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# NANOCOMPOSITES: A PROMISING DRUG DELIVERY IN PHARMACEUTICAL INDUSTRIES

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#### **ABSTRACT**

Nanotechnology is the field of science which deals with the development of materials lesser than the normal size. The field generally, focuses upon nanoscale product development using various methodologies. The size range for such a product lies in between 1 to 100nm scale. Nanocomposite is one of the promising nanotechnological tool which has abundant applications into the pharmaceutical field, tissue engineering, cell culture development, medical devices, cell culture development etc. The issues related with conventional therapeutics like stability, drug toxicity, poor patient compliance, drug delivery associated with the candidates having low

solubility, and low permeability, drug resistance into the body are widely taken into consideration. To overcome those problems nanocomposites are designed, developed and produced in modern practice of medical science. They have been developed with the decreased gas, water, hydrocarbon permeability, modified surface properties, thermal stability, mechanical properties like shape & strength, which has high surface-volume ratio and optical clarity. This review will detail the advantages, characteristics, types of nanocomposites also, different techniques used to produce the nanocomposites etc. Briefly the review will focus on the pharmaceutical industrial applications of nanocomposites especially for the targeted drug delivery system.

**KEYWORDS:** Nanocomposites, Clay-based, Polymer-matrix, Hydrogels, Films. Nanoparticles.

#### INTRODUCTION

The field of nanotechnology is one of the most popular areas for current research and development in basically all technical fields. This includes polymer science and technology and in this field the investigations cover a broad range of topics. What are composites? The term "composite" refers to something that is comprised of two or more separate pieces. It is a combination of two or more different materials that are mixed in an effort to blend the best properties of both. "A nanocomposite" is a composite material in which at least one of the components has a size of 10-09m or less.<sup>[1]</sup> Nanocomposite material is a novel product containing nano fillers which are dispersed in the matrix. [2] A nanocomposite is a multiphase material in which, in contrast to microcomposites, one of the phases has one, two, or three dimensions of less than 100nm, or the composite phases have nanoscale distances between them<sup>[2]</sup> .Nanocomposites are composite materials having one of the phases with dimension in the nanometer range. When material dimensions are reduced to the nanoscale level, phase interfaces are created, which are critical for improving material characteristics Due to their superior and enhanced qualities, nanocomposites may be a viable alternative to microcomposites and monolithics.<sup>[3]</sup> The basic thing related to nanotechnology is the size that makes it feasible to be used in many different fields. The nano size of the materials provides advantages like high surface area and low surface defects in the material thereby improving material properties. [4] Proven benefits of nanocomposites such as mechanical properties, barrier properties and contribution to fire retardancy, polymer nanocomposites are used in various applications.<sup>[4]</sup>

The constituent that is present in greater quantity is called the matrix. The constituent that is embedded into the matrix material to improve the mechanical properties of nanocomposites is called reinforcement (or nanomaterials). Reinforcement is in the form of nanosized filler materials. Because of the varied characteristics of elements and inhomogeneous reinforcing distribution, nanocomposites generally exhibit anisotropy (properties are directionally dependant)<sup>[4]</sup>. There are different types of clays with differences in their formula, properties and structures. Polymer/clay nanocomposites can be classified in a number of ways including in situ polymerization, melt blending, solution mixing and latex methods.<sup>[5]</sup>

#### • Advantages of nanocomposites<sup>[6]</sup>

Nanocomposites have more advantages than conventional composites in many parameters. The following are some of the advantages of nanocomposites:-

- a. Nanocomposites differ from conventional composite materials due to the exceptionally high surface to volume ratio of the reinforcing phase and/or its exceptionally high aspect ratio.
- b. Due to the addition of small percentage of nanofiller materials, nanocomposites are lighter in weight with compared to conventional composites.
- c. Nanomaterials are having size dependent properties with improved thermal, chemical, mechanical, optical, magnetic and electrical properties to a much greater extent than conventional composites.
- d. In contrast to traditional composites, nanocomposites can enhance matrix material qualities by adding a little amount of nanofiller materials, whereas conventional composites require a large concentration of micro particles to increase properties.
- e. The area of the interface between the matrix and nano-reinforcement is typically an order of magnitude higher than the conventional composites. New tech.
- f. Nanocomposites are highly dispersible in aqueous medium and have Uniform distribution of the active agent over an extended period of time which gives Controlled release of the drug to Reduces frequency of administration and to provide augmented stability. Also, it Penetrate regions inaccessible to other delivery systems.

