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Engineering Nanocomposites For Precision Medicine And Therapeutic Applications-A Review

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ABSTRACT

Nanocomposites, based on the inclusion of two or more phases in which at least one phase is nanoscale, have drawn immense interest due to their emergent properties based on synergistic interactions between their constituents. These materials have great value particularly in biomedicine. Nanocomposites represent a strong contender in drug delivery, dermatology, oral care, cancer therapy, vaccines, gene therapy, and enhancing blood circulation. The paper aims at comprehensively reviewing the current state of nanocomposite applications in biological fields, especially relating to their application in therapy and the challenges that accompany them. Nanocomposites have many unique advantages, such as controlled drug release, better biocompatibility, and enhanced efficacy in targeted delivery. All these features make them highly effective in medical treatments across various biological applications. Nonetheless, the current review's findings do emphasize that while these materials are promising, there is still a way to go in terms of safety assessment, precision of drug release, targeted delivery, and biocompatibility. Additionally, challenges arise from the scalability and reproducibility of the processes, environmental impact studies, standardization, and issues at the regulatory level all contribute to additional barriers for widespread implementation. Scaling up in production, reduction of environmental impacts, and developing comprehensive regulatory frameworks will be important to completely enhance the potential of nanocomposites within biomedical applications. Research and studies in these areas should thus be targeted to ensure an optimization of their use and to surpass the present barriers in the field.

Keywords: *Biological application, Eco friendly, Nanoscience, Drug delivery, Nanoparticles, Nanocomposite.*

1. INTRODUCTION

Nanocomposites are advanced solid materials composed of multiple phases, with at least one phase exhibiting dimensions in the nanometer range (1-100 nanometers). These materials integrate nanoscale components to achieve enhanced properties through the synergy of their constituents. Key nanomaterials in nanocomposites include nanoparticles, nanofibers, and nanoclays. These components, when reduced to critical sizes, exhibit unique properties that significantly differ from their bulk counterparts, leading to advanced material characteristics [1].

Composition and Structure of Nanocomposites

Nanocomposite materials are typically composed of at least one component with nanometric dimensions and can be made from various materials, including non-metallic, metallic, and polymeric substances. This specific process of combining materials at the nanoscale provides the advantage of retaining primary features while overcoming defects and introducing new characteristics [2].

Such materials represent a multiphase system consisting of:

a) Matrix Material**:** The continuous phase that supports the nanomaterial, which can be metallic, inorganic non-metallic, or polymeric.

b) Reinforcing Material**:** The dispersed phase, which is often fibrous, such as glass fiber, carbon fiber, or organic fibers. This phase is crucial for providing enhanced mechanical and physical properties.

Importance of Nanoscale Dimensions

At the nanoscale, the properties of materials can change drastically due to the increased surface area-to-volume ratio and the prominence of quantum effects. For instance, materials at this scale often exhibit enhanced mechanical, thermal, and electrical properties [3]. The critical size threshold is the point below which these properties become pronounced, offering novel functionalities not seen in larger scale materials.

Phase Interface Interactions

Reducing material dimensions to the nanometre scale fosters significant phase interface interactions. These interactions are crucial for enhancing the properties of the material. The high surface area of the reinforcing phase interacts intensely with the matrix material, leading to improved load transfer, increased mechanical strength, and enhanced thermal stability [4]. The ratio between the surface area and volume of the reinforcing material is pivotal in understanding and optimizing the structure-property relationship of nanocomposites. Chitosan is used in a wide variety of sectors, including those that deal with biomedicine, cosmetics, papermaking, wastewater treatment, agriculture, pharmaceuticals, and other fields. The following section provides more details on the applications, including an explanation of biomedical applications and a description of how chitosan is specifically used in the industry. Chitosan provides various advantages for biomedical applications, including biocompatibility and control over biodegradability, which cause items to break down. Also, it has no negative effects and has no risky side effects. In addition, because chitosan possesses adjustable functional groups, it may be altered by blending it with other polymeric materials like cellulose, which increases the stability of blends. In summary, combining chitosan-based products with other appropriate biopolymers that can be used commercially can increase their stability.

