Copper Nanoparticles in Cancer Care: From Bench to Bedside

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Abstract- ***Copper nanoparticles (CuNPs) have emerged as a groundbreaking tool in cancer therapy, attributed to their exceptional physicochemical properties, biocompatibility, and versatility for multifunctional applications. They offer unique advantages such as high surface reactivity and the ability to be tailored for specific biological interactions, making them ideal for targeted cancer therapies and diagnostics. This review delves into the synthesis techniques, diverse mechanisms of action, and the wide array of therapeutic applications of CuNPs in oncology. Furthermore, it addresses the critical translational challenges, including toxicity, scalability, and regulatory barriers, which must be overcome to achieve clinical success. By effectively bridging the gap between innovative laboratory research and practical clinical implementation, CuNPs represent a transformative potential to revolutionize cancer care, paving the way for safer, more efficient, and personalized treatment strategies.***

Index Terms- ***Copper Nanoparticles, Nanomedicine Applications, Targeted Drug Delivery, Cancer Therapy, Photothermal and Chemotherapy.***

I. INTRODUCTION

Cancer continues to be a leading cause of death worldwide, underscoring the urgent need for novel and effective therapeutic strategies [1], [2]. Conventional treatments, including chemotherapy and radiotherapy, while life-saving, often suffer from significant drawbacks, such as lack of specificity and detrimental side effects on healthy tissues [3], [4]. Nanotechnology has revolutionized cancer treatment by offering precise and targeted solutions, minimizing harm to non-cancerous cells [5], [6]. Within this domain, copper nanoparticles (CuNPs) have gained particular attention due to their multifaceted properties, such as high reactivity, ease of surface modification, and catalytic activity [7], [8], [9]. These attributes enable their application in targeted drug delivery, enhanced imaging techniques for better tumor visualization, and innovative therapeutic modalities such as photothermal and photodynamic therapies [10], [11]. Furthermore, CuNPs can be engineered to selectively induce oxidative stress in cancer cells, triggering apoptosis while sparing normal cells [8], [12], [13]. With continued advancements in nanotechnology and interdisciplinary research, CuNPs hold the promise of not only augmenting existing therapies but also enabling a new era of personalized and efficient cancer care [11], [14], [15]. This review explores the transformative journey of CuNPs from laboratory research to clinical applications, examining their potential to overcome the limitations of traditional cancer treatments. It also highlights the challenges associated with their clinical translation, including issues of toxicity, scalability, and regulatory compliance.

II. PROPERTIES AND SYNTHESIS OF COPPER NANOPARTICLES

Copper nanoparticles (CuNPs) are characterized by remarkable properties that make them highly valuable for biomedical applications. Their high surface-to-volume ratio enables enhanced interaction with biological molecules, increasing their efficacy in drug delivery and other therapeutic roles [10], [13], [16]. The plasmonic resonance of CuNPs allows them to be utilized in advanced imaging techniques and photothermal therapies, where they can efficiently convert light into heat for targeted cancer treatment [11], [15]. Additionally, their catalytic activity plays a critical role in generating reactive oxygen species (ROS), which can selectively induce cancer cell apoptosis [8], [17].

The synthesis of CuNPs can be broadly categorized into several methods, each tailored to achieve specific nanoparticle characteristics. These include:
Chemical Methods: Chemical synthesis of copper nanoparticles typically involves the reduction of copper salts such as copper sulfate or copper chloride using a reducing agent, often in the presence of stabilizing agents to prevent nanoparticle aggregation

[18], [19]. The choice of reducing agents, which may include hydrazine, sodium borohydride, or ascorbic acid, plays a critical role in controlling the size, shape, and uniformity of the nanoparticles [20], [21]. Stabilizers such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), or citrates are commonly added to maintain colloidal stability and prevent the particles from clumping together [14], [22]. The reaction conditions, including pH, temperature, and concentration, significantly influence the final properties of the CuNPs [23], [24]. This method is widely used due to its simplicity and cost-effectiveness, enabling the production of CuNPs at various scales for potential biomedical applications [25], [26]. However, careful optimization is required to minimize the presence of residual chemicals and ensure biocompatibility for therapeutic uses [27], [28].