### • Disadvantages of nanocomposites<sup>[7,8]</sup>

- A. Though it is an effective approach towards an efficient drug delivery it has economical issues like high cost of raw materials, fabrication and assembly.
- B. As compared to matrix carriers composites are weak in the out of plane direction and have low resistance to temperature and moisture.
- C. Nanocomposites are more difficult to repair if damage happens due to their small size as compare to conventional composites.

#### Nanocomposites can dramatically improve properties like

- Mechanical qualities including strength, modulus and dimensional stability
- Electrical conductivity, Flame retardancy, Thermal stability, Chemical resistance, Surface appearance, Optical clarity.
- Decreased gas, water and hydrocarbon permeability

# Basic ingredients used in nanocomposites<sup>[1,9]</sup>

The wide variety both thermoplastic and thermosetting nature polymeric materials are available, that can be made to meet specific performance characteristics, necessitates a clear identification of the property and processing requirements of the material to be used as a matrix in the composite. Depending on the size, the composites can be defined as normal or as nanoscale.

Polymer nanocomposites consist of polymeric materials with reinforcement of nano- particles embedded into matrix form. These Polymeric materials can be incorporate into the polymeric species itself. Most commonly used polymers are of 4 types viz. Thermoplastics, Thermosets, Elastomers, Natural and Biodegradable polymers. The examples of such a polymers used as a basic ingredients in nanocomposites are given below:

- Carbon nanofibers
- Nanosilica (N-silica)
- Nanoaluminum oxide (Al2O3)
- Nanotitanium oxide (TiO2)
- Montmorillonite organoclays (MMT)
- Polyhedral oligomericsilsesquioxane (POSS)
- Carbon nanotubes

There are two most important and major challenges in developing nanocomposite materials after desired polymer is getting selected. The choice of nanoparticles requires an interfacial interaction within the polymer matrix or it has to be compatible with the polymer matrix. Secondly, there should be a proper uniform dispersion and distribution of nano particles within the polymer matrix with the proper aggregation.

- Types of nanocomposites<sup>[3]</sup>
- Clay based nanocomposites
- Ceramic-matrix nanocomposites
- Polymer-matrix nanocomposites
- Metal-matrix nanocomposites
- Magnetic nanocomposites
- Elastomeric nanocomposites
- Bionanocomposites

There are stages of nanocomposites that can be considered before examining the kinds.

Most nanocomposites are made up of two phases, which are regarded to be technologically vital as well as important when developing for drug delivery in the pharmaceutical industry.

These are divided into three categories.<sup>[2]</sup>

- A. Nano layered composites: These are made up of alternating nanoscale layers.
- B. Nano filamentary composites: matrices with incorporated nanoscale diameter filaments (generally aligned).
- C. Nano particulate composites: matrices containing nanoscale particles incorporated in them.

# $\textbf{1.} \quad \textbf{Clay based nanocomposites}^{\textbf{[10,11,12,13,14]}}$

Clays are extensively utilised as excipients, active compounds, or in a variety of dosage forms in the pharmaceutical business. Several studies have linked the co-administration of clays with a reduction in oral absorption of a variety of drugs, yet it may have technical and biopharmaceutical benefits. As a result, the usage of clays in systems of customized drug release employing various kinds of clays began here. Because of colloidal particle size, crystalline structure, compatibility with other excipients, easy availability, Charge, greater cation exchange capacity, and swelling capacity are all advantages of having a large specific surface area, natural clay minerals are suitable for use in modified drug delivery systems. They can be inserted into a polymeric host carrier to modulate the diffusion rate of a distributed slow-release substance, allowing the release to be delayed.

A nanoclay particle increases the length of the diffusion channel for the aim of regulating the diffusion pace by reducing the porosity of the polymer or by holding the diffusion of the active substance being released.

This also aids in slowing the release of the delayed release polymers. Clays are inexpensive materials that may be modified by ion exchange, metal/metal complex impregnation, pillaring, and acid treatment to produce catalysts with specified characteristics. Organically modified layered-silicates or nanoclay have become an attractive class of organic—inorganic hybrid materials because of their potential use as in polymer nanocomposites, in paints, inks, greases as a rheological modifier, as a absorbent for several toxic gases, in a cosmetic industry, and most importantly in the drug delivery system as a carrier. The clays used for the

preparation of nanoclay belong to smectite group clays which are also known as 2:1 phyllosilicates, the most common of which are Montmorillonite, Hectorite, Beidillite, Nontronite, Saponite etc.