2. BIOMEDICAL APPLICATIONS OF NANOCOMPOSITES: INNOVATIONS IN DRUG DELIVERY, CANCER THERAPY, AND BEYOND

2.1 Drug Delivery

Nowadays, regulated drug administration offers several benefits to people, including improving efficacy and lowering or eliminating undesirable side effects as well as drug levels. Chitosan has some unique qualities that make it perfect for use in drug delivery systems. Anti-bradykinin B2 conjugated chitosan nanoparticle systems can also improve the inhibition of HIV replication. Chitosan is only employed in the pharmaceutical sector to lessen cardiotoxicity, one of the negative effects of cancer treatment. Chitosan nanoparticles are used to contain the medication. These chitosan nanoparticles have the ability to improve doxorubicin's absorption in the small intestine. Chitosan tripolyphosphate (TPP) nanoparticles are the kind of chitosan nanoparticles that are frequently employed in this particular business. Moreover, chitosan nanoparticles can increase the stability of tea polyphenols and stop them from degrading or oxidising in the digestive system [5]. As a result, chitosan made from polyethylene glycol is probably acceptable for use as a medication carrier with controlled release. When processing chitosan for this use, it is crucial to take into account factors such chemical stability, particle sizes, toxicity, release kinetic profiles, and kind of delivery method. Depending on the purpose and applications of the carrier, chitosan can be applied in a variety of ways [6]. Here is a tabular column 1 summarizing the application of nanocomposites in drug delivery.

Table 1 Summarize the application of nanocomposites in drug delivery

Sl.no	Application Area	Characteristics
1	Polymer Nanocomposites	Polymer nanocomposites are extensively developed for drug delivery, showing promising results in various therapeutic applications [24].
2	Targeted Drug Delivery	Nanocomposites enable targeted delivery systems that enhance the efficacy of therapeutic agents while minimizing side effects [6].
3	Cancer Treatment	These systems have been particularly effective in delivering anticancer drugs and increasing their therapeutic efficacy [25].
4	Bioavailability Improvement	Nanocomposites help improve the bioavailability of natural

		products, enhancing their therapeutic effects [26].
5	Controlled Release Systems	Recent advancements emphasize the use of nanocomposites for controlled and sustained release of drugs, enhancing treatment regimens [6].
6	Biocompatibility and Safety	Emphasizing biocompatibility and biodegradability, modern nanocomposites are designed to ensure safety in medical applications [24].
7	Combination Therapies	Nanocomposites are facilitating multi-drug delivery systems, allowing combination therapies for improved patient outcomes [24].
8	Nano cellulose Applications	Nano cellulose-based materials have been utilized in drug delivery, enhancing the stability and functionality of therapeutic agents [27].

2.2 Dermatology and Skin Care

Chitosan is a natural cationic polymer used in cosmetic applications that becomes viscous when neutralised with acid and functions as a cationic humectant in cosmetics and topical formulations. Creams, lotions, and other cosmetic preparations are made with it. Chitosan is also well-known for its use as a moisturising and film-forming agent. Moreover, chitosan offers advantages for skin safety since it improves water resistance in sun protection emulsions, which are combined with chitosan. Chitosan is frequently used as a skin permeability enhancer in drug delivery systems because it alters the keratin structure and is absorbed to the negative charges of the skin surface. Because of its hydrophilic hydroxyl groups, which allow it to interact with water molecules, chitosan also increases the fluidity of the cell membrane and raises the stratum corneum's water content [7]. Chitosan can be employed as a percutaneous drug delivery vehicle because of its positive charges, large molecular weight, and ability to stick to the skin. The use of chitosan to make nanoparticles that transport active chemicals for skin-care products and medications has gained popularity in recent years. Nanoparticles made of chitosan have been utilised to treat infections and malignant melanoma of the skin locally [8].

2.3 Cosmetics for Oral Care Products

The cosmetics business frequently uses and concentrates on natural substances like chitin, chitosan, and its derivatives since oral care products have an impact on human health. Chitosan, which has a lower molecular weight and has been suggested as a potential anti-cavity agent, inhibits the oral adsorption of streptococci. Chitosan is also capable of interfering with other aspects and the adherence of microorganisms. The effectiveness of chitosan in actual formulations against the development of dental plaque [9]. In the trial, chitosan was added to rinses, toothpastes, and other products. It has been demonstrated that chitosan, which is used in toothpaste and mouthwashes to prevent biofilm development in the mouth since *Streptococcus mutans* is present and decreases the formation of colonies. As chitosan has a broad antibacterial spectrum, many researchers have investigated its effectiveness against different bacterial strains linked to dental caries [10].

