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Analyses of Polymer Nanocomposites Development in Biomedical Applications

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Abstract

Polymer nanocomposites (PNCs) are known for being an effective method to impart materials with exceptional properties that cannot be achieved by the individual components on their own. Utilizing the interfaces between the two phases of nanoscale compounds with high specific surface areas is advantageous for creating composites that incorporate nanofillers. The primary difficulty with nanocomposites lies in managing the interfacial interactions between the two phases. Polymer nanocomposites have gained significant research attention in recent years because of their promising potential in various electric, magnetic, optical, and biological applications. Over conventional materials, polymeric nanocomposites provide several advantages, such as light weighting, flexibility, processing simplicity, and low cost of the finished product. Biomedical applications have become a top study area among the disciplines due to the significance of medical technology, which has raised the criteria for biomedical materials. Demand for new materials with specific properties is high. Biomedical polymer-silicate nanocomposites hold great potential for advancing biomedical applications, including diagnostic and therapeutic devices, tissue regeneration, drug delivery systems, and various biotechnologies inspired by biology but with limited direct ties to biomedicine. A deep understanding of polymer-nanoparticle interactions is essential to regulate the structure-property relationships of materials, ensuring they function effectively within the chemical, physical, and biological limitations imposed by their intended applications. This review compiles the latest published strategies for designing and developing polymer-silicate nanocomposites, including clay-based silicate nanoparticles and bioactive glass nanoparticles, for various biological applications. Emerging application areas are being explored, and recent advancements in biotechnological and biomedical nanocomposites are highlighted.

Keywords: Nanocomposites, polymer, silicates, clay, biopolymer, mechanical properties, miomedical applications

INTRODUCTION

Scientists have been paying close attention to the development of a new class of hybrid materials known as polymer matrix-based nanocomposites over the past two decades. Using polymer composites, it is possible to improve the structural and useful properties of polymers. It frequently happens that the properties of nanoparticle-reinforced polymer composites outperform those of the polymer alone. Polymer nanocomposites are made by mixing polymers with inorganic/inorganic nanofillers. Low- and high-interfacial area-to-volume ratio nanostructures with sizes under 100 nm are known as nanofillers [1]. The most used nanofillers include carbon nanotubes, silicates, metals, metal oxides, and ceramics. These fillers exhibit a range of properties, including mechanical, chemical, thermal, and electrical characteristics. In this view, a fundamental understanding and knowledge of

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nanostructures are necessary for the development of materials for specific purposes. The interaction between nanofillers and the polymer matrix plays a crucial role in determining the mechanical and functional properties of polymer nanocomposites. By modifying various parameters and controlling the interaction between nanostructures and polymers, specific property combinations can be created [2, 3].

Using the unique properties of nanoparticles and the appropriate polymer matrix, a variety of novel nanocomposites materials have been developed. Possibilities exist for polymer nanocomposites right now since they may be used for a variety of purposes and satisfy different functional criteria [4]. The polymer-based nanocomposites have gained a lot of interest for their numerous biological and biotechnological applications [5]. Researchers from the domains of materials science, nanotechnology, and biological science collaborate on research in the interdisciplinary topic of biomaterials based on polymer nanocomposites. The synergistic combination of physical, chemical, and biological properties of nanocomposites offers an attractive platform for the design and development of improved materials for biomedical applications [6, 7].

Polymer nanocomposites with improved mechanical characteristics can be used to replicate high performance materials like bone and silk [8]. Nature gives methods to model biological tissues with both hard and soft components. In order to generate biologically inspired materials, which can be formed through a specific combination of soft polymer matrix and hard nanostructure, these novel composite materials are being produced by dispersing hard inclusions in polymer matrix [9]. Nonetheless, uniform dispersion of nanofillers into polymer matrix is one of the key issues encountered during fabrication of polymer-based nanocomposites, for which numerous processing procedures have been studied by academics [10]. Another crucial issue that needs to be considered when creating nanocomposites for biomedical applications is their biocompatibility. By balancing mechanical characteristics, functions, and biocompatibility aspects, polymer nanocomposites are thus finding numerous fascinating applications in the new technologies, such as tissue engineering, biomedical imaging, sutures, surgical implants, drug delivery-based applications, etc.

Due to the multidisciplinary nature of the polymer nanocomposite biomaterials field, researchers from several disciplines, including biology, chemistry, physics, materials and biomedical engineering, are increasingly cooperating. A typical result of such joint work is the development and adoption of new terminology and definitions that are applicable to all pertinent fields. The conventional definition of biomaterials from 1999, for instance, has allegedly changed over time as a result of the materials' employment in a variety of biologically inspired medical and non-medical technology [11, 12]. As a result, it is more difficult to distinguish between polymer nanocomposite biomaterials used for non-medical biotechnological purposes and those made for biomedical devices (e.g., renewable resources). This article will explore polymer nanocomposite materials that have the potential to serve as biomaterials in the biomedical field, focusing on their interactions with tissues and tissue-related components. There is a wealth of literature on the subject, and polymeric biomaterials have been created to replace and repair biological tissues [13, 14]. One of these innovative strategies involves developing self-assembling and intelligent nanocomposite biomaterials that respond to environmental cues, such as optical, temperature, mechanical, electric, and magnetic fields [15–17]. The sensitivity of these materials to external stimuli is crucial in designing smart implants, drug delivery systems, and innovative biotechnologies, including biosensors, actuators, in vitro diagnostics, cell culture matrices, contrast agents, and bioassays.

