



## CHALLENGES AND PERSPECTIVES OF POLYMERIC NANOCOMPOSITES FOR BIOMEDICAL APPLICATION

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### Abstract

This article shows that polymers have become one of the most important parts of almost everything humans do. Polymer nanocomposites (PNCs) have been recognised as an efficient means of endowing materials with exceptional properties that would be impossible to attain with the components alone. Nanoscale polymer matrices and reinforcing phases constitute polymer nanocomposites (either organic or inorganic constituents). Various characteristics are used to divide polymer nanocomposites into distinct classes. This page discusses the preparation procedures. They include the sol-gel method, in-situ polymerization, solution mixing, melt mixing, and in-situ intercalative polymerization. Proteins (for example, soy, collagen, and fibrin gels), polysaccharides (for example, starch, alginate, and chitin/chitosan), and synthetic polymers such as poly(hydroxyl butyrate) (PHB), poly(lactic acid) (PLA), poly(glycolic acid) (PGA), and poly(caprolactone) (PCL) may have biomedical applications. These non-hazardous compounds are biocompatible and decompose at a rate that may be regulated. For biomedical applications, polymeric nanocomposites must overcome numerous challenges, including their manipulation and handling. Due to their high surface free energy, nanoparticles readily accumulate in the air and can be oxidised or contaminated. These miracles are capable of altering the antibacterial properties of nanocomposites containing metal nanoparticles. The amount of microbe surface area in contact with metal nanoparticles influences the nanoparticles' antibacterial activity. Nanoparticles can eradicate bacteria in a variety of ways due to their small size and high surface-to-volume ratio. Moreover, we have discussed the inherent properties of polymer matrices, the reinforcing effects of nanofillers, and the manufacturing processes.

**Keywords:** Polymer, Polymeric nanocomposites, biomedical application, challenges, microorganism, antimicrobial.

## Introduction

As the science of materials advances, there is a growing demand for polymers with a variety of forms, functions, and properties.

Nearly fifty years of research have been devoted to nanocomposites. 1950 marks the first mention of them. 1976 saw the discovery of polyamide nanocomposites by Farzana Hussain and Mehdihojjati (D.R. Paul and L.M. Robeson, 2008). Toyota Research Group was instrumental in generating interest in this field (Robert O. 2000).

Within the realm of nanocomposites, the diameter of a phase must fall between 10 and 100 nanometers. Fillers with particle sizes on the nanoscale scale include a limited number of atoms per particle. As a consequence, these fillers may exhibit properties that are unique to them and matrix interactions that are stronger than those of the bulk material. Filler particles are broken down into their constituent molecules, which can impact the performance of polymers. Through the incorporation of molecular or nanoscale fillers, polymer nanocomposites research seeks to improve the tensile strength and abrasion resistance of polymeric materials. In comparison to conventional composites, composites whose structure and composition change on a nanometer scale have exhibited significant improvements in their physical properties.

In the world of nanocomposites, the size of a phase must be between 10 and 100 nanometers. Fillers with nanoscale particle sizes contain a restricted number of atoms per particle. As a result, these fillers may possess unique characteristics and matrix interactions that are stronger than those of the bulk material. Combining at least two phases, each of which has a distinct structure or composition, and at least one of which varies in size from 10 to 100 nanometers, produces nanocomposites (nm). Polymer nanocomposites frequently employ molecular or nanoscale fillers in order to produce polymeric parts that are more robust and less subject to wear and tear. It has been shown that polymer nanocomposites, also known as PNCs, are an effective approach for endowing materials with unique properties that are impossible to achieve from the individual components alone. During the fabrication of nanofiller composites, it is advantageous to develop interfaces with large, specific surface areas between the two phases of nanoscale compounds. The most difficult aspect of these materials, however, is the interfacial interactions between the two phases of a nanocomposites, which have recently piqued the interest of researchers due to their promise. Electrical engineering, magnetic engineering, optical engineering, and biology all seem like good places to use polymers. The many benefits of polymeric nanocomposites come from the fact that they have improved properties, such as being light, flexible, easy to work with, and

cost-effective as a final product. Due to the importance of medical technology, which makes more demands on biomedical materials, biomedical applications has become a separate field of research within the ones listed above. There is a large demand for compounds with unique properties. This chapter introduces polymer nanocomposites and explores their manufacture, processing, structural composition, and possible medical applications (Rahmani, S., et al., 2022).

- *Following is a list of applications for polymer nanocomposite systems, which are utilised in numerous fields:*
- *Classification of polymer*

The word "polymer" comes from two Greek words that mean, respectively, "many" and "parts" or "molecules." So, a polymer is a big molecule, also called a macromolecule, which is made up of a lot of small chemical units (Robert O., 2000). There are numerous ways to classify polymers. The primary distinction between polymers is whether they are natural or synthetic. According to their structures, processes, or thermal reactions, polymers can be classified into many groups (Choudhury et al., n.d.).

ξ *Natural polymer nanocomposites vs Synthetic polymer nanocomposites* Both natural and synthetic polymers exist. Enzymes are in charge of all metabolic processes within the human body (e.g., the production of energy from our food intake). Without these enzymes, the extinction of all life forms is possible. Polymers derived from biological sources include enzymes, nucleic acids, and proteins. Their ordinarily intricate organisational structures remained a mystery up to that point. Starch is a fundamental component of the diets of virtually all human societies, whereas cellulose and natural rubber are examples of plant-derived polymers with more straightforward structures than enzymes and proteins. VBERs, elastomers, plastics, and adhesives are some of the many synthetic (man-made) polymer families. There are subgroups within each family (Robert O. 2000). ξ *Perspectives of Polymeric Nanocomposites*

Polymer nanocomposites are made by mixing polymers with inorganic or organic fillers on a nanoscale. Researchers have access to a wide range of biopolymers and fillers, which is one reason why these new materials can be used for many different things. Biopolymers that are now in use include polysaccharides, aliphatic polyesters, polypeptides and proteins, and polynucleic acids. Fillers include polynucleic acids, clays, hydroxyapatite, and nanoparticles of metal (E. Ruiz-Hitzky et al. 2005).

Nanotechnology is a field that is growing quickly and has led to a lot of new polymer nanocomposites that have interesting new properties. You can make the child substance by putting together the qualities of the parent substances into a single substance. In addition, it is possible that the materials will acquire qualities that were not previously present. (Gubin SP, et al. 2002).

A nanocomposite is a type of composite made from a material with a surface area on the nanometer scale. Even though there are many nanoreinforcements, there is a lot of interest in layered silicate clay materials because they are easy to find, cheap, and don't hurt the environment. Clay is often used as filler in making composites, and its nanoscale size makes the surface area bigger (Fukushima K. et al. 2009).

Typically, melt intercalation is the standard procedure for producing nanocomposites from thermoplastic polymers. As depicted in Figure 2, the procedure begins with kneading the composite material, then annealing the polymer matrix at high temperatures, adding the filler, and annealing the composite once more to achieve uniform distribution. Because it contains no solvents, the product is environmentally friendly. In addition, it can be used in manufacturing processes like injection moulding and extrusion due to its compatibility with these techniques. This makes its implementation more viable and economical. Unfortunately, the high temperatures generated by the technique can hinder the filler's surface modification. Organoclays treated with alkyl ammonium fail at temperatures above 140 degrees Celsius. In contrast, melt intercalation processing requires melting temperatures between 190 and 220 degrees Celsius (Abedi, S. and Abdouss, M. 2014).

- *Interface Effects*

The power-law percolation model is hard to use everywhere because there have been many reports of different critical exponent values. Numerous studies believe that the variations in the critical exponent are due to the complexity of the significant tunnelling phenomena occurring in the conductive network, the variability of the inherent nanofiller properties (especially for CNTs), and the complications that arise for CNT junctions (Mutiso RM, 2015). Functionalization refers to the addition of functional groups to the atomic structure of a nanofiller phase by means of either covalent or noncovalent bonding. PNCs are frequently functionalized in order to facilitate the separation of aggregated carbon nanoparticles. (Sahoo NG, 2010).

Polymer nanocomposites are capable of significantly more than merely enhancing the properties and barriers of traditional engineering materials. The research demonstrates advances in electrical phenomena, UV stabilisation, flammability, and polymer crystallisation

control. A decade ago, nanocomposite technology was a concept with great potential. Future prosperity is inevitable (selvin p.thomas, et al., n.d.).

