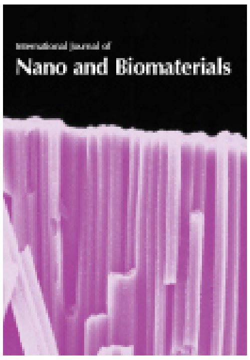

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Polymeric bio-nanocomposite in the biomedical field: a review of the current status and challenges

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Polymeric bio-nanocomposite in the biomedical field: a review of the current status and challenges

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Abstract: The development of polymer nanocomposite has emerged as a promising class of materials in biomedical applications. The various formulations and chemistries of compositions, improvement techniques in surface modification, and advancements in technologies and polymerisation techniques have led to applications in dentistry, bone reconstruction, tissue engineering, etc. The polymeric nanocomposite material has shown superior hardness, toughness, stiffness, strength, electrical and thermal conductivity, chemical resistance to corrosion, etc. This paper presents state-of-the-art applications and efforts made to develop advanced materials in the biomedical field. Additionally, an approach was discussed to improve the performance of materials using modifications in filler technology. The last section highlighted several characteristics, prospective uses, and challenges of polymeric nanocomposite materials in the biomedical industry.

Keywords: nanocomposite; polymeric materials; mechanical properties; biomedical applications; nanofiller; nanofibre; carbon nanotube.

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1 Introduction

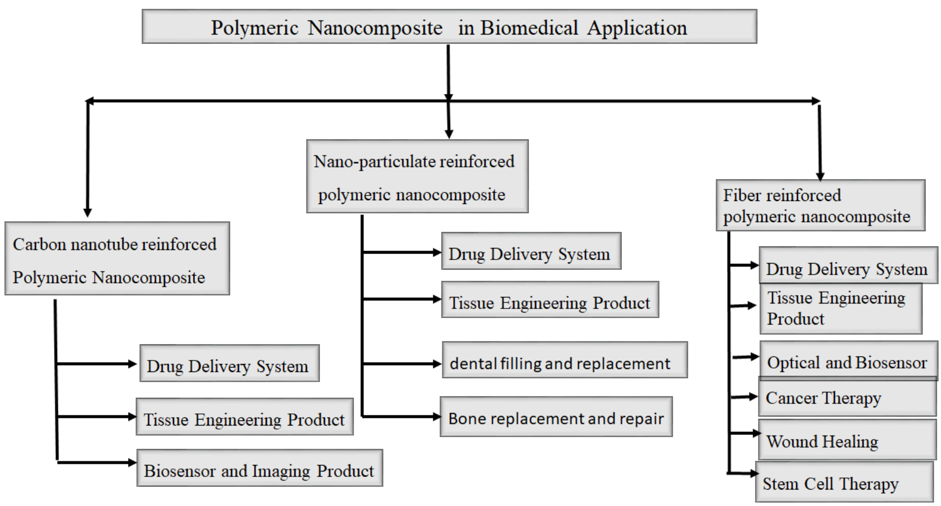
Due to ease in manufacturing, low processing cost, light weight, mechanical flexibility, availability and low thermal conductivity, polymer composites have been considered as the main or alternative material for a large number of applications.

Major strategies for modifying the formulation of polymer composite have been considered by varying filler contents, filler size and filler type. Polymer composite consists of mainly resin and filler/fibre. Polymer composite are prepared by many conventional methods such as hand layup methodology, compression moulding, resin mould transfer moulding, injection moulding etc. and advanced methods such as 3D printing technology (Kumar, 2022; Kumar et al., 2020).

The purpose of adding a matrix is to bind fillers/fibres and allow them to provide interfacial strength. The purpose of adding fillers is to enhance the physical, mechanical, thermal, chemical and wear properties of composite materials. Decreasing the size of filler and increasing the filler content enhance the physical and mechanical performances of composite materials. In this regard, nanofillers are generally added to composite materials and termed as nanocomposite is the best option to modify the properties of composite materials. In biomedical applications, polymer composite has been used in a wide range of applications due to better mechanical stiffness and strength, wear resistance, and biocompatibility of polymers (Figure 1). In biomedical applications, the introduction of nanotechnology has provided novel methods for treating human ailments, as well as the replacement of body parts.