Physical Methods: Physical synthesis techniques for copper nanoparticles (CuNPs) involve processes that rely on physical forces or high-energy inputs to produce nanoparticles with controlled size and properties [20], [29]. Techniques like laser ablation and thermal decomposition are prominent in this category. Laser ablation involves focusing a high-energy laser beam onto a copper target submerged in a suitable liquid medium. This process vaporizes the copper, leading to the formation of nanoparticles in the liquid. The parameters of the laser, such as wavelength, pulse duration, and energy, can be adjusted to control the size and distribution of the nanoparticles [13], [20], [25]. Thermal decomposition, on the other hand, involves the breakdown of copper-containing compounds under high temperatures in the presence of stabilizing agents. This method is advantageous for producing CuNPs with high purity and uniformity [20], [30]. Physical methods are often favoured for their ability to avoid chemical contaminants, making them suitable for biomedical applications [26], [31]. However, they may require sophisticated equipment and are often more energy-intensive compared to chemical or green synthesis methods.

Green Synthesis: Green synthesis of copper nanoparticles (CuNPs) leverages biological systems such as plant extracts, bacteria, fungi, and algae to create eco-friendly nanoparticles with reduced toxicity. This method avoids harmful chemicals and focuses on sustainable practices, making it an attractive option for biomedical applications [26], [32]. Plant extracts contain natural reducing agents, such as phenolics, flavonoids, and alkaloids, which facilitate the reduction of copper ions into nanoparticles while simultaneously stabilizing them [29], [33]. Similarly, microorganisms like bacteria and fungi produce enzymes and metabolites that act as natural reducing and capping agents, ensuring biocompatibility [34], [35]. Green synthesis not only minimizes environmental impact but also enhances the biocompatibility of CuNPs, reducing the risk of adverse biological reactions. Additionally, this approach allows for the incorporation of bioactive compounds from plants or microbes, potentially imparting therapeutic properties to the nanoparticles. The scalability of green synthesis and its alignment with principles of green chemistry make it a promising avenue for producing CuNPs suitable for clinical applications in cancer care [8], [21], [32].

The synthesis method chosen for copper nanoparticles (CuNPs) is a critical determinant of their physicochemical properties, including size, shape, and surface characteristics. These attributes play a pivotal role in defining the nanoparticles' interaction with biological systems and their overall therapeutic performance. For instance, smaller nanoparticles with a higher surface-to-volume ratio typically exhibit enhanced cellular uptake and bioactivity, making them more effective in targeted drug delivery [13], [36]. Similarly, the shape of CuNPs, whether spherical, rod-like, or cubic, influences their optical and catalytic properties, which are crucial for imaging and therapeutic applications such as photothermal therapy [37], [38]. Surface characteristics, including charge and functional groups, impact nanoparticle stability, biodistribution, and biocompatibility, directly affecting their efficacy and safety profile. Therefore, tailoring the synthesis method to achieve specific properties enables the optimization of CuNPs for targeted biomedical applications, enhancing their potential in cancer therapy and other medical interventions [8], [39], [40].

III. MECHANISMS OF ACTION IN CANCER THERAPY

CuNPs exhibit multiple mechanisms that contribute to their anticancer activity, encompassing a wide range of biochemical and physical interactions that target cancer cells selectively while minimizing harm to healthy tissues [8], [21]. These mechanisms leverage the unique properties of CuNPs, including their ability to induce oxidative stress, disrupt essential metabolic processes, and serve as multifunctional agents in advanced therapeutic modalities like photothermal and photodynamic therapies [41], [42]. Furthermore, CuNPs can be tailored for precision drug delivery, enhancing the therapeutic index of existing treatments. Together, these mechanisms position CuNPs as a versatile and potent tool in the fight against cancer, offering opportunities for synergistic and innovative treatment approaches [13], [40].

