: Analytical overview of nanostructured Boron properties.

Property Category	Scientific Description	Biomedical Relevance	Analytical Insight
Surface Area	High surface-to-volume ratio due to nanoscale morphology.	Enhances drug loading and target interaction.	Facilitates functionalization and targeted delivery.
Density	Lower bulk density enables lighter structures.	Suitable for injectable or aerosolized systems.	Improves biodistribution and compatibility with soft tissues.
Mechanical Stability	Maintains structure under physiological stress.	Useful for implantable or sustained-release systems.	Ensures durability in dynamic biological environments.
Thermal Stability	Resists degradation under heat or metabolic processes.	Supports use in photothermal therapies and temperature-sensitive treatments.	Maintains functionality in extreme or prolonged exposures.
Chemical Reactivity	Forms stable bonds with drugs or ligands.	Enables precise conjugation of therapeutic agents.	Critical for controlled and targeted therapy.
Physicochemical Flexibility	Allows control over size, shape, and dispersibility.	Supports effective circulation and tissue penetration.	Enable customization for multiple administration routes.
Biocompatibility	Low toxicity and favorable clearance behavior.	Safe for systemic use with minimal long-term risk.	Supported by toxicological evaluations in biological models.

Multifunctionality	Integrates therapeutic, diagnostic, and structural roles.	Enables combined treatment and imaging (theranostics).	Ideal for precision medicine and next-generation nanomedicine platforms.

3.1 Systems. chemical properties

These materials have remarkable chemical stability, facilitating extended in vivo retention without considerable degradation. Their adaptable bonding ability enables the attachment of medicinal or diagnostic substances, while their antioxidant characteristics aid in cellular protection. Their multifunctional characteristics enable a single chemical to serve as a transporter, imaging agent, and medicinal entity [7], [22], [23], [24].

3.2 Physical properties

The physical characteristics of nanostructured boron, including nanoscale dimensions, extensive surface area and adjustable porosity, provide accurate drug encapsulation and regulated release. Their structural rigidity, low density, and corrosion resistance facilitate their application in extreme biological conditions. These properties play a crucial role in contemporary drug delivery and cancer treatment methods [3], [25], [26].

3.3 Biocompatibility

Biocompatibility tests demonstrate that laser-synthesized elemental boron nanoparticles, even at elevated concentrations, do not elicit harmful effects and are effectively eliminated from biological systems. Boron carbides and boron carbon oxynitride particles demonstrate comparable low-toxicity characteristics and can be monitored by multimodal imaging techniques. Despite ongoing obstacles, such as nanoparticle aggregation, surface modification, and functionalization techniques are demonstrating efficacy in improving their biological performance [5], [18], [27], [28].

4. Drug delivery systems

Nanostructured boron compounds provide essential characteristics that render them suitable for medication delivery systems. Their homogeneous particle size, extensive surface area, and advantageous biological interaction facilitate both passive and active targeting methods. Boron nitride nanotubes, boron carbide, and boron-doped graphene have been utilized to enhance the targeting accuracy of chemotherapeutics. Functionalization with ligands like folate or hyaluronic acid increases selectivity and absorption by tumor cells [29], [30], [31], [32], as illustrated in Figure 1.

