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Nanostructured Materials in Pharmaceutical Chemistry: Revolutionizing Cancer Immunotherapy

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Abstract: Nanotechnology has been extensively used in the advance of new strategies for drug delivery and cancer therapy. In medicine and pharmacy, advances in nanotechnology have been widely used, particularly in the domain of nano-delivery systems. The use of nanotechnological solutions in the prevention and treatment of a variety of diseases has significant benefits nowadays. Its treatment results in lowering adverse responses and enhance drug efficacy at intended site. Nanostructured drug delivery vehicles have been used in numerous studies to transport various cargoes as a possible alternative for the treatment of diseases such as cancer, autoimmune diseases, infectious diseases, and immunological and allergy disorders. In this regard, the development of nanomaterials and nanostructured drug delivery systems is presented in this study as a strong foundation for advances in immunotherapy and cancer treatment.

Keywords: Nanotechnology, Nanostructured drug delivery, Cancer therapy, Immunotherapy

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Introduction

Nanomaterials and nanostructured substances have been used in a variety of biomedical and therapeutic domains (Gaur *et al.*, 2021). One of two primary methods—the top-down technique or the bottom-up approach-- is usually used to create nanomaterials. In recent years, the production of nanomaterials by the use of physical vapor deposition, chemical vapor deposition, electrospinning, 3D printing, biological synthesis, and supercritical fluid has grown in importance. These techniques are combined with other techniques to increase the synthesis efficiency (Rehan *et al.*, 2019; Abdel-Haleem *et al.*, 2019). A vital component in preserving homeostasis, the

immune system is a complex network of defense systems. These systems have developed to eliminate viruses and external materials, shielding the body from danger (Sorci *et al.*, 2013; Mitarotonda *et al.*, 2022; Azevedo *et al.*, 2022). Numerous immune cells, signaling channels, and biological mechanisms are all involved in the intricate interactions that nanomaterials can have with the immune system (Croitoru *et al.*, 2024). By lowering non-specific toxicity and significantly increasing the therapeutic efficacy of the loaded chemotherapeutic medicines, nanomaterials will enable safe and efficient cancer treatment (Bae *et al.*, 2011).

Creation and advancement of nanostructured materials:

Large-scale material delivery methods have significant limitations, including poor absorption, stability, bioavailability, and solubility, which can reduce their effectiveness and target specificity. Using nanoparticles as drug carriers has the primary goal of lowering medication toxicity while increasing bioavailability, target specificity, and delivery without compromising therapeutic effects (Chen *et al.*, 2014; Klymchenko *et al.*, 2020; Tan *et al.*, 2021; Li *et al.*, 2023) Targeting the immune system precisely is made possible by biomedical nanotechnology, which involves the development of complex biomaterials and drug delivery systems (Panda, 2022). Nanomaterials have at least one dimension between 1 and 100 nm, making them extremely small. Additionally, their size helps them reach certain sites for the release of carrying substances and penetrate physiological barriers that are ordinarily intact. Therefore, immune cells and nanoparticles interact molecularly to produce the immune system's reaction to stimulation or suppression, modifying the immune system and making it possible to use them therapeutically (Wang *et al.*, 2013; Liu *et al.,* 2022). Polymeric nanoparticles are very useful for immunotherapeutic approaches because they have the ability to target dendritic cells, which are essential for triggering immunological reactions. Additionally, research indicates that enhancing the nanoparticles' size, shape, hydrophobicity, and surface charge improves the delivery of immunotherapeutic drugs to cancers. This exact control makes it easier to combine immuno-therapy therapies, prevents tumors from recurring, encourages the formation of persistent immunological memory, and improves patient outcomes by lowering adverse events and immune system toxicity. (Craparo *et al.*, 2012; Yu *et al.,* 2023). Polymers with a highly branching structure are called dendrimers. Doxorubicin (DOX)-loaded pegylated thermoresponsive aliphatic polyester G5 dendrimers were synthesised well. When cytotoxicity was assessed in SKOV-3 ovarian cancer cells, it was shown that dendrimers devoid of medications are non-toxic, but the DOX material reduced cell viability. Excellent drug encapsulation and controlled drug release capabilities were demonstrated by G5 dendrimers (Khatri *et al.,* 2014). Lipid nanoparticles (LNPs) also provide intriguing immunotherapy prospects. LNPs may be produced on a massive scale while retaining exact control over their morphology and lipid composition (Aldosari *et al.,* 2021). Recent research has shown that DNA and RNA nanostructures are interesting biological tools, especially for medication delivery. Nanomaterials can be broadly categorized into four classes based on their dimensionality 0D, in which width, height, and length are all fixed at one location; Carbon nanotubes are an example of a 1D material; graphene is an example of a 2D material; and length, height, and width are examples of a 3D material (Kumar *et al.,* 2017). Tetrahedral DNA nanostructures, or TDNs, are gaining more and more interest because of their exceptional stability, ease of synthesis, high level of biocompatibility, and ease of functionalization (Sharma *et al.,* 2024). The frequency of drug delivery may be decreased by employing nano-carriers to enhance pharmacokinetic parameters such as absorption, distribution, metabolism, and excretion. This enhancement may lead to increased compliance and, eventually, improved clinical results (Alghamdi *et al.,* 2022). Nevertheless, these drug-carrying NPs can be

taken up by immune phagocytic cells, which will stop the drugs from reaching therapeutic concentrations. This will cause the drugs to be distributed in the body in an unspecific manner, hinder their effective passage through blood vessels, interfere with their intracellular internalisation mechanism, and cause multidrug resistance (Blanco *et al.,* 2015).