This study seeks to highlight the most significant findings in the literature, provide an overview of recent developments in nanocomposite materials and their applications in diverse biomedical fields, and provide possible opportunities for future developments and perspectives. An introduction to polymer nanocomposite and associated techniques is given first. The critical investigation of the application of nanotechnology and polymer composite in biomedical applications is one of the major challenges faced by the researcher. Hence, in this regard, the paper can be helpful in the research and development of materials for biomedical applications. The study of polymeric nanocomposite can be carried out in three categories which are Carbon nanotube filled Polymeric nanocomposite, Nano-particulate filled polymeric nanocomposite and Fibre reinforced polymeric nanocomposite. CNTs are prepared by any of fabrication techniques such as Arc discharge method, Laser ablation method and Chemical vapour deposition method etc. Nanoparticles, carbon nanotubes or nanofibres are added to the resin to form nanocomposite and to impart excellent mechanical, electrical, thermal and wear properties in the product.

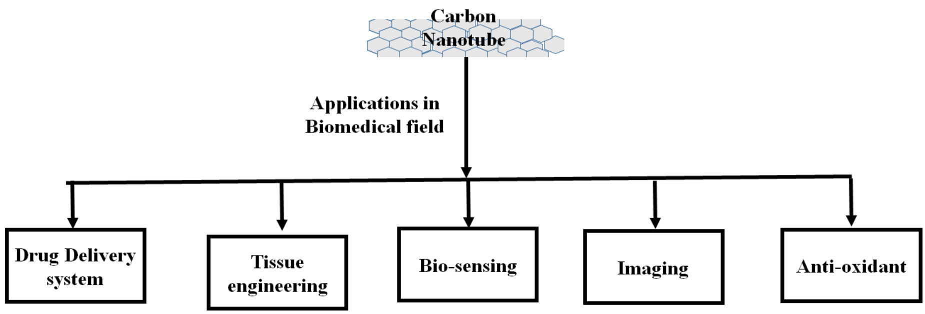
Figure 1 Polymeric nanocomposite in biomedical applications



2 Carbon nanotube filled polymeric nanocomposite

Carbon nanotubes (CNTs) are cylindrical rolled sheet of single layer carbon atom i.e., graphene or multi-layer of such graphene atoms. As a result, both single- and multi-walled carbon nanotubes are possible. Carbon nanotubes have a diameter of less than 1 nanometre. However, in the case multi-walled carbon nanotube, the length of the tube can reach up to several millimetres or micrometres. Excellent electrical properties, lighter in weight, mechanical properties, thermal, properties, chemical stability and extreme corrosion resistance make CNTs promising materials in many applications. The uniform dispersion of CNT filler into resin provides better strength to the materials. However, the dispersion can be improved by treating CNT with clay which leads to improvement in the mechanical and electrical properties (Liu and Grunlan, 2007). Carbon nanotubes are treated with nitric and sulphuric acid to form a carboxylic functional group on the surface. Due to the presence of a functional group in CNT, the interfacial bonding strength between resin and filler is increased which leads to better mechanical strength such as hardness and compressive strength. The applied load is transferred from resin to inorganic and organic fillers (Maron et al., 2017). The detail application of carbon nanotube has been depicted in Figure 2.

Figure 2 Application of carbon nanotube in biomedical field (see online version for colours)



In the biomedical industry, the formation of a shield to protect chemicals from the outside environment makes it suitable for drug delivery systems. It can be used to contain various nanomaterials to separate and protect it from the environment. It is also used for biosensors. Apart from light weight and outstanding mechanical properties, carbon nanomaterials remain unresolved in a medium which makes them very high chemical resistance. The most commonly used carbon nanomaterials are nano-diamonds, carbon nanotubes and some types of graphene such as graphene oxide, few-layer graphene, and reduced graphene oxide (Wick et al., 2014). Its superior mechanical properties make it suitable for applications such as scaffolding for bone tissue engineering, implant, and restoration (Neves et al., 2012). It is reported in various literatures that the addition of CNT as reinforcement in composite improved material performance as such hardness, tensile strength and elastic modulus (Ramnath et al., 2014). The application of nanotechnology in medicine and biomedical engineering spans a variety of fields, including tissue engineering (Arumugam and Ju, 2021; Farah et al., 2016), prosthetics and orthotics (Medupin et al., 2019, 2020; Hovorka et al., 2021), and more recently, diagnosis and therapy.