People are becoming more concerned about the environment, and technology keeps getting better, so it is likely that the trend of getting materials from quickly renewable natural resources will continue. This refers to polymer matrices, additives, and reinforcements within the context of composites. Nanocellulose-based reinforcements are potentially intriguing. Due to their lower density, nanocellulose reinforcements might be better in a number of ways. Moreover, these nanocellulose reinforcements have a low CTE, are transparent, and have barrier properties. These are only a handful of the benefits. However, the use of nanocellulose as a reinforcement is still in its infancy, and these materials have not yet reached their full reinforcing potential. This is due in part to the challenges associated with mass-producing nanocellulose. Prior to this moment, the inaccessibility of huge quantities of nanocellulose impeded the advancement of large-scale research and development efforts relating to the application of these materials. Recent announcements of commercial and government pilot programmes, in addition to large-scale production facilities, are expected to improve the situation (Zeng X. et al., 2011).

As the amount of energy necessary to convert cellulose fibres to NFCs has diminished, interest in NFCs as a reinforcement material has increased (Feng C. et al. 2013). Numerous obstacles must be overcome before it can be used effectively and affordably as reinforcement. Identifying improved and more efficient methods for producing nanocellulose with optimal properties is crucial. Numerous applications of these substances' hydrophilicity will require additional research. Techniques and chemistry are needed to effectively distribute nanocellulose reinforcements or change them into a form that can be mixed into a variety of matrices and hold them in place. They can be successfully attached to the matrix to do this. In order to attain optimal performance, it is important to enhance the control of structures at many scales. For instance, improved control over the porosity and fibre volume should result in enhanced material strength, stiffness, and fracture behaviour. Innovative analytic methods are required to simulate the fabrication of nanocellulose-based structures and precisely predict their mechanical properties. To build a connection between the modelling of NFC distributions and the optimization of characteristics, it is required to model the process. It is essential to discover pertinent applications, undertake pertinent research, and establish their validity. In addition, it is essential to comprehend and address nanoscale-related health and safety concerns.

These changes are quite unlikely to occur on their own. Almost definitely, they will need to be included in larger infrastructures. Paper mills, for example, could be converted into facilities for the production of biofuels and other chemicals, helping to mitigate the effects of climate change by reducing the amount of greenhouse gases released into the atmosphere. Here is an illustration of how this type of facility could be utilised. In the event that nanocellulose applications of great value are identified, biorefineries may be able to incorporate it into their material flows, contributing to economic growth (Chaurasia AK. et al. 2014).

- *Blending and Nanocomposite Cross-Linking*

In accordance with standard operating procedure, the following actions must be taken to dissolve 5 grammes of EPM-g-furan rubber in 50 millilitres of THF: When suspended in 50 mL of THF, CNT at concentrations ranging from 0.5 to 10% (relative to EPM-g-furan) was sonicated for 30 minutes. After 15 minutes of stirring and 30 minutes of ultrasonification, the two solutions were eventually combined and homogenised after a total of 45 minutes of mixing. The mixture was heated for 24 hours after dissolving 1000 ppm of phenolic anti oxidant in about 2 mL of THF and adding 0.5 molar equivalent of cross-linking agent (BM or DCP). The amount of cross-linking agent required will be determined by the amount of furan in EPM-g-furan. A phenolic anti-oxidant at a concentration of one million parts per million was then administered. After combining all of the ingredients, the solvent was removed, and the resulting mixture was baked at 50 degrees Celsius for twenty-four hours. The nanocomposite was heated at 50 °C for three days after being squeezed and shaped for thirty minutes at 150 °C and 100 °F. The samples were reprocessed by grinding them in a ball mill at 195 degrees Celsius, pressing the resulting powder into new sample bars at 150 degrees Celsius for 30 minutes, and heating them at 50 degrees Celsius for three days. (Guilia Gorrasi).

## **2. Characterization of nanocomposites for Biomedical**

Electroanalysis (EA) and Fourier transform infrared spectroscopy (FT-IR) were employed to convert EPM-g-MA to EPM-g-furan. The Perkin-Elmer Spectrum 2000 is the instrument used in the FT-IR spectrum recording procedure (Perkin Elmer, Waltham, MA, USA). After compression moulding rubber films with a thickness of 0.1 mm at 150 °C and 100 bar for 30 minutes in a KBr tablet holder, the films were thermally annealed for maximum DA cross linking, and the results were then analysed. The area between 4000 and 600 cm<sup>2</sup> was measured with a resolution of 4 cm<sup>2</sup> and 32 co-averaged scans. The regions under each FT-IR peak were measured using deconvolution ( $R^2 > 0.95$ ). Using the relative differences in

peak area, the conversion of the reaction was computed. As an internal standard, the 723 cm<sup>-1</sup> methyl rocking vibration peak was chosen because it can't be changed chemically and comes from the EPM backbone. used to determine the quantity of EPM-g-MA that is converted to EPM-g-furan during the EPM-g-MA and EPM-g-MA reactions. The 723 cm<sup>-1</sup> methyl rocking vibration peak was selected as the internal standard since it cannot be altered chemically and originates from the EPM backbone. used to determine the quantity of EPM-g-MA that is converted to EPM-g-furan during the EPM-g-MA and EPM-g-MA reactions(Okamoto, K., et al. 2006).

Regardless of whether or not the C-O-C symmetrical stretch vibration was adjusted to 1013 cm<sup>-1</sup>, the cross-linking reaction was the same. Using a Euro EA element analyzer, N, C, and H were analysed. Although unmodified CNT does not contain any nitrogen, it was discovered that the nitrogen concentration is related to the furan- and amine-functionalization of CNT, as mentioned in a previously disclosed approach (Makadia, H.K. et al., 2011), (Makadia, H.K. et al., 2011).

Surface pictures of the nanocomposites were taken using a scanning electron microscope (SEM) with a Philips XL30 Environmental SEM FEG. This was done in order to characterise the surfaces (Philips, Amsterdam, The Netherlands). Using cryogenic fracturing permitted the creation of CNT-exfoliated surfaces on sample surfaces.

For X-ray photoelectron spectroscopy, a Surface Science Instrument SSX-100 spectrometer, made by Fisons plc and situated in Ipswich, Suffolk, United Kingdom, was utilised (XPS). This apparatus had a monochromatic AlK X-ray source with a pressure of 3.1010 mbar at its base. The source had a hV value of 1,486.6 eV. After being resuspended in toluene and deposited on gold substrates, CNT sample components were created in this manner. After removing the solvent, the samples were placed in a machine with a very powerful vacuum. This was done to eliminate all traces of the solvent. ASTM D412 directed us to utilise an Instron 5565 (Instron, High Wycombe, UK) fitted with a 15-mm clamp length when measuring the tensile strength (Tb) and elongation at break of the material. This was accomplished with an Instron 5565 (Eb). Five hundred millimetres per minute was the rate of displacement that was being utilised. Ten samples were examined for each measurement, and the two outliers were omitted from the calculation of the average. The figures depict the stress-strain curves at the median level. Experiments on cyclic hysteresis were done with the same equipment as before, plus a clamp that was 3 cm long. The samples were stretched at a

rate of 10% of their total length per minute and put through five cycles of 5%, 10%, 15%, and 20% strain (Giuliana Gorrasi). The percolation threshold was compared to the results of tests on nanocomposites composed of carbon nanotubes that were conducted under extremely sensitive conditions. To determine the strain-induced conductivity of nanocomposites, a Tinius Olsen H25KT tensile tester with a one-centimeter-long clamp was utilised (Tinius Olsen TMC, Horsham, Pennsylvania, United States). A GossenMetrawattMetrahit 18S multimeter made by GMC-I Messtechnik GmbH in Nürnberg, Germany, was used to clamp nanocomposite sample bars between manually stretched copper sheets for 30 seconds at 2 mm intervals.

GMC-I Messtechnik GmbH's headquarters can be found in the German city of Nürnberg. After a minimum of twenty-four hours of deformation, each sample underwent a total of three cycles of deformation before the statistical analysis findings were generated full recovery of the original elasticity of the specimen A camera equipped with Fluke Ti10 IR Fusion Technology was utilised to record thermographic images of steady-state heat generation for the purpose of visualising the Joule effect (Fluke Corporation, Everett, WA, USA). To determine the results, a scratch test and re-annealing of fractured tensile test samples were utilised, it was determined that nanocomposites can accelerate the healing of cracks generated by welding. To conduct scratch tests, a nanocomposite film was cast onto a glass microscope slide, and then its surface was scratched with a knife. The film was then submitted to a thirty-minute test in which it was exposed to a 7-volt, 0.05-ampere potential source. This was achieved by attaching metal wires to the film's edges and placing them between the glass microscope slide substrate and a second covering slide. This allowed the film to maintain its shape during the entire process. With the use of a Zeiss axioscope equipped with an HCS MX5 framegrabber, the gradual removal of the scratch was identified. (Zeiss, Oberkochen, Germany). Most rubber nanocomposites were joined together by cutting sample bars in half and then pressing the two halves together.