Optimizing complex polymer bio-nanocomposite materials for advanced applications, such as scaffolding, tissue regeneration, and controlled drug delivery paves the way for faster and more effective disease treatment.

One of the most fascinating but equally difficult issues facing researchers today is the production of polymeric nanocomposites with better performance and mechanical properties as well as acceptable biological function. For instance, despite appearing to be non-cytotoxic in a test tube, a polymer nanocomposite may not be biocompatible with a real creature [18]. Although though there has been great success in controlling the chemical and biological aspects of live tissues independently, it is difficult to replicate the physical features of living tissues, particularly their mechanical qualities. The mechanical performance of complex biological tissue is superior to that of most synthetic polymer materials, and further investigation is necessary to determine why this is the case. Many research groups have looked at the mechanical properties of specific biological tissues and found that these properties are typically the result of a polymer nanocomposite structure, and that nanoscale hard inclusions are frequently scattered within a softer biopolymer matrix (such as bone) [19–22]. The unique combinations of hard and soft components seen in biological tissues inspired material scientists to design and produce polymer nanocomposites with outstanding mechanical characteristics [23, 24]. Some of these polymer nanocomposites hold potential for use as biomaterials.

One strategy to enhance the performance of materials is to synergistically combine their chemical, physical, and biological properties. Polymer nanocomposites have the potential to combine the best features of the polymer matrix with those of the nanoparticles and nanostructures, if they are successful. By simultaneously adjusting many parameters, a variety of capabilities are being created, and these functions can be used to create new materials for specific biomedical products. This article provides an overview of the most recent techniques for developing polymeric nanocomposite materials for various biological applications. A variety of polymeric bio-nanocomposite materials are created by integrating inorganic nanoparticles with synthetic or natural polymers (Figure 1).

Review of biomedical polymer and silicate nanoparticle-based nanocomposites is done while highlighting their benefits and drawbacks in the biotechnological and medical domains.

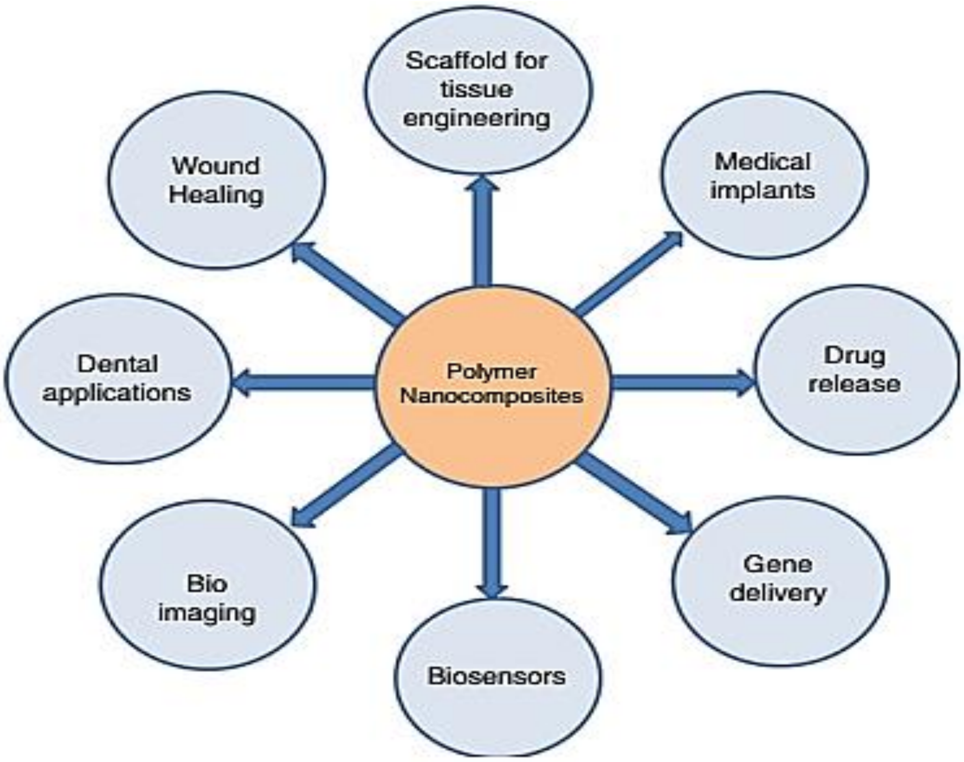

Figure 1. Applications of polymer nanocomposites in biomedicine and biotechnology.

Ultimately, the literature review will demonstrate that only a limited range of material properties can be modified to enhance specific functionalities and improve performance in a biological environment. Basic examinations of structures and properties, along with molecular analyses, are emphasized as essential design principles that become increasingly important for optimizing and formulating existing biomaterials. The development of polymer nanocomposites for various applications, including biomedical nanotechnology, is discussed alongside emerging advancements in biotechnological polymer nanocomposites that may hold biological significance in the future. The design of polymer nanocomposite biomaterials is subsequently guided by an overview of potential challenges and trends.

Biomedical polymers enhanced with clay-based silicate nanoparticles.

By adding silicate nanoparticles, the mechanical properties of synthetic and natural polymers have been dramatically improved (Table 1). The resulting polymer nanocomposites often exhibit significant enhancements in their structure, modulus, strength, and toughness, which cannot be attained by using the polymer alone[25–27]. To enhance polymers commonly used in biomedical applications, silicate nanoparticles have been incorporated into them. However, only a limited number of studies concentrate on polymer nanocomposites that may be relevant to biomedicine. When developing silicate-reinforced polymers for biomedical applications, several challenges must be addressed, such as the accumulation of non-degradable silicate nanoparticles in vivo and concerns regarding the long-term biocompatibility of these materials. It's important to note that in vivo biocompatibility does not always equate to non-cytotoxicity.