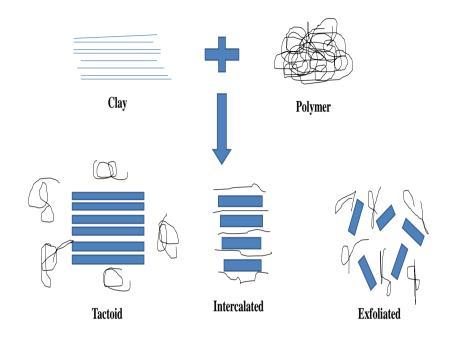


Fig. 1: Preparation methods of clay-based nanocomposites.

### Mechanisms of clay-drug interactions<sup>[11,12,14]</sup>

Clay minerals may undergo ion exchange with basic drugs in solution as they are naturally occurring inorganic cationic exchangers. As compared to other pharmaceutical silicates (such as kaolin, talc and fibrous clay minerals) Smectites, especially montmorillonite and saponite, have been the more commonly studied, due to their higher cation exchange capacity.

The following are the main processes of drug intercalation into montmorillonite:

- (1) Absorption of the drug onto the free surface of the montmorillonite.
- (2) Replacement of the drug with sodium in the interlayer.
- (3) Replacement of the drug with clay containing -OH groups to form ionic bonds with Al3+ and Mg2+ in the montmorillonite.

The first two mechanisms are considered as the major mechanisms for drugs absorption onto the montmorillonite by a concentration gradient (diffusion mechanism). When the concentration gradient is equal between inside and outside of the montmorillonite, after soaking for a particular period of time the diffusion would stop automatically as it fulfills the condition with the concentration gradient. "Counterions" in biological fluids can displace the drug from the substrate and distribute it into the body while the exchanger is removed.

#### • In-vivo Drug release mechanism

Biological counter ions are exchanged with cationic drug particles located on the surface of nanoclay when produced nanocomposites are delivered into the body. Free drug molecules are accessible for absorption, and unloaded submicron-sized particles pass through the intestinal wall and into the bloodstream for further processing. The unloaded particles were eliminated through the kidney.

# 2. Ceramic-matrix Nanocomposites<sup>[15,16]</sup>

Ceramic matrix nanocomposites belong to a group of composite materials and a subgroup of ceramics. They consist of ceramic fibers which are embedded in a ceramic matrix. Both the fibres and the matrix can be made of any ceramic material, including carbon and carbon fibres, which can be utilised as a ceramic material. They can be easily prepared by various methods such as matrix deposition from a gas phase, matrix forming via pyrolysis, chemical reaction, sintering, and electrophoresis. Carbon nanotubes are the most widely used ceramic-matrix nanocomposites as a drug delivery tool for efficient drug release in pharmaceutical industries. The properties like good stability, thermal stability at elevated temperature, electrical resistivity, and most importantly stability towards corrosion makes it highly popular.

# ${\bf 3.}\ \ {\bf Polymer-matrix}\ nanocomposites^{[10,17]}$

A polymer or copolymer with nanoparticles or nanofillers distributed in the polymer matrix is called a polymer *nanocomposites* (*PNC*). These may be of different shape (e.g., platelets, fibers, spheroids), but at least one dimension must be in the range of 1–50 nm. Addition of nanoparticulates to a polymer matrix can enhance its performance (these materials are better described by the term *nanofilled polymer composites*). By uniformly dispersing the fillers into the matrix properties of the matrix can be enhanced also, it for the effective performance and high yield this strategy is effective. There are several polymeric nanocomposites used for bone tissue engineering applications such as carbon nanotubes, molybdenum disulfide, graphene and tungsten disulfide. A range of polymeric nanocomposites are used for several biomedical applications such as drug delivery, cellular therapies etc. Polymeric network are combined with ceramic, metal oxide or carbon based nanomaterials to obtain desired property

combinations. Methods used to prepare such a nanocomposites are In situ polymerization, solution induced intercalation method, melt processing method. There are several natural and synthetic polymers including starch, cellulose, alginate, chitosan, gelatin, fibrin, PVA, PEG etc. are used in combination with nanocomposites to make it highly temperature resistant. Such a nanocomposites are suitable to develope a thermally stable drug delivery system.

