Metadata of the chapter that will be visualized online

Chapter Title	Nanofillers: A Promising Future for Pharmaceutical Industry	
Copyright Year	2024	
Copyright Holder	Springer Nature Singapore Pte Ltd.	

Author	Family Name	**Mishra**
	Particle	
	Given Name	**Suchitra S.**
	Suffix	
	Organization/University	Dadasaheb Balpande College of Pharmacy
	City	Nagpur
	Country	India AU1
Corresponding Author	Family Name	**Mahajan**
	Particle	
	Given Name	**Nilesh M.**
	Suffix	
	Organization/University	Dadasaheb Balpande College of Pharmacy
	City	Nagpur
	Country	India AU1
Author	Family Name	**Kharwade**
	Particle	
	Given Name	**Rohini**
	Suffix	
	Organization/University	Dadasaheb Balpande College of Pharmacy
	City	Nagpur
	Country	India AU1

Abstract

Nanotechnology holds immense promise for transforming the realm of pharmaceutical science, analogous to the groundbreaking impacts of biotechnology and genetic engineering. Nanofillers, characterized by their minute particle sizes ranging from 1 to 100 nanometers, have long been in existence and encompass materials such as precipitated calcium carbonate, synthetic silicas, and carbon blacks. The careful selection of nanofillers, taking into consideration their unique physical and dimensional characteristics, allows for customization to meet specific application needs. Due to their nanoscale dimensions, fillers exhibit significantly enhanced properties compared to pure polymers, including heightened modulus and strength, exceptional barrier characteristics, improved resistance to solvents and heat, and reduced flammability.

Among the various nanofillers, carbon nanotubes (CNTs) have emerged as a recent and remarkable filler, extensively utilized due to their exceptional attributes. Nanofillers exhibit remarkable thermal, mechanical, and electrical properties that surpass those of traditional materials, making them highly advantageous. Currently, nanofillers find extensive use in various fields, including rigid containers, automotive components, packaging films, industrial components, and medical devices. Within this chapter, we explore the diverse pharmaceutical applications of nanofillers across various domains, including disease diagnosis, prevention, and treatment.

Keywords (separated by “-”)	Nanofillers - Carbon blacks - Carbon nanotubes - Gene technology - Synthetic silicas

Nanofillers: A Promising Future for Pharmaceutical Industry

Suchitra S. Mishra, Nilesh M. Mahajan, and Rohini Kharwade

Contents

S. S. Mishra · N. M. Mahajan (✉) · R. Kharwade
AU1 Dadasaheb Balpande College of Pharmacy, Nagpur, India

S. Mallakpour, C. M. Hussain (eds.), *Handbook of Nanofillers*,
https://doi.org/10.1007/978-981-99-3516-1_49-1

Abstract

Nanotechnology holds immense promise for transforming the realm of pharmaceutical science, analogous to the groundbreaking impacts of biotechnology and genetic engineering. Nanofillers, characterized by their minute particle sizes ranging from 1 to 100 nanometers, have long been in existence and encompass materials such as precipitated calcium carbonate, synthetic silicas, and carbon blacks. The careful selection of nanofillers, taking into consideration their unique physical and dimensional characteristics, allows for customization to meet specific application needs. Due to their nanoscale dimensions, fillers exhibit significantly enhanced properties compared to pure polymers, including heightened modulus and strength, exceptional barrier characteristics, improved resistance to solvents and heat, and reduced flammability.

Among the various nanofillers, carbon nanotubes (CNTs) have emerged as a recent and remarkable filler, extensively utilized due to their exceptional attributes. Nanofillers exhibit remarkable thermal, mechanical, and electrical properties that surpass those of traditional materials, making them highly advantageous. Currently, nanofillers find extensive use in various fields, including rigid containers, automotive components, packaging films, industrial components, and medical devices. Within this chapter, we explore the diverse pharmaceutical applications of nanofillers across various domains, including disease diagnosis, prevention, and treatment.

Keywords

Nanofillers · Carbon blacks · Carbon nanotubes · Gene technology · Synthetic silicas

Introduction

As posited by Drexler, nanotechnology encompasses the manipulation of substances at the molecular scale, enabling the construction of intricate nanostructures and facilitating the development of various nanomachines. The fundamental characteristic of nanotechnology lies in its ability to operate on a scale that renders it applicable across diverse domains. The nanosized dimensions of materials provide notable advantages, including minimal surface defects and a large surface area-to-volume ratio, resulting in improved material properties. Nanomaterials have found utility in an array of applications, including organic light-emitting diodes for AU2 AU3

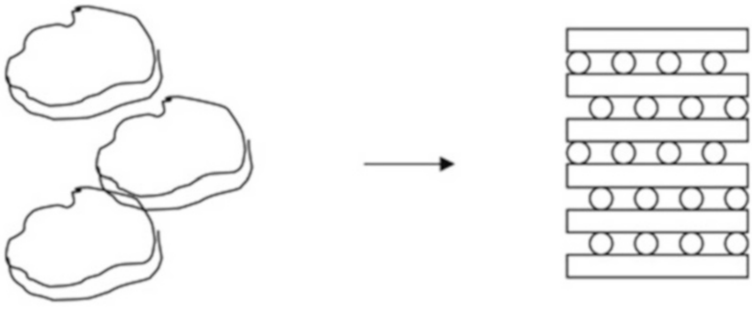

Fig. 1 Schematic structure of nanofillers (Composites 2014)

displays, human hip joints, pacemakers, water-splitting processes, and ear implants (Shanbhag et al. 2019).

The emergence of nanoparticles in the commercial market has significantly heightened the potential for amalgamated substances with unique or improved physical characteristics. Nanosized additives, characterized by their small dimensions and enlarged surface area, exhibit distinct qualities compared to larger-scale materials and conventional fillers at the micron scale. The definition of nanofillers encompasses fillers with geometric dimensions typically below 1–100 nm, with particle sizes falling within the range of 1–100 nm. Examples of such nanofillers include carbon black and synthetic silicas (Ohani et al. 2015).

Nanofillers, as depicted in Fig. 1, consist of platelet-shaped elementary particles with a thickness on the order of 1 nm and a diameter on the order of 100 nm. These primary particles are formed through the stacking of multiple elementary particles, resulting in aggregates with a thickness of approximately 10 nm (Composites 2014).

In polymer matrices, nanofillers are incorporated at mass fractions ranging from 1% to 10%. They are introduced alongside traditional fillers, additives, and, in some cases, conventional reinforcement fibers such as glass, carbon, or aramid fibers. The utilization of nanofillers with small dimensions offers a notable advantage in the form of a significant surface-to-volume ratio, which is dependent on the geometrical characteristics of particles. The characteristics and attributes of polymer nanocomposites can be precisely tailored by selecting the appropriate type of nanoscale filler for the system. Various commercially available nanofillers exist presently, including Montmorillonite (MMT) or clay, which has been extensively studied in polymer nanocomposites. Variants in fillers encompass aluminum oxide, carbon, and silica. The subsequent subcategories provide specific options of these fillers (Harsha AU4 and Ajayan 2002).

Traditionally, fillers have been regarded as additives that could only bring about moderate changes in polymer characteristics due to their geometric features rendered undesirable, chemical composition, or surface area. Their primary role was to reduce material costs by replacing more expensive polymers, with additional benefits including faster molding cycles resulting from elevated thermal conductivity.

As per the specific filler variant, other properties of the polymer could be influenced. For instance, the incorporation of fibrous materials could significantly increase melt viscosity. Conversely, thermal expansion and mold shrinkage were commonly reduced as a result of incorporating inorganic fillers (Ajyan and Kim 2008; Siegmeth et al. 2009; Landgraeber et al. 2008; Lenz et al. 2009; Hatton et al. 2003).

The true milestone, marking a distillation of the impact of these fillers, is mostly attributed to the initial studies on polyamide-6 filled with nanoclays conducted by Usuki et al. (1993) and Okada A. (1995) at Toyota R&D. These studies referred to the material as a "hybrid" material. Subsequently, research efforts rapidly expanded, and the term "nanocomposites" first appeared in 1994 through publications by Lan and Pinnavaia (1994), Lan et al. (1995), and Giannelis (1996). Following the pioneering work of these researchers, investigations into various fillers gained momentum. The continuous pursuit of enhancing the performance of thermoset polymer and thermoplastic materials has fostered the emergence of these novel technologies. Over the years, the list of nanofillers has expanded significantly, encompassing nanoclays, nanooxides, carbon nanotubes, POSS, and more. Similarly, advancements have been made in the matrices consumed and the interactions with conventional fillers.

Currently, the advancement of polymer nanocomposites stands as a highly active field within nanomaterial development. Nanoparticles offer diverse properties, with a particular emphasis on enhancing electrical conduction, providing barrier properties against gases and liquids, temperature, and potentially improving fire resistance. Nanocomposites (Biron 2004; Gloaguen and Lefevre 2007) represent a novel generation of dual-phase materials, akin to the reinforcement of polymer chains at the molecular level, similar to fibers on a macroscopic scale. In this approach, a fundamental matrix is combined with nanofillers integrated between the polymer chains.

By incorporating nanofillers, the aspects of the composite materials can be, to a great degree enhanced or adjusted, encompassing mechanical, optical, thermal, electrical, and fire-retardant characteristics, often in synergy with traditional fillers. The ratio of the organic matrix to the nanofillers can have quite an impact on the composite material's aspects.

The objective of the ongoing chapter is to provide an overview of common fillers employed in the pharmaceutical industry, examining their advantages and disadvantages and their application in the preparation of nanocomposites. Additionally, several examples of material applications, along with their future prospects, will be presented to enhance understanding in this domain.

Classification of Nanofillers

"Filler" – this term encompasses a span of category of materials, including a diverse range of solid particulate substances, both inorganic and organic. These fillers exhibit significant variations in their forms, shapes, chemical structures, sizes, and inherent properties. Typically, fillers are rigid materials that do not mix along with the matrix in either the solid or molten states (Hatton et al. 2003). Nanofillers, on the other hand, are classified using different criteria, such as their shape, size, geometry, chemical constituents, properties, and applications.

On the Basis of Geometry

Nanofillers are commonly classified into three distinct geometries, as illustrated in Fig. 2:

(a) Equi-axial particles
(b) Rod-shaped structures resembling fibers
(c) Sheet-like forms

When considering nanorods and nanoplatelets, the aspect ratio (L/D), defined as the ratio between the longest size (L) and the smallest size (D) of the particle, is commonly utilized to characterize the geometric anisotropy of the nanofiller. These very primary particles have a tendency to aggregate into particle clusters, necessitating exfoliation to achieve a homogeneous dispersion within a nanocomposite (Imai 2017).