Table 1. Nanoparticles of cloisite (modified MMT clay) and montmorillonite (MMT clay) are present in some biomedical polymers.

Nanoparticles	Polymer	Experimental Observations	References
MMT	PLG	Toughness and elongation of the nanocomposites enhanced due to addition of nanoparticles. Physical cross-linking between polymer and nanoparticles triggered a toughening mechanism via multiple crazing and shear yielding.	[28]
MMT	PLLA	Increase in tensile modulus observed with addition of MMT. Enhanced surface interaction between nanoparticles and polymer decreased polymer crystallinity and promoted degradation of the nanocomposite.	[29]
MMT	PLLA	MMT improved structural integrity of the nanocomposites.	[30, 31]
MMT	PLLA	MMT improved compression properties and hydrophilicity of the polymeric matrix.	[32]
MMT	PLLA	Higher amounts of MMT and fully exfoliated structures gave rise to stiffer materials. Addition of MMT suppressed polymer crystallization due to enhanced surface interactions.	[33]
MMT	Gelatin chitosan	Lower degradation rate and enhanced cell adhesion observed after addition of MMT to the polymer blend.	[34]
Cloisite	Ethylene vinyl acetate	10% clay concentration produced materials with the higher moduli and enhanced cell proliferation.	[35]
Cloisite	Polyurethanes	Nanocomposites had a 5 fold lower permeability towards water vapor and enhanced mechanical properties.	[36, 37]

Although a substantial portion of the research in this field focuses on enhancing mechanical properties, biological limits are often not adequately addressed. For example, poly(lactic-co-glycolide) (PLG), which is biocompatible and biodegradable but brittle, has been researched for applications, such as sutures, resorbable meshes, and controlled drug release. Incorporating small quantities of surface-modified clay nanoparticles (natural montmorillonite clay, MMT = multilayer silicate) can enhance this polymer's toughness and elongation in tensile tests, increasing from 7% for the pure polymer to 210% for the polymer nanocomposite. The researchers suggest that the strength and toughness of these composites result from the physical crosslinking between the polymer chains and MMT silicate nanoparticles. With repeated crazing and shear yielding, these physical cross-links increase the polymer's capacity to degrade and initiate a toughening mechanism.

In a different study, Lee et al. improved the mechanical properties of poly L-lactic acid (PLLA) model scaffolds using silicate clay nanoparticles (MMT). The resulting polymer nanocomposite scaffolds had a tensile modulus that was 40% greater than that of pure PLLA scaffolds. The nanocomposite scaffolds created by adding MMT nanoparticles showed a faster rate of biodegradation than the pure polymer [29, 38]. Lee et al [30]. Carried out different research using silicate clay. The researchers concluded that the mechanical stability and biodegradation of PLLA nanocomposites could be precisely regulated through the incorporation of layered silicate nanoparticles. In earlier publications by the same authors and others, the biodegradation morphology of silicate-PLLA nanocomposites was characterized in more depth. The scaffolds generated using fiber-spinning showed better structural integrity during the biodegradation of the polymer. Potential exists for the application of fiber scaffolds at the ligament, cartilage, and bone interfaces. This is so because porous, fibrous materials facilitate cellular penetration and have strong mechanical qualities. Unfortunately, the study did not address the fate or degradation of the natural montmorillonite clay (MMT) within the PLLA scaffolds, which remains a significant challenge, particularly since the authors aim to utilize these materials as biodegradable scaffolds for tissue engineering. The following sections of this review will show how the inclusion of silicate nanoparticles may facilitate bone growth and healing; as a result, PLLA-clay nanocomposites may have significant biological potential.

Polymer/particle leaching and micro compounding were used by [32] to make porous PLA-MMT nanocomposites. The inclusion of MMT improved the compressive performance of the polymer nanocomposites, approaching cancellous bone qualities. Cell adhesion was directly influenced by the surface hydrophilicity of the polymer nanocomposite. For instance, the change in the water contact angle from 60.7° to 31.4° was 3% MMT. This is attributed to an increase in the hydrophilicity of the PLA surface, resulting from a reduction in the interfacial tension between the polymer and water. Like Krikorian et al. [33] discovered that the addition of MMT significantly improved the mechanical characteristics of PLLA. In contrast to microphase-separated or intercalated composites, higher concentrations of MMT and exfoliated structures resulted in stiffer materials. Nanoparticles that had been exfoliated prevented polymer crystallization because they had better surface interactions. Moreover, when silicate concentration and exfoliation rose, PLLA-MMT nanocomposites grew stiffer and more transparent. No prospective applications of the authors' materials in biology were mentioned. [34] demonstrated that the intercalated structure of MMT-gelatin-chitosan degrades more slowly than a gelatin-chitosan scaffold. By adjusting the MMT concentration, the deteriorating rate can also be altered. Increased cell adhesion and proliferation were observed on the MMT-gelatin-chitosan nanocomposite film. Chitosan can be used to create glycosaminoglycans, which can aid with cartilage integration.