However, it is also one of the major concerns that the use of nanomaterials in the human body can lead to serious health concerns. Therefore, many biocompatibility and cytotoxicity tests must be performed before introduction into the human body. Another major concern of CNT is its hydrophobicity that makes it difficult to disperse properly in the resin.

2.1 CNT as a carrier in drug delivery system

CNTs have been used as a carrier in many drug delivery applications. The major advantages of CNT include good drug loading capacity and better cell transfection capabilities. Oxidised CNTs are used to load a drug which is popularly known as Doxorubicin (DOX) and is used in the treatment of variety of malignancies (Fabbro et al., 2012). As a drug delivery device, CNTs are favoured over other tubes because of presence of carboxylic groups on their surface that readily functionalise with the intended components. According to Liu et al. (2007, 2009), Doxorubicin (DOX) was loaded polyethylene glycol conjugated single walled carbon nanotube surface to increase permeability and retention. DOX remained attached to CNT and easily released in any toxic neutral and alkaline environment within the healthy body parts (Wells et al., 2018). Another drug used in the treatment of cancer, 10-hydroxycamptothecin (HCPT) was loaded through MWCNT delivery (Wu et al., 2009). Another anticancer drug cis-dichlorodiammine platinum (II) need proper delivery to reduce cytotoxic effect. Ultrashort CNTs (US-tubes) are used for the loading of small molecules of cisplatin. Cisplatin drug is loaded inside the nanotube in the form of nanocluster.

2.2 CNT in tissue engineering

The objective of tissue engineering is to replace damaged tissue with biological tissue. The development in Tissue engineering has been progressing continuously due to advancements in cell and organ transplantation and materials science and engineering. Scaffolding materials with specific properties are required to make cells for the replacement of dead or harmed tissues

The tissue engineering product should have better mechanical properties, biocompatible and good cell adhesive properties (Li et al., 2012). It is also reported that the addition of carbon nanotube scaffolding composite materials enhances the mechanical properties (Andrews and Wiesenberger, 2004). In a similar work, it was found that an addition of 1 weight percentage of single-walled carbon nanotube improved the tensile strength of tissue near to that of natural tissues (Yildirim et al., 2008).