The volume fraction of the inorganic filler relative to the polymer is a crucial parameter influencing the microstructure of the nanocomposite, contingent upon the geometric shape of the nanofiller. In the case of nanoplatelets, a high-volume fraction of nanofillers leads to the formation of a hierarchical layered structure, wherein inorganic platelets are stacked, with the polymer matrix positioned between each layer. This hierarchical arrangement often exhibits similarity to the brick-and-mortar structure observed in biological materials like nacre (Tang et al. 2003; Morits et al. 2017; Niebel et al. 2016; Podsiadlo et al. 2007; Abba et al. 2015; Mäkiniemi et al. 2015). Conversely, at volume fractions below a critical value, the structure formation

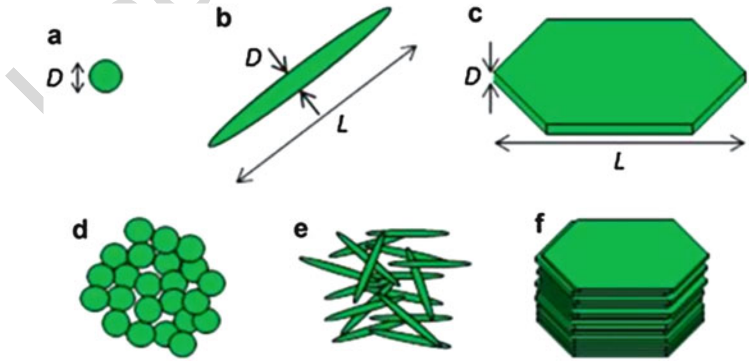

Fig. 2 Types of nanofillers: (**a**) spherical; (**b**) rod shaped; (**c**) sheet like; and (**d-f**) aggregate of each type of nanofillers (Imai 2017)

is dictated by the polymer matrix, resulting in a disordered, random dispersion of inorganic platelets within the polymer matrix (Wang and Hare 2012).

On the Basis of Dimensions (Marquis et al. 2009)

The classification of nanofillers based on their dimensions, as depicted in Fig. 1 of ISO/TS27687 (2008), is as follows (Fig. 3):

(a) One-dimensional nanofillers: These nanofillers exist in the form of shells, lamina, or plates.
AU5
(b) Two-dimensional nanofillers: This category includes nanotubes and nanofibers with diameters smaller than 0.1 μm.
(c) Three-dimensional nanofillers: Iso-dimensional nanoparticles, such as nanometric silicabeads, are representative of this classification.

On the Basis of Chemical Constituents (Jamróz et al. 2019)

There are four distinct categories of nanofillers:

(a) Clays: This group encompasses nanofillers derived from clays.
(b) Organic: The organic nanofillers consist of natural biopolymers such as cellulose and chitosan.
(c) Inorganic: Inorganic nanofillers include metallic agents like silver, as well as metal oxides such as ZnO and TiO2.
(d) Carbon nanostructures: Carbon nanostructures can be distinguished as per various types, such as nanofibers, graphene, fullerenes, and carbon nanotubes (Fig. 4).

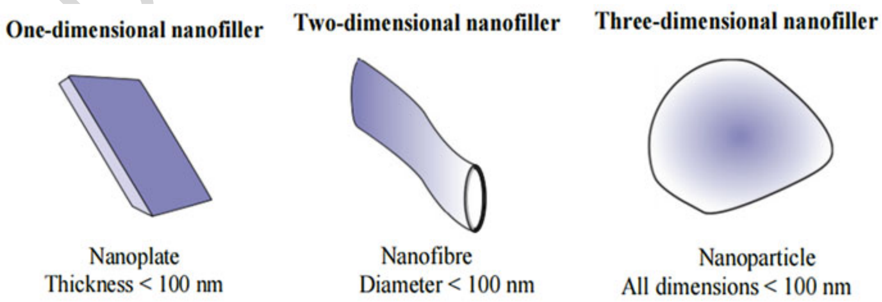

Fig. 3 Types of nanofillers on the basis of dimensions (Marquis et al. 2009)

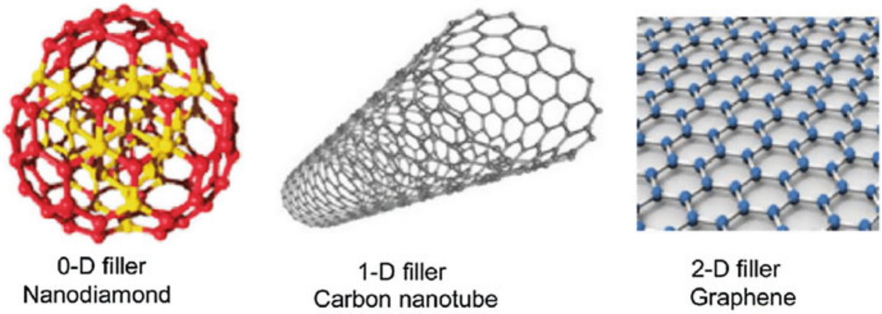

Fig. 4 Different types of carbon-based nanofillers

t.1 **Table 1** Chemical families of nanofillers for polymers

	Chemical family	Examples
t.2	Inorganic oxides	Glass fibers, spheres, hollow spheres, flakes, MgO, and SiO2r S!CQ1
t.3	Hydroxides	$A(OH)_3$, $mg(OH)_2$
t.4	Salts	$CaCO_3$, $BaSO_4$, and $CaSO_4$
t.5	Silicates	Talc, Mica, Kaoline, Montmorillonite, NanoclaY, and Felrlsnar- Asbestos
t.6	Metals	Steel, boron
t.7	Carbon - graphite	Carbon fibers, graphite fibers, and carbon black
t.8	Natural polymers	Cellulose fibers, wood flour and fibers, cotton, and starch
t.9	Man-made polymer	Polyamide-polyester, aramid, and poly vinyl alcohol polymers

On the Basis of Functional Group (Germain 2019; Purdue et al. 2006; Vataio et al. 2005; Tsukamoto et al. 2008; Tateiwa et al. 2008; Fisher et al. 2006; Thbei et al. 2010)

Nanofillers are classified into two broad groups based on their composition: inorganic and organic substances. These groups can be further subdivided based on their chemical families and specific functional properties. Table 1 shows chemical families of nanofillers.

On the Basis of Functions (Germain 2019; Purdue et al. 2006; Vataio et al. 2005; Tsukamoto et al. 2008; Tateiwa et al. 2008; Fisher et al. 2006; and Thbei et al. 2010)

The functions of fillers changed with the ratio of different types of fillers according to their physicochemical properties. The various functions of these fillers like permeability, bioactivity, radiation absorption, and stability get affected by different types of nanofillers used (Table 2).

t.1 **Table 2** Nanofillers with their functions

	Primary function	Fillers examples	Secondary functions	Fillers examples	
t.2	Enhancement processability	Thixotropic, antisag, thickeners, and acid scavengers: colloidal silica' bentonite, hydrotalcite	Improved dimensional stability Modification of optical properties Control of darning	Isotropic shrinkage, reduced warpage: particulate fillers, glass beads, and mica Nucleators, clarifiers, and inidescent pigments: fine particulates, mica/pigment hybrid flake fillers, glass, and BaSO4	AU6
t.3	Modification of surface properties	Antiblock, lubricating: silica, CaCO3, PTFE, MoS2, and graphite	Radiation Absorption	Metal particles, lead oxide, and leaded glass	
t.4	Modification of electrical and magnetic properties	Conductive, nonconductive, and feromagnetic: metals, carbon fibers and nanotubes, carbon black, and mica	Degradability	Organic fillers: starch, cellulose	
t.5	Enhancement of fire retardancy	Hydrated fillers: Al(OH)3, Mg(OH)2	Bioactivity	Bone regeneration: hydroxyapatite, tricalcium phosphate, and silicate glasses	
t.6	Modification of mechanical properties	High-aspect ratio: glass fibers, mica, nanoclays, carbon nanofibers, carbon / graphite fibers, and aramid/synthetic/ natural fibers Low aspect ratio: talc, CaCO3, kaolin, wood, glass, and wollastonite	Control of permeability	Reduced permeability: impermeabic plate-like fillers: mica, talc, nanoclays, and glass flakes Enhanced permeability: stress concentrators for inducing porosity: CaCO3, dispersed polymers	

Advantages (Shanbhag et al. 2019; Chothave et al. 2022; Reshmi 2021)

Based on the concise review of the significance of nanofillers, the following conclusions have been deduced:

(a) Nanofillers greatly elevate the electrical, thermal, and mechanical properties of composites as opposed to unfilled materials or conventional alternatives.
(b) The high surface-to-volume ratio that nanofillers exhibit, which also raises the material's hardness, is to blame for the noticeable improvement in properties. Moreover, nanofillers offer cost advantages.

(c) Extensive research indicates that nanofillers have a significant impact in contemporary times due to their intriguing characteristic behavior and unique features while occupying minimal space and cost. Furthermore, there is substantial potential for future research in this field.
(d) Nanofillers expand the application of nanocomposites across major sectors such as aerospace, automotive, sports goods, and electronic parts.
(e) The combination of reinforcing fillers and polymeric matrices results in desired qualities, including strength, high stiffness, flame resistance, scratch/wear resistance, electromagnetic shielding, toughness, thermal/electrical conductivity, coefficient of thermal expansion, wear, and damping resistances (Zheng-Ming et al. 2003; Rohan et al. 2007; Lin et al. 2012a, b).
(f) The morphing from micro to nanoparticles is supposed to elevate the surface area-to-volume ratio (Thakur et al. 2014a, b), culminating in an enhancement in the behavior of surface atoms. This, in turn, influences the properties of the particles during interactions with other particles (Yuan-Qing et al. 2008).
(g) The increased specific surface area of nanoparticles leads to intensified interactions with other particles in the mixture, resulting in favorable properties such as corrosion resistance, high temperature resistance, noise damping, ductility, low manufacturing cost, high specific stiffness and strength, high thermal conductivity, and a low coefficient of thermal expansion (Dubois and Alexandre 2006).
(h) Another advantage of polymeric nanofillers is their ability to be efficiently and accurately fabricated using rapid manufacturing techniques such as compression and injection molding.
(i) Nanocomposites exhibit distinct characteristics compared to conventional composites due to the significantly higher surface-to-volume ratio of the reinforcing phase and/or its exceptional aspect ratio.
(j) The incorporation of a small percentage of nanofiller materials in nanocomposites results in reduced weight compared to conventional composites.
(k) Nanomaterials possess properties that are size-dependent and offer significantly enhanced mechanical, thermal, optical, chemical, magnetic, and electrical properties compared to conventional composites.
(l) Unlike traditional composites, nanocomposites can enhance the qualities of the matrix material with a small concentration of nanofiller materials, while conventional composites require a higher concentration of microparticles to achieve similar property improvements.
(m) The interface area between the matrix and nano-reinforcement in nanocomposites is typically an order of magnitude larger than that in conventional composites.
(n) Nanocomposites exhibit excellent dispersibility in aqueous media and provide a uniform distribution of active agents over a considerable span of time, enabling the controlled release of drugs and reducing the administration frequency. Additionally, nanocomposites can penetrate regions that are not accessible to other delivery systems, thereby enhancing stability.

Disadvantage (Chothave et al. 2022)

(a) While efficient drug delivery is achieved through the use of nanofillers, economic challenges arise due to the high costs associated with raw materials, fabrication, and assembly.
(b) In comparison to matrix carriers, nanofiller composites exhibit lower strength in the out-of-plane direction and reduced resistance to temperature and moisture.
(c) Nanocomposites incorporating nanofillers pose greater challenges in terms of repairability in the event of damage, primarily due to their smaller size when compared to conventional composites.