Other nanocomposites composed of ethylene vinyl acetate and natural cloisite clay were also investigated by Lewkowitz-Shutoff et al. [35]. In addition to examining the adhesion and growth of human dermal fibroblasts on the surfaces of polymer nanocomposite materials, these researchers also studied the mechanical properties of clay. Clay concentrations of 10% produced materials with the highest moduli, according to the findings of the mechanical testing. Comparable outcomes were found for cell growth, which demonstrated that it was greatest on polymer nanocomposites surfaces containing 10% clay. The substrates utilized for fibroblast cell culture had higher clay content, which led to poor growth curves and crooked actin filaments. Iron adsorption on cloisite clay resulted in magnetic polymer nanocomposites, which promoted the proliferation of MC3T3 osteoblast cells on the material's surface. Enhanced osteoblast cell growth was achieved by culturing osteoblast cells on electrospun aligned fibers in a continuous magnetic field. Its capacity to coordinate various cell types enables the ongoing development of this system for tendon or bone repair. Additionally, the barrier properties of polymer nanocomposites can be utilized in sealed medical devices to protect pacemakers and power sources from the body's moist environment. For instance, biomedical polymers used in the construction of pacemakers, implantable artificial hearts, and left ventricular assist devices must not only possess the appropriate mechanical properties but also be non-thrombogenic, exhibit reduced calcification, and have low permeability rates. Polyurethanes are among the traditional biomaterials commonly used for these applications due to their excellent flexural performance and favorable blood compatibility. Since polyurethanes are typically porous to water, air, and water vapor, this porosity may lead to the failure of the microelectronics they are designed to encapsulate [39]. Organic modified silicate nanoparticles (modified MMT = cloisite clay) were incorporated into biomedical polyurethanes to decrease permeability while maintaining the desired biocompatibility and mechanical properties [40]. The resulting polyurethane-silicate nanocomposites exhibited a fivefold reduction in permeability to water vapor compared to the original polymer. The mechanical properties of the polymer nanocomposite were also considerably improved.

Silicate-Based Hydrogels for Potential Medical Applications

Silicate nanoparticles derived from layered clay can also be utilized to greatly enhance the mechanical properties of polymer hydrogels, in addition to bulk materials (Table 2). Hydrogels have gotten a lot of attention in the realm of biomedical engineering due to how much they mimic soft tissues. Yet, the low mechanical strength of hydrogels typically precludes their application in practical settings. Silicate nanoparticles (clay) have been used in several publications as either fillers or cross-linkers to strengthen the polymer network in hydrogels with potential applications in biomedicine and boost their mechanical strength [40]. Laponite, a type of silicate, is commonly used as a physical or covalent cross-linker in polymers. It is made up of artificial and charged silicate nanoparticles. Synthetic laponite provides several benefits over natural montmorillonite, such as single layer nanoparticle dispersions, high purity, gelation properties, and a history of use in pharmaceutical and cosmetic applications. Silicate cross-linked polymer hydrogels are created using two polymers: poly (acrylamide) and poly (ethylene oxide) (PEO) [41, 42]. Desirable biomaterials that are used as culture dishes for cell sheet engineering, bioseparation devices, and drug delivery systems include stimuli-responsive poly(N-isopropylacrylamide) (PNIPAM) hydrogels. Due to its lower critical solution temperature and thermosensitive coil to globule transition, PNIPAM can be used in a variety of biological applications.

Table 2. Hydrogels made of polymer-Laponite nanocomposites having promise for biomedicine.

Nanoparticles	Polymer	Experimental Observations	References
Laponite	PNIPAM	Ultrahigh elongation with near-complete recovery, rapid deswelling responses to temperature changes and large equilibrium swellings were observed due to addition of Laponite to the polymeric matrix.	[43–45]
Laponite	PNIPAM	Cell sheet easily detached by changing temperature.	[41]
Laponite	PEO	Cells cultured on the surfaces of PEO-Laponite gels attached and proliferated easily.	[46, 47]

Although the precise molecular interactions between the polymer and silicate nanoparticles remain unclear, cross-linking PNIPAM to Laponite involves initiating monomer polymerization from the silicate nanoparticles [48]. Stresses can be released during mechanical deformation thanks to the structural homogeneity of the silicate cross-linkers utilized to make the hydrogels. Mechanical testing findings show that these PNIPAM-Laponite hydrogels have extraordinarily high elongation with almost complete recovery, rapid de-swelling reactions to temperature variations, and considerable equilibrium swellings. Extensive elongations of greater than 1000% were produced by tensile moduli ranging from KPa to MPa [43]. Both the compressive and tensile moduli were affected by the silicate concentration. The compressive moduli can be further enhanced by incorporating additional covalent cross-linkers [49]. This polymer nanocomposite approach has been tested with a variety of silicate nanoparticle and polymer combinations, but only a small number of organizations have investigated its potential for biomedical applications. In the introduction of their paper, the researchers note that their highly extensible hydrogels demonstrate excellent blood compatibility and minimal inflammation when tested in an animal model.

The first PNIPAM-Laponite nanocomposite hydrogels were developed by Haraguchi et al. Following this, they investigated cell cultivation and cell sheet detachment on the hydrogel surfaces. Human hepatoma cells, cutaneous fibroblasts, and umbilical vein endothelial cells exhibited varying levels of adhesion and proliferation based on the concentration of silicate present. By utilizing the temperature-responsive behavior of PNIPAM nanocomposites, confluent cell sheets were able to be spontaneously detached from the hydrogel surfaces (Figure 2). This method offers innovative approaches for designing cell sheets. The new PNIPAM nanocomposite is classified as a biomaterial or biomedical material due to its direct interaction with living cell sheets.