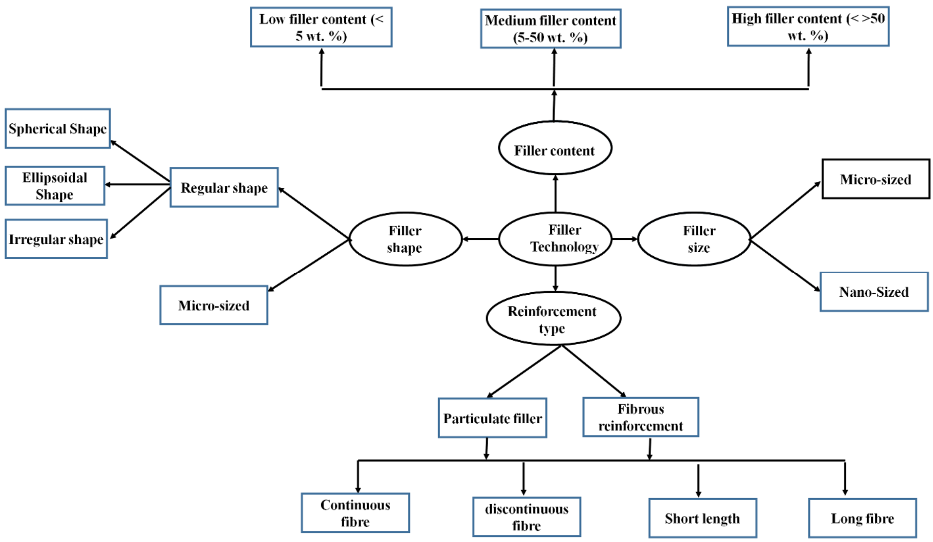
2.3 CNT in biosensor

CNT has been used to identify and monitor defects and bacterial infections in the human body, In this regard, there are many research focusing on in vivo detection of glucose by developing low-cost biosensors. The wide use of carbon nanotubes as glucose biosensors is due to high specific surface area, electrochemical stability and electrical conductivity. In this regard, the Use of carbon nanotubes for electrochemical monitoring for salmonella detection was obtained at less detection time (Punbusayakul et al., 2013). In another research, it was proposed that the addition of CNT improved the sensitivity for electrochemical detection on the surface due to electron transfer. Enhancement of electrical conductivity with the addition of CNT was used as an alternative method for non-enzymatic glucose detectors (Wayu et al., 2019).

3 Nano-particulate filled polymeric nanocomposite

Polymers such as polyamide, polyesters, polysaccharides, and poly nucleic acids, are mixed with nanoparticles of inorganics oxide such as nanoalumina, nanosilica, hydroxyapatite etc. to enhance mechanical and biological properties (Zhang et al., 2018). Fillers are added to the polymer resin to modify the performance of the polymer composite. The strategies related to the addition and modification of filler in the polymer composite are known as filler technology. Filler technology includes the concept of varying filler types, sizes, shapes, and content (Figure 3). Therefore, these nanocomposites are used in various applications such as tissue engineering, drug delivery, dental filling and replacement, and bone replacement/repair. However, a polymer nanocomposite implant must possess standard design criteria that include biocompatibility, biodegradability, physical properties mechanical properties and/or aesthetic properties.

Figure 3 Major factors of filler technology (see online version for colours)



Nanoparticles such as nanoalumina, nanosilica, nanozirconia, nanotitania and nano-hydroxyapatite based polymer composite have been developed by researchers and are being used in many biomedical applications. These ceramic nanoparticles add two important properties to a soft polymer matrix i.e., excellent hardness due to the addition of ceramic particles and excellent binding strength due to the addition of nano-sized filler particles providing good mechanical properties. Due to such outstanding performances of nanofillers, Nano-particulate filled dental composites have been used for dental restoration applications (Kumar and Patnaik, 2022; Kumar and Sharma, 2023; Mahna et al., 2019; Sharma et al., 2019).

Adding nanoalumina and nanosilica improves the mechanical properties of dental composite (Meena et al., 2016, 2019; Kumar et al., 2016a, 2016b, 2018a; Sonal et al., 2018). Adding nanozirconia and nanohydroxyapatite improves the wear resistance of dental composite (Kumar et al., 2016c, 2018b; Bhat et al., 2017). One of the most biocompatible materials such as hydroxyapatite (HAP) based polymer nanocomposites has been used for the replacement of orthopaedic parts.

4 Nanofibre reinforced polymer composite

One of the most common methods for the preparation of nanofibre-reinforced polymer composite is the electro-spinning method. Fibres are different from particulate fillers. It has larger length to diameter ratio. Nanofibres have two exterior dimensions less than 100nm and one dimension that is significantly more. This nano-sized dimension provides high surface area to volume ratio, controllable porosity, superior adhesion with resin component and superior mechanical performance (Bhardwaj and Kundu, 2010; Turky et al., 2017). Due to their exceptional qualities, nanofibres are an excellent choice for a variety of biomedical applications, including as drug delivery systems, dressings for wound healing, biomedical devices, and tissue-engineered scaffolds (such as skin, cartilage, bone, and blood vessels) (Sill et al., 2008). With the extraordinary capabilities of nanofibres, such as efficient control over drug release kinetics for drug delivery applications, it is possible to choose biodegradable or non-biodegradable materials to offer outstanding properties.