Properties of Nanofillers Support Phamaceutical Products

The properties of nanocomposites that make them suitable for pharmaceutical applications include their large surface area, tensile strength, formation of a network within the matrix, nanocrystallinity, and nanosized polymer. It has been observed that the tensile strength of a composite elevates with the concentration of nanofillers till a certain extent and then plateaus. For example, the input of nanocrystalline cellulose with up to 5% w/w) in a chitosan matrix enhances the tensile strength of the composite, but after this concentration, the tensile strength will remain constant (Sharpe 1972; Manson and Sperling 1976; Ishida and Koenig 1978).

Nanoparticles prepared from polysaccharide nanocrystals exhibit strong interactions, such as hydrogen bonding, leading to the formation of nanoparticle agglomerates. In a nanocomposite, these interactions are welcomingly effective for creating a filler network inside the matrix. Magnetic nanoparticles are sensitive to outside alternating magnetic fields, which can be utilized in nanocomposites to control drug release (Shanbhag et al. 2019).

One challenge with nanocomposite hydrogels is undesired dehydration during drug delivery. However, studies have shown that the addition of montmorillonite (MMT) nanoclay to a polyvinyl alcohol (PVA) hydrogel improves its water retention properties. Nanocomposites of PLGA-MMT with the drug paclitaxel have demonstrated enhanced cellular uptake of paclitaxel in cancerous cells and improved interaction of nanoparticles with the gastrointestinal tract (GIT). Improved tensile strength and enhanced water/moisture sensitivity were observed in a blend film of chitosan and silk fibroin nanocomposites (Khan et al. 2012; Sermsantiwanit and Phattanarudee 2012; Dong and Feng 2005). The thermal stability of poly(ester-amide)-functionalized ZnO nanocomposites was enhanced compared to the pristine polymer. In the case of PLGA (poly(lactic-co-glycolic acid)), which was the only one to show an inflammatory response in the spinal cord, the inflammatory reaction was significantly reduced when PLGA was combined with hyaluronan and methylcellulose nanocomposites. PLA (polylactic acid) has limitations such as low cell adhesion and inflammatory reactions, which can be overcome by incorporating calcium phosphate in the composite. The degradation rate of the

PLA/hydroxyapatite composite was lower than that of pure PLA (Abdolmaleki et al. 2011; Zhang et al. 2009).

Celecoxib, an adjuvant used for the treatment of colon cancer, was found to exhibit hemolysis when used alone. However, when loaded into a nanocomposite of hydroxyapatite-chitosan, the hemolytic activity decreased due to the stiff structure of the composite, which was noninteractive with the red blood cell membrane. The biodegradability and biocompatibility of nanocomposites are essential properties that enable their use in various drug delivery systems (Yilmaz et al. 2010; Deborah and Chung 2002).

Recently Used Nanofillers

Clay Nanofiller

Clay nanosheets have gained significant attention as an inorganic component in high filler-content nanocomposites, primarily owing to their versatility, low cost, and wide availability. These inorganic, nanometer-sized sheets possess negative charges and offer numerous hydroxyl groups for potential cross-linking. Montmorillonite (MTM), vermiculite (VMT), laponite (LAP), and saponite (SA) are the commonly utilized clays for the production of polymer-clay nanocomposites. Figure 5. illustrates the structure of a 2:1-layered silicate (Beyer 2002). The uncommon intercalation and exfoliation characteristics and high-aspect ratio of these materials contribute to their extensive research focus (Alexandre and Dubois 2000). MTM and VMT clays exhibit elevated cation exchange capacities and targeted surface areas compared to other clay nanofillers. In particular, MTM clay nanofillers possess smaller crystallite sizes and rougher platelet surfaces than other clays (Ho et al. 2012). The incorporation of clay nanofillers into polymer-clay nanocomposites yields favorable mechanical properties, improved gas barrier properties, and enhanced flame retardancy (Pavlidou and Papaspyrides 2008; Beyer 2002). Consequently, MTM clays have undergone expansive studies and are widely employed as clay nanofillers in the research literature.

The first bentonite clay nanopaper was successfully manufactured by Hauser in 1938 (Hauser and Okada 2006). However, this material exhibited opacity and undesirable gas barrier properties. From the 1970s, significant research efforts have been dedicated to polymer-clay nanocomposites, aiming to enhance their physical properties. In most cases, these composites primarily consisted of the organic phase, with clays comprising a minor component (10 vol%). It was observed that increasing the clay content beyond 10% led to mechanically weak nanocomposites. This weakness was attributed to the formation of clay agglomerates resulting from the inhomogeneous dispersion of clay sheets within a brittle material (Okada and Usuki 2006). Moreover, the aspect ratio decreased as multiple silicate layers reformed, and the total thickness of aggregates increased, diminishing the advantages of nanocomposite formation.

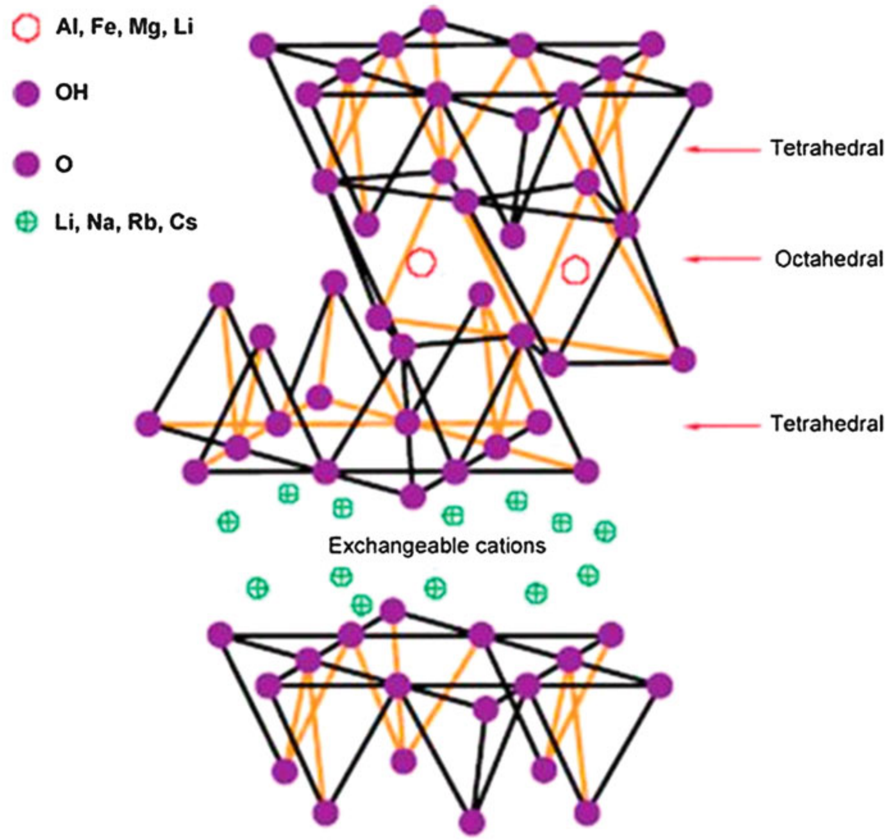

Fig. 5 The structure of layered silicate (Beyer 2002)

Graphene Oxide Nanofiller

Graphene (G), a two-dimensional nanomaterial, exhibits exceptional physical properties attributed to its pure sp2 hybridization network. It is renowned for its outstanding mechanical properties, remarkable thermal and electrical conductivity, making it highly promising with varied applications like aerospace, flexible supercapacitor electrodes, artificial muscles, and tissue engineering. Pristine graphene is typically obtained through top-down methods like mechanical exfoliation or bottom-up methods such as chemical vapor deposition (CVD) (Novoselov et al. 2013). However, these methods face limitations in terms of scalability and time-consuming procedures. As a result, attention has shifted to graphene oxide (GO), a precursor of graphene. GO is commonly synthesized using Hummers' method (Hummers and Offeman 1958) or modified versions that involve chemical functionalization of mineral graphite flakes. Nevertheless, these methods suffer from certain drawbacks, including a low-yielding and potentially toxic gas production. To address these

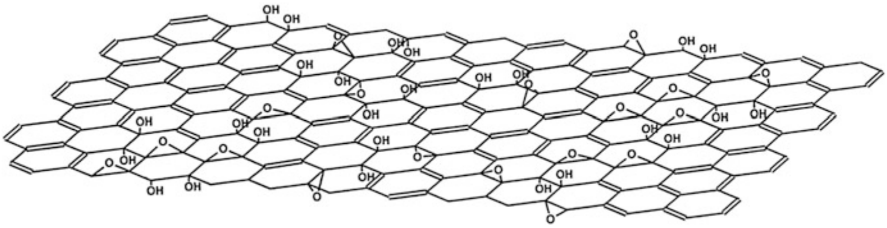

Fig. 6 Schematic representation of structure of graphene oxide (He 1998)

issues, researchers have proposed modified and improved approaches. These include the elimination of NaNO3 (Chen et al. 2013), preoxidation before the Hummers' procedure, adjustment of the KMnO4/NaNO3 ratio (Marcano et al. 2010), and substitution of KMnO4 with K2FeO4 without the use of NaNO3 (Peng et al. 2015).

The resulting graphene oxide (GO) sheets, which are water-soluble derivatives of graphene, exhibit favorable characteristics for the fabrication of artificial nacre. These sheets possess numerous functional groups, such as hydroxyl and epoxide groups, that avail themselves for cross-linking (He et al. 1998). In fact, GO stands out among platelet nanofillers due to the presence of reactive functional groups on its basal plane, enabling covalent bond formation (Fig. 6) (He 1998). In contrast, silicate layers obtained from clay do contain hydroxyl groups, but these groups are enclosed within the silicate layer and are inaccessible for covalent bonding. Covalent bonds can be formed only by the exposed silanol groups at the edge plane. The planar nature of GO sheets facilitates their assembly into paper-like structures through self-assembly and filtration techniques (Dikin et al. 2007; Chen et al. 2009). The exceptional mechanical properties of monolayered GO sheets, with a tensile strength of 63 GPa and a Young's modulus ranging from 200 to 500 GPa, in conjunction with their high surface areas, add to the production of nanocomposites with outstanding mechanical performance (He 1998; Paci et al. 2007; Chen et al. 2008).

Ceramic Matrix Nanofillers (Naslain et al. 1989; Simon 2005)

Ceramic matrix nanofillers are a category of ceramics composed of ceramic fillers embedded within a ceramic matrix. Both the fibers and the matrix may have various ceramic materials, including carbon and carbon fibers, which possess ceramic properties. These nanofillers can be conveniently prepared using different techniques such as gas-phase matrix deposition, pyrolysis-based matrix formation, chemical reaction, sintering, and electrophoresis. Among them, carbon nanotubes are extensively employed in ceramic matrix nanocomposites, particularly as a means of efficient drug delivery in the pharmaceutical industry. These nanocomposites are highly valued due to their desirable attributes, including excellent stability, thermal resistance at high temperatures, electrical resistivity, and, most importantly, corrosion resistance.