Other polymer nanocomposite hydrogels with potential biomedical uses are made using PEO that has been physically bonded to Laponite [50]. PEOs are some of the synthetic water-soluble polymers that have received the most attention from researchers and have attracted a lot of interest in the biomedical sector [51]. Materials with PEO modifications can help cells develop because of their biocompatibility and ability to stop protein denaturation. When coupled with laponite nanoparticles, PEO rapidly adsorbs and desorbs from their surfaces, resulting in injectable, self-healing, and mechanically resilient hydrogels. Despite the fact that this type of hydrogel has been the subject of published research for more than ten years [52]. The molecular interactions between polymers and silicate nanoparticles are not yet fully understood. PEO-Laponite hydrogels are among the most extensively studied model systems for exploring fundamental polymer-clay interactions and shear orientations. Recently, cell growth studies have indicated for the first time the biomedical relevance of PEO-Laponite gels, showing that murine fibroblast cells cultured on their surfaces adhere and proliferate readily. Incorporating chitosan into PEO-Laponite hydrogels enhanced cell adhesion and spreading while preserving mechanical strength, injectability, and self-healing properties, which are primarily influenced by the synthetic polymer and laponite components. Consequently, a nanocomposite hydrogel containing small amounts of chitosan maintains its mechanical strength while also benefiting from the properties of chitosan.

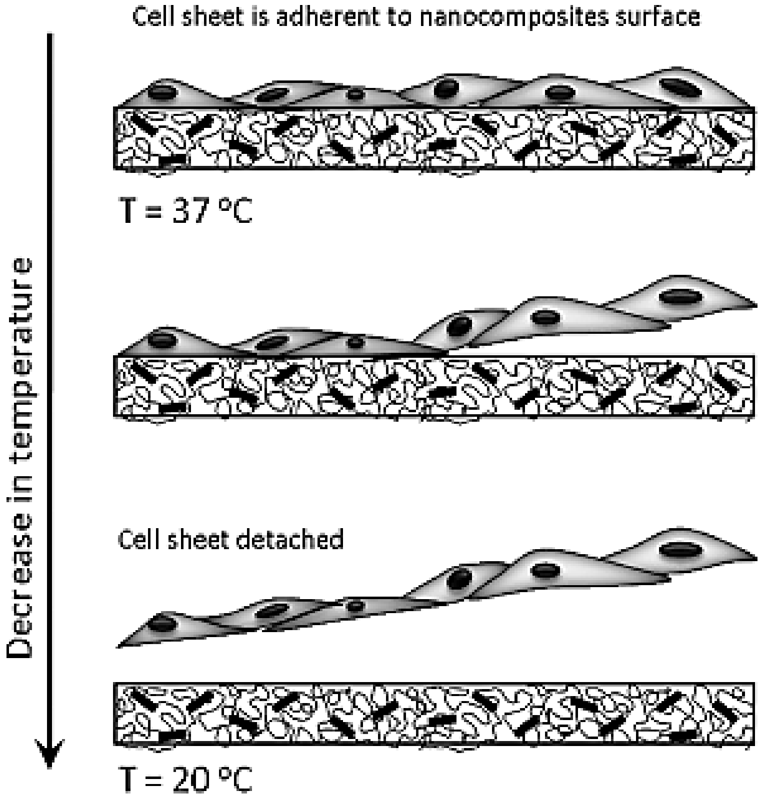

Figure 2. Cell sheets can be split by growing cells atop temperature-responsive polymer nanocomposite materials, allowing for separation upon lowering the temperature below the lower critical solution temperature, which induces a conformational change in the polymer.

Recent Advances in Polymer Layered Silicate Nanocomposite for Drug Delivery Applications

One problem that needs to be resolved by biomaterials for drug delivery is the burst release of pharmaceuticals that are encapsulated or confined. By controlling the release kinetics of a drug, one can enhance the therapeutic effects and alter its biological activity. Silicate-based polymer nanocomposites offer good barrier qualities because of the challenging diffusion pathways that small molecules must travel through the substance to pass through it (Figure 3) [53]. This trait can be used in the creation of applications for delayed medication release. Model drugs have been added to nanocomposites made of diverse biomedical polymer and clay mixtures (Table 3). For instance, cloisite clay-based organic modified silicate nanoparticles were added to polyethylene (ethylene-co-vinyl acetate) to assess the release kinetics of dexamethasone [54]. The authors found that a sustained release of dexamethasone and a higher mechanical strength of the polymer nanocomposite were caused by an increase in the concentration of silicate nanoparticles. It was proposed that the silicate nanoparticle's aspect ratio and degree of dispersion influenced the drug release kinetics [54].

It is also possible to deliver injectable medication using polymer nanocomposites that respond to environmental factors like temperature [55]. Discussed the temperature-dependent sol-gel transitions in thermosensitive nanocomposite hydrogels composed of pluronic-type polymers and laponite nanoparticles in their research injectable applications rely significantly on pluronics, which are triblock copolymers consisting of poly (ethylene oxide), poly (propylene oxide), and poly (ethylene oxide) (PEOxPPOy-PEOz). Due to their rapid disintegration, pure pluronic hydrogels are unsuitable for applications that necessitate long-term drug release. The temperature of the pluronic phase transition was shown to be changed by the inclusion of silicate nanoparticles, which also increased the hydrogels' resistance to dissolution. Thus, a drug called albumin, a macromolecular model, may leave the body for longer.