Induction of Reactive Oxygen Species (ROS): Copper nanoparticles (CuNPs) play a pivotal role in cancer therapy through the induction of reactive oxygen species (ROS), which are highly reactive molecules containing oxygen. The catalytic activity of CuNPs facilitates the conversion of intracellular oxygen into ROS, such as superoxide anions, hydrogen peroxide, and hydroxyl radicals. Elevated levels of ROS disrupt the redox homeostasis in cancer cells, leading to oxidative stress [43], [44]. This oxidative stress damages critical cellular components, including lipids, proteins, and DNA, impairing cellular functions and triggering apoptotic pathways. Notably, cancer cells are more vulnerable to oxidative stress due to their already elevated basal ROS levels compared to normal cells, making them selectively susceptible to CuNP-induced apoptosis [21], [45]. Additionally, the generation of ROS by CuNPs can synergize with other therapies, such as chemotherapy and radiotherapy, enhancing their efficacy [11], [45]. The ability of CuNPs to target cancer cells while sparing normal cells highlights their potential as a promising therapeutic agent. However, the precise modulation of ROS levels is crucial to minimize potential off-target effects and toxicity in healthy tissues, underscoring the need for careful design and optimization of CuNP-based treatments [8], [11], [41].

Disruption of Cellular Metabolism: Copper ions, released from copper nanoparticles (CuNPs), play a critical role in disrupting the metabolic processes of cancer cells, significantly impairing their growth and proliferation. Cancer cells exhibit a heightened metabolic activity to sustain rapid division and survival under stressful microenvironments [15], [42]. Copper ions interfere with key metabolic pathways, including glycolysis, oxidative phosphorylation, and lipid metabolism, leading to energy depletion and reduced biosynthetic capabilities [42]. For instance, copper can inhibit enzymes critical to the electron transport chain, causing mitochondrial dysfunction and the subsequent loss of ATP production [15], [41]. Additionally, the accumulation of copper ions induces endoplasmic reticulum stress, disrupting protein synthesis and folding, which further hampers cancer cell viability. These metabolic disruptions render cancer cells more susceptible to apoptosis and necrosis, providing a dual mechanism of action alongside other therapeutic approaches. Importantly, the selectivity of CuNPs in targeting cancer metabolism while sparing normal cells underscores their potential as a therapeutic tool. This metabolic interference, combined with CuNPs' other anticancer properties, highlights their versatility in overcoming tumor growth and resistance mechanisms [17], [42], [45].

Photothermal and Photodynamic Therapy: Copper nanoparticles (CuNPs) are highly effective in photothermal and photodynamic therapy, offering a targeted approach to cancer treatment [21], [46], [47]z. In photothermal therapy, CuNPs absorb light, typically in the near-infrared (NIR) region, and convert it into localized heat. The efficiency of this heat generation depends on the plasmonic properties of the nanoparticles, which can be tuned during their synthesis. This localized hyperthermia selectively destroys tumor cells while minimizing damage to surrounding healthy tissues [11], [47], [48]. Photodynamic therapy, on the other hand, involves the generation of reactive oxygen species (ROS) when CuNPs are exposed to light in the presence of oxygen [13], [21]. The ROS induce oxidative stress, leading to cell membrane disruption, protein damage, and DNA fragmentation, ultimately causing apoptosis or necrosis in cancer cells. Combining these therapies with CuNPs offers a synergistic effect, enhancing their overall therapeutic efficacy [17], [49]. Furthermore, the ability to functionalize CuNPs with targeting ligands or biomolecules ensures precise delivery to tumor sites, reducing off-target effects. These

modalities demonstrate the versatility of CuNPs in offering non-invasive and efficient cancer treatments [8], [41].