Polymer-Matrix Nanofillers (Hussain et al. 2006; De Sousa et al. 2013)

Polymer filler-based nanocomposites (PNC) refer to polymers or copolymers with nanoparticles or nanofillers distributed within the polymer matrix. These nanofillers can have various shapes, such as platelets, fibers, or spheroids, with an eligibility of one dimension, at least, falling within the range of 1–50 nm. The addition of nanoparticles to the polymer matrix can improve its performance, resulting in materials known as nanofilled polymer composites. By effectively dispersing the fillers uniformly throughout the matrix, the aspects of the polymer can be enhanced, leading to enhanced performance and productivity (Fig. 7).

Bone tissue engineering is a field which employs various polymeric nanocomposites, including carbon nanotubes, molybdenum disulfide, graphene, and tungsten disulfide. These materials find applications in biomedical fields such as drug delivery and cellular therapies. To achieve desired property combinations, polymeric networks are combined with ceramic, metal oxide, or carbon-based nanomaterials. Different methods, such as solution-induced intercalation, in situ polymerization, and melt processing, are used to prepare such nanocomposites.

Both natural and synthetic polymers, including cellulose, starch, cellulose, gelatin, alginate, chitosan, PVA, fibrin, and PEG, are used in conjunction with nanocomposites to create highly temperature-resistant materials. These nanocomposites are suitable for developing thermally stable drug delivery systems.

Metal-Matrix Nanofillers (Krishna et al. 2017)

Metal matrix nanofillers refer to toughened metal matrix composites, which can be differentiated as continuous or noncontinuous reinforced materials. Among these, carbon nanotube metal matrix stands out as a significant nanofiller. It is an emerging material that offers the advantageous electrical conductivity and enhanced tensile strength of carbon nanotube materials. Various techniques are employed for the processing of metal matrix nanocomposites, including spray pyrolysis, vapor techniques, liquid metal infiltration, electrodeposition, rapid solidification, and chemical

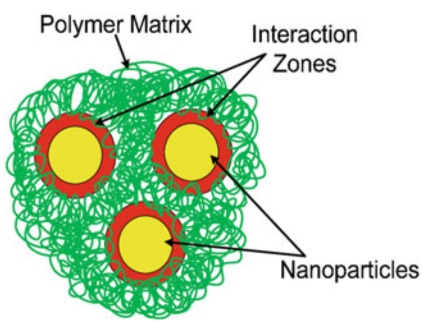

Fig. 7 Polymer-matrix nanofillers

methods such as colloidal and solgel methods. These materials find wide-ranging applications in the development of structural components.

Magnetic Nanofillers (Behrens and Appel 2016)

Magnetic nanofillers are composite materials composed of nanoscale magnetic materials that exhibit a response to external stimuli, such as static or alternating magnetic fields. Extensive research has been conducted to explore innovative nanocomposites by combining a wide range of materials, including gels, silica, liquid crystals, carbon, renewable polymers, or metal-organic frameworks, with varied magnetic particles. These combinations hold immense potential for diverse usages in fields such as medical therapy and diagnosis, separations, actuation, and catalysis, offering promising prospects for advancements in various industries.

Elastomeric Nanofillers (Malaki et al. 2019)

Elastomeric nanofillers refer to polymers that possess rubber-like elasticity. These nanosized particles, known as elastomeric nanoparticles (ENPs), have found extensive use in polymer modification, where they exhibit nanoscale effects. For instance, when incorporated into plastics, ENPs have the ability to simultaneously enhance the toughness and heat resistance of the material.

Bionanofillers (Qiao 2020)

Bionanofillers are a distinct class of materials consisting of a combination of biopolymers, which are naturally occurring polymers, and inorganic nanomaterials. They are also referred to as "green nanofillers" because of their utilization of natural polymers. These bionanofillers can be categorized as polymer-matrix materials and can be prepared using similar methods as those employed for polymer nanocomposites. Their size, which is typically less than 1000 nm, renders them highly significant in drug delivery applications. Specifically, they find widespread use in gene drug delivery for anticancer therapy.

Other Nanofillers

Layered double hydroxides (LDH) belong to a class of lamellar compounds characterized by brucite-like layers with positively charged ions and an interlayer region comprising of anions and solvation molecules. Electrophoretic deposition (EPD) is a widely employed and effective technique for producing LDH-based nanocomposites with high filler content, due to the ionic nature of the inorganic filler. Another commonly utilized inorganic filler is alumina (Al2O3), commonly called aluminum oxide, which exhibits thermodynamic stability and possesses a trigonal symmetry. Al2O3 has been extensively employed in the fabrication of optimum-performance nanocomposites due to its favorable physical properties.

Additional nanofillers usually found in the literature include boron nitride (BN), carbon nanotubes (Ansorge and Papailiou 2015; Teng et al. 2011), and silica nanoparticles (Goertzen and Kessler 2008; Zhang et al. 2006). While more recent nanofillers like MoS2 (Wang et al. 2017) and black phosphorus (phosphorene) hold promise due to their unique properties, there are currently no reported attempts at manufacturing high nanofiller-content nanocomposites with these materials.

Black phosphorus, being a graphite analogue, offers numerous potential applications, provided that environmental challenges can be overcome. Recent reports indicate progress in developing black phosphorus-based nanocomposites that partially address these concerns (Fonsaca et al. 2017).

Table 3 presents a compilation of various nanofillers and their associated properties as examples.

Hybrid materials, composed of both organic and inorganic components, have garnered increasing interest across diverse research domains. Organic-inorganic hybrid materials possess unique attributes that stem from the combination of inorganic elements (such as rigidity, dimensional stability, and thermal stability) with the properties exhibited by organic materials (such as tenacity and workability) (Wu et al. 2017). These characteristics distinguish them from traditional materials.

Pharmaceutical Applications of Nanofillers in the Form of Nanocomposites

Nanofillers offer the potential for site-specific drug delivery, surpassing conventional approaches by enabling controlled release. These controlled-release nanofillers containing nanocomposites present a promising avenue for the development of sustained and regulated dosage forms. Various nanofillers matrix in the form of nanocomposites, including carbon nanotubes, chitosan-based hydrogels, nanospheres, graphene nanotubes, and magnetic nanocomposites, hold great promise for diverse applications. Magnetic hydrogel nanocomposites, for instance, can be utilized in pulsatile drug delivery systems, while nanofillers rich nanocomposite beads demonstrate potential for oral pharmaceutical formulations and the treatment of spinal cord injuries (Das et al. 2022) (Fig. 8). AU7

Controlled Release

In pulsatile drug delivery systems, magnetic nanocomposites of hydrogel can be employed. N-isopropyl acrylamide (NIPAAm) magnetic nanocomposite is used to construct remote controlled medication release. NIPAAm is a temperature-sensitive hydrogel, and iron oxide is employed as a remote heating device. Heat is produced in nanocomposites as a result of the high-frequency magnetic field's alternation, t.1 **Table 3** Recent examples of nanofillers with their characteristics

	Type of nanofillers	Properties added to the film	Reference
t.2	Inorganic nanofillers		
t.3	SeNPs	Antimicrobial effect	Jamroj (2018)
t.4		Antioxidant activity	Kalishwaralal et al. (2016)
t.5	AgNPs	Antimicrobial effect	Divya et al. (2019)
t.6		UV shielding properties	Roy et al. (2019)
t.7		Antioxidant activity	Kadam et al. (2019)
t.8		Photocatalytic effect	Farshchi et al. (2019)
t.9	SNPs	Antimicrobial effect	Shankar (2018)
t.10	TiO2 NPs	Antifouling effect	Natarajan et al. (2018)
t.11		Antimicrobial activity	Jbeli et al. (2018)
t.12		Photocatalytic activity	Noshirvani et al. (2017)
t.13		UV shielding properties	Fathi (2018)
t.14	CuNPs	Antimicrobial effect	Shankar (2014)
t.15		UV shielding properties	Roy et al. (2019)
t.16	Organic nanofillers		
t.17	Nanocellulose	Blood compatibility	Poonguzhali et al. (2017)
t.18		Antibacterial effect	
t.19		Thermal stability	Adel et al. (2018)
t.20		Good mechanical stability	Curvello et al. (2019)
t.21		Low cytotoxicity	
t.22	Chitosan nanoparticles	Biocompatibility	
t.23		Biodegradability	Yu et al. (2019)
t.24		Low toxicity	Martins et al. (2019)
t.25		Antimicrobial activity	Pan et al. (2019)
t.26	ZnO NPs	Antifungal effect	
t.27		UV shielding properties	Abdeen et al. (2018)
t.28		Antimicrobial effect	Ponnamma et al. (2019)
t.29		Dielectric properties	
t.30		Electromagnetic shielding	
t.31		Thermal conductivity	Tripathi et al. (2019)
t.32	Clay nanofillers		
t.33	MMT, Hal, etc.	UV shielding properties	Fathi (2018)
t.34		Good mechanical stability	Zhu et al. (2019)
t.35		Thermal stability	
t.36	Carbon nanofillers		
t.37	Graphene, graphene oxide, etc.	Lightweight Processing benefits, flexibility, and resistance to corrosion Extraordinary electrical, mechanical, and thermal properties	Wu et al. (2017)

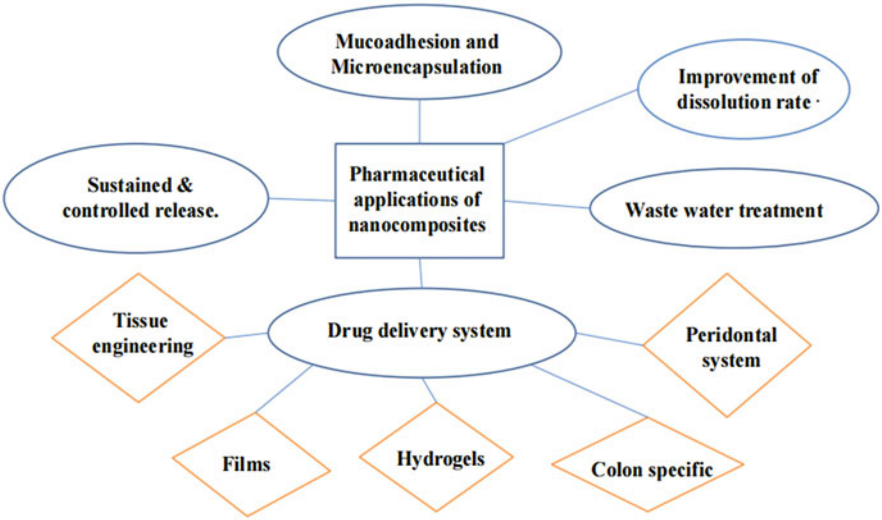

Fig. 8 Pharmaceutical applications of nanofillers

forcing the hydrogel's transition to swelling. It was discovered that when the temperature rose, the medication release reduced (Shailesh et al. 2016; Wen et al. 2011).

Sodium alginate nanocomposite shows controlled release of diclofenac sodium. Oral medicinal formulations may be created using nanocomposite beads, when compared to sodium alginate hydrogel beads, and the release of diclofenac sodium was extended by nanocomposites for an additional 8 hours (Shailesh et al. 2016; Bergese et al. 2003).