### *Moisture Effect*

The structure was solvated with increasing amounts of water molecules so that researchers could assess how the epoxy/SWCNT nanocomposite interacts with water. This created an environment similar to the various stages of water absorption. (Prolongo, S.G., et al., 2012) - The highest level of moisture recorded for an epoxy nanocomposite is less than 4 percent by weight (Gkikas, G., et al., 2015). During the course of this experiment, the nanocomposite

model's moisture content varied between 1.0 and 4.0 wt%. Saturation is expressed as a weight percentage and is signified by the molar mass of the structure, which is 4.0. Initially, the influence of moisture is characterised based on the model systems by observing local structural changes in the nanocomposite as the moisture concentration varies. This is done to determine the effect of moisture on the nanocomposite. The nanocomposite epoxy matrix consists of two functional oxygen-containing groups: Hydroxyl groups and oxygen atoms are present in ether. These oxygen-containing functional groups are essential potential hydrogen bonding sites and tend to form H-bonds with the absorbed water molecules and among themselves. In addition, ether oxygen atoms are distributed throughout the matrix. Polar interactions between functional groups and water molecules are capable of altering the nanocomposite's water distribution. Prior to determining the water distribution, it is required to establish the configuration of the functional groups that surround the SWCNT segment. In the majority of cases, the radial distribution function (RDF), commonly known as the RDF, is used to calculate the normalised probability of locating one thing at a distance  $r$  from another object. This will result in the provision of helpful information regarding the configuration of the functional group.

The RDFs were shown with respect to the relative humidity. According to Chakraborty, S., et al. (2012), the RDFs for polymer dispersion in a range of nanocomposites have comparable structures. Larin, S.V., et al. (2014) The fact that there are only a few small hydroxyl RDF peaks between 2.5 and 5 shows that these functional groups are advantageously dispersed in the interfacial layer surrounding the SWCNT. Despite the fact that there are much fewer hydroxyl groups than ether groups in the structure, it is feasible for dispersed hydroxyl groups in the interfacial layer to congregate at a specific distance due to H-bond interactions. This results in the development of minute peaks. This is due to the fact that there are fewer hydroxyl groups than ether groups in the molecule. The SU-8 monomers can be looked at in relation to the axis of the SWCNT in the following ways: The layout of the epoxy matrix in the various nanocomposite models is generally consistent, independent of the moisture content.

#### *Biomedical Applications of CNT Polymer Nanocomposites*

In the past few years, there has been more interest in how carbon nanostructure-reinforced polymer nanocomposites could be used in biotechnology and medicine. They have a wide range of possible uses in the realm of biology. Carbon nanotube-based polymer composites are the subject of a substantial amount of research that is now being undertaken. In the realm of biomaterials research, Polymers and nanotube nanocomposites have garnered considerable

interest in research and development. Biomaterials composed of polymers and nanotube nanocomposites have been the subject of a substantial amount of study and scholarly writing.

### *Tissue Engineering*

In the last few years, carbon nanotubes (also called CNTs) and polymeric composites (also called PMCs) have become more popular as scaffolds for engineering bone. Tissue engineering produces scaffolds that allow cell adhesion, development, and transformation, the synthesis of extracellular matrix (ECM), and the repair of damaged tissue. To be effective, the optimum scaffold for tissue regeneration must possess the necessary mechanical properties. Carbon nanotubes are capable of providing the structural integrity required for tissue scaffolding. (Armentano et al., 2010). Carbon nanotubes are anticipated to be incorporated into these scaffolds in the not-too-distant future in order to improve the overall mechanical qualities of the scaffolds as well as facilitate and direct the formation of new bone tissue. It is possible to significantly boost the polymer matrix's mechanical strength by adding a minute quantity of carbon nanotubes to the matrix (Chen, G.X., Kim, H.S., et al., 2005). According to the study's findings, the inclusion of MWCNTs into chitosan produced a material with much greater mechanical capabilities than chitosan alone (Wang, S.-F., et al., 2005). In vitro research has demonstrated that CNT scaffolds possess characteristics typical of biological systems. On carbon nanotube-based polymer composites, different types of cell growth have been shown to be effective. Jell et al. have outlined the TIPS method for the fabrication of porous thermoplastic polyurethane–multiwalled carbon nanotube (CNT) foams (Jell, G., et al. 2008). They discovered that the addition of CNTs to the nanocomposite scaffold significantly increased the structure's compression strength and stiffness. According to the results of in vitro investigations, the concentration of the active angiogenic factor The amount of VEGF (vascular endothelial growth factor) produced by osteoblasts increased inversely with CNT loading. This indicates that nanocomposite scaffolds are capable of influencing their surroundings. Shi and his colleagues used a method that involved thermal cross-linking and particle leaching to make nanocomposite scaffolds with a porous structure. (Shi, X.B., et al., 2007) Using an in vitro culture approach, researchers determined that mesenchymal stem cells (MSCs) adhere to and can survive on all PPF-SWNT scaffolds. In order to test the level of biocompatibility of porous PPF-SWNT scaffolds(Sitharaman et al. (2008). used a rabbit as a model. They found that PPF-SWNT implants exhibited comparatively mild inflammatory responses. Twelve weeks after implantation, PPF-SWNT nanocomposite scaffolds revealed substantial bone ingrowth and enhanced collagen matrix production (Figs. 12 a, b, and 1). For making a scaffold out of carbon nanotubes, it is important to think about ways to make sure that the nanotubes are spread out evenly in the polymer matrix. This will enable the needed electrical conductivity and mechanical strength to be achieved. When carbon nanotubes are spread out evenly over the surface of a polymer matrix, the load that the polymer matrix is carrying is transferred to the nanotubes. This process must be performed to improve the composite's mechanical and electrical qualities.Armentano, I., and coworkers (2010) studied a number of techniques for enhancing CNT dispersion in a variety of polymer matrices. In the fields of medicine and biotechnology,

the number of uses for polymer nanocomposites is growing (Figures 12 a, b). After carbon nanotubes have been given functions, it may be possible to find a way to make them spread out more. Because of the functionalization process, carbon nanotubes are now more water miscible and biocompatible than they previously were. By attaching chemical functional groups to the side walls and tips of CNTs either covalently or noncovalently, it is possible to control how polymers and nanotubes interact. This can be accomplished by utilising a variety of chemical functional groups. The kind of functional group that is located on the surface of the CNT has an impact on the way in which it interacts with cells. Lin and colleagues (2011) developed nanocomposites by mixing poly (lactic-co-glycolic acid) with carboxyl functionalized multiwalled carbon nanotubes (c-MWCNT) (PLGA).

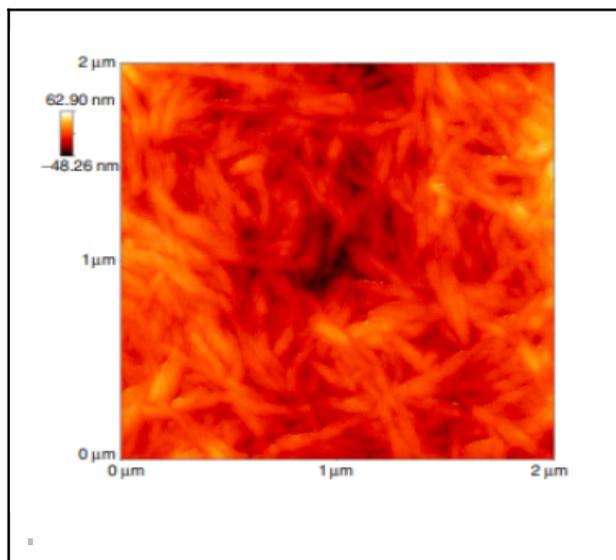
### *Matrix*

Biotechnology and biomedicine have a strong interest in expanding the possibilities beyond cell growth scaffolds (Qing et al., 2010). Current research focuses on these biomaterials, which unite the disciplines of biology and nanotechnology. Combining the physical, biological, and chemical properties of nanocomposites is an innovative way to make and sell better biomedical materials (G. X. Chen et al., 2005; Lu Y., Yang B., et al., 2002). This chapter goes into more detail about how polymer nanocomposites can be used besides as "scaffolds" for cell growth. It focuses on the wide range of biological uses for these materials. With their huge surface areas, metal nanoparticles exhibit a wide variety of intriguing features. Not only does the material have a large active surface area and overall area, but it also has a greater volume-to-surface area ratio than the majority of other materials. Recent attention has been drawn to silver as a result of its effectiveness against numerous forms of germs. Biomedical and environmental uses embrace silver nanoparticles. For the production of polymers and silver nanoparticles, scientists employ a vast array of methods, including in situ polymerization. (H. Palza et al.). (2012).