Drug Delivery Vehicles: Copper nanoparticles (CuNPs) serve as highly versatile platforms for drug delivery, with the capability to be functionalized for carrying chemotherapeutic agents [8], [39]. The surface of CuNPs can be modified with ligands, antibodies, or polymers, enabling precise targeting of cancer cells while sparing healthy tissues. This functionalization enhances drug delivery efficiency by improving the stability, solubility, and bioavailability of the therapeutic agents [8], [10], [32]. CuNPs can encapsulate drugs or conjugate them directly on their surface, facilitating controlled and sustained drug release at the tumor site. This targeted delivery reduces systemic toxicity and minimizes off-target effects, addressing one of the major limitations of conventional chemotherapy [8], [21], [40]. Additionally, the inherent catalytic and ROS-generating properties of CuNPs can synergize with the delivered drugs, enhancing their cytotoxic effects on cancer cells [44], [50]. Emerging research also explores the use of CuNPs in combination therapies, where they act as dual agents for drug delivery and photothermal or photodynamic therapy, further amplifying therapeutic outcomes. These multifaceted capabilities position CuNPs as promising candidates for next-generation drug delivery systems in oncology [21], [44].

IV. PRECLINICAL APPLICATIONS

Preclinical studies have demonstrated the potential of CuNPs in various oncological applications, highlighting their role as transformative agents in cancer care. These studies have revealed the diverse functionalities of CuNPs, including their ability to serve as dual-purpose theranostic tools, targeted therapy agents, and enhancers in combination therapies [17], [39]. By leveraging their unique properties such as high catalytic activity, ROS generation, and customizable surface functionalization, CuNPs have shown promise in improving therapeutic specificity and efficacy while minimizing side effects [8], [21]. Furthermore, preclinical investigations have underscored their potential to overcome traditional treatment challenges, such as drug resistance and limited tumor penetration. These findings set the stage for the integration of CuNPs into innovative treatment paradigms, bridging the gap between laboratory discoveries and clinical applications. However, the transition to human trials requires addressing critical issues like biocompatibility, scalability, and regulatory compliance to ensure safety and effectiveness [8], [32].

Theranostics: Copper nanoparticles (CuNPs) represent a cutting-edge advancement in the field of theranostics, integrating diagnostic and therapeutic functions into a single platform. Their unique physicochemical properties allow them to serve as contrast agents in imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), and photoacoustic imaging, facilitating precise tumor localization [15], [47]. Simultaneously, CuNPs can deliver therapeutic agents or induce therapeutic effects, such as photothermal or photodynamic therapy, directly at the tumor site. This dual functionality significantly enhances treatment efficiency by enabling real-time monitoring of therapeutic outcomes and dynamic adjustment of treatment strategies [11], [21], [41], [47]. The ability to functionalize CuNPs with targeting ligands or biomarkers further improves specificity, ensuring that the nanoparticles preferentially accumulate in tumor tissues while sparing healthy cells [8], [51]. Moreover, theranostic CuNPs can be engineered for controlled and sustained release of drugs, reducing systemic toxicity and improving patient compliance. The integration of diagnostic and therapeutic capabilities within a single nanoparticle platform exemplifies the potential of CuNPs to revolutionize personalized oncology, paving the way for non-invasive, precise, and efficient cancer care [47], [52].

Targeted Therapy: Functionalized copper nanoparticles (CuNPs) have revolutionized targeted cancer therapy by significantly enhancing the specificity of drug delivery to cancer cells. This is achieved through surface modifications that enable CuNPs to recognize and bind selectively to molecular markers overexpressed on cancer cells [8], [21], [40]. These functionalizations often involve conjugating CuNPs with ligands, antibodies, peptides, or small molecules that exhibit high affinity for cancer-specific receptors. Once bound to the target cells, CuNPs

facilitate localized delivery of chemotherapeutic agents, reducing systemic drug distribution and minimizing adverse effects on healthy tissues [11], [32], [41]. Moreover, the ability of CuNPs to penetrate tumor microenvironments ensures efficient drug delivery even to hypoxic or densely packed tumor regions that are often inaccessible to conventional therapies. This enhanced targeting capability not only improves the therapeutic efficacy of the encapsulated or conjugated drugs but also reduces the required dosage, thereby lowering toxicity risks. By integrating advanced targeting strategies, CuNPs are paving the way for safer and more effective cancer treatments [11], [41], [53].