Controlled release of drug was also observed in glycolic acid-g-chitosan-gold-nanoflower nanocomposites. The nanohybrid scaffolds were found to be stable toward pH of the medium. The prepared nanohybrid scaffolds are biocompatible. These nanocomposites showed controlled drug release rate in the buffer solution of pH 7.4. It was observed that gold nanoflowers are the viable additive for the glycolic acid-grafted chitosan-based system, for drug delivery (Shailesh et al. 2016; Sivanesan et al. 2012; McCarthy et al. 2021; Niezabitowska et al. 2018; Zhang et al. 2018; Hu and Niemeyer 2020).

Sustained Release (Shailesh et al. 2016; Zhang et al. 2010)

Additionally, nanocomposites in the form of biomaterials have the potential to revolutionize sustainable drug delivery. Sudipa Das et al. have successfully developed sustainable biomaterials incorporating nanocellulose for drug delivery purposes.

Hyaluronan and methylcellulose hydrogel nanocomposites with PLGA nanoparticles were effectively created as sustained release products for the treatment of spinal cord injury. Biocompatibility and safety were determined to be present. It was well tolerated in the intrathecal area of wounded rats for 28 days and had no influence on the animals' ability to move or on the amount of inflammation, scarring, or cavities compared to the control.

Mucoadhesion and Microencapsulation

The stability, permeability, degradation, absorption, toxicity, and compatibility issues associated with certain drugs can be addressed through the microencapsulation of drugs using nanocomposites. In addition, mucoadhesives are employed to prolong drug absorption time. Researchers have extensively investigated this approach, which demonstrates immense avenues for usages in the field of pharmaceutical drug delivery systems. An example of such an approach is the development of Carmellose Mucoadhesive Oral Films containing vermiculite/chlorhexidine nanocomposites as innovative biomaterials for treating oral infections. The mucoadhesion of montmorillonite chitosan nanocomposites involves the extraction of naturally occurring polymers. Similarly, an iodine-loaded poly(silicic acid) gellan nanocomposite mucoadhesive film is utilized for antibacterial applications. Furthermore, the effect of bentonite on the physical properties and drug-release behavior of bentonite nanocomposite hydrogels for mucoadhesive purposes has been investigated. Another example includes the preparation of an alginate-based nanocomposite for the microencapsulation of probiotics, evaluating the impact of cellulose nanocrystals and lecithin.

Improvement of Dissolution Rate (Ohani et al. 2015)

Enhancing the dissolution rate of drugs which exhibit poor water solubility is a crucial aspect of pharmaceutical technologies, and one effective approach is the design of nanocomposites. By incorporating these drugs into nanocomposite structures, their molecular size is significantly reduced, leading to a substantial increase in surface area. This improved surface area facilitates enhanced dissolution rates. Clay-based nanocomposites are particularly utilized to enhance drug wettability thanks to the hydrophilic properties inherent in clay materials.

Waste Water Treatment (Paravastu et al. 2019)

Various techniques are currently employed in the market to eliminate organic molecules from water, such as air strippers, reverse osmosis, activated charcoal, and granular-activated carbon. However, a limitation of these systems is their inability to effectively remove larger molecules, such as humic acid and water contaminated with oil and grease. To address this issue, the use of organoclays has emerged as an effective approach for the treatment of oily wastewater. Organoclays have demonstrated promising results in efficiently treating such wastewater, overcoming the challenges associated with the removal of large molecules.

Drug Delivery System (Massoud et al. 2019; Sivanesan 2021; McCarthy et al. 2021; Niezabitowska et al. 2018; Zhang et al. 2018; Hu and Niemeyer 2020; Salahuddin et al. 2020)

In recent times, a novel approach has emerged to address the challenges and limitations associated with conventional dosage forms. Nanocomposites have emerged as effective tools for efficient drug delivery within the body. These nanocomposites find various usages, like colon-specific drug delivery, tissue engineering, periodontal systems, and targeted drug delivery systems. Different types of nanocomposites, including films, hydrogels, and carbon nanotubes, are utilized for drug transportation within these systems.

Researchers have made significant contributions in this field. Jonathan et al. developed a photomechanical polymer nanocomposite drug delivery system that enables laser-triggered drug release. Iyyakannu et al. prepared curcumin-loaded chitosan-based nanocomposites, while Pumtiwitt et al. developed a chitosan hydrogel with applications in wound healing, drug delivery, and sensor development.

Other studies focused on the combination of carbon nanotubes with polycaprolactone (PCL) to produce nonspherical nanocomposites (Edyta et al.), the development of water-dispersible polymer nanocomposites containing PEG-curcumin/amine functionalized covalent organic framework for drug delivery of doxorubicin in cancer treatment (Zhang et al.), and targeted drug delivery through carbon nanotubes and hydrogels loaded with anthracycline drugs for treating HeLa cancer cells (Yong Hu et al.).

Moreover, Nehal et al. designed and synthesized a norfloxacin drug delivery system based on PLA/TiO2 nanocomposites, exhibiting antitumor and antibacterial activities. Peeyush Kumar et al. utilized a photopolymerization technique for 3D printing nanocomposite pills for drug delivery purposes, utilizing approved nutraceuticals.

These studies highlight the advancements in utilizing nanocomposites for drug delivery, demonstrating the applications of this approach in various therapeutic avenues.

Anticancer (Shailesh et al. 2016; Zhang et al. 2009)

Because of its poor GIT absorption and first pass impact, the anticancer medication paclitaxel cannot be administered orally. For oral administration, PLGA-MMT (nanofiller) was used to formulate nanofillers that included paclitaxel nanocomposites. By increasing cellular uptake by CaCo-2 and HT-29 cells, PLGA-MMT nanocomposites showed enhanced GIT absorption. The drug release analysis revealed a rapid initial release followed by a moderate, continuous release that was not significantly impacted by the MMT component.

It was discovered that nanofillers with nanocomposite particles outperform the negative effects of free celecoxib. Additionally, hydroxyapatite and celecoxib nanocomposites had stronger anticancer efficacy compared to free celecoxib.

Antianemic (Shailesh et al. 2016; Sirousazar et al. 2011)

Iron oxide nanodispersion in arabinogalactan matrix, which was used to make the ferroarabinogalactan nanocomposite, showed improved antianemic action. Siberian larch contains arabinogalactan, which has antianemic properties. Due to the interaction between iron nanoparticles and arabinogalactan, it has been found that this nanocomposite stimulated hemopoiesis and stabilized iron.

Antibacterial and Antifungal (Shailesh et al. 2016; Venkatesan et al. 2011)

Magnetic nanocomposites of silver and iron oxide can be used to deliver effective and safe antibacterial and antifungal drugs. Nanocomposites did not show acute cytotoxicity toward mice embryonal fibroblasts at the reported minimal inhibitory concentration. The ability of these nanocomposites to be employed in antibacterial and antifungal applications as targeted drug delivery systems was established by the synergistic impact of the magnetic capabilities of iron oxide nanoparticles and the antimicrobial activity of silver nanoparticles.

Future Scope

The use of nanofillers in nanocomposite has seen a sharp increase in recent years. According to reports, in less than 2 years, the global output is expected to surpass 600,000 tonnes, and in the next 5–10 years, it is planned to cover the following important areas:

- New scratch-/abrasion-resistant materials
- Superior strength fibers and films
- UV protection gels
- Lubricants and scratch-free paints
- Drug delivery systems
- Fire-retardant materials

Future nanocomposite preparations might greatly benefit from the use of nanofillers if procedures for their extraction, separation, refinement, and surface modification can be devised in a systematic manner. Nanofillers are anticipated to initially find use in high-end products where their restricted usage offers considerable benefits. These items can need to have both high transparency and better mechanical qualities, such as membranes and filters, wound dressings, dental implants, sophisticated glue systems, and strong adhesive tapes (Paravastu et al. 2019).

Recent studies have shown that nanofillers not only enhance mechanical but also exhibit high optical transparency when carefully selected polymer matrix host materials are used. As large-scale and cost-effective production of nanocomposite continues to develop, the main challenge for their industrial implementation lies in refining extraction procedures and establishing simple methodologies for surface modification. Interestingly, some recent literature suggests that nanocomposite can enhance barrier properties, indicating their potential use in environmentally friendly packaging materials.

Multilayered silicates are preferentially selected as barrier modifiers in the plastics industry; however, they are not renewable or biodegradable. In contrast, polymeric nanofillers matrices possess these desirable characteristics, making them a promising alternative. Implementing nanofillers and nanocomposite as protecting agents in packaging films would be a beneficial efford toward creating a more sustainable environment (Composite 2014).

In order to achieve a true nanocomposite that goes beyond the typical reinforcement provided by a filler, it is essential to disrupt the structure of the primary particles in one of two ways:

- Complete destruction: This involves dispersing the individual elementary particles within the macromolecules, resulting in a delaminated nanocomposite.
- Partial destruction: This entails inserting macromolecules between the elementary particles, leading to the formation of an intercalated nanocomposite.

The natural layered silicate montmorillonite is widely recognized as the most popular nanofiller, undergoing specific treatments. These treatments and the effectiveness of the mixing process have an impact on the properties of the resulting nanocomposite (Composite 2014).

The Global “Nanofillers Market” [Apr 27, 2023 (The Expresswire)] research report offers a comprehensive analysis of the market, segmented by regions, countries, companies, and other relevant factors. Key players such as Eka Chemicals AB, Galaxy Corporation, Reade, DuPont, 3 M, Shenzhen Nanotechnology Development, Intelligent Materials Private Limited, Henkel Corporation, Shanghai Yaohua Nanotech, and Fuso Chemical dominate the global nanofillers market. These players have implemented diverse strategies to enhance their market presence and strengthen their position in the industry. Stakeholders and other participants in the market can leverage this report as a valuable resource for their business requirements.

This market study on nanofillers is the result of intensive primary and secondary research. Along with a competitive analysis of the market divided by application, kind, and geographical trends, it offers a thorough explanation of the market’s present goals and future possibilities. A dashboard summary of the past and present performance of the top corporations is also included in the study. To guarantee accurate and complete information on the nanofillers market, a variety of approaches and analysis are used (Nanofillers Market – Competitive and Segmentation Analysis n.d.).

The global nanofillers market is projected to experience significant growth during the forecast period from 2022 to 2030. The market exhibited steady growth in 2021, and with the implementation of strategic measures by key players, it is expected to continue its upward trajectory in the foreseeable future (Nanofillers Market – Competitive and Segmentation Analysis n.d.).

Global Nanofillers Market Analysis and Insights (Polymer Nanocomposites Report by University of Wisconsin-Stout March 2005)

In light of the COVID-19 pandemic, the estimated value of nanofillers market around the globe in 2022 is projected to be USD million. However, due to the economic impact of this health crisis, the market size is expected to readjust to USD million by 2028, with a compound annual growth rate (CAGR) of percent during the review period. Within the nanofillers market, organic nanofillers accounted for a percentage of the global market in 2021 and are anticipated to reach a value of USD million by 2028, growing at a revised percentage CAGR in the post-COVID-19 period. The construction segment is projected to experience a percentage CAGR throughout the period forecasted. AU8

In 2021, the nanofillers market in China was valued at USD million, while the market sizes in the USA and Europe were USD million and USD million, respectively. The market proportion in the USA was percent in 2021, whereas China and Europe accounted for percent and percent, respectively. It is predicted that China's market proportion will reach percent in 2028, with a CAGR of percent during the analysis period. Noteworthy markets in Asia include Japan, South Korea, and Southeast Asia, which are expected to grow at CAGRs of percent, percent, and percent, respectively, over the next 6 years. In the European nanofillers landscape, Germany is projected to reach USD million by 2028, with a CAGR of percent over the forecast period.

