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Review

Elastomer nanocomposites: Applications in medicine

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ABSTRACT

Polymer nanocomposites represent a family of materials that have assumed great importance in recent years and are the focus of extensive research in academia and industry. They are based on a hybrid product made of a macromolecular matrix and an organic or mineral reinforcement (filler) where in at least one of the physical dimensions can be measured in the range of nanometres; the filler is introduced in a very small amount or volume. A number of recent studies deal with their applications in engineering field and in medicine. Besides thermoplastic and thermoset polymer nanocomposites, the elastomer nanocomposites are studied for potential uses in different fields. This review focuses on the studies done recently concerning applications of elastomer nanocomposites in various areas of medicine such as therapy, tissue engineering scaffolds, antimicrobials, and drug delivery. The elastomers covered in recent studies are polyurethane, natural rubber, nitrile rubber, ethylene-propylene diene monomer, silicon rubber.

KEYWORDS: elastomer nanocomposites, polyurethane, rubbers, applications in medicine.

INTRODUCTION

Thermoplastics, thermosets and elastomers are used more and more to obtain new kinds of composites known as polymer nanocomposites. Because of the nanometric size features of one of its components, nanocomposites possess unique properties not shared by conventional polymer micro and macro composites and offer new research possibilities.

These polymer composites capture much attention in academia, industry and government; their properties are far better than those of many polymers and conventional polymer composites [1-3]. They are based on a hybrid material made of a macromolecular matrix and an organic or mineral filler with at least one physical dimension in the range of nanometres; this nano component is introduced in a very small amount or volume. The most commonly used nanoparticles are layered silicate, spherical nanosilica, carbon black (CB), carbon nanotube (CNT), graphene, bionanofillers, layered double hydroxide, mica, vermiculite, ZnO, CuO, Ag, etc. The properties of polymer nanocomposites depend greatly on the interaction between polymer and nanofiller. Many studies deal with this important aspect of polymer nanocomposites. A recent one provides a new method to quantitatively characterize the elastomer-nanofiller CNT interface at nanoscale resolution [4].

As previously mentioned, besides thermoplastics and thermosets, elastomers are also used for obtaining nanocomposites with interesting applications [5, 6].

Many studies are done on the uses of elastomer nanocomposites in engineering areas such as aerospace, transportation, construction, packaging,

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as well as fabrication of household items, and many others. They are also gaining importance in medicine and biomedical fields such as tissue engineering, manufacture of antimicrobial products, drug delivery, gene therapy, cancer detection and treatment.

The medical field dealing with nanocomposites is known as nanomedicine.

The present review covers a few studies done recently regarding the use of elastomer nanocomposites in medicine. It focuses on elastomers such as polyurethane (PU), natural rubber (NR), nitrile rubber (NBR), silicone rubber and ethylene-propylene-diene monomer (EPDM).

Polyurethane

PUs as commercial polymers constitute one of the most complete and versatile class of macromolecular materials known today. They are obtained by step-growth polymerization in which the chain length increases steadily as the reaction progresses. These polymers can be considered in terms of flexible (soft) segments and much shorter rigid (hard) units. So far, due to its characteristics PU is the most studied elastomer for applications in medicine.

The earliest mention of the use of PUs in medicine was in 1991 [7].

The limitations of Pus' properties led to development of polyblends and composites and more recently to nanocomposites characterized by high biocompatibility, biostability, excellent blood compatibility, and good low-temperature flexibility. They show no toxicity. The improved shape memory of PU composites can be used for applications such as biosensors, synthetic skin bioengineering, tissue engineering, implantable pancreas, ophthalmic devices, cardiovascular stents, etc.

PU without nanofiller has also been studied for its applications in the medical field. Herein, only a few examples of studies done in this regard will be mentioned. Being biostable and biocompatible, it was used in cardiac prostheses, small vascular shunts, and tracheal tubes [8]. Due to its biodegradation rate and other properties including the mechanical ones, PU is suitable for tissue engineering [9]. Porous PU scaffolds were obtained in one study by using solvent casting/particulate leaching technique combined with thermally induced phase separation [10].

PU films have been shown to have antibacterial characteristics through their release of sulfathiazole; this was evaluated based on the inhibition of *Escherichia coli* growth [11].

An amphiphilic poly(ether urethane) was synthesized in an earlier study [12] from a triblock copolymer, an aliphatic diisocyanate and an amino acid-derived diol. By varying the amount of poly(ether urethane), hydrogels which could suit applications such as *in situ* drug-cell delivery or bioprinting of the scaffolds were prepared [12].

Polyurethane nanocomposites

PU/biocellulose nanofiber nanocomposites have been studied for producing porous scaffolds. Biodegradation investigation showed that over a 5-week period the scaffold samples exhibited a mass loss which ranged from 17 to 29%. The loss was higher when soft segment content was higher. This range of biodegradation demonstrates potential application in short-term implants [13].

A research paper [14] proved the development of a multifunctional antimicrobial and fluorescent PU/ZnO nanocomposite coating with azide-alkyne click chemistry. The obtained PU nanocomposites are extremely resistant towards various bacterial and antifungal attacks. Such resistance is attributed to the presence of ZnO nanoparticles having attached pyrene fluorophore. The antibacterial activity of PU foam/ZnO nanocomposites against *Staphylococcus aureus* and *Eschericia coli* was also investigated [15].

Similar nanocomposites obtained by using polyadition process based on 44'-methylene (cyclohexyl isocyanate, poly (ε-caprolactone) diol and 1, 4 butandiol exhibit antibacterial characteristics against the same bacteria [16].