Combination Therapy: Copper nanoparticles (CuNPs) are emerging as potent agents in combination cancer therapies, enhancing the efficacy of established treatments such as chemotherapy, radiotherapy, and immunotherapy [8], [11], [15]. By acting as sensitizing agents, CuNPs improve the responsiveness of cancer cells to these therapies, overcoming common resistance mechanisms. For instance, in chemotherapy, CuNPs can facilitate more effective drug delivery and synergize with chemotherapeutic agents by inducing oxidative stress or disrupting cellular metabolism [11], [41], [45]. In radiotherapy, CuNPs enhance radiation-induced damage by generating reactive oxygen species (ROS) and amplifying DNA damage within cancer cells, thereby increasing therapeutic efficacy at lower radiation doses [46], [54]. Similarly, CuNPs complement immunotherapy by modulating the tumor microenvironment to make it more amenable to immune cell infiltration and activation [55]. The multifunctional nature of CuNPs allows them to be tailored for specific combinations, enabling personalized treatment regimens that maximize therapeutic outcomes while minimizing systemic toxicity [11], [15], [56]. Ongoing research continues to refine the integration of CuNPs into combination therapies, paving the way for innovative approaches that leverage their unique properties to combat cancer more effectively [26], [54].

V. CHALLENGES IN CLINICAL TRANSLATION

Despite promising preclinical results, the translation of CuNPs to clinical settings faces several hurdles that need to be addressed for effective clinical implementation. Addressing these challenges will be crucial to bridging the gap between preclinical success and clinical application of CuNPs in cancer therapy. These challenges are multifaceted and involving:

Toxicity and Biocompatibility: High doses of copper nanoparticles (CuNPs) have been shown to cause toxicity in healthy tissues, presenting a critical barrier to their clinical application. This toxicity is primarily attributed to the generation of excessive reactive oxygen species (ROS) and the release of copper ions, which can disrupt normal cellular functions and induce oxidative stress in non-cancerous cells. Key organs such as the liver, kidneys, and spleen, which are involved in nanoparticle metabolism and clearance, are particularly vulnerable to such effects [42], [49], [56]. Furthermore, the prolonged accumulation of CuNPs in the body can lead to inflammatory responses, cellular damage, and long-term health complications [8], [57], [58]. To mitigate these risks, dose optimization strategies are essential. This involves determining the therapeutic window- the range of doses that maximize anticancer efficacy while minimizing harm to healthy tissues. Advanced functionalization techniques, such as surface coating with biocompatible materials and the use of targeting ligands, can enhance the selective delivery of CuNPs to tumor sites, reducing off-target effects. Additionally, the development of controlled-release formulations and biodegradable CuNPs may further improve their safety profile. Rigorous preclinical studies and in vivo toxicity assessments are crucial to refine these approaches and establish safe dosing guidelines, ultimately paving the way for the clinical translation of CuNPs in cancer therapy [8], [11], [41], [42], [59].

Stability and Scalability: Ensuring the stability of copper nanoparticles (CuNPs) during storage and large-scale production is a pivotal concern in their clinical translation [39]. Stability encompasses maintaining the physicochemical properties of CuNPs, such as size, shape, and surface functionality, over extended periods and under varying environmental conditions [8], [20], [26]. Factors like oxidation, aggregation, and degradation can compromise their effectiveness and safety, posing significant hurdles for therapeutic applications [60]. To address these challenges, researchers are exploring advanced

stabilization techniques, such as coating CuNPs with biocompatible materials like polymers, lipids, or silica, which can shield them from environmental degradation [13], [20], [61]. Additionally, optimizing storage conditions, including temperature, pH, and packaging, plays a crucial role in preserving their integrity [35]. Scalability, on the other hand, requires the development of cost-effective and reproducible synthesis methods capable of producing large batches of uniform nanoparticles [14], [39]. Techniques like green synthesis and continuous-flow manufacturing are gaining attention for their potential to meet industrial-scale production demands while maintaining quality and reducing environmental impact [8], [35], [59], [62]. Overcoming these stability and scalability challenges is essential for ensuring the reliable and consistent performance of CuNPs, ultimately paving the way for their successful adoption in clinical settings [63], [64], [65].