Key manufacturers of nanofillers globally include Eka Chemicals AB, Galaxy Corporation, Reade, DuPont, 3 M, Shenzhen Nanotechnology Development, Intelligent Materials Private Limited, Henkel Corporation, and Shanghai Yaohua Nanotech, among others. In terms of revenue, these top five players held a share of approximately 1% in 2021.

This report examines the nanofillers market from production and sales perspectives. It investigates the growth rate, production, capacity, growth rate, market share of manufacturers, and regional analysis (at both the regional and country levels) from 2017 to 2022, with forecasts extending to 2028. On the sales side, the report focuses on the sales of nanofillers by region, company, type, and application from 2017 to 2022, with projections for the period up to 2028.

Future of nanofillers as nanocomposite: According to estimates, the flexible and rigid packaging industry is projected to utilize 5 million pounds of nanocomposite materials in the beverage and food sectors by 2009, with consumption expected to reach 100 million pounds by 2011. Among these, beer consumption is anticipated to be the highest by 2006, utilizing 3 million pounds of nanocomposites, while carbonated soft drink bottles are predicted to surpass this figure and consume 50 million pounds of nanocomposites by 2011 (Butschli 2004). Polymer nanocomposites hold significant promise for the global packaging industry's future. As production costs decrease and materials become more affordable, companies will increasingly adopt this technology to enhance product stability and survivability throughout the supply chain, delivering higher quality to customers while achieving cost savings. The advantages offered by nanocomposites outweigh the associated costs and concerns, and with further refinement and development of processes, the technology will continue to advance. Ongoing research into alternative nanofillers, such as carbon nanotubes, enables the creation of new nanocomposite structures with improved properties, further expanding their application in diverse packaging sectors.

By coprocessing drugs (naproxen, indomethacin, progesterone, ketoprofen, ibuprofen, and nitrendipine) with 50–90 wt% silicate nanoparticles (A200, Neusilin®, and kaolin), amorphous pharmaceutical composites with enhanced physical stability have been achieved. These composites demonstrate long-term stability for several months at 40 °C/75% RH, surpassing the stability of the neat amorphous drugs. The improved stability is owing to the surface immobilization of the drug at the filler particle surface, facilitated by interactions such as hydrogen bonding between the drug and filler particles (rigidification). However, Bahl et al. discovered that physically stable composites of indomethacin with silicate clay nanoparticles (MMT and kaolin) can be achieved even at drug fractions that exceed the monolayer coverage of the nanofillers. This finding suggests that surface immobilization alone cannot fully explain the increased physical stability observed.

Conclusion

This comprehensive chapter provides an in-depth exploration of nanofillers and their significant role in enhancing the performance of components compared to traditional materials. Nanomaterials exhibit unique properties that are well-suited for meeting the evolving demands of various scientific applications. The chapter discusses the classification of nanofillers based on matrix materials, such as elastomeric nanocomposites, bionanocomposites using natural polymers, clay-based nanofillers, and their respective applications.

However, achieving proper dispersion of nanophases within polymer matrices remains a challenge for some approaches. Nevertheless, researchers are actively seeking solutions to overcome this obstacle and explore the full potential of nanomaterials. Polymer nanocomposites having nanofillers have already found applications in diverse fields. They offer advantages such as extended half-life, excellent biocompatibility, reduced immunogenicity, targeted delivery, and enhanced drug permeation through nanoparticle-based drug delivery systems.

Furthermore, smart materials that can alter their structure and functionality in response to environmental cues have emerged due to recent advancements. These nanocomposites show immense promise in tissue engineering and neuronal regeneration within biological systems. Additionally, nanocomposites serve as potential carriers for active pharmaceutical ingredients (APIs) in drug delivery systems. Several nanocomposite-based drug delivery systems have undergone clinical trials, while others are still in the nascent stages of development. These systems demonstrate the ability of smart polymer matrices to release pharmaceuticals in response to specific environmental changes, enabling more effective medication delivery.

The utilization of polymer-clay nanocomposites in drug delivery systems represents a burgeoning area in nanotechnology applications. These nanocomposites hold great promise for drug delivery as well as in tissue engineering and nerve growth regeneration within biological systems. Polymer-clay nanocomposites serve as a highly promising nanocarrier for the efficient delivery of drug molecules. In particular, when employed in oral multiparticulate systems, they enable controlled and sustained drug release while enhancing mechanical integrity.

By harnessing the potential of nanoparticle-based drug delivery, polymer-clay nanocomposites offer advantages such as prolonged half-life, excellent biocompatibility, minimal immunogenicity, targeted drug delivery, and the ability to overcome membrane barriers. Furthermore, recent advances in smart materials have brought forth significant breakthroughs, enabling these materials to dynamically alter their structure and function in response to environmental stimuli. The development of smart drug delivery systems, which trigger the release of drugs in response to particular environmental cues, has successfully used this remarkable capability.

In parallel, novel approaches utilizing bottom-up and top-down nanofabrication technologies have enabled the creation of precisely controlled nanoparticulate delivery systems with tailored sizes and shapes. These advancements contribute to the continued progress and refinement of drug delivery systems based on nanofillers.

References

AU9

Abba M, Hunger P, Kalidindi S, Wegst U (2015) Nacre-like hybrid films: structure, properties, and the effect of relative humidity. J Mech Behav Biomed Mater 55:140–150. https://doi.org/10.1016/j.jmbbm.2015.10.013

Abdeen Z, Farargy A, Negm N (2018) Nanocomposite framework of chitosan/polyvinyl alcohol/ZnO: preparation, characterization, swelling and antimicrobial evaluation. J Mol Liquids 250: 335–343

Abdolmaleki A, Mallakpour S, Borandeh S (2011) Preparation, characterization and surface morphology of novel optically active poly (Ester-amide)/functionalized Zno bionanocomposites via ultrasonication assisted process. Appl Surf Sci 257:6725–6733

Adel A, El-Shafei A, Ibrahim A, Al-Shemy M (2018) Extraction of oxidized nanocellulose from date palm (Phoenix dactylifera L.) sheath fibers: Influence of CI and CII polymorphs on the properties of chitosan/bionanocomposite films. Ind Crop Prod 124:155–165

Ajayan PM, Schadler LS, Braun PV Nanocomposite science and technology. Wiley-VCH, Weinheim, pp 122–113

Alexandre M, Dubois P (2000) Polymer-layered silicate nanocomposites: preparation, properties and uses of a new class of materials. Mater Sci Eng R Rep 28:1–63. https://doi.org/10.1016/S0927-796X(00)00012-7

Alizadeh-Sani M, Khezerlou A, Ehsani A (2018) Fabrication and characterization of the bionanocomposite film based on whey protein biopolymer loaded with TiO_2 nanoparticles, cellulose nanofibers and rosemary essential oil. Ind Crop Prod 124:300–315

Ansorge S, Papailiou K (2015) Mechanical properties of silicone rubber under high loadings of alumina trihydrate filler. J Elastomers Plast:1–29. https://doi.org/10.1177/0095244315580452

Behrens S, Appel I (2016) Magnetic nanocomposites. Curr Opin Biotechnol 39:89–96. https://doi.org/10.1016/j.copbio.2016.02.005

Bergese P, Colombo I, Gervasoni D (2003) Microwave generated nanocomposites for making insoluble drugs soluble. Mater Sci Eng 23C:791–795

Beyer G (2002) Nanocomposites: a new class of flame retardants for polymers. Plast Addit Compd 4:22–28. https://doi.org/10.1016/S1464-391X(02)80151-9

Chen H, Müller M, Gilmore K, Wallace G, Li D (2008) Mechanically strong, electrically conductive, and biocompatible graphene paper. Adv Mater 20:3557–3561. https://doi.org/10.1002/adma.200800757

Chen C, Yang Q, Yang Y, Lv W, Wen Y, Hou P (2009) Self-assembled free standing graphite oxide membrane. Adv Mater 21:3007–3011. https://doi.org/10.1002/adma.200803726

Chen J, Yao B, Li C, Shi G (2013) An improved Hummers method for eco-friendly synthesis of graphene oxide. Carbon N Y 64:225–229. https://doi.org/10.1016/j.carbon.2013.07.055

Chothave M, Chandramore A, Jagatap V, Bhambar K (2022) Nanocomposites: a promising drug delivery in pharmaceutical industries. 11(7):337. ISO 9001:2015 certified journal

Composites (2014) Thermosets and composites: material selection, applications, manufacturing and cost analysis, 2nd edn Chapter no 6

Curvello R, Raghuwanshi V, Garnier G (2019) Engineering nanocellulose hydrogels for biomedical applications. Adv Colloid Interface Sci 267:47–61

Das S, Ghosh B, Sarkar K (2022) Nanocellulose as sustainable biomaterials for drug delivery. Sens Int 3. https://doi.org/10.1016/j.sintl.2021.100135

De Sousa RL, Figueiras A, Veiga F, de Freitas R, Nunes L, da Silva FE, da Silva LC (2013) The systems containing clays and clay minerals from modified drug release: a review. Colloids Surf B: Biointerfaces 103. https://doi.org/10.1016/j.colsurfb.2012.10.0680

Deborah D, Chung L (2002) Composite materials: functional materials for modern technologies. Springer-Verlag London Ltd

Dikin D, Stankovich S, Zimney E, Piner R, Dommett G, Evmenenko G (2007) Preparation and characterization of graphene oxide paper. Nature 448:457–460. https://doi.org/10.1038/nature06016

Divya M, Kiran G, Hassan S, Selvin J (2019) Biogenic synthesis and effect of silver nanoparticles (AgNPs) to combat catheter-related urinary tract infections. Biocatal Agric Biotechnol 18:101037

Dong Y, Feng S (2005) Poly (D,L-Lactide-Co Glycolide)/montmorillonite nanoparticles for Oral delivery of anticancer drugs. Biomaterials 26:6068–6076

Farshchi E, Pirsa S, Roufegarinejad L, Alizadeh M, Rezazad M (2019) Photocatalytic/biodegradable film based on carboxymethyl cellulose, modified by gelatin and TiO2 Ag nanoparticles. Carbohydr Polym:216, 189–196

Fathi Achachlouei B, Zahedi Y (2018) Fabrication and characterization of CMC-based nanocomposites reinforced with sodium montmorillonite and TiO2 nanomaterials. Carbohydr Polym 199:415–425

Fisher L, Lin Z, Tipper J, Stone M, Ingham E (2006) Tribolory of alternative bearings. Clin Orthop Relat Res 453:25–34

Fonsaca J, Domingues S, Orth E, Zarbin A (2017) Air stable black phosphorous in polyaniline-based nanocomposite. Sci Rep 7. https://doi.org/10.1038/s41598-017-10533-5