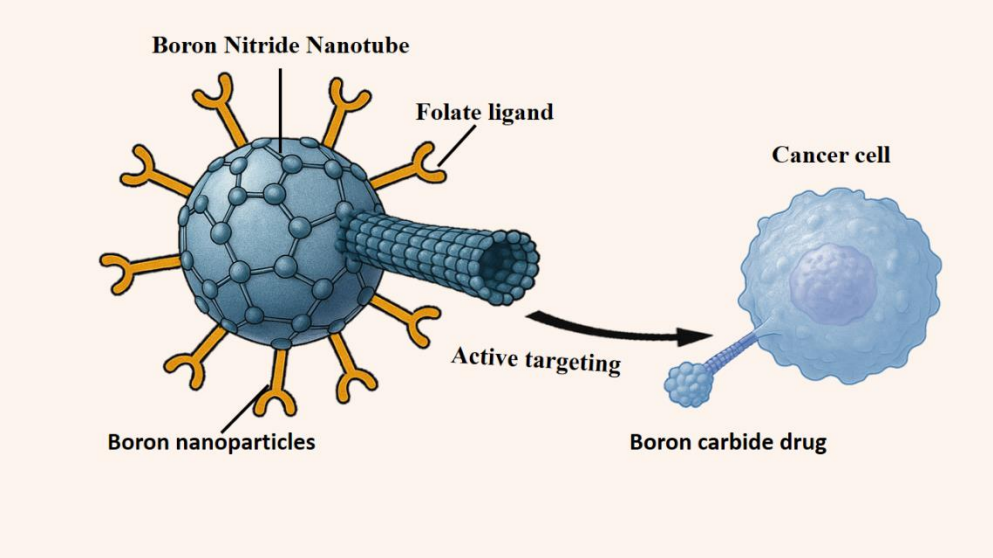

Figure 1. Nanostructured Boron compounds for targeted pharmaceutical drug delivery.

4.1 Mechanisms of drug delivery

These molecules provide regulated drug release and enhanced bioavailability by utilizing significant sorption capacity, chemical stability, and surface functionalization. Nanotubes and hollow nanospheres can encapsulate pharmaceutical compounds, releasing them in response to specified stimuli such as pH or temperature. Surface ligands facilitate preferential attachment to cancer cells, thereby permitting focused therapeutic interventions while reducing damage to healthy tissue [33], [34], [35], [36].

4.2 Nanocarriers for drug delivery

Four principal categories of boron nanocarriers are recognized: elemental boron structures, boron organic frameworks, boron oxides, and boron nitride variants. Each offers distinct benefits for mechanical strength, drug-loading capability, and biocompatibility. Recent advancements feature hydroxylated boron nitride (OH-BN) with remarkable drug-loading capacity and surface-engineered composites that provide multiple therapeutic and diagnostic functions within a single platform [35], [37], [38].

4.3 Targeted Drug Delivery

Targeted administration is accomplished via active ligands that identify overexpressed receptors on cancer cells, like folate or transferrin receptors. Boron-based nanocarriers exhibit effective internalization by receptor-mediated endocytosis, with acidic intracellular conditions initiating drug release. These technologies improve therapy accuracy and diminish systemic adverse effects, highlighting their significance in oncology [1], [39], [40].

5. Imaging applications

Boron nanostructures play a crucial role in imaging technologies owing to their distinctive optical, magnetic, and neutron absorbing characteristics. They function as contrast agents across various modalities, including MRI, optical fluorescence, and photoacoustic imaging. Functionalized boron compounds, adorned with gadolinium or europium, improve signal specificity and facilitate multimodal imaging techniques that aid in diagnostic and treatment evaluation [41], [42], [43], [44], as illustrated in Figure 2.