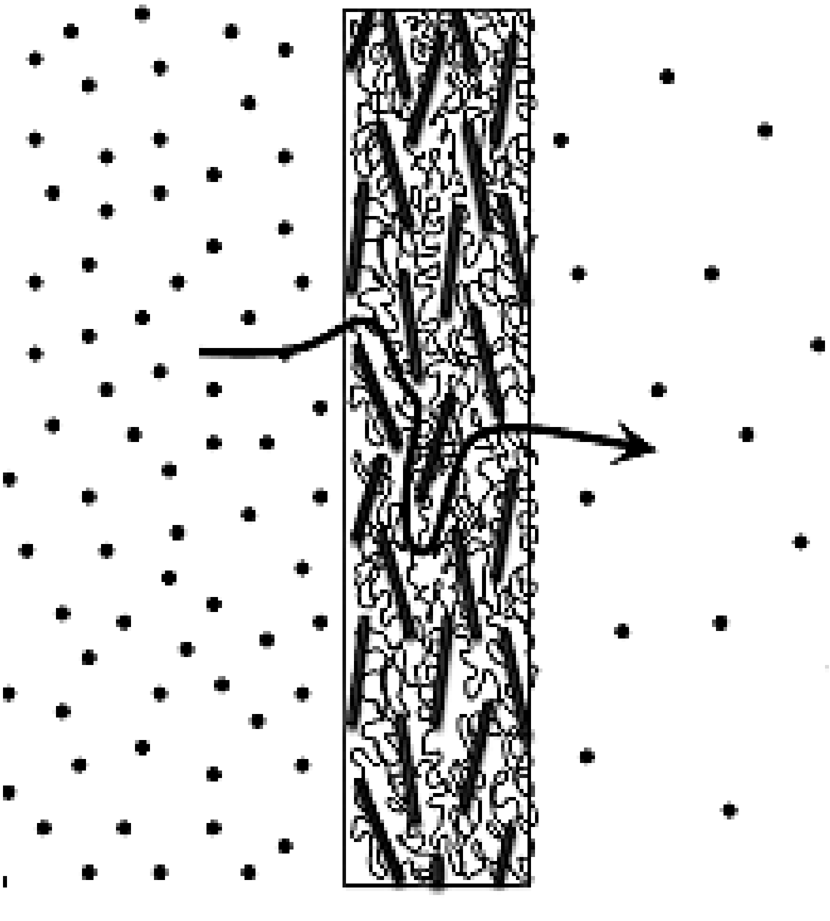

Figure 3. Silicate-based polymer nanocomposite materials display reliable barrier properties because of the challenging path that small molecules must travel through the material, which makes them useful in sustained drug delivery applications.

Table 3. Advancements in polymer-layered silicate nanocomposite materials for drug delivery uses.

Nanoparticles	Polymer	Experimental Observations	References
Cloisite	Poly (ethyleneco-vinyl acetate)	Addition of nanoparticle resulted in slower release of dexamethasone. Moreover, release kinetics were dependent on the aspect ratio and degree of dispersion of the nanoparticle.	[54]
Laponite	Pluronic	A temperature dependent sol-gel transition was observed in the nanocomposites. Laponite enhanced the dissolution resistant properties of the hydrogels and release of entrapped macromolecular drug was slowed down.	[55]
Bentonite	Acrylic acid PEG methyl ether acrylate	Elution kinetics strongly depended on the interactions between the surface charges of the clay and the drug.	[56]
Laponite	PEO polyamide	Molecular interactions between Laponite and drug resulted in sustained release profiles.	[57]

In a study by Lee and Chen [56], model medications were delivered using hydrogels made of natural Bentonite clay nanoparticles and acrylic acid-poly (ethylene glycol) methyl ether acrylate. The researchers discovered that the elution kinetics were notably affected by the interactions between the drug and the surface charges of the clay. Vitamins B12 (zwitterionic), B2 (uncharged), crystal violet (cationic), and phenol red (anionic) were employed as model pharmaceuticals in the study. Attractive interactions between the negatively charged silicate surfaces and the drug led to slower release rates, while repulsive interactions between them accelerated the rate of drug elution. The authors' hydrogels' mucoadhesive properties, which increased the efficiency of drug administration, are highlighted. In a separate study, Takahashi et al. [57] reported the ability of a PEO-polyamide block copolymer-Laponite nanocomposite to transport the uncharged hydrophobic model drug pyrene. The sustained release drug delivery patterns to a period of weeks were produced by the molecular interactions between the pyrene and laponite.

Bioactive Glass Nanocomposites for Tissue Engineering and Repair

Studies from the past and the present show that silicon dioxide-containing bioactive nanostructured materials, such as silicate, bioglass, wollastonite, and silicon-doped calcium phosphate, combine well with biodegradable polymers to exhibit excellent bioactivity and encourage apatite formation both in vitro and in vivo [58]. Early studies revealed that silicon, which occurs naturally in living things, is essential for cell metabolism and the growth of cartilage and bone [59–61]. For instance, studies by Schwarz et al. [60] and Hensch et al. [62] examined how live tissue interacted with bioactive glasses, whereas found that silica may work as a cross-linking agent in connective tissue. Hensch et al. [62] enhanced these bioactive glasses for the treatment of bone defects and to promote cell growth (Figure 4). Vogel et al. also investigated the effect of bioactive glass solubility on the adhesion of implants to bone. During implant studies of bioactive glasses in rabbits, these materials were found to be nontoxic and noninflammatory [63]. Bioactive glass ceramics' properties have typically been carefully studied. Several studies examining implants made of bioactive silicate found that the implants induce bone growth, enhance osteogenic proliferation, and activate genes associated to bone [64, 65]. The ability of these implants to promote bone tissue growth at their surface and attach to the surrounding tissue allows for implant fixation in hard tissue engineering applications [66, 67].