Regulatory Hurdles: Meeting stringent regulatory requirements for safety and efficacy remains a significant barrier. Regulatory bodies such as the FDA and EMA mandate comprehensive evaluations to ensure the safety, efficacy, and quality of new medical technologies [66], [67], [68]. This process involves rigorous preclinical studies, clinical trials, and documentation, which are time-consuming and resource-intensive. For copper nanoparticles (CuNPs), challenges include establishing standardized protocols for synthesis, stability, and characterization, as well as demonstrating biocompatibility and long-term safety [8], [20], [26]. The lack of harmonized guidelines for nanomaterials adds complexity, requiring innovators to navigate varying regulatory frameworks across regions [69]. Furthermore, the dynamic nature of nanotechnology often outpaces existing regulations, necessitating adaptive and proactive approaches. Overcoming these hurdles demands collaboration among researchers, regulatory agencies, and industry stakeholders to create clear pathways for approval, facilitate risk assessments, and streamline the clinical translation of CuNP-based therapies.

VI. FUTURE DIRECTIONS AND PROSPECTS

To harness the full potential of CuNPs in cancer care, future research should focus on:

Advanced Functionalization: Developing CuNPs with enhanced specificity and reduced toxicity requires integrating advanced surface engineering and bioconjugation strategies. For enhanced specificity, functionalizing CuNPs with ligands, antibodies, or peptides that target cancer-specific biomarkers can direct the nanoparticles to tumor sites while sparing healthy tissues [41], [70]. Technologies such as aptamer-based targeting and CRISPR-Cas systems can further refine this precision by addressing heterogeneity in tumor biology [71], [72], [73]. To reduce toxicity, utilizing biocompatible coatings, such as polyethylene glycol (PEG) or liposomes, can improve stability and minimize adverse immune responses [21], [44], [74]. Controlled drug release systems, triggered by stimuli such as pH, temperature, or enzymes unique to the tumor microenvironment, offer an additional layer of safety and efficacy [15], [21], [75]. Additionally, employing green synthesis techniques that incorporate natural antioxidants or bioactive compounds can mitigate residual toxicity while enhancing therapeutic outcomes [76], [77], [78]. Combining these approaches will enable the development of CuNPs that are not only effective in targeting cancer cells but also safe for clinical application.

Clinical Trials: Clinical trials of CuNP-based therapies are advancing our understanding of their potential in cancer treatment. Early-phase studies focus on assessing the safety, biocompatibility, and pharmacokinetics of CuNPs, aiming to minimize toxicity and optimize their therapeutic window [8], [40], [75]. These trials evaluate their efficacy in various cancer types, emphasizing CuNPs' roles in targeted drug delivery, photothermal therapy, and reactive oxygen species (ROS) generation to induce cancer cell apoptosis [8], [42], [46]. Additionally, combination therapies involving CuNPs and conventional treatments, such as chemotherapy and radiotherapy, are under investigation for their synergistic effects in overcoming drug resistance and improving therapeutic outcomes. Researchers are leveraging functionalized CuNPs to enhance targeting specificity, ensuring that nanoparticles accumulate predominantly in tumor tissues while sparing healthy cells. Preliminary results from these studies highlight the promising antitumor effects of CuNPs, with reduced systemic side effects compared to traditional

therapies. However, challenges such as standardizing nanoparticle formulations, scaling up production, and meeting regulatory standards remain critical hurdles. Ongoing trials are also exploring the integration of CuNPs with personalized medicine approaches, tailoring treatments based on individual tumor profiles. These efforts underscore the transformative potential of CuNP-based therapies, paving the way for innovative, precise, and efficient cancer care [8], [15], [21], [40], [59].