Polymer-modified gold nanoparticles have a lot of potential to be used in new materials, as was found recently (D. Li, Q. He, and J. Li, Smart Score 2009). To improve conductivity, magnetic nanoparticles containing cobalt and nickel oxides are manufactured (K. Murali et al., 2016). Applications of these nanocomposites in electric field research include magnetic sensors and high-density recording devices (J. Husainc et al., 2015).

When Fe nanoparticles and Ni were mixed to make nanocomposites, they were spread out using different amounts of epoxy. Using an impedance analyzer, H. Sharma et al. (2015) determined several composite properties, including permeability and permittivity. During the biological process, nanocellulose becomes contaminated with a variety of impurities,

including biological agents such as microorganisms and enzymes as well as numerous soluble media components. The Trichoderma fungus makes NCC by breaking down MCC with the help of bacteria. Thus, the purification of the NCC is one of the most essential steps in the process of producing it using biological means. Once the fermentation phase of the process is complete, the broth was subjected to separation.



**Fig. 1 AFM image of the NCC produced during microbial hydrolysis under control**

In the sedimentation process, any particles with a radius greater than one millimetre are separated by centrifugation. Based on Prasad (S. et al. (2011)). This allowed water and solutes with low molecular weights to pass through while the NCC was removed with an ultrapure water jet. Therefore, it was determined that differential centrifugation coupled with ultrafiltration is an effective method for cleaning NCC. This method can be used to clean up any more nanoparticles that are made by the biological process. As seen in Figure 1, the researchers were able to determine the dimensions and form of the cleaned-up NCC using atomic force microscopy. A dynamic light scattering particle size analyzer was used to make Figure 2 and figure out the size distribution of the particles. Afterwards, the data were analysed.

There are numerous mechanical, Chemical and biological processes are involved in the production of nanocellulose. Mechanical procedures can produce greater yields, but they are not only prohibitively costly but also extremely energy-intensive. Extremely time-consuming are biological procedures involving cultures of bacteria and fungi (Bismarck A., et al., 2011). It is more efficient to produce cellulose nanoparticles by hydrolyzing cellulose with acids,

bases, and oxidising agents. These methods aren't perfect, though. They are corrosive, change the surface of the cellulose, and don't work well with the environment. These disadvantages diminish the desirability of these strategies. The manufacture of nanocellulose using cellulose exposed to enzymatic hydrolysis has the potential to be an efficient and cost-effective approach. This technology is suitable for creating nanocellulose at a low cost of energy and with negligible byproducts, and it is acceptable for doing so. N.(Vigneshwaran et al. 2011).

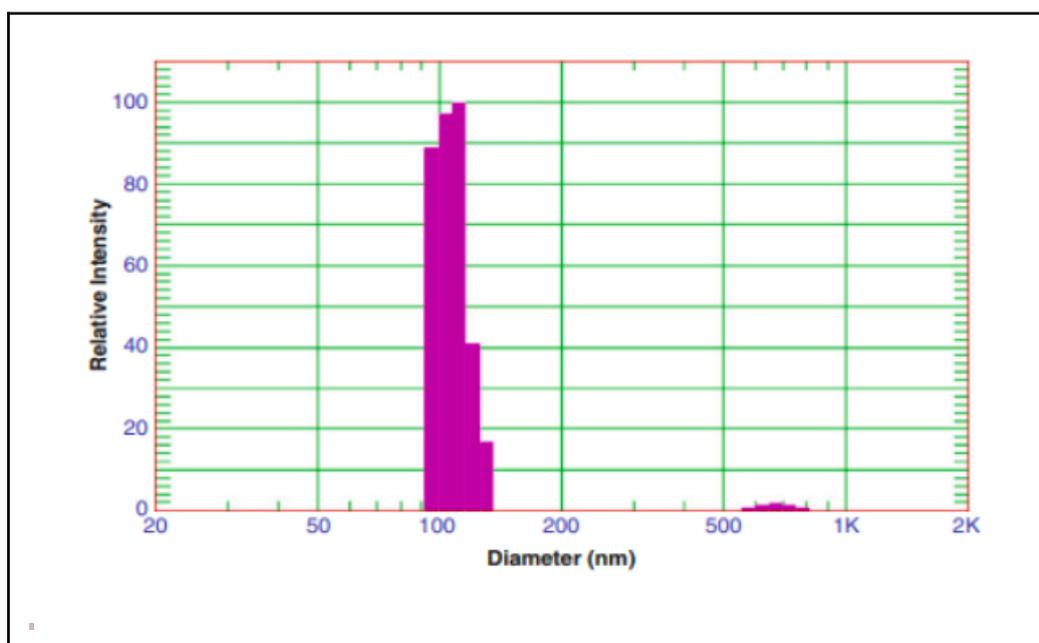


Figure 2 shows how the controlled microbial hydrolysis changes the size of the NCC particles (N. Vigneshwaran et al 2011)

Several enzymes serve as natural catalysts for the transformation of cellulosic compounds. Several biostripping and biofinishing products for cotton fabrics based on enzymes are currently available on the market. Cellulase is a typical enzyme capable of hydrolyzing cellulose's glycosidic bonds. Under controlled conditions, they can degrade macromolecular cellulose chains to nanoscale dimensions (KM, Bhatwadekar SP., 1984).

By combining the effects of three enzyme components, the polymer chains in cellulose can be broken apart. The rate of hydrolysis is affected by temperature, the pH of the medium, the amount of enzyme, and the amount of substrate. Based on the research that has been done, the best conditions for acid cellulases to work are between 45 and 50 degrees Celsius and a pH of 4.8 (Serrano, M.C., et al., 2014). Usually, the concentration of the substrate is raised to reduce the surface binding of enzymes that don't work. In addition, the rate of reaction at the beginning of the process is the fastest and utilises the most reactants. During this time, cellulose molecules undergo rapid hydrolysis. The duration of substrate-enzyme interactions

dictates the extent of hydrolysis. Introducing a disruption into the hydrolysis procedure allows for the collection of nanocellulose. Either disengaging the enzyme from the partially hydrolyzed substrate or isolating the partially hydrolyzed cellulose from the partially hydrolyzed substrate using ultrafiltration are effective strategies for achieving this objective (via denaturation). As a result, the separation procedure can produce cellulose nanoparticles, and it is possible to increase yield by performing the procedure repeatedly on unhydrolyzed cellulosic material.

A new method for making nanocellulose is to use enzymes to break down a cellulosic substrate. There is extensive research on how enzymatic hydrolysis can be used to convert cellulosic materials into biofuel, yet, few papers examine the idea of utilising enzyme combinations as Prior to the introduction of additional chemicals, pretreatments are performed. Hydrolysis of microcrystalline cellulose with the cellulase enzyme was one of the earliest methods reported for producing nanocellulose with a 50-nm diameter. Due to the difficulty of maintaining optimal hydrolysis conditions, enzymatic hydrolysis is rarely employed to produce nanocellulose.

Because of its unusually wide size dispersion, nanocellulose can only be used for a limited number of distinct applications.

Although having significant disadvantages, this approach is growing in popularity. This is because it consumes less energy and money, and most importantly, it is environmentally friendly.

Enzymes can therefore be easily modified to enhance the creation of biological nanocellulose. This method can be industrialised for the production of nanocellulose if the operating conditions are further optimized. Boosting the effectiveness of a process by recycling the used enzyme. This nanocellulose production method may become standard due to its increased output, low operating costs, and environmental friendliness.

### **3. Treatments of nanocomposites for Biomedical Application - Review**

#### *Chemical Treatment*

The water-borne hyacinth weeds were washed for a total of six hours in a Soxhlet apparatus with a mixture of toluene and ethanol with a volumetric ratio of 2:1 (v/v). The dewaxed fibres were bleached and boiled in a pH-4 solution that contained 3% by weight of sodium chlorite.

Three hours were spent keeping the suspension at 80 degrees Celsius before leaving it overnight to settle. The bleaching procedure was repeated twice, and the tissues were washed until every trace of acid was eliminated. To get rid of the hemicelluloses, the tissues were put in a solution with 1% sodium hydroxide for 24 hours at 60 degrees Celsius. Following the centrifugation stage, the specimens were washed in deionized water. The elimination of lignin required the treatment of samples with a 1% sodium chlorite solution in an acidic atmosphere with vigorous stirring at 75 degrees Celsius for 48 hours, followed by centrifugation and rinsing with distilled water. Following 24 hours of stirring a 5% NaOH solution at 55 degrees Celsius, any remaining hemicelluloses were degraded and eliminated, resulting in the formation of pure cellulose fibres. The remaining residues were passed through a centrifuge and then rinsed with distillate water when this procedure was complete.