Some polymer bioglass composite materials can be used for both hard and soft tissue engineering. For example, the use of poly(DL-lactic acid) (PDLLA) bioglass composites for bone tissue engineering has been studied by Verrier et al. [68]. Meanwhile, Verrier et al. [69] demonstrated that the porous foams of PDLLA bioglass support and positively influence the proliferation and behavior of human osteosarcoma cells and human lung carcinoma cells, thereby opening new avenues for lung tissue engineering applications. Research conducted by Day et al. [70] investigated the morphology of fibroblasts and observed neovascularization in polyglycolic acid meshes that were coated with bioglass. While the bioglass particles used in these three studies were micron-sized, nanoparticles may also prove to be effective. Nanophase or nanoparticle-containing ceramic materials (with grain sizes less than 100 nm) have an advantage over conventional ceramic materials (with grain sizes greater than 100 nm) in terms of osteoblast adhesion, proliferation, and an increase in alkaline phosphatase production, as well as mineralization [71]. Due to their inadequate mechanical properties, bioactive glasses cannot be used independently for applications that require strength, such as in orthopedic surgery. Combining polymers and bioactive glasses is a potential method to improve mechanical strength and toughness. As a result, bioactive silicate nanoparticle-containing polymer nanocomposites could offer novel prospects and methods in the sectors of dentistry and bone repair. Many techniques direction have been reported (Table 4).

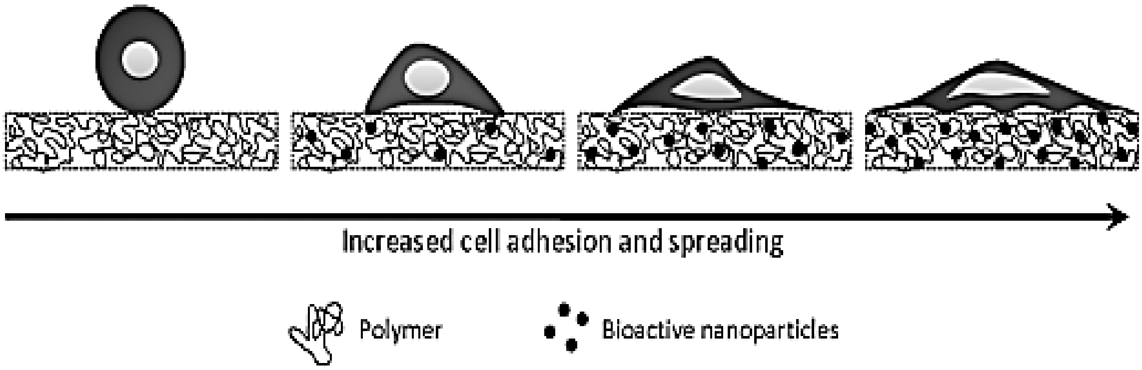

Figure 4. Oftentimes, adherent cells have an odd spherical form and are unable to connect to unaltered polymers. Yet, the addition of bioactive nanoparticles like bioglass enables a more organic cell form.

Table 4. Glass nanocomposites containing bioactive polymers.

Nanoparticles	**Polymer**	**Experimental observations**	**Ref.**
Bioglass	P3HB	Nanocomposite supported osteoblast cell attachment, proliferation and differentiation.	[72]
Bioglass	P3HB	Addition of nanoparticles enhanced modulus and strength of the nanocomposite compared to microcomposite. Addition of bioglass resulted in deposition of hydroxyapatite when submersed in simulated body fluid.	[73]
Wollastonite	PCL	Addition of wollastonite improved the nanocomposite young’s modulus, tensile strength and fracture toughness. Nanocomposites supported in vitro formation of apatite.	[74, 75]
Bioglass	PLA	Addition of bioglass fiber enhanced in vitro bioactivity of the nanocomposite. Significant increase in alkaline phosphatase activity observed in nanocomposite compared to pure PLA.	[76]
Bioglass	Poly L-lactide	Increase in bioglass concentration reduced water absorption capacity but enhanced degradation rate.	[77]
Bioglass	Chitosan and chitosan gelatin	Bioactive nanocomposite scaffolds promoted osteoblast cell adhesion and spreading.	[78, 79]
Silica	Chitosan	Improved mechanical properties observed due to addition of bioglass. Bioglass aided in significant increase in cell adhesion, proliferation and alkaline phosphatase activity. Enhanced bone regeneration observed when the nanocomposite was implanted in vivo.	[80]
Silica	Collagen	Improved bioactivity of the material; accelerated the formation of bone-like apatite and led to the differentiation of human monocytes into osteoclast-like cells.	[81]
Silica	Chitin	Chitinous organic matrix provided a template for biodirected deposition of the silicate mineral phase.	[82]
Silica	Silk	High toughness and strength due to deposition of silica.	[83]
Wollastonite	Silk	Wollastonite enhanced both the mechanical strength and bioactivity of the nanocomposites. In vitro cell attachment and proliferation were also observed on the nanocomposites.	