Germain M, Hatton A, Williarns S, Matthews J, Stone M, Fisher J, Ingham E (2003) Comparison of the cytotoxicity of clinically relevant cobalt-chromium and aiumina ceramic wear particles in vitro. Biomaterials 24:469–479

Goertzen W, Kessler MR (2008) Dynamic mechanical analysis of fumed silica/cyanate ester nanocomposites. Composites 39:761–768. https://doi.org/10.1016/j.compositesa.2008.02.006

Harsha AP, Tewari US (2002) Tribo performance of polyaryletherketone composites. Polym Test 21:697–709

Hatton A, Williarns S, Matthews J, Stone M, Fisher J, Ingham E (2003) Comparison of the cytotoxicity of clinically relevant cobalt-chromium and aiumina ceramic wear particles in vitro. Biomaterials 24:469–479

Hauser E, Le Beau D (1938) Studies on gelation and film formation of colloidal clays I. J Phys Chem 1938:961–969

Hauser E, Le Beau D (1939) Studies in gelation and film formation. II. J Phys Chem 43:1037

He H, Klinowski J, Forster M, Lerf A (1998) A new structural model for graphite oxide. Chem Phys Lett 287:53–56. https://doi.org/10.1016/s0009-2614(98)00144-4

Heijnsbergen D, Demyk K, Duncan M, Meijer G, Helden G (2015) Structure determination of gas phase aluminum oxide clusters. Phys Chem Chem Phys 2515. https://doi.org/10.1039/b212654k

Ho T, Ko Y, Zimmermann T, Geiger T, Caseri W (2012) Processing and characterization of nanofibrillated cellulose/layered silicate systems. J Mater Sci 47:4370–4382. https://doi.org/10.1007/s10853-012-6291-8

Hu Y, Niemeyer C (2020) Designer DNA-silica/carbon nanotube nanocomposites for traceable and targeted drug delivery. J Mater Chem B 8. https://doi.org/10.1039/c9tb02861g

Hummers W, Offeman R (1958) Preparation of graphitic oxide. J Am Chem Soc 80:1339–1339. https://doi.org/10.1021/ja01539a017

Hussain F, Hojjati M, Okamoto M, Gorga R (2006) Review article: polymer-matrix nanocomposites, processing, manufacturing, and application: an overview. J Compos Mater 40. https://doi.org/10.1177/0021998306067321

Imai Y (2017) Encyclopedia of polymeric nanomaterials. https://doi.org/10.1007/978-3-642-36199-9

Ishida H, Koenig J (1978) The reinforcement mechanism of fiber-glass reinforced plastics under wet conditions: a review. Polym Eng Sci 18:128–145. https://doi.org/10.1002/pen.760180211

Jamróz E, Kulawik P, Kopel P (2019) The effect of nanofillers on the functional properties of biopolymer-based films: a review. Polymers 11:675. https://doi.org/10.3390/polym11040675

Jbeli A, Hamden Z, Bouattour S, Ferraria A, Conceição D, Ferreira L, Chehimi M, do Rego A, Rei Vilar M, Boufifi S (2018) Chitosan-Ag-TiO2 films: an effective photocatalyst under visible light. Carbohydr Polymn 199:31–40

Kadam D, Momin B, Palamthodi S, Lele S (2019) Physicochemical and functional properties of chitosan-based nano-composite films incorporated with biogenic silver nanoparticles. Carbohydr Polym 211:124–132

Kalishwaralal K, Jeyabharathi S, Sundar K, Muthukumaran A (2016) A novel one-pot green synthesis of selenium nanoparticles and evaluation of its toxicity in zebrafish embryos. Artif Cells Nanomed Biotechnol 44:471–477

Khan A, Khan R, Salmieri S, Le Tien C, Riedl B, Bouchard J, Chauve G, Tan V, Kamal M, Lacroix M (2012) Mechanical and barrier properties of nanocrystalline cellulose reinforced chitosan based nanocomposite films. Carbohydr Polym 90:1601–1608. https://doi.org/10.1016/j.carbpol.2012.07.037

Kim WY, Greidanus NV, Duncan CP, Masri BA, Garbuz DS (2008) Porous tantalum uncemented acetabular shells in revision total hip replacement: two to four year clinical and radiographic results. Hip Int l8:17–22

Kovtyukhova N, Ollivier P, Martin B, Mallouk T, Chizhik S, Buzaneva E (1999) Layer-by-layer assembly of ultrathin composite films from micron-sized graphite oxide sheets and polycations. Chem Mater 11:771–778. https://doi.org/10.1021/cm981085u

Krishna G, Kumar P, Swapna N, Rao B, Bhargava N (2017) Metal-metal composites-an innovative way for multiple strengthening. Mater Today Proc 4(8):8085–8095. https://doi.org/10.1016/j.matpr.2017.07.148

Landgraeber S, Knoch M, Loer F, Wegner A, Tsokos M, Hussmann B, Totsch M (2008) Exfinsic and intrinsic pathways of apoptosis in aseptic loosening after total hip replacement. Biomaterials 29:444–450

Lenz R, Mittekneier W, Ilansmann D, Brem DP, Fritsche A, Bader R (2009) Response of human osteoblasts exposed to wear particles generated at the interface of total hip stems and bone cement. J Biomed Mater Res 89:370–378

Lerf A, He H, Forster M, Klinowski J (1998) Structure of graphite oxide revisited. J Phys Chem B 102:4477–4482. https://doi.org/10.1021/jp9731821

Lin T, Huang W, Jun I, Jiang P (2008) Electrophoretic deposition of biomimetic nanocomposites. Electrochem Commun 11:14–17. https://doi.org/10.1016/j.elecom.2008.10.018

Lin T, Huang W, Jun I, Jiang P (2009) Electrophoretic co-deposition of biomimetic nanoplatelet-polyelectrolyte composites. Electrochem Commun 11:1635–1638. https://doi.org/10.1016/j.elecom.2009.06.017

Mäkiniemi R, Das P, Hönders D, Grygiel K, Cordella D, Detrembleur C (2015) Conducting, self-assembled, nacre-mimetic polymer/clay nanocomposites. ACS Appl Mater Interfaces 7: 15681–15685. https://doi.org/10.1021/acsami.5b04676

Malaki M, Xu W, Kasar A, Menezes P, Dieringa H, Varma R, Gupta M (2019) Advanced metal matrix nanocomposites. Metals 9. https://doi.org/10.3390/met9030330

Manson J, Sperling L (1976) Polymer blends and composites. Springer US, Boston, MA. https://doi.org/10.1007/978-1-4615-1761-0

Marcano D, Kosynkin D, Berlin J, Sinitskii A, Sun Z, Slesarev A (2010) Improved synthesis of graphene oxide. ACS Nano 4:4806–4814. https://doi.org/10.1021/nn1006368

Marquis D, Éric G, Joly C (2009) Properties of Nanofillers in Polymer, Laboratoire national de métrologie et d'essais (LNE), France

Martins G, Segalla Petrônio M, Furuyama Lima A, Martinez Junior A, Oliveira Tiera V, Freitas Calmon M, Leite Vilamaior P, Han S, Tiera M (2019) Amphipathic Chitosans improve the physicochemical properties of siRNA-chitosan nanoparticles at physiological conditions. Carbohydr Polym 216:332–342

Massoud M, Xu W, Kasar A (2019) Advanced metal matrix nanocomposites. Metals 9. https://doi.org/10.3390/met9030330

McCarthy P, Zhang Y, Abebe F (2021) Review recent applications of dual-stimuli responsive chitosan hydrogel nanocomposites as drug delivery tools. Molecules 26. https://doi.org/10.3390/molecules26164735

Morits M, Verho T, Sorvari J, Liljeström V, Kostiainen M, Gröschel A (2017) Toughness and fracture properties in nacre-mimetic clay/polymer nanocomposites. Adv Funct Mater 27:1–9. https://doi.org/10.1002/adfm.201605378

Nanofillers Market – Competitive and Segmentation Analysis (n.d.) https://www.360researchreports.com/enquiry/request-sample/20410807

Naslain R, Langlais F, Fedou R (1989) The cvi-processing of ceramic matrix composites. Le Journal de Physique Colloques 50. https://doi.org/10.1051/jphyscol:1989526

Natarajan S, Lakshmi D, Thiagarajan V, Mrudula P, Chandrasekaran N, Mukherjee A (2018) Antifouling and anti-algal effects of chitosan nanocomposite (TiO2/Ag) and pristine (TiO2 and Ag) films on marine microalgae Dunaliella salina. J Environ Chem Eng 6:6870–6880

Niebel T, Carnelli D, Binelli M, Libanori R, Studart A (2016) Hierarchically roughened micro-platelets enhance the strength and ductility of nacre-inspired composites. J Mech Behav Biomed Mater 60:367–377. https://doi.org/10.1016/j.jmbbm.2016.02.008

Niezabitowska E, Smith J, Prestly M, Akhtar R, Aulock F, Lavallée Y, Mcdonald T (2018) Facile production of nanocomposites of carbon nanotubes and polycaprolactone with high aspect ratios with potential applications in drug delivery. RSC Adv 8. https://doi.org/10.1039/c7ra13553j

Noshirvani N, Ghanbarzadeh B, Mokarram R, Hashemi M, Coma V (2017) Preparation and characterization of active emulsified films based on chitosan-carboxymethyl cellulose containing zinc oxide nano particles. Int J Biol Macromol 99:530–538

Novoselov K, Fal V, Colombo L, Gellert P, Schwab M, Kim K (2013) A roadmap for graphene. Nature 490:192–200. https://doi.org/10.1038/nature11458

Ohani OR, Phatak AA, Chaudhari PD (2015) Use of nanocomposites in drug delivery systems. Pharma Times 47:33–35

Okada A, Usuki A (2006) Twenty years of polymer-clay nanocomposites. Macromol Mater Eng 291:1449–1476. https://doi.org/10.1002/mame.200600260

Olayil R (2021) A brief review on effect of nano fillers on performance of composites. IOP Conf Ser Mater Sci Eng 1059:012006

Paci J, Belytschko T, Schatz G (2007) Computational studies of the structure, behavior upon heating, and mechanical properties of graphite oxide. J Phys Chem 111:18099–18111

Pan C, Qian J, Fan J, Guo H, Gou L, Yang H, Liang C (2019) Preparation nanoparticle by ionic cross-linked emulsified chitosan and its antibacterial activity. Colloids Surf A Physicochem Eng Asp 568:362–370

Paravastu V, Yarraguntla S, Suvvari A (2019) Role of nanocomposites in drug delivery. GSC Biol Pharm Sci 8. https://doi.org/10.30574/gscbps.2019.8.3.0150

Pavlidou S, Papaspyrides C (2008) A review on polymer-layered silicate nanocomposites. Prog Polym Sci 33:1119–1198. https://doi.org/10.1016/j.progpolymsci.2008.07.008

Peng L, Xu Z, Liu Z, Wei Y, Sun H, Li Z (2015) An iron-based green approach to 1-h production of single-layer graphene oxide. Nat Commun 6. https://doi.org/10.1038/ncomms6716