2.4 Cancer Therapy

Nanoparticles have garnered significant interest in the field of cancer treatment due to their unique properties and potential applications. However, it's essential to acknowledge that while nanoparticles offer numerous advantages, they also come with certain disadvantages. One major use of nanoparticles in cancer treatment is drug delivery. Nanoparticles can be engineered to encapsulate anticancer drugs, allowing for targeted delivery to tumor sites while minimizing damage to healthy tissues. This targeted drug delivery approach can enhance the therapeutic efficacy of anticancer drugs and reduce the side effects associated with traditional chemotherapy [11]. Another application of nanoparticles in cancer treatment is as imaging agents. Nanoparticles can be functionalized to carry imaging agents, such as fluorescent dyes or magnetic nanoparticles, which enable the precise visualization of tumors. This aids in early detection, accurate diagnosis, and monitoring of the treatment's progress. Furthermore, nanoparticles are used for hyperthermia therapy, where magnetic nanoparticles are introduced into tumors and then exposed to an external magnetic field. This localized heat generation can effectively destroy cancer cells or sensitize them to radiation therapy.

Despite these promising uses, nanoparticles also have their disadvantages. One significant concern is the potential for toxicity. The small size and high surface area of nanoparticles can lead to unpredictable interactions with biological systems, potentially causing harm to healthy tissues [12]. Moreover, the long-term effects of nanoparticles on the human body are not yet fully understood, raising concerns about their safety. Additionally, nanoparticles can face challenges in terms of clearance from the body. Their small size may hinder the body's natural mechanisms for eliminating foreign substances, leading to potential accumulation and long-term exposure. Table 2 represents characteristic of nanocomposite in cancer therapy.

There's also the issue of cost and scalability. The production and functionalization of nanoparticles for medical applications can be expensive, limiting their widespread use, especially in resource-constrained healthcare settings [13].

TABLE 2 Application Area of Nanocomposite in Cancer Therapy

Sl.no	Application Area	Characteristics
1	Targeted Drug Delivery	Nanocomposites are engineered for targeted delivery of chemotherapeutic agents, selectively enhancing drug concentration at tumor sites while minimizing toxicity to healthy tissues [28].
2	Combination Therapy	They are used in combination therapies, facilitating the concurrent delivery of multiple therapeutic agents to enhance overall efficacy [28].
3	Photo thermal Therapy (PTT)	Nanocomposites are utilized in PTT, where they absorb light and convert it to heat, effectively destroying cancer cells.
4	Gene Therapy	Nanocomposites play a role in gene therapy by delivering nucleic acids directly to cancer cells, improving stability and therapeutic effects [25] [29].
5	Immunotherapy Enhancement	They enhance immunotherapy by facilitating the targeted delivery of immune stimulatory agents to remodel the tumor microenvironment.
6	Diagnostic Applications	Certain nanocomposites are incorporated into biosensors for detecting cancer biomarkers, leading to early diagnostics and personalized treatment approaches [30].
7	Biocompatibility Improvement	Recent advancements have focused on improving the biocompatibility and biodegradability of nanocomposites for safer cancer treatment applications [31].
8	Tissue Engineering	Nanocomposites are being explored for use in tissue engineering approaches to aid in reconstructive surgeries post-cancer treatment [28].