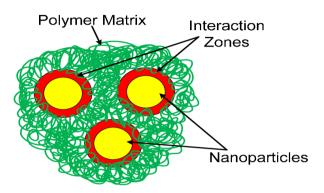


Fig. 2: Polymer-matrix nanocomposites.

#### 4. Metal-matrix nanocomposites<sup>[18]</sup>

Metal matrix nanocomposites are nothing but reinforced metal matrix composites. This are classified as continuous and non-continuous reinforced materials. One of the most important nanocomposites amongst them is Carbon nanotube metal matrix composites, which is developed as an emerging new material which has an advantage of the electrical conductivity and greater tensile strength of carbon nanotube materials. The common techniques by which the processing of metal matrix nanocomposites is done are spray pyrolysis, liquid metal infiltration, vapour techniques, rapid solidification, electrode position and chemical methods, which includes colloidal and sol-gel methods. They have wide applications in the development of structural components.

### 5. Magnetic nanocomposites<sup>[19]</sup>

*Magnetic nanocomposites* are multi-component materials, which contains nanosized magnetic materials to trigger the response to an external stimulus (i.e., an external static or alternating magnetic field). Up to now, the search for novel nanocomposites has lead to the combination abundance materials (e.g., gels, liquid crystals, renewable polymers, silica, carbon or metal organic frameworks) with various types of magnetic particles, offering exciting perspectives for application in various fields, including medical therapy and diagnosis, separations, actuation, or catalysis.

### 6. Elastomeric nanocomposites<sup>[20]</sup>

*Elastomeric nanocomposites* are nothing but polymers which exhibit rubber like elasticity. Elastomeric nano-particles (ENPs) have been used widely and they show nano-scale effects when used in polymer modification. For example, when blending ENPs with plastics ENPs could increase toughness and heat resistance of plastics simultaneously.

#### 7. Bionanocomposites<sup>[21]</sup>

Nanocomposites that contain biopolymer which is normally occurring polymers mixed with an inorganic nanomoiety make it a different class of materials called *Bionanocomposites* (BNCs). They are also known as "green composites," as they contain natural polymers. They can be considered as polymer-matrix nanocomposites. They can be prepared by the methods as the same way as polymer nanocomposites are prepared. They have significance in the drug delivery due to the size less than 1000nm. They are widely used in gene drug delivery in anticancer therapy.

#### **4** Pharmaceutical Applications of nanocomposites

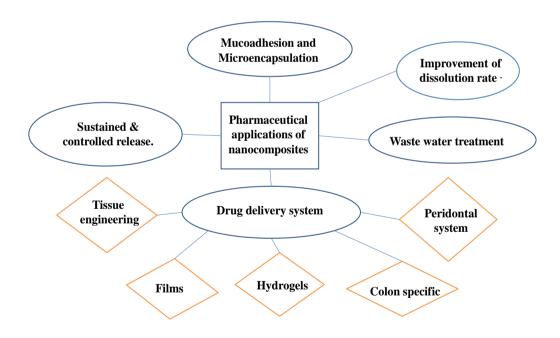


Fig. 3: Applications of nanocomposites.

### 1. Sustained and controlled release<sup>[22]</sup>

Nanocomposites can be designed for the site-specific delivery of many drugs. They are more advantageous than the conventional approach because there release can be controlled. There

are many nanocomposites available which can be promising approach to develop a sustained and controlled release dosage form. This controlled release nanocomposites have wide range of applications in the form of carbon nanotubes, chitosan-based hydrogels, nanospheres, grapheme nanotubes, magnetic nanocomposite etc. Nanocomposites of magnetic hydrogel can be used in pulsatile drug delivery system. Prepared nanocomposite beads could be used in the production of oral pharmaceutical formulations Nanocomposites for treatment of spinal cord injury. Nanocomposites in the form of biomaterials can be used for developing sustainable drug delivery. Sudipa das et al. prepared sustainable biomaterials containing nanocellulose for drug delivery.