PU/chitosan (CS)/PU/alginate (ALG) nanoparticles showed better encapsulation efficiency, sustained swelling and *in vitro* insulin release than CS/PU/ALG and PU/CS/ALG nanocomposites. PU-incorporated nanoparticles were also found to be nontoxic and safe to be used as drug delivery devices. Acute toxicity studies that included a histopathological test showed evidence for the

safe use of the developed core-shell PU/ALG/CS polymer nanocomposites as oral insulin-delivery medium [17, 18].

Concerning the occurrence of in-stent restenosis and stent thrombosis of stent implantation with balloon angioplasty, a dual-induced self-expandable stent based on biodegradable shape memory PU nanocomposites has been developed. Due to very good dual-responsive shape memory properties, desirable mechanical properties, biocompatibility and biodegradability, the polylactide-based PU/Fe_3O_4 nanocomposites show potential application in biomedical devices such as vascular stents [19].

Memory behaviour showed that recovery stress for PU/CNT samples was increased to a maxium of 100% and no harmful effects on shape recoveries were observed [20].

To upgrade the PU shape memory and other useful properties, CNT and grahphene are recommended as nanofillers [21].

PU-carotino oil nanocomposites in the form of a patch showed delayed blood clotting properties suggesting the antithrombogenic nature of the patch in comparison with pure PU. The newly developed nanocomposites possessing blood compatibility might open the doors for their use as a substitute product in the regeneration of cardiac and graft tissues [22].

A PU/CuO nanocomposite was obtained *via* several electrical processes. Films were produced with antimicrobial properties against methicillin-resistant *Staphylococcus aureus.* Significant reduction of population was demonstrated with 10% w/w CuO over a 4-h period. This approach demonstrates the potential of generating tailored antimicrobial structures for applications in designer filters, patterned coatings, breathable fabrics, adhesive films (as opposed to sutures) and mechanically supporting structures [23].

PU/cellulose nanofibrils (5 wt.%) have been used for various versatile medical implants [24].

The water-borne PU/regenerated cellulose nanoparticles also have great potential to be used in medical applications [25].

Nanopolyester/ether-urethane can be easily designed to modulate the hydrophilic balance and to embed specific functional groups, thus representing a promising solution as a targeted delivery system in combination with cytotoxic drugs [26].

Dox-loaded poly(ortho ester urethanes) nanoparticles show prolonged blood circulation time and improved accumulation in solid tumors, leading to enhanced therapeutic efficacy [27].

Other elastomer nanocomposites

Natural rubber (NR) latex obtained from *Hevea Brasiliensis* showed no toxicity and allowed osteoblast adhesion, proliferation and mineral extracellular matrix deposition, thereby proving to be suitable for guided bone regeneration [28].

A polyblend NBR/NR/montmorillonite (MMT) was produced in a previous study [29] by using a revised two-roll technique. The obtained elastomer nanocomposite acts strongly against a spectrum of microbials, both bacteria and yeasts.

The Ketjenblack-reinforced deproteinized NR nanocomposite was successfully tested in a previous study [30] for the real-time monitoring of finger pressure. Farther accessory movements of bone (grade 1 and 2) were demonstrated on a subject with spinal pain, using the developed system for the first time in real life situations.

An elastomer nanocomposite based on EPDM, using nano rice husk powder was prepared in a previous study. The surface of the nanofiller was grafted with maleic anhydride (MA)-g-EPDM to improve its compatibility with the elastomer. The *in vitro* study indicated that the nanocomposites were non-toxic for human gingival fibroblast and could be developed for future medical uses [31].

Nanocomposites made from silicon rubber solution vulcanized at room temperature/CNT/CB can be used in the manufacture of medical equipments such as feeding tubes, catheters, respiration masks, synthetic muscles, seals and gaskets [32].

Poly (polyol alkanoate)s elastomers have been intensively investigated due to their potential for soft tissue engineering. A family of novel hyperbranched elastomers based on pentaerythritol and adipic acid modified with poly (ethylene glycol) was synthesized. Paclitaxel release tests proved to be sustained and constant for a period of time. Anti-proliferation studies

have shown that plain materials have cytostatic effects, preventing cancer cells from proliferating. These new products can find application in controlling cancer tumor growth [33].

Block copolymer nanocomposites containing polybutylene segments have been studied for their application in cancer therapy [34], and their use as antimicrobial agents [35].

Copolymers of poly[2-(dimethylamino) ethyl methacrylate]-poly (butylene succinate)-poly [2-(dimethylamino) ethyl methacrylate] could form spherical nanomicelles with small particle size. Drug loading and release experiments have been conducted using doxorubicin as a hydrophobic model drug [36].

CONCLUSION

According to recent studies, besides PU, its nanocomposites show potential in biomedical equipment manufacturing applications such as scaffold forming, tissue engineering, drug delivery, blood vessel reconstruction and the manufacture of some medical equipment.

Nanocomposites based on other elastomers such as NR, NBR, EPDM, siliconic, and polybutilen copolymers also show promise for various applications in medicine.

CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

ABBREVIATIONS

AG	:	Alginate
CB	:	Carbon black
CNT	:	Carbon nanotube
CS	:	Chitosan
EPDM	:	Ethylene-propylene-diene monomer
MA	:	Maleic anhydride
MMT	:	Montmorillonite
NBR	:	Nitrile rubber
NR	:	Natural rubber
PU	:	Polyurethane

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