2.5 Vaccines and Immunotherapy

Nanoparticles have gained prominence in the field of vaccines and immunotherapy due to their ability to address some key challenges and enhance the efficacy of these treatments. One prominent use of nanoparticles in vaccines is as carriers for antigens, ensuring controlled and sustained release of antigens to the immune system, which can lead to a stronger and longer-lasting immune response. This is particularly advantageous for developing vaccines against infectious diseases and cancers. Additionally, nanoparticles can improve the delivery of immunotherapeutic agents, such as checkpoint inhibitors or monoclonal antibodies, by increasing their stability and targeting their release to specific sites [14]. However, their use in this context also comes with certain disadvantages. Nanoparticles can sometimes evoke unintended immune responses, potentially diminishing the efficacy of vaccines or immunotherapies. Moreover, there are concerns about the long-term safety of nanoparticles within the body, including issues related to their potential accumulation in organs and tissues. Regulatory and ethical considerations regarding the use of nanomaterials in vaccines and immunotherapies also need to be carefully addressed to ensure patient safety and public trust in these advanced medical interventions. Therefore, while nanoparticles hold significant promise in vaccines and immunotherapy, their disadvantages underscore the importance of rigorous research, monitoring, and safety assessment in their application [15].

2.6 Gene therapy

Nanoparticles have shown promise in the field of gene therapy, offering innovative solutions for the delivery of genetic material into cells. One of the primary uses of nanoparticles in gene therapy is their role as efficient carriers for delivering therapeutic genes to target cells. These nanoparticles can protect the genetic material from degradation in the bloodstream and facilitate its entry into the target cells. Additionally, nanoparticles can be engineered to release their cargo at specific locations within the body, ensuring precise targeting and reducing the potential for off-target effects. However, there are certain disadvantages associated with the use of nanoparticles in gene therapy. One significant drawback is the potential for immunogenicity and toxic responses to the nanoparticles themselves, which can trigger unwanted immune reactions [16]. Controlling the release kinetics and ensuring that the genetic material reaches the intended cells can also be challenging. Furthermore, long-term safety concerns regarding the persistence of nanoparticles in the body and the potential for unintended side effects necessitate thorough investigation and monitoring. Despite these challenges, nanoparticles remain a promising avenue for advancing gene therapy, and ongoing research aims to address these issues and optimize their use in this critical medical application [17].

2.7 Blood circulation enhancement

Nanoparticles have shown promise in the field of blood circulation enhancement, particularly in addressing conditions like clotting disorders and thrombosis. By engineering nanoparticles to improve blood flow, several potential applications have emerged. For instance, magnetic nanoparticles can be guided by external magnetic fields to break up blood clots or enhance drug delivery to targeted sites. While these approaches hold great potential, they are not without their disadvantages. One significant concern is the potential for nanoparticles to cause blockages in smaller blood vessels or capillaries [18]. If not carefully designed and controlled, nanoparticles may also interact with blood components, leading to unintended consequences or immune responses. Additionally, the long-term safety of nanoparticle-based blood circulation enhancement methods needs further investigation to ensure they do not pose health risks or complications over time. As such, while nanoparticles offer innovative solutions for improving blood circulation, their application in this context requires rigorous research and thorough consideration of potential disadvantages and risks to ensure patient safety and efficacy [19].

3. NAVIGATING THE CHALLENGES OF NANOPARTICLE RESEARCH ACROSS DISCIPLINES

Research involving nanoparticles spans a wide array of disciplines, including nanomedicine, materials science, and environmental science, offering substantial potential for advancing technology and addressing pressing global issues. However, this burgeoning field is accompanied by its own unique set of research challenges, which can be categorized into several overarching themes [20].

Safety Evaluation and Toxicity Assessment:

Among the most critical issues in nanoparticle research lies the imperative need to assess their safety, whether in medical or environmental applications. It is imperative to ascertain the potential toxicity of nanoparticles and gain comprehensive insight into their long-term impact on both human health and the environment. To ensure secure utilization in various contexts, researchers must establish standardized testing protocols and evaluation methods.

Biocompatibility and Immunogenicity:

Within the realm of nanomedicine, achieving biocompatibility in nanoparticles and averting unwanted immune responses is of utmost importance. The design of nanoparticles capable of evading the immune system effectively and minimizing adverse reactions represents a substantial challenge. Researchers are actively devising strategies to enhance the biocompatibility of nanoparticles, particularly when deployed in fields such as drug delivery and gene therapy.

Precise Drug Release Control:

In the sphere of drug delivery, the quest for precise control over the release of therapeutic agents from nanoparticles stands as a pivotal challenge. Researchers are diligently working towards the development of nanoparticles featuring adaptable release profiles, ensuring that drugs are administered at the appropriate dosage and rate. Striking the delicate balance between sustained release and the mitigation of side effects remains a complex conundrum.