Integration with Personalized Medicine: Integration of copper nanoparticles (CuNPs) with personalized medicine represents a groundbreaking approach in precision oncology, offering the potential to tailor cancer treatments to individual patient profiles. By leveraging the unique properties of CuNPs- such as their ROS-generating capabilities, surface functionalization potential, and ability to deliver therapeutic agents- treatments can be customized based on a patient's genetic makeup, tumor microenvironment, and disease progression [44], [50], [56]. For example, CuNPs can be engineered to target specific biomarkers expressed on cancer cells, ensuring precise delivery of therapies while minimizing damage to healthy tissues [8], [21], [75]. Moreover, the diagnostic capabilities of CuNPs, including their use in advanced imaging modalities, enable real-time monitoring of treatment efficacy, allowing for dynamic adjustments to therapeutic regimens. This integration not only enhances the efficacy and safety of cancer therapies but also aligns with the principles of personalized medicine by addressing tumor heterogeneity and patient-specific factors [11], [41], [59]. As advancements in genomic and proteomic technologies continue to refine patient stratification, CuNPs are poised to play a pivotal role in the development of bespoke oncological interventions, ultimately improving patient outcomes and reducing the burden of side effects associated with traditional cancer treatments [79], [80].

Sustainable Manufacturing: Sustainable manufacturing of copper nanoparticles (CuNPs) through green synthesis methods represents a vital step toward eco-friendly and cost-effective production [26], [33], [35], [81]. Green synthesis employs biological systems such as plant extracts, fungi, bacteria, and algae, which act as natural reducing and stabilizing agents, eliminating the need for toxic chemicals typically used in conventional methods. This approach aligns with principles of green chemistry, minimizing environmental impact and enhancing the biocompatibility of the resulting nanoparticles [26], [34], [61], [77], [82]. Plant-derived antioxidants like flavonoids and phenolics, or microbial enzymes, not only reduce copper ions to nanoparticles but also confer bioactivity, potentially enhancing their therapeutic properties [21], [29], [33], [35], [83], [84]. Moreover, green synthesis methods enable scalability while maintaining uniform nanoparticle size and shape, crucial for biomedical applications [85], [86]. The integration of green synthesis into CuNP production offers a dual benefit: reducing production costs and environmental hazards while producing nanoparticles optimized for clinical use. This sustainable approach is particularly significant for advancing the application of CuNPs in cancer care, where eco-friendly and biocompatible nanoparticles can meet the growing demand for safer and more efficient therapies. By adopting green manufacturing practices, researchers can ensure that the development of CuNPs is both technologically innovative and environmentally responsible, paving the way for their broader adoption in medical and industrial sectors [34], [35], [87], [88].

CONCLUSION

Copper nanoparticles represent a promising frontier in cancer therapy, offering multifaceted applications that span diagnostics, therapeutics, and combination treatments. Their ability to be engineered for precision targeting, coupled with their unique physicochemical properties, positions them as transformative agents in oncology. CuNPs have demonstrated exceptional promise in preclinical studies, showcasing their potential to overcome limitations of traditional treatments, such as non-specificity, systemic toxicity, and drug resistance. By enabling innovative approaches like photothermal and photodynamic therapies, targeted drug delivery, and theranostics, CuNPs provide a platform for integrated and efficient cancer care.

However, despite their potential, the clinical translation of CuNPs faces significant hurdles, including challenges related to toxicity, scalability,

and regulatory compliance. Addressing these barriers will require a concerted effort from interdisciplinary teams spanning materials science, molecular biology, pharmacology, and regulatory sciences. Advanced functionalization techniques, robust preclinical studies, and well-designed clinical trials will be essential to ensure the safety, efficacy, and scalability of CuNP-based therapies.

Furthermore, the integration of CuNPs into precision oncology, leveraging patient-specific data to tailor treatments, represents an exciting future direction. Sustainable manufacturing methods, such as green synthesis, can further enhance the scalability and eco-friendliness of CuNP production, making these technologies more accessible for widespread clinical use.

In conclusion, copper nanoparticles hold immense potential to revolutionize cancer care. Their success will depend on overcoming translational challenges and fostering collaborative efforts across disciplines. With sustained research and innovation, CuNPs can bridge the gap from bench to bedside, ushering in a new era of personalized, efficient, and safer cancer therapies.

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