One of these techniques was explored by Misra et al., who studied the impact of bioactive glass nanoparticles on the bioactivity, degradation, and in vitro cytocompatibility of poly (3-hydroxybutyrate) nanocomposite. As is typical for polymer nanocomposites, incorporating nanoparticles into the polymer enhanced its mechanical properties, such as strength and modulus, compared to the inclusion of micron-sized particles. The formation of hydroxyapatite on the surface of the materials indicated that the polymer nanocomposites exhibited high bioactivity. Improvements must be done for this system to be stable over the long term because weight loss and water intake were found to rise with increasing bioactive glass content. The polymer nanocomposites are favorable for cell attachment, proliferation, and differentiation, according to cytocompatibility experiments that included osteocalcin synthesis and alkaline phosphatase activity using human MG-63 osteoblast-like cells. Another approach suggested by [74] involved the development of polymer nanocomposites using polycaprolactone (PCL) and wollastonite nanoparticles for bone repair. Wollastonite, a naturally occurring calcium silicate with bioactive properties, significantly enhanced the young’s modulus, tensile strength, and fracture toughness of the materials when modest amounts were added. When apatite production was noticed on the wollastonite surfaces, the bioactivity of the polymer nanocomposite was validated. Overall, our findings are consistent with those that Wei et al. previously achieved on polycaprolactone calcium silicate nanocomposites [75]. Kady’s research on nanocomposites made of poly L-lactide and bioactive glass nanospheres [77] as well as the work of Kim et al. Two further research on nanocomposites that have been investigated for bone tissue engineering and healing are on PLA bioactive glass nanofiber composites [76].

By mixing natural polymers like chitin and chitosan with bioactive silicate nanoparticles, biocompatible, biodegradable, and cost-effective biomaterials can be created. According to recent publications by [78], nanocomposite scaffolds were made by lyophilizing a chitosan solution that contained bioactive glass. In place of a chitin gel, a chitosan solution or chitosan-gelatin mixture can be employed to manage the scaffold’s properties, including swelling, degradation, and bioactivity. Adjusting cell adhesion, growth, migration, and differentiation may be possible with the addition of gelatin to chitosan bioglass composites. The fact that these polymer nanocomposite scaffolds have the requisite basis to be enhanced for application in tissue engineering was noted by the authors [79].

In a different work, Lee et al. [80] created chitosan-silicate nanocomposite membranes for bone regeneration by employing the sol-gel method. The resulting silicate xerogel was found to be uniformly dispersed within the chitosan matrix at the nanoscale. As anticipated, the incorporation of silicate enhanced the mechanical properties of the nanocomposite in comparison to pure chitosan. When immersed in artificial body fluid, the chitosan-silicate nanocomposites led to the deposition of calcium phosphate minerals, showing in vitro bioactivity. The addition of silicate enhanced the adhesion, proliferation, and alkaline phosphatase activity of osteoblasts. The histological results from the implantation of the polymer nanocomposite in a rat calvarium model demonstrated a significant increase in bone regeneration compared to pure chitosan. Overall, the addition of bioactive silica nanostructures was reported to enhance the mechanical and biological properties of the chitosan matrix. VA has been widely used in drug administration, dialysis membranes, wound dressings, and other biomedical devices even though pure poly (vinyl alcohol) (PVA), which has less, has better biodegradability than modified PEO and PLGA, which have lower levels. Therefore, polyvinyl alcohol (PVA) and bioactive glass, or a combination of PVA, chitosan, and bioactive glass, can be utilized to create scaffold materials that integrate the mechanical strength of synthetic PVA with the hemocompatibility, bactericidal properties, and biodegradability of natural chitosan polymers, along with the bioactive characteristics of silicate.

Heinemann et al. replicated the bio silicification process using a different method to produce xerogels from silica and collagen in ambient conditions [81]. Novel nanocomposite materials were synthesized using sol-gel methods by altering the ratios of collagen and silicate. The bioactivity of these materials was further improved with the addition of calcium phosphate cements, which facilitated the formation of bone-like apatite and transformed human monocytes into osteoclast-like cells. In a related study, silica-chitin-based bionanocomposites derived from living glass sponges were also reported [82]. The study revealed that the chitin-based organic matrix can facilitate the bio-directed deposition of silicate minerals, resulting in structures suitable for tissue engineering applications in both bone and cartilage. To examine self-assembled nanocomposites made of fibrous proteins, like silk, Winey and Vaia [83] combined chimeric silk proteins with silica nanoparticles. Films and fibers were made from spider silk that had been coated with silica nanoparticles through the application of silicification methods. The shape and structure of the silica nanoparticles were controlled via formulation, improving the mechanical qualities, such as toughness and strength. Silk proteins were also linked with wollastonite to produce bioactive scaffolds that promote cell development and are mechanically robust.

Trends and Challenges for the Future

Polymer nanocomposites offer promising advancements for biomedical materials due to their adaptable nanoparticles, allowing for improved mechanical properties over pure polymers. These composites show potential for hard and soft tissue repair and responsive biomedical devices with refined temporal and spatial control. However, challenges include a lack of established structure-property relationships and limited theoretical models to predict polymer-nanoparticle behavior. Biocompatibility remains uncertain, as polymer nanocomposites can yield varying cytotoxicity results across labs, and their in vivo behaviour is not well understood. Research is currently focused on biocompatible options, especially bioglass-based nanocomposites for tissue engineering and drug delivery, showing promising preliminary results.

CONCLUSIONS

Developing polymeric biomaterials using polymer nanocomposites is a promising approach, offering superior mechanical properties compared to pure polymers. These nanocomposites can be applied in both soft and hard tissue repair. However, challenges remain, including the lack of established structure-property correlations and theories to predict the behavior of polymer-nanoparticle combinations. Biocompatibility is also uncertain, as in vitro cytotoxicity results vary across studies. Further research is needed to understand the complex interactions between nanoparticles, polymers, and biological systems. While preliminary findings in biomedical applications like tissue engineering and drug delivery are promising, much remains to be explored.

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