It can be short fibre or long fibre depending upon the length of fibre. It is usually thin and flexible. These fibres add some major properties such as physical, mechanical and wear properties and some minor properties such as thermal properties, and dynamic mechanical properties, to the polymer composite. Fibres in nano-size length are used to develop nanofibre-reinforced polymer composite. However, fibre can be natural and synthetic. Some of the popular synthetic fibres are aramid, glass and carbon. These fibres also provide an aesthetic look, thermal conductivity, and corrosion resistance. Natural fibre attracts researchers to fabricate the best suitable and optimised polymer composite due to its lighter weight, low cost, better mechanical properties and renewable and biodegradable resources.

During electro-spinning, a polymer jet is created by applying high voltage to the polymer matrix. These nanofibre-reinforced polymer nanocomposites have been used in optical and biosensors (Wang et al., 2002), tissue engineering (Wnek et al., 2003; Shalumon et al., 2009) and drug delivery system (Sanders et al., 2003; Jayakumar et al., 2010). In recent research, Ag nanofibre-reinforced polymer composite has been used in chemical and electronic parts due to the presence of good catalytic and electronic properties. Further, the composite has also shown better antibacterial properties and hence promised a good choice for wound healing, recovery and tissue engineering applications (Jayakumar et al., 2012). Some of the major findings in biomedical applications are presented in Table 1.

Table 1 Recent findings on biomedical application of application of polymer nanocomposite

Reference	*Composite detail (Resin and filler)*	*Fabrication method*	*Remark/conclusion*	*Applications*
Alkurdi et al. (2022)	Cromolyn polyamide-disulphide nanocomposites	Gelation method	Cromolyn has shown significant effect on % loading efficiency and zeta potential of polyamide-disulphide nanocomposites	Drug delivery system
Fernandes et al. (2009)	Chitosan based nanocomposite	Ex situ method	Improvement in the mechanical properties, antibacterial properties, transparency and flexibility	Skin tissue regeneration
Nampoothiri et al. (2010)	Polylactic based nanocomposite	Extrusion and polymerisation	Good mechanical properties, intrinsic biocompatibility	Tissue engineering
Mishra et al. (2014)	Inorganic nanoparticles based polymer nanocomposite	Fabrication of PNC film by carbodiimide coupling	Probe orientation was excellent with an immunosensor and detection capacity was 10 ng/ml	Identifying CRP antigen

Table 1 Recent findings on biomedical application of application of polymer nanocomposite (continued)

Reference	*Composite detail (Resin and filler)*	*Fabrication method*	*Remark/conclusion*	*Applications*
Lakouraj et al. (2013)	Poly(p-phenyldiamine)/ Fe_3O_4 nanocomposites	Emulsion polymerisation	The antioxidant activity of the nanocomposite enhanced by up to 54%	Antioxidant
Cinay et al. (2017)	poly(methacrylic acid-g-ethylene glycol)	Visible light-induced synthesis	Controlled PH-triggered release of therapeutic molecules	Drug delivery
Marrella et al. (2017)	Graphene oxide hydrogel	Chemical crosslinking	Cellular growth and biomechanical loads	Articular tissues

Therefore, various factors such as economical aspect, mechanical properties and biocompatibility issues should be taken into consideration before selection of types of polymer composite for particular application in biomedical field.

5 Conclusion

Nanoparticles have become an important constituent in every component of biomedical applications. Significant efforts are being done to find its further application for newly arising problems in biomedical applications. On the other side, researches are also being conducted to evaluate possible toxic effects of the nanoparticle. Biocompatibility tests seem to be one of the important challenges faced by researchers. The incorporation of Carbon nanotube in polymer matrix nanocomposite results in excellent electrical properties, lighter in weight, mechanical properties, thermal, properties, chemical stability and extreme resistance to corrosion. Addition of nanoparticles in polymer matrix provides biocompatibility, biodegradability, physical properties mechanical properties and/or aesthetic properties. Nanofibre such as Ag nanofibre reinforced polymer composite indicated good catalytic, electronic properties, better antibacterial properties and better mechanical properties which make them suitable for various biomedical applications like wound healing and recovery.

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