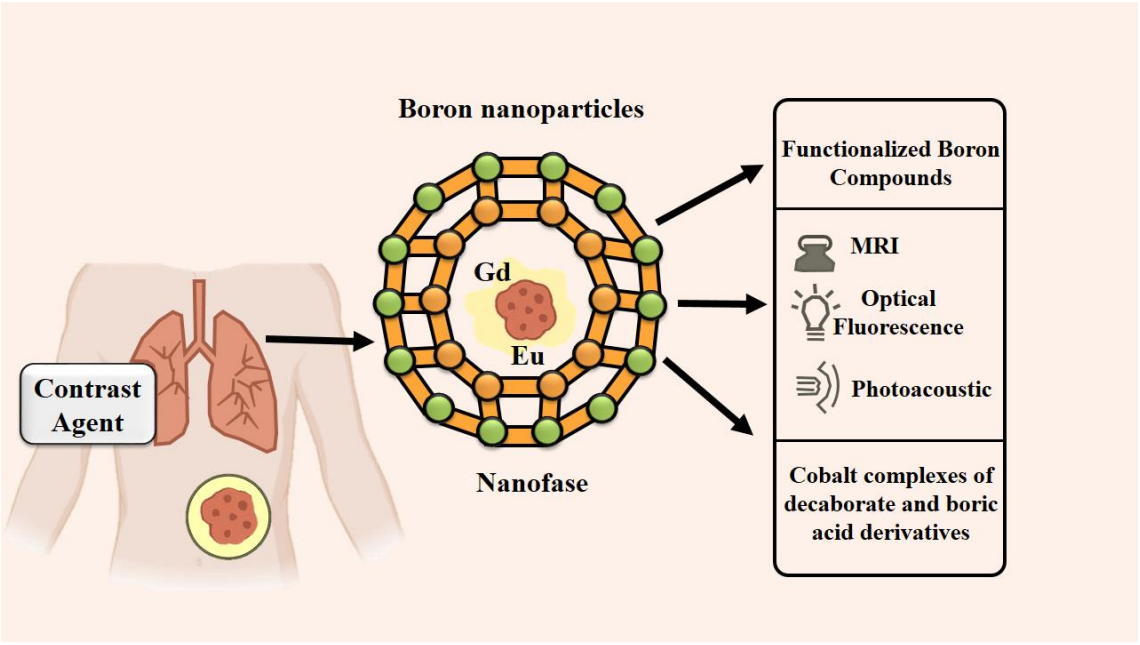

Figure 2. Imaging applications of Boron nanostructures.

5.1 Contrast Agents in medical imaging

Boron-based contrast agents enhance resolution and targeting in imaging modalities by their high atomic number, adjustable surface chemistry, and compatibility with biological systems. They facilitate precise tumor localization and evaluation, especially when used alongside boron neutron capture treatment (BNCT). Functionalized nanoparticles, including decaborate cobalt complexes and boric acid derivatives, offer improved imaging capabilities for real-time monitoring and therapeutic evaluation [45], [46], [47], [48], [49].

6. Cancer therapy applications

Boron compounds possess unique anticancer properties that have been investigated extensively in recent years. They can disrupt cellular metabolism by interfering with nutrient transport and may induce apoptosis and inhibit proliferation and migration in malignant cells. Nanostructured boron compounds offer additional advantages for cancer therapy in their capacity to carry and deliver drugs in a targeted manner and to enhance imaging techniques for tumour visualization [50], [51], [52], [53], [54].

Neutron-capturing boron compounds have attracted interest for the selective destruction of tumour cells by boron neutron capture therapy (BNCT). Irradiation with neutrons generates ionizing alpha particles and 7Li ions that have a very short travelling distance and can selectively kill tumour cells without extensive damage to the surrounding tissues [2], [55], [56], [57], [58].

Boron compounds are increasingly applied as effective adjuvants for radiation therapies. Boron compounds can cause multiple cytogenetic damage, including DNA breaks, base damage and crosslinks, and assist radiotherapy with cell-killing mechanisms. Furthermore, boron-associated drugs can work synergistically with photothermal therapy to enhance tumour cell necrosis, leading to enhanced anticancer efficacy. These properties are demonstrated by their specific binding to sialic acid overexpressed on the surface of several cancer cells. BSH and BPA are the two boron drugs approved for BNCT. Several clinical trials have demonstrated the effectiveness of BPA and BSH for treating different types of incurable tumours. Nanostructured boron compounds increase the repertoire of boron delivery agents available for cancer therapy, facilitating the selective destructuring of cancerous tumours [56], [59], [60], [61], as illustrated in Figure 3.