Targeted Delivery:

The promise of nanoparticles in achieving targeted drug delivery and enabling precision medicine is significant. Nevertheless, the effective targeting of nanoparticles to specific cells or tissues within the body presents a substantial challenge. Researchers are actively exploring diverse strategies, encompassing approaches such as ligand-based targeting and nanoparticles responsive to external stimuli, to augment the precision of drug delivery.

Manufacturing Scalability:

The production of nanoparticles at a scale suitable for practical applications poses a formidable challenge. Researchers are diligently engaged in the development of manufacturing methods for nanoparticles that are both scalable and cost-effective, all the while preserving their quality and consistency. These methods must also meet environmental standards and regulations.

Environmental Consequences:

The deliberate or inadvertent release of nanoparticles into the environment carries inherent risks. Researchers are engaged in the study of the ecological impact of nanoparticles, their persistence within natural systems, and their potential to accumulate in organisms. The understanding and mitigation of these environmental effects hold paramount significance.

Standardization and Characterization:

The establishment of standards for characterizing and classifying nanoparticles is of utmost importance to ensure research reproducibility and comparability. The ongoing challenge lies in the development of universally accepted measurement and characterization techniques.

Regulatory and Ethical Considerations:

As nanoparticles find increasingly widespread applications, regulatory agencies face the challenge of crafting comprehensive guidelines for their safe deployment. Ethical considerations surrounding nanoparticle research, particularly within medical and environmental contexts, necessitate sustained attention to ensure responsible and advantageous implementation.

4. DISCUSSION

Significant advancements have recently been made in the processing, design, and field of polymer nanocomposites. Its employment in a variety of applications is still constrained by the inherent issues with damage restoration, though. The field of polymers and composites' self-healing chemistries has made it possible to use these systems in polymer nanocomposites. While various self-healing techniques have mostly been used on polymers and composites, nanocomposite systems have received little attention. In this article, we examine the chemistries of self-healing polymer nanocomposites and give examples of some of these materials [21].

Next-Generation Nanocomposites for Targeted Delivery, Regenerative Medicine, and Biosensing

Nanocomposite also have the added advantage of drawing intense focus on their biomedical applications and include biosensing, drug delivery, and tissue engineering. Among these applications, carbon-based nanocomposites will be particularly important in addressing some deficiency in biomedical research work such as unstable biomolecules and low biosensor sensitivity. Additionally, there are challenges associated with the specific targeted delivery of therapeutic agents. Both single-walled and multi-walled carbon nanotubes have been previously noted for their high aspect ratio, significant mechanical strength, and electrical conductivity and thus can be appropriate in the reinforcement of polymer matrices to develop nanocomposites for tissue engineering scaffolds and drug delivery systems. Graphene and its derivatives, graphene oxide, and reduced graphene oxide enhance the mechanical strength of biomaterials, facilitate drug delivery, and provide antimicrobial coatings for medical devices [30]. Carbon dots (CDs) are used in polymer nanocomposites for biosensing, bioimaging, and biomimetic implants due to their photoluminescence, biocompatibility, and low toxicity. DLC coatings for medical implants are applied to improve wear resistance and reduce bacterial adhesion due to their properties, such as high hardness, chemical inertness, and biocompatibility. The recent developments in carbon-based nanostructures include functionalized graphene oxide nanocomposites, which exhibit superior mechanical strength and biocompatibility, and CNT-based sensors that can detect proteins at nanogram levels, which is promising for diagnostics and therapy. Protein-guided biomimetic nanocomposites utilize the natural properties of proteins to develop multifunctional materials. [29] These composites combine organic and inorganic components, using proteins to template, nucleate, and structure nanomaterials for specific biological functions. For instance, silk fibroin is used in biomimetic mineralization to synthesize hydroxyapatite nanocomposites for bone regeneration. The targeted drug delivery and imaging are facilitated by engineering ferritin and albumin into theranostic nanocomposites. Ferritin composites may allow for the controlled release of drugs in cancer therapy, while albumin increases the bioavailability of hydrophobic drugs. Laccase may be applied in an enzyme-based method to form conductive nanocomposites for biosensors. Proteins stabilize nanoparticles in composites, such as silver nanoparticles coated by bovine serum albumin (BSA) that increase its antibacterial property. Protein-guided nanocomposites are also used in regenerative medicine, where collagen-nanoparticle scaffolds mimic extracellular matrices to support cell adhesion and tissue growth, as well as in imaging and biosensing applications using fluorescent and protein-modified electrodes [31].