#### 2. Mucoadhesion and Microencapsulation

There are several drugs which have issues related stability, permeability, degradation, low absorption, toxicity, compatibility with other excipients. To cover those issues microencapsulation of drug using nanocomposites can be done. Also to increase the time for the absorption of the drug mucoadhesives are used. Many researchers have investigated this type of approach and they have wide variety of applications in the pharmaceutical drug Carmellose Mucoadhesive Oral Films delivery system. Containing Vermiculite/Chlorhexidine Nanocomposites as Innovative Biomaterials for Treatment of Oral Infections is one of the example of this approach. mucoadhesion of montmorillonite chitosan nanocomposite is done by extraction of naturally occurring polymer. Iodine-loaded poly (silicic acid) gellan nanocomposite mucoadhesive film used for antibacterial application. Effect of bentonite on the physical properties and drug-release behavior of bentonite nanocomposite hydrogels for mucoadhesive etc. are the examples of mucoadhesion using nanocomposites. Alginate based nanocomposite for microencapsulation of probiotic was prepared to check the effect of cellulose nanocrystal (CNC) and lecithin.

# 3. Improvement of dissolution rate<sup>[2]</sup>

By designing nanocomposites containing poorly water-soluble drugs the dissolution rate of such a drugs can be improved which is the most important step for the pharmaceutical technologies. As nanocomposites are smaller in molecular size the surface area of such drugs can be widely improved and thus, helps in the Improvement of dissolution rate. Clay based nanocomposites are used to enhance the drug wettability due to the hydrophilic properties of the clay.

### 4. Waste water treatment<sup>[7]</sup>

There are some common techniques which are available in the market for removal of organic molecules from water including activated charcoal, reverse osmosis, air strippers. Granularactivated carbon. But the problem with such a system is that they are unable to remove large molecules like humic acid, water which contains oil and grease. To encounter this organoclays have proven to be an effective way for treating oily waste waters.

# 5. Drug delivery system $^{[23,24,25,26,27,28,29]}$

Recently, to encounter the problems or disadvantages associated with conventional dosage forms novel approach is being used. In this area nanocomposites have contributed towards a successful and effective tool to transport the drug into the body. There are various applications like colon specific drug delivery, tissue engineering, periodontal systems, targeted drug delivery system etc. films, hydrogels, carbon nanotubes and other types of nanocomposites are available for the transportation of the drug into such system. Jonathan et al. developed photomechanical polymer nanocomposites drug delivery system fabricating laser triggered drug delivery. Iyyakannu et al. Prepared curcumin-loaded Chitosan based nanocomposites. Pumtiwitt et al. developed chitosan hydrogel which has several applications in drug delivery, wound healing, sensor development & others. Edyta et al. worked on the carbon nanotubes combined with polycalprolactone (PCL) to produce non-spherical nanocomposites. Zhang et al. develop a series of water-dispersible polymer nanocomposites containing PEG- curcumin/ amine functionalized covalent organic framework which is used to develop drug delivery tool for drug doxorubicin to treat cancer. Yong hu et al. developed an approach towards targeted drug delivery by preparing carbon nanotubes & hydrogels containing anthracyclin drug to treat HeLa cancer cells Nano10). Nehal et al. designed and synthesized norfloxacin drug delivery system based on PLA/TiO<sub>2</sub> nanocomposites which has antibacterial and antitumor activities. Peeyush kumar et al. used photopolymerization technique for 3D printing of nanocomposite pills for drug delivery reason by using approved neutraceutical.

#### CONCLUSION

This review article covers the fundamentals of nanocomposites, as well as the methods for making them. Nanomaterials possess these features, which aid in enhancing component performance when compared to conventionally processed components. New technologies necessitate materials with innovative properties; nanomaterials have these properties.

Nanomaterials are the best materials for meeting the growing demands of the scientific community in this area. The classification of nanocomposites based on matrix materials, elasticity of materials (e.g. elastomeric nanocomposites), natural polymers (e.g. bionanocomposites), clay based nanocomposites, as well as their preparation, are also discussed in the article. However, dispersion of nanophase in polymer matrix is a difficult for some of these approaches. As a result, researchers will have more opportunities to solve the problem of nanomaterials. Polymer nanocomposites have been employed in a variety of applications already. It can give enhanced half-life, excellent biocompatibility, and minimal immunogenicity, site targeting, and overcome membrane barriers via nanoparticle drug delivery. Major and novel identifications in smart materials that change their structure and function in response to the environment have been established in the recent period as well. Aside from that, these nanocomposites have major applications in tissue engineering and neuron regeneration in biological living