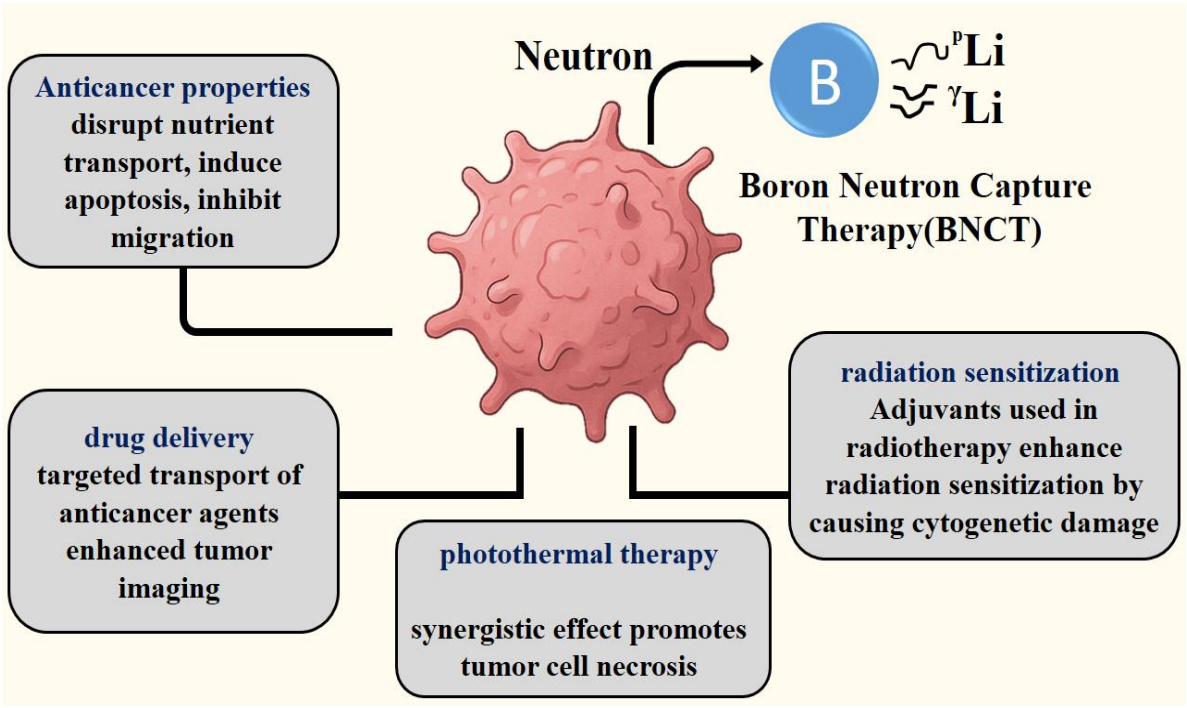

Figure 3. Applications of Boron compounds in cancer therapy.

6.1 Mechanisms of Action against Cancer Cells

The boron-containing materials are used for cancer treatment, such as boron neutron capture therapy (BNCT), anticancer drugs, genetic engineering, and boron delivery systems. The selective localization and accumulation of boron in cancer cells are one of the key challenges that should be solved before these materials can be used for biomedical applications. Nanostructured boron compounds are versatile for nanomedicine because they integrate drug delivery, imaging, and cancer therapy into the same platform [62], [63], [64], [65], [66], [67].

Many investigations focus on drug delivery systems and imaging applications, whereas high-potential cancer therapy systems are still under development. As future development, anticancer drug boron compounds should exhibit combined boron delivery and stimulation in the same nanostructured compound. Development based on existing boron compounds is highly anticipated to realize a cancer treatment nanoplatform for practical applications. The unique characteristics of nanostructured boron compounds make them a multifunctional platform for drug delivery, imaging, and cancer therapy. Such multifunctionality is not available with other nanostructured materials. Specific boron effects in cancer therapy are achieved with boron compounds [68].

6.2 Combination therapies

Cancer is complex and often adapts to treatment, necessitating combination therapies to enhance therapeutic effectiveness. Such strategies involve either coupling different therapeutic agents or integrating multiple modalities into a single delivery system, enabling simultaneous treatments in a localized manner. Nanostructured boron compounds are highly advantageous platforms for implementing combination therapies, given their unique ability to concurrently serve as drug delivery and imaging agents, in addition to their inherent anticancer activity. Studies have demonstrated the efficacy of polymer-coated non-(10) B-enriched boron nanocarriers for simultaneous doxorubicin delivery and fluorescence imaging, highlighting the potential for integration with boron neutron capture therapy (BNCT). Similarly, laser-synthesized elemental boron nanoparticles and polymer-coated boron carbon oxynitride nanocarriers have shown promise in efficiently delivering conventional chemotherapy and photodynamic agents, respectively, underlining the multifaceted therapeutic capabilities of these materials [47], [49], [53], [69], [70], [71], [72].

Given the high toxicity and side effects associated with conventional chemotherapy, the development of new treatment strategies prioritizes the use of boron nanostructures as both therapeutic and diagnostic (termed boron theranostic) agents. The integration of boron's imaging and anticancer properties into a single platform expands the possibilities for designing novel combination therapies, underscoring the versatility and clinical potential of nanostructured boron compounds in enhancing cancer treatment outcomes [73], [74], [75], [76].