#### *Mechanical Treatment*

When the samples were put through a mechanical method with high shear, After being treated with chemicals, energy is transferred at a fast rate and has a big effect, they got worse. After being obtained through a chemical process, Using a centrifugal ball mill, the cellulose fibres were micronized after being dried for twenty-four hours at a temperature of one hundred degrees Celsius (Retsch PM100, Germany). It required 20 minutes of centrifugation at 550 rpm and 550 rpm, respectively, to separate 5 grammes of sample from 10 millimeter-sized agate balls in a 50-milliliter liquid-filled cap.

After generating a homogenous nanofiber dispersion in water via ball milling, the fibres were cryocrushed with high impact in a mortar and pestle to release the nanofibers. After 15 minutes of ultrasonication, a homogeneous nanofiber dispersion was obtained. Suspensions were sonicated and then lyophilized in order to produce cellulose nanofibers (Thiripura Sundari, M., & Ramesh, A. 2012).

#### *Combining Scanning Electron Microscopy (SEM) with Optical Microscopy to Evaluate Morphology*

Shimadzu utilised scanning electron microscopy in order to examine the morphology of cellulose nanofibers and fibres (SEM). Following chemical and mechanical treatment, the samples were placed on aluminium stubs, coated with platinum or gold using an ion sputter coater to avoid charging, and examined with a scanning electron microscope. (SEM). The image analyzer was utilised for the purpose of estimating the diameters of SEM images.

Before being converted into cellulose fibres, Raw water hyacinth fibres were subjected to solutions of acidified sodium chlorite and sodium hydroxide in a series of treatments. The purpose of these treatments was to clear the fibres of any soluble components so that cellulose could be recovered from them after processing. The bleaching of water hyacinth fibres with a thickness between 25 and 50 millimetres (Fig. 3). To examine the fibre morphology, optical microscopy was employed (Zeiss, Germany). Optical micrographs collected at various magnifications demonstrate that the sample's hemicelluloses were effectively removed by the chemical treatment, lignin, and other solubilized pollutants from the fibre bundles. Figures 4.a and b illustrate these outcomes.

Individual cellulose fibres with a diameter of 7 millimetres are discernible in the SEM images (Figs. 5.a and 5.b) at 4 K and 3 K magnification, respectively (Alemdar A et al. 2008). The mechanical treatment consists of grinding the cellulose fibres to submicron levels using a ball mill. This was followed by a process of cryocrushing, which resulted in fibre aggregation and a moderate reduction in fibre diameters. After fifteen minutes of ultrasonication, the fibres were separated into nanofibers. According to an examination of a 40 K SEM image, the nanofibers in the suspension had a diameter between 20 and 100 nm (Fig. 6. a). As a result, nanofibers with a structure resembling a network were generated.

#### *Morphology Evaluated by Transmission Electron Microscopy*

Transmission electron microscopy (TEM) was used in the research to investigate the nanofiber microstructure of cellulose. On a carbon-coated grid, a single drop of diluted nanofiber suspension was examined using transmission electron microscopy (TEM) at 20–200 kV with 2.4 Å resolution. When TEM images were acquired, an image analyzer was used to determine the length and width of any identifiable fibres present in the samples.

*Isolation and Characterization of Cellulose Nanofibers and Their Properties* Fig. 3 SEM image of bleached raw water hyacinth fibers

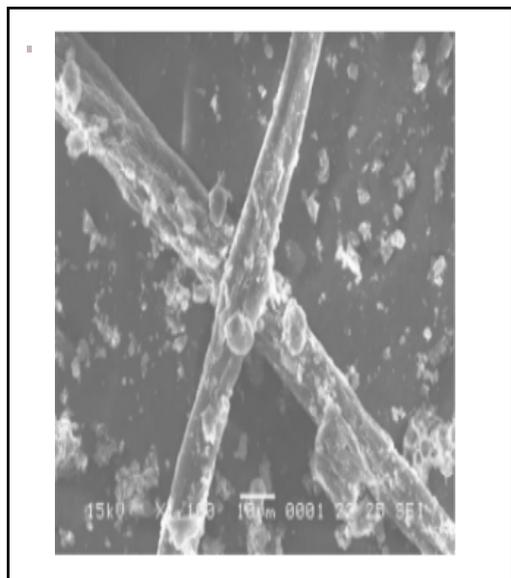


Fig. 4 the pure cellulose fibres are obtained by submitting the crude fibres to a series of chemical treatments, as illustrated by an optical micrograph (a) at 10 magnifications and (b) at 100 magnifications.

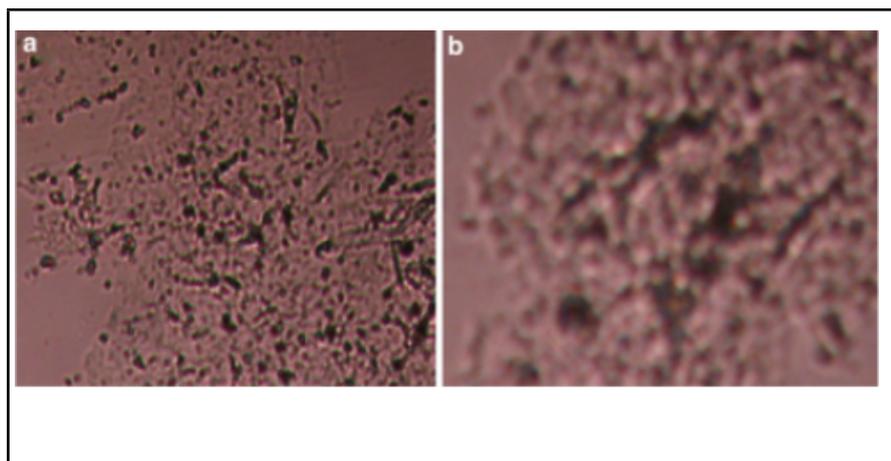


Fig. 5 SEM images (a) at 4K and (b) at 3K magnifications

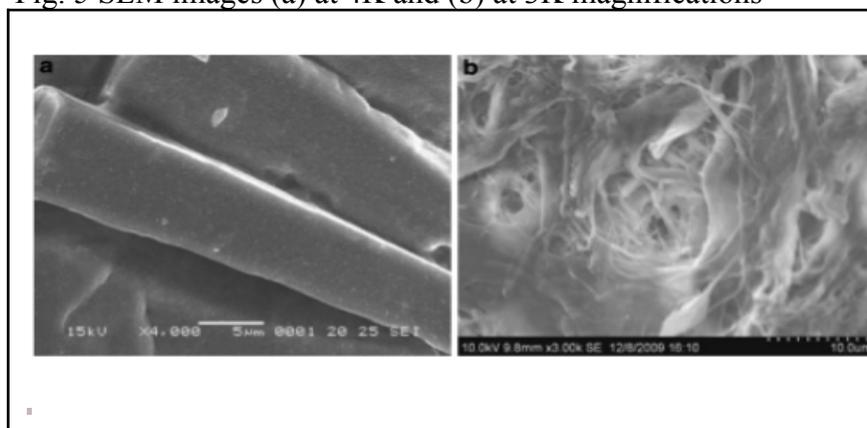


Fig. 6. (a) This image obtained by a scanning electron microscope reveals bundles of cellulose nanofibers prior to sonication.