Nanostructured materials in cancer immunotherapy delivery:

Cancer immunotherapy has increased survival in instances that were previously thought to be deadly by modifying the body's immune system to target tumours (Varshney *et al.,* 2021; Li *et al.,* 2022*)*. Drug delivery strategies based on nanotechnology have been seen as viable ways to improve the effectiveness of TLR7/8 agonists in cancer immunotherapy. Several nanocarriers can be used to improve treatment outcomes and reduce dose-limiting toxicities, particularly with tiny molecular immune therapeutics (Radzi *et al.,* 2023; Vasantha and Mohini, 2025). Hydrogels made to transport tetracycline and DOX, which exhibit varying levels of biodegradability at pH 1.2 and 7.4, are examples of such nanocarriers. They exhibit reversible volume loss of more than 80% of the starting volume at pH 1.2 (Xu *et al.,* 2018). Guanosine- and uridine-rich single-stranded RNA (GU-rich RNA), which is known to be an agonist of TLR7 and TLR8, are used as the therapeutic agent. In this regard, the scientists created a hydrogel assembly of GU-rich RNA/DNA that is nanostructured and has a sustained release. The delivery mechanism is regarded as a useful adjuvant in cancer immuno-therapy since it was effectively internalised in murine dendritic cells and produced strong immunostimulatory activity (Komura *et al.,* 2020).Stimuli-triggered nanosystems provide for more accurate spatiotemporal control over TLR7/8 agonist activity in response to specific tumor microenvironment (TME) variables, such as hypoxia, acidity, and hypoglycemia, than passive delivery vehicles. In treatments like magnetic hyperthermia, chemotherapy, and radiation therapy, nanobiotechnological systems can enhance immunogenic cell death by selectively releasing their cargo in response to changes in temperature, pH, or redox potential. They can also cross biological barriers. (Souza *et al.,* 2023). For imiquimod administration, the researchers particularly created nanometric self-assembling micelles with vitamin E and newly synthesized fatty acid-protic ionic liquids (FA-PILs). Because it allowed the controlled release of the TLR agonist in cancer tissues, which were triggered by the acidic conditions of the TME, the developed nanosystem has promise for the treatment of skin cancer (Tampucci *et al.,* 2020). Successful tests against melanoma were conducted using polydopamine nanoparticles coated with the membranes of B16-F10 cancer cells (CC) and bacterial outer membrane vesicles (OMV)(Wang *et al.,* 2020).Immune checkpoint inhibition is another approach that may be used to treat cancer. Specifically, it has been demonstrated that immune checkpoint blockade (ICB), particularly anti-PD1/PD-L1 and anti-CTLA-4 therapies, is effective in treating solid cancers. Anti-PD1/PD-L1 antibody therapy is effective in treating high-mutational-load malignancies, including urothelial bladder carcinoma, renal cell carcinoma, non-small lung cancer, melanoma, and Hodgkin's lymphoma (Crispen *et al.,* 2020). A combination technique was employed in the instance of PTX and the P-glycoprotein inhibitor zosuquidar. To address drug resistance, which frequently arises during the treatment of hepatocellular carcinoma, both medications were added to nanoliposome conjugated with programmed death ligand. The medication created in this manner demonstrated a strong synergistic impact of active ingredients and a high encapsulation capacity, suggesting low toxicity and antitumor efficacy (Gu *et al.,* 2022). Nanostructured delivery techniques usually hold considerable promise for improving cancer immunotherapy, as numerous studies demonstrate their potential for improved targeting, greater cargo internalization, and synergistic benefits. Even better results have been obtained using modern combinatorial techniques,

which have produced promising results against a variety of cancer types that are otherwise challenging to treat. However, more thorough testing is necessary for these novel approaches.

Conclusion

Immunotherapy's usage of nanostructured drug delivery systems has demonstrated significant potential in improving therapeutic efficacy and specificity; these systems are particularly utilized in cancer applications. Numerous studies in the field have demonstrated that the inherent immunomodulatory properties and versatility of nanomaterials used as carriers can significantly boost the effectiveness of nanostructured materials systems in the delivery of immunotherapeutic medications. In nanomedicine research groups, the use of various nanoparticles to deliver gene therapy or monoclonal antibodies, or to transport specific drugs to damaged cells, such as cancer or tumor cells, is without a doubt the trend. In conclusion, nanostructured drug delivery methods provide a solid foundation for additional therapeutic advancements in the immune system. To get over the present obstacles and fully utilize the promise of these cutting-edge therapeutic techniques, multidisciplinary cooperation, and ongoing development will be crucial.

Ethical Statement

No animal or microbes have been used or sacrificed for this study, hence Ethical Approval not required.

Author Contributions

Each author has contributed equally in designing the research, conducting thorough analysis, drafting the manuscript, and refining its content. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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