6.3 Clinical trials and outcomes

Boron compounds have been exploited extensively for neutron capture therapy. The idea behind this strategy is to deliver boron to the tumor in a targeted and efficient manner before treating the tissue with a neutron beam to create a radiation-enhanced tumor environment. Several clinical trials involving boronated compounds such as BSH, BPA, BPA-fructose, and L-BPA are listed on clinicaltrials.gov. The main issue is that these compounds must be administered in kilogram-scale quantities to meet the minimum boron concentration in the tumor tissue, which challenges their applicability and underscores the need for efficient delivery agents [2], [77], [78], [79], [80], [81], [82].

Liposomes can carry high amounts of boron compounds and additional therapeutic agents, and their surfaces may be functionalized with targeting moieties. Consequently, numerous studies have been conducted on liposome-based formulations. Cell-derived nanosystems may assist in overcoming limitations related to biocompatibility, purity, and pharmacokinetics affecting synthetic formulations. However, challenges remain, including batch-to-batch variability, scaling issues, and the lack of standardized purification and characterization guidelines. Combining cell-derived vesicles with synthetic nanoparticles in hybrid systems offers a potential solution by incorporating the advantages of both components. Most investigations focus on evaluating efficacy in vivo after irradiation. Unfortunately, limited access to suitable neutron irradiation facilities hinders rapid clinical translation and testing of new boron-vehiculating nanosystems [47], [49], [83], [84], [85].

7. Challenges and limitations

7.1 Toxicity and safety concerns

One of the primary limitations is the potential toxicity of these materials. Although boron-based nanostructures can be engineered to enhance biocompatibility, they may still pose risks to both human health and the environment. The degree of toxicity depends on multiple factors including the synthesis method, dosage, route of administration, and duration of exposure. While surface modification and functionalization techniques can help mitigate some of these risks, they do not eliminate them. This ongoing concern significantly affects their clinical acceptance.

7.2 Regulatory barriers

There is a noticeable gap in regulatory frameworks specifically tailored for nanotechnology-based medical products. Despite following general drug approval procedures, the lack of specialized guidelines for nanostructured materials complicates the approval process. Additionally, due to the novelty of boron-based systems, there is limited expertise available for conducting long-term safety evaluations. The absence of standardized synthesis methods can also lead to inconsistencies in product quality, making it difficult to ensure reproducibility and reliability in clinical use.

7.3 Scalability and manufacturing limitations

Large-scale nanostructured boron compound production is difficult and expensive. Traditional synthesis is complicated, time-consuming, and expensive. Laser-based synthesis in liquids and polymer coating of boron particles may improve stability and biocompatibility. These approaches need more development to suit clinical and industrial scaling needs. For broad medical application, boron-based nanomaterials must be consistently high-quality, safe, and efficacious.

8. Future Directions

Nanostructured boron compounds will be studied for biological uses and enhanced synthesis. Creating boron nitride nanosheets with near-infrared responsiveness and high photoluminescence can improve cancer treatment and multimodal imaging. Nanostructures with specific chemical and physical properties can be synthesized via laser ablation, chemical etching, and transformation from bulk boron. These materials' biocompatibility, sustained circulation, and great selectivity make them promise for targeted medication delivery and diagnostic imaging. Their roles in BNCT and multifunctional treatment platforms are growing. Interdisciplinary research has shown new medicinal systems based on boron-containing molecules. These cross-disciplinary advances should lead to novel medical, pharmacological, and other uses.

9. Conclusion

In conclusion, nanostructured boron compounds represent a versatile and powerful platform in biomedicine, combining drug delivery, imaging, and cancer therapy within a single material system. Evidence from preclinical studies highlights their ability to achieve enhanced drug uptake, improved imaging contrast, and tumor-selective destruction in BNCT, with minimal toxicity under controlled conditions. Among their diverse applications, BNCT and multifunctional nanocarriers currently stand out as the most promising translational directions, demonstrating reproducible tumor suppression and theranostic capability.

Nevertheless, significant barriers remain. Clinical application is limited by toxicity concerns at higher doses, the absence of standardized regulatory guidelines, and scalability challenges in nanoparticle synthesis and functionalization. These issues must be addressed before boron nanostructures can move beyond experimental use.

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