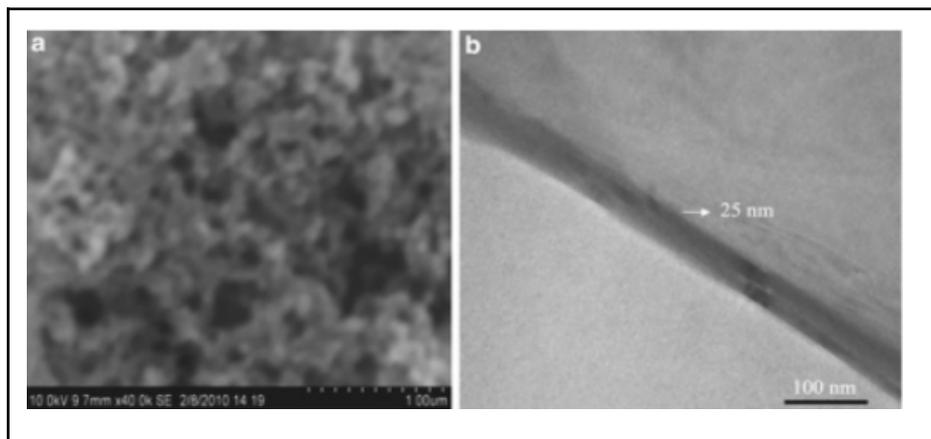
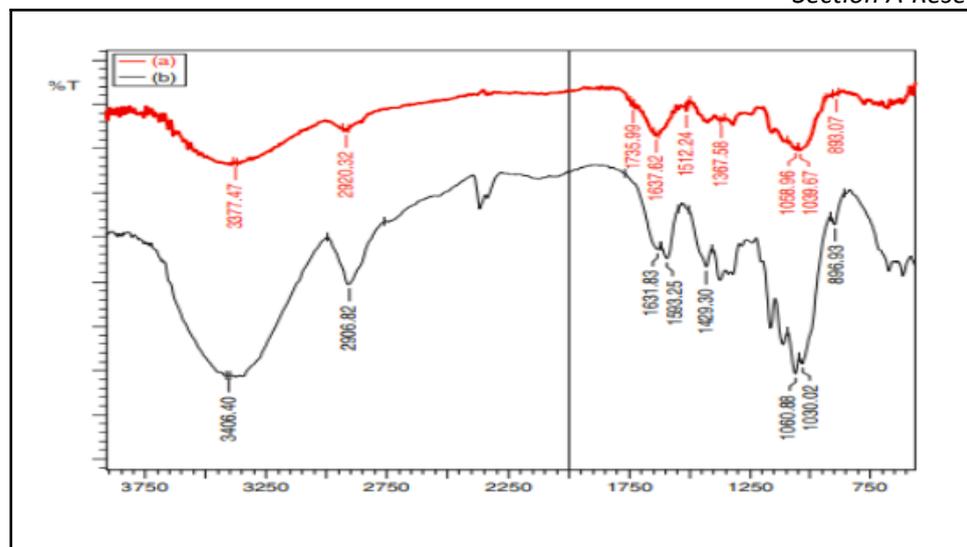


Figure 6 a transmission electron micrograph displaying cellulose nanofibers formed mechanically from water hyacinth. Sonication has been utilised to generate individual fibres with diameters of 25 nm and lengths of several microns (Thiripura Sundari, M., & Ramesh, A., 2012)

*Using spectroscopy and Fourier transform infrared analysis, the chemical composition was determined.*

Using Fourier transform infrared spectroscopy, changes in the chemical composition of water hyacinth fibres that had been exposed to chemical treatment were studied. First, untreated and treated fibre samples were analysed after being ground into a powder and combined with potassium bromide to form a thin pellet (KBr). In order to get FTIR spectra (FTIR 8400S), Shimadzu's Fourier transform infrared spectroscopy was needed. The spectrum was obtained by gathering data in transmission mode at frequencies spanning from four thousand to four hundred centimetres.

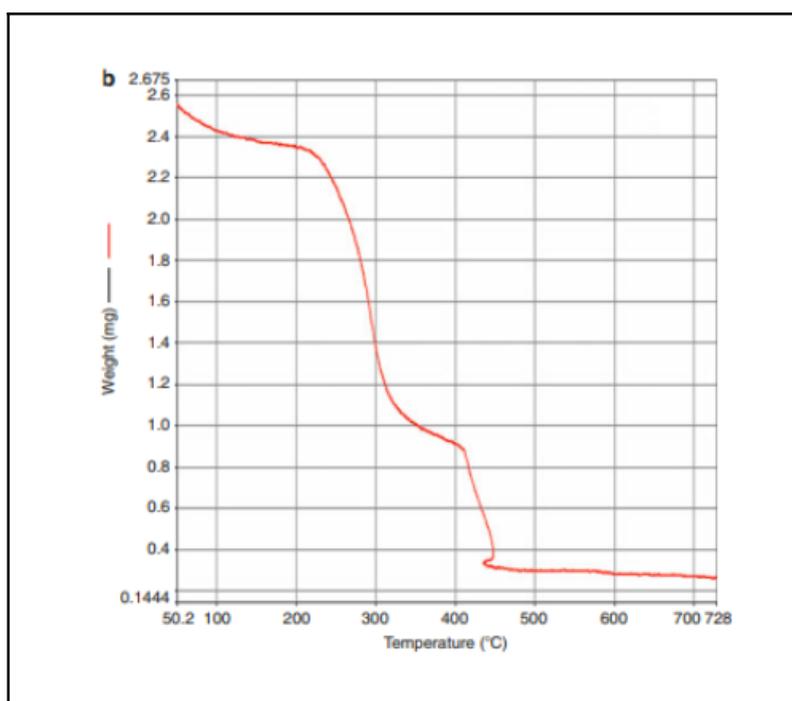
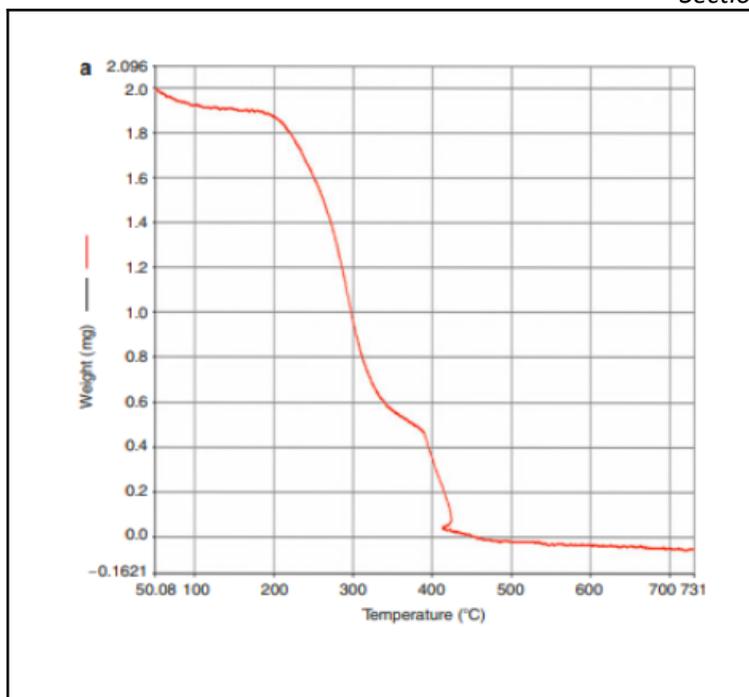
Figure 7: FTIR spectra of water hyacinth (a) original crude fibres and (b) cellulose nanofibers



### *Thermogravimetric Evaluation Performed on WHNF to Determine Its Thermal Stability (TGA)*

The thermal properties of untreated and treated cellulose fibres were evaluated using a thermogravimetric analyzer (TGA) at temperatures ranging from 50 to 700 degrees Celsius in a nitrogen environment at a heating rate of 20 degrees per minute. Figure 8 depicts the thermogravimetric data for untreated and chemically treated water hyacinth fibres. The TG curves reveal that the absorption of water causes the first temperature to fall between 50 and 150 degrees Celsius. Untreated plant fibres began to break down at a temperature of around 206 degrees Celsius. This is due to the fact that hemicelluloses, lignin, and pectin begin to disintegrate at significantly lower temperatures. (Gaharwar, A.K., et al., 2012). The temperatures required for the degradation of the original crude fibres and the pure cellulose fibres have been determined to be 202 and 254 degrees Celsius, respectively. At 500 degrees Celsius, both treated and untreated fibres include carbonaceous components in their residue. The TGA test revealed that the purified cellulose fibres contained negligible amounts of residual bulk. This was presumably the result of removing these unneeded components.

Figure 8: TGA examination of (a) beginning raw materials for fibre production and (b) the cellulose fibres of water hyacinth (Source: Thiripura Sundari, M., & Ramesh, A., 2012)



It consists of hemicelluloses as well as lignin. The application of the chemical treatment greatly improved the thermal stability of the cellulose fibres compared to the state of the fibres' thermal stability prior to the application of the chemical treatment.

### Clay-Based Nanocomposites

For a range of biomedical applications, silicate-based polymer nanocomposites are expected to be the materials of the next generation. This is because the interactions between silicate nanoparticles and polymer chains work best close to the surface.