The antioxidant properties in cerium oxide nanoparticles (CeO_2NPs) allow them to scavenge ROS. However, direct application may lead to cytotoxicity, and integration of CeO_2NPs into PCL fibers can reduce the cytotoxic effects of free CeO_2NPs. The one-stage methods to synthesize these nanocomposites encapsulate the nanoparticles into electrospun PCL fibers, thus retaining ROS-scavenging capabilities that reduce oxidative stress in cellular environments while improving biocompatibility compared to free CeO_2NPs. Applications range from tissue engineering scaffolds that encourage cell proliferation to wound healing by abating oxidative stress, and controlled therapeutic delivery [21]. Polyetheretherketone (PEEK) well known for its mechanical strength and biocompatibility suffers from bio-inertness. Decoration of PEEK with silver nanoparticles AgNPs overcomes this problem as these impart antimicrobial properties since the release of silver ions inhibits bacterial growth. AgNP-coated PEEK is used in orthopaedic and dental implants, as well as surgical instruments that advance functional uses along with safety.

Advances in Nanocomposite Hydrogels, Metal-Organic Biohybrids, and Self-Healing Polymers

Nanocomposite hydrogels are promising in drug delivery and tissue engineering by incorporating nanoparticles into hydrogel networks. The porous structure of hydrogels enables drug encapsulation and stimuli-responsive release, whereas the mechanical properties can be designed according to requirements by tuning the system. Biopolymer-based nanocomposite hydrogels are recently reported that exhibit antibacterial properties for wound healing. Research is ongoing despite challenges related to nanoparticle distribution and scalability toward improving these materials for clinical applications. MOBs are hybrid structures acquired by coupling of metal ions or clusters with biological molecules. [27] The biomedical applications of the hybrid structures are transportation carriers of therapeutic agents, anticancer therapies, antimicrobial coatings, and imaging tools. For example, the cytotoxic effect was determined to occur in cancer study with copper-based MOBs, and the silver-cysteine MOBs were tested to determine the presence of antimicrobial activity. In bioluminescent biological imaging, MOBs based on lanthanides are employed. Their biocompatibility, tunability, and functional versatility enable targeted drug delivery, diagnostics, and therapy. Further improvements in synthesis techniques and deeper insights into their interactions with biological systems will be expected to further expand the utility of MOBs in medicine. In summary, these innovative materials foster transformative solutions in biosensing, drug delivery, tissue engineering, among other applications.

The study of nanocomposites' capacity for self-healing is still in its infancy. The many polymerization techniques used by the self-healing mechanisms in polymer nanocomposites are covered in this article. There is a lot of room for advancement and the creation of new self-healing polymer nanocomposites in the field of polymer nanocomposites. Even though various chemistries have been reported for a variety of materials, there is still little knowledge about self-healing polymer nanocomposites [22]. To incorporate these materials for various applications, self-healing nanocomposites must overcome a number of obstacles. The design of polymer nanocomposite materials must be optimised in order to facilitate their efficient synthesis and use. These nanocomposite materials should be able to mend themselves repeatedly so that they are perfect for applications that require multiple functions. Moreover, it would make it possible to create nanocomposites with increased sustainability [23]. The new advanced high-strength polymer nanocomposite would benefit from creative study on the self-healing of polymer nanocomposites. The development of self-healing polymer nanocomposites will be dependent on the identification and use of cutting-edge chemistries that enable the regulated, quick, and easy synthesis of novel materials.

5. CONCLUSION

Nanocomposites have advanced cancer therapy by improving drug delivery through the enhanced permeability and retention (EPR) effect and tumor-specific targeting. They also play a pivotal role in cancer diagnostics, enabling early detection and precise imaging for timely intervention. Despite their potential, challenges like durability and damage repair remain, with self-healing polymer nanocomposites still under development. Continued research is essential to unlock their full capabilities.

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