Podsiadlo P, Liu Z, Paterson D, Messersmith P, Kotov N (2007) Fusion of seashell nacre and marine bioadhesive analogs: high-strength nanocomposite by layer-by layer assembly of clay and L-3,4- dihydroxyphenylalanine polymer. Adv Mater 19:949–955. https://doi.org/10.1002/adma.200602706

Polymer nanocomposites are the future alyssa downing-perrault university of wisconsin-stout March 2005 AU10

Ponnamma D, Cabibihan J, Rajan M, Pethaiah S, Deshmukh K, Gogoi J, Pasha S, Ahamed KJ, Chandrashekar B (2019) Synthesis, optimization and applications of ZnO/polymer nanocomposites. Mater Sci Eng 98:1210–1240

Poonguzhali R, Basha S, Kumari V (2017) Synthesis and characterization of chitosan-PVP-nanocellulose composites for in-vitro wound dressing application. Int J Biol Macromol 105:111–120

Purdue P, Koulouvaris P, Nestor B, Sculco T (2006) The central role of wear debris in peri-prostheticosteolysis. HSS J 2:102–113

Qiao J (2020) Elastomeric nano-particle and its applications in polymer modifications. Adv Ind Eng Polym Res 3(2):47–59. https://doi.org/10.1016/j.aiepr.2020.02.002

Roy S, Rhim J, Jaiswal L (2019) Bioactive agar-based functional composite film incorporated with copper sulfide nanoparticles. Food Hydrocoll 93:156–166

Salahuddin N, Abdelwahab M, Gaber M, Elneanaey S (2020) Synthesis and design of norfloxacin drug delivery system based on PLA/TiO2 nanocomposites: antibacterial and antitumor activities. Mater Sci Eng C 108. https://doi.org/10.1016/j.msec.2019.110337

Sermsantiwanit K, Phattanarudee S (2012) Preparation of bio-based nanocomposite emulsions: effect of clay type. Prog Org Coat 74:660–666

Shailesh P, Prasad J, Surendra G (2016) Nanocomposites: a new approach to drug delivery system. Asian J Pharm 10(4):646

Shanbhag P, Rane D, Chandra R, Lande S, Deshmukh P, Patil P, Gawade T (2019) Nanocomposites: a newer technology in drug delivery systems. Int J Pharm Sci Rev Res 56(2):144–154

Shankar S, Rhim J (2018) Preparation of sulfur nanoparticle-incorporated antimicrobial chitosan films. Food Hydrocoll 82:116–123

Sharpe L (1972) The interphase in adhesion. J Adhes 4:51–64. https://doi.org/10.1080/00218467208072210

Siegmeth A, Duncan CP, Masri BA, Kim WY, Garbuz DS (2009) Modular tantalum augments for acetabular defects in revision hip arthroplast. Clin Orthop Relat Res 467:199–205

Simon R (2005) Progress in processing and performance of porous-matrix oxide/oxide composites. Int J Appl Ceram Technol 2. https://doi.org/10.1111/j.1744-7402.2005.02016

Sirousazar M, Kokabi M, Hassan Z (2011) Dehydration kinetics of polyvinyl alcohol nanocomposite hydrogels containing NaMontmorillonite Nanoclay. Sci Iran Found 18:780–784

Sivanesan I, Gopal J, Muthu M, Shin J, Mari S, Oh J (2012) Green synthesized chitosan/chitosan nanoforms/nanocomposites for drug delivery applications. Polymers 13. https://doi.org/10.3390/polym13142256

Tang Z, Kotov N, Magonov S, Ozturk B (2003) Nanostructured artificial nacre. Nat Mater 2: 413–418. https://doi.org/10.1038/nmat906

Tateiwa T, Clarke I, Williams P, Garino J, Manaka M, Shishido T, Yamamoto K, Imakiire A (2008) Ceramic total hipatoplasty in the United States: safety and risk issues revisited. Am J Orthop 37: 826–831

Teng C, Ma C, Lu C, Yang S, Lee S, Hsiao M (2011) Thermal conductivity and structure of non-covalent functionalized graphene/epoxy composites. Carbon N Y 49:5107–5116. https://doi.org/10.1016/j.carbon.2011.06.095

Thbei A, Mubarak Y, Abdrabo M (2010) Dielectric properties response of lndustrial applications by nanocomposite materials. In: 2nd International conference on energy engineering, high institute of energy. South Valley University, Aswan, Erypt

Tripathi R, Narayan A, Bramhecha I, Sheikh J (2019) Development of multifunctional linen fabric using chitosan film as a template for immobilization of in-situ generated CeO2 nanoparticles. Int J Biol Macromol 121:1154–1159

Tsukamoto R, Williarns P, Shoji H, Hirakawa I, Yamamoto K, Tsukamoto M, Clarke I (2008) Wear of sequentially enhanced 9- MRAD polyethylene in l0 million cycle KNEI simulation study. J Biomed Mater Res B Appl Biomater 86:119–124

Vataio S, Bersaglia G, Rocchi M, Taddei P, Fagirano C, Toni A (2005) Wear behaviour of cross-linked polyethylene assessed in vitro under severe conditions. Biomaterials 26:3259–3267

Venkatesan P, Puvvada N, Dash R, Prashanth Kumar B, Sarkar D, Azab B, Pathak A, Kundu S, Fisher P, Mandal M (2011) The potential of celecoxib-loaded hydroxyapatite-chitosan nanocomposite for the treatment of colon cancer. Biomaterials 32:3794–3806. https://doi.org/10.1016/j.biomaterials.2011.01.027

Wang Q, Hare D (2012) Recent advances in the synthesis and application of layered double hydroxide (LDH) nanosheets. Chem Rev 112:4124–4155. https://doi.org/10.1021/cr200434v

Wang J, Cheng Q, Tang Z (2012) Layered nanocomposites inspired by the structure and mechanical properties of nacre. Chem Soc Rev 41:111–129. https://doi.org/10.1039/C1CS15106A

Wang X, Xing W, Feng X, Song L, Hu Y (2017) MoS2/polymer nanocomposites: preparation, properties, and applications. Polym Rev 57:440–466. https://doi.org/10.1080/15583724.2017.1309662

Wang C, Murugadoss V, Kong J, He Z, Mai X, Shao Q, Chen Y, Guo L, Liu C, Angaiah S (2018) Overview of carbon nanostructures and nanocomposites for electromagnetic wave shielding. Carbon 140:696–733

Wen Y, Gallego M, Nielsen L, Jorgensen L, Everland H, Møller E, Nielsen H (2011) Biodegradable nanocomposite microparticles as drug delivering injectable cell scaffolds. J Control Release 156:11–20

Wu Q, Sun Y, Gao J, Dong S, Luo G, Li H, Zhao L (2017) Applications of hybrid organic–inorganic materials in chiral separation. TrAC Trends Anal Chem 95:140–148

Yilmaz O, Cheaburu C, Durraccio D (2010) Preparation of stable acrylate/montmorillonite nanocomposite latex via *in situ* batch emulsion polymerization: effect of clay types. Appl Clay Sci 49:288–297

Yu S, Xu X, Feng J, Liu M, Hu K (2019) Chitosan and chitosan coating nanoparticles for the treatment of brain disease. Int J Pharm 560:282–293

Zhang H, Zhang Z, Friedrich K, Eger C (2006) Property improvements of in situ epoxy nanocomposites with reduced interparticle distance at high nanosilica content. Acta Mater 54: 1833–1842. https://doi.org/10.1016/j.actamat.2005.12.009

Zhang M, Ishii A, Nishiyama N (2009) Pegylated calcium phosphate nanocomposites as smart environment sensitive carriers for Si RNA delivery. Adv Mater 21:3520–3525. https://doi.org/10.1002/adma.200800448

Zhang J, Wang Q, Wang A (2010) In situ generation of sodium alginate/hydroxyapatite nanocomposite beads as drug controlled release matrices. Acta Biomater 6:445–454. https://doi.org/10.1016/j.actbio.2009.07.001

Zhang G, Li X, Liao Q, Liu Y, Xi K, Huang W, Jia X (2018) Water-dispersible PEGcurcumin/amine-functionalized covalent organic framework nanocomposites as smart carriers for in vivo drug delivery. Nat Commun 9. https://doi.org/10.1038/s41467-018-04910-5

Zhu T, Zhou C, Kabwe F, Wu Q, Li C, Zhang J (2019) Exfoliation of montmorillonite and related properties of clay/polymer nanocomposites. Appl Clay Sci 169:48–66

Index Terms:

Author Queries

Chapter No.: 49-1 519127_0_En

Query Refs.	Details Required	Author's response
AU1	Please be aware that your name, affiliation and email address and if applicable those of your co-author (s) will be published as presented in this proof. If you want to make any changes, please correct the details now. Note that corrections after publication will no longer be possible. Please note that we standardly publish professional e-mail addresses, but not private ones even if it is provided in the manuscript. If you have a different preference regarding publication of your email address, please indicate this clearly on the proof. If no changes are required, please respond with "Ok".	
AU2	The index terms are available in a separate tab, please review the index terms and make any changes, if required. If no changes are required, please respond with "Ok".	
AU3	Could you confirm that necessary permission has been obtained from the copyright holders for any material used from other works and that references to the original publications are included?	
AU4	Please provide details of "Harsha and Ajayan (2002), Ajyan and Kim (2008), Usuki et al. (1993), Lan and Pinnavaia (1994), Lan et al. (1995), Giannelis (1996), Biron (2004), Gloaguen and Lefevre (2007), Germain (2019), Reshmi (2021), Zheng-Ming et al. (2003), Rohan et al. (2007), Lin et al. (2012a, b), Thakur et al. (2014a, b), Yuan-Qing et al. (2008), Dubois and Alexandre (2006), Hauser and Okada (2006), He (1998), Jamroj (2018), Shankar (2018), Fathi (2018), Sivanesan (2021), Butschli (2004)" in reference list.	

AU5	Please check if the list “One-dimensional nanofillers. . . of this classification.” is part of Figure 3 caption.	
AU6	Please check the edit is correct in the phrase “Thixotropic, antisag,thickeners, and acid scavengers:colloidal silica’ bentonite,hydrotalcite” in Table 2.	
AU7	Please check if inserted citation for Figures 3, 4, 7, 8 and Table 2 are fine	
AU8	Please check the phrases “USD million” and “of percent” for completeness in the sentences “In light of. . . the review period.”	
AU9	References "Ajayan et al. (n.d.), Alizadeh-Sani et al. (2018), Fathi Achachlouei & Zahedi (2018), Germain et al. (2003), Harsha & Tewari (2002), Hauser & Le Beau (1938), Hauser & Le Beau (1939), Heijnsbergen et al. (2015), Kim et al. (2008), Kovtyukhova et al. (1999), Lerf et al. (1998), Lin et al. (2008), Lin et al. (2009), Olayil (2021), Shankar & Rhim (2018), Wang et al. (2018), Wang et al. (2012), Thermosets and Composites (2014), Nanofillers Market (n.d.), Polymer nanocomposites (2005)" were not cited anywhere in the text. Please provide in text citation or delete the reference from the reference list.	
AU10	Please provide complete details for “Polymer nanocomposites...(2005)”.	

Note:
If you are using material from other works please make sure that you have obtained the necessary permission from the copyright holders and that references to the original publications are included.