**Figure 9: Clay based nanocomposites**

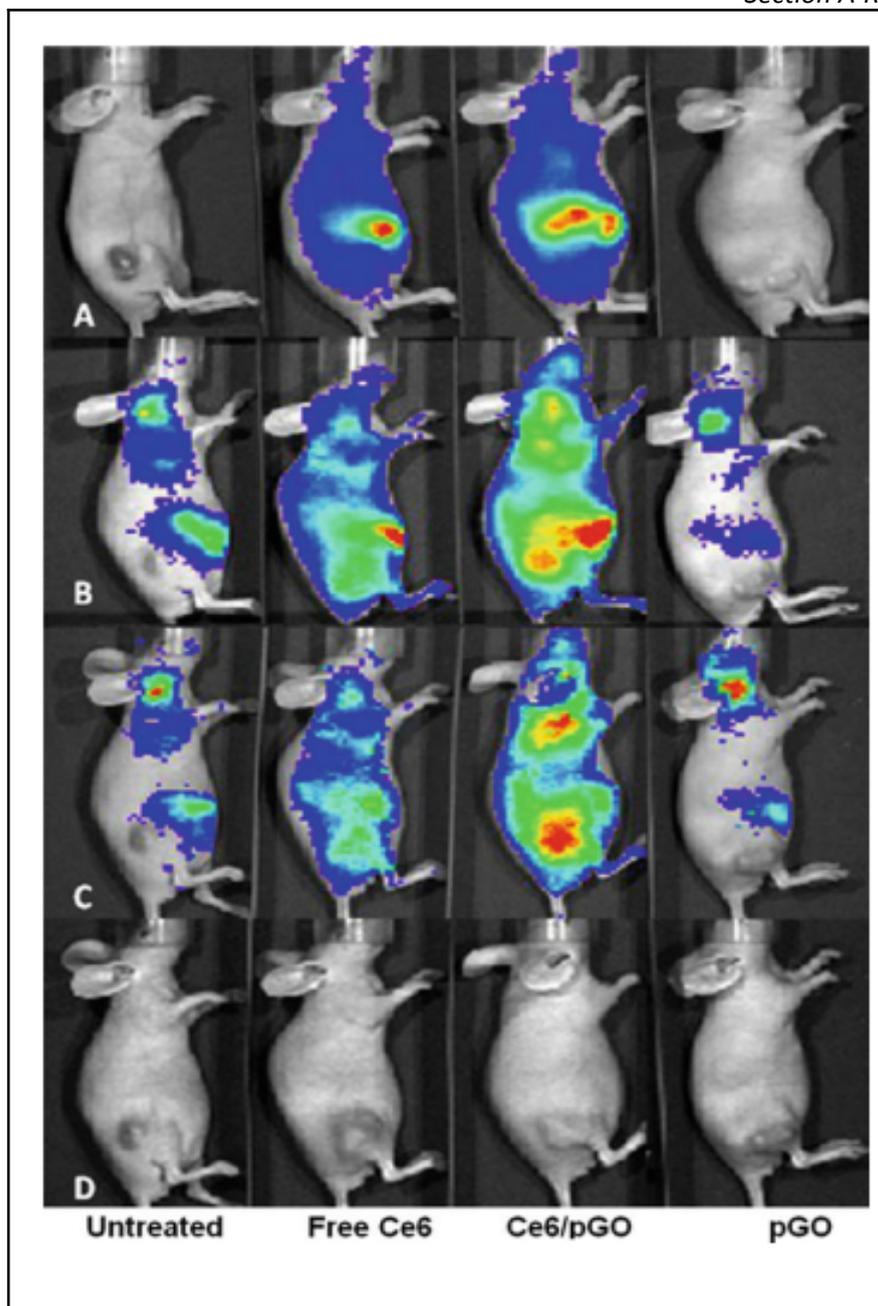


Figure 9 shows how far pGOnanophysisorplexes have spread, showing that they are in all living things. Intravenous infusions of pGO, free Ce6, Ce6/pGO, or Ce6/Dox/pGO at a dose of 10 mg/kg Ce6 and 5 mg/kg Dox were administered to SCC7-carrying mice. In addition, harmless injections of a placebo were administered to the mice. One hour following the initial dose, the in vivo distributions of Ce6 fluorescence were evaluated using a molecular imaging instrument.

(a), 24 hours (b), and 48 hours (c) after administration of kg Ce6 and 5 mg/kg Dox to SCC7-carrying mice. (a) One hour after receiving kg Ce6 and 5 mg/kg Dox (b) After 24 hours (b) After 48 hours (c) Using a molecular imaging system, Once one hour had passed, the in vivo

distributions of Ce6 fluorescence were investigated(a), twenty-four hours (b), and forty-eight hours (c). According to Miao, the availability of optical images for cancer diagnosis is as follows: (2013)

*Biomedical applications of graphene-based polymer nanocomposites*

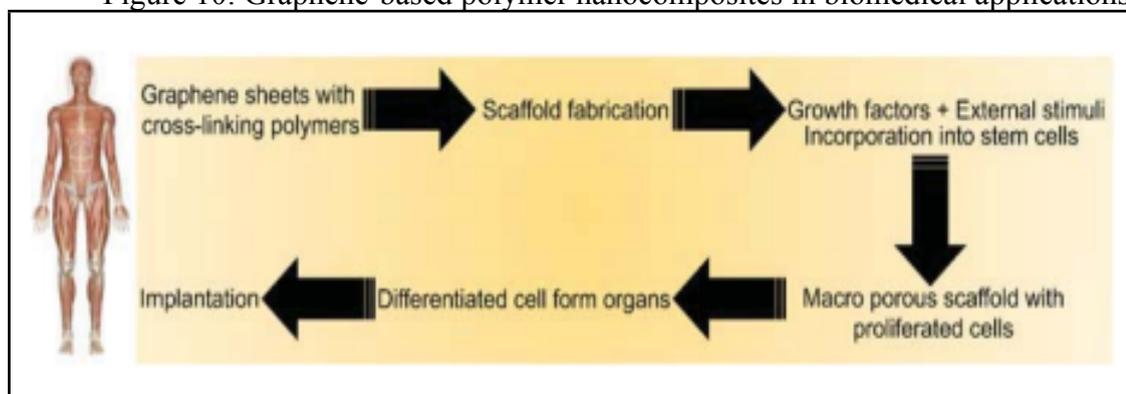
Zhang et al. (2012) found that graphene-based nanomaterials are necessary for continuous growth, controlled adhesion, and better differentiation (Figure 10). This is because they are more flexible and elastic and can stretch to fit both flat and oddly shaped surfaces. Chitosan and the graphene-coated surface of polyvinyl, which was tested by Lu et al., helped skin wounds heal completely after ten days of treatment, which was not seen in graphene-free control groups (B. Lu, T. Li, et al., 2012). PNCs are manufactured with graphene-based materials and biodegradable polymers. They could be utilised in a range of biomedical applications. This is because they have a bigger surface area, are more toxic to bacteria, and are less toxic to human cells. Scaffolds are used in the framework of tissue engineering, one of the most important and rapidly growing scientific fields. Scaffolds are used to treat tissues as well as to improve their biological activity. (M. Bera et al. 2017).

R. Subbiah and his colleagues made Fn-Tigra, a synthetic matrix, on pure titanium (Ti) substrates in 2014 using an electrodepositing process and a coaxial needle for which a patent had previously been issued. Graphene oxide and fibronectin (Fn) were the two constituents of the synthetic matrix (GO). This is pertinent to the discussion concerning bone tissue engineering. Within the field of tissue engineering, it has been recognised that graphene-based polymer composites have the potential to serve as advantageous solutions for drug delivery and other biological applications. utilised for the purpose of productively loading soluble medicines Gene therapy has been the focus of extensive research as a potential treatment for numerous diseases, including cancer and Parkinson's disease, for a very long period. Gene therapy needs to go through many tests, but the most important one is making a protected gene vector. This vector protects DNA against deterioration and facilitates its uptake by cells. Several distinct research approaches have demonstrated that graphene forms bind with single stranded DNA but not with double-stranded DNA.

Graphene can protect oligonucleotides from the deteriorating effects of enzymes. After combining GO and PEI for delivery purposes, graphene has been studied for these applications (Y. Zhang et al. 2012). Numerous biomedical applications have been characterised and implemented utilising sensors comprised of diverse materials. Sensors have

played a significant role in biomedical applications for a considerable amount of time (A. Chen et al. 2013).

Figure 10: Graphene-based polymer nanocomposites in biomedical applications



Numerous biomedical applications of Blood flow (P. Bingger et al. 2012), pulse rate (S. Park et al. 2014), respiration (S. Ryu et al. 2015), knee movement (M. Amjadi et al. 2015), etc. For many years, mercury strain gauges have been used for strain sensing; however, their strain range and mercury's application in the biomedical sector are currently their limitations (L. Cai et al. 2015). Graphene and other conductive materials, including Z. Jing et al. Researchers are utilising Qin et al. (2015) to create strain sensors with increased sensitivity. By evaluating either the gauge factor or the conductivity, you may evaluate the extent of the system's improvement. Even if some of these sensors have the potential to provide enhanced sensitivity, their development can be costly (S.-H. Bae et al., 2013), and there are a number of technological obstacles to overcome. (L. Cai et al. 2013). Despite this, graphene and graphene-based nanocomposites are desired materials due to graphene's extraordinarily high specific surface area and remarkable electron mobility. This potential device is capable of altering the electrodes for electrochemically sensing a wide range of biomolecules, including DNA, proteins, and glucose, among others (Y. Liu, et al. 2010), (Q. Zeng, et al. 2010).

Recent research (O. Akhavan et al., 2010) has shown that bacteria don't like graphene. These results suggest that graphene could be used to make antimicrobial agents. As test organisms, *E. coli* and *Staphylococcus aureus* were used to find out how dangerous graphene oxide and graphene oxide reduction are. Reduced graphene oxide, often known as rGO, has proven to be more effective than graphene oxide at killing microorganisms.

*Polymer nanocomposites for biomedical applications*

Figure 11: Polymer Nanocomposites for Biomedical and Biotechnology Applications (figure 12 a,b)

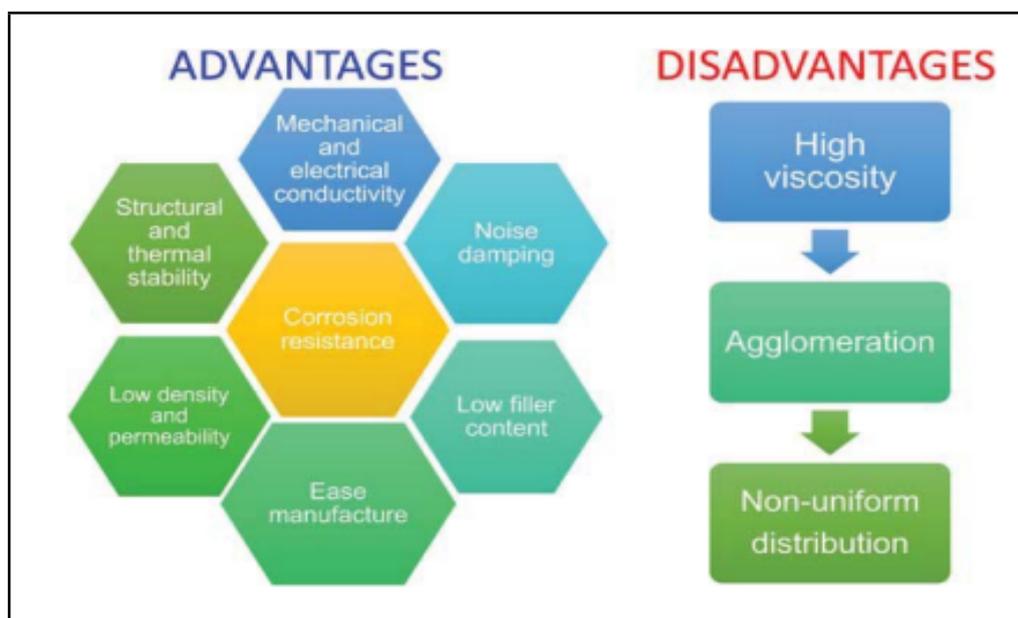
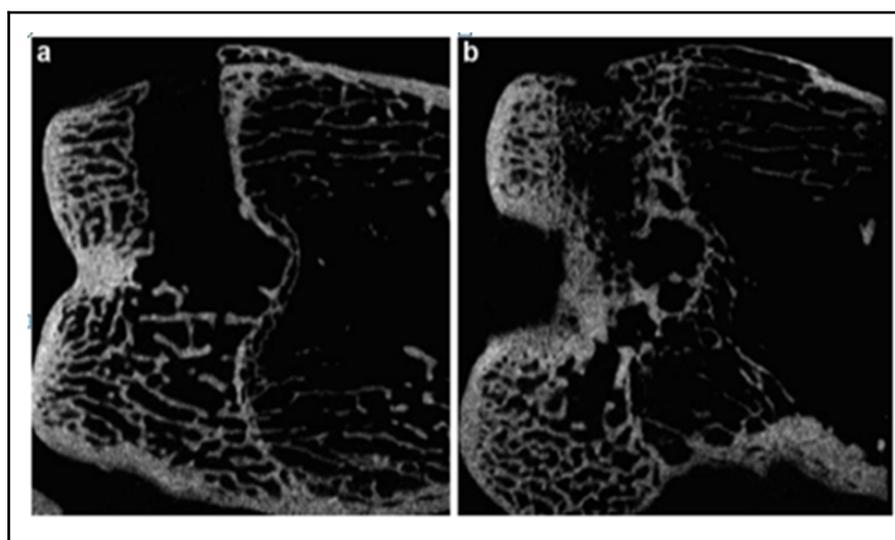


Figure 12: 12 weeks following implantation of either (a) or (b) a US-tube PPF scaffold into the femoral condyle of a rabbit, these typical micro-CT images were collected (Adapted from Sitharaman (2008))



#### 4. Challenges in Biomedical Application for nanocomposites

Polymer nanocomposites have many pros and cons when it comes to their use in medical applications (Fig. 11). Due to the way polymers are made and the many things that affect how

polymers behave, polymer nanocomposites can be used in many different ways in technology. A nanocomposite sample may contain more than one type of nanoscale-sized metal or polymer. By putting together the different chemical makeups, physical properties, and shapes of the different phases, it is possible to make a wide range of features and uses. This enables the concurrent development of features and applications. This is possible due to the interaction of the numerous phases that comprise the entire. Due to the potential for advancement, other biomedical applications, such as probes for electron microscopy to visualise cellular components, tissue engineering for bone implants, and others, are ripe for development. People and communities may have much to gain from the industrial production of polymer and metal nanocomposites, which should be considered in light of the possible economic ramifications of such endeavours. Large-scale production of high-quality goods is unachievable without first standardising the synthesis pathway and production process (Y. Zare, et al. 2016).

## 5. Conclusion

Polymer-based nanocomposites have advanced considerably since their inception. This is because nanostructured reinforcing materials have unique properties that make them useful. When nanofillers are manufactured and endowed with functions, new avenues are opened for investigating their inclusion into polymer-based nanocomposites for biomedical applications. [Bibliography needed] In a number of ways, these polymer nanocomposites are vastly superior to virgin polymer, which has resulted in a number of breakthroughs in their medical applications. Polymer-based nanocomposites for bioapplications will not reach their full potential, no matter how many times they are made, until a number of problems are solved. Before these nanocomposites may be utilised as biomaterials, biocompatibility and biodegradability are two of the most crucial requirements that must be addressed. In addition to these criteria, there are a number of other things that must be studied thoroughly through the right preclinical studies so that people don't have too high of hopes. The biological approach to making nanocellulose is new and better for the environment, but the main problem is that it doesn't make as much NCC as the chemo-mechanical process, which is already used in the business world. By creating nanocellulose with a low energy footprint and incorporating it into high-value products, it is possible to compensate for the biological route's low NCC yield. In addition, by employing a continuous production system, the yield of NCC can be significantly enhanced. In general, the biological process for the production of NCC has a substantial degree of commercial application potential that is applicable to a

variety of businesses. To separate cellulose nanofibers from the water hyacinth plant, a species of aquatic weed, both chemical and mechanical techniques were employed. The SEM investigation revealed that the application of the chemical treatment resulted in the creation of pure cellulose fibres. The transmission electron microscopy analysis determined that the isolated nanofibers have a length of 1 micron and a diameter of 25 nm. By measuring the FTIR spectrum, it was found that acidified sodium chlorite and sodium hydroxide solutions at different temperatures and times removed lignin and hemicelluloses from the sample. This finding was reached following treatment of the sample. According to the findings of the TGA test, repeated chemical treatments increased the temperature at which fibres disintegrated. Our research has demonstrated that an aquatic weed traditionally recognised as a severe pollutant possesses certain beneficial qualities. In addition, it has been demonstrated that it is possible to create cellulose nanofibers, which may have future applications.

Due to the unique features that nanostructured reinforcing materials provide, they are very advantageous. Polymer-based nanocomposites have been made successfully. When nanofillers are made and given functions, it opens up new ways to look into how they can be used to make polymer-based nanocomposites for bioapplications. Because of this, a lot of progress has been made in using them for new technologies like delivering drugs and genes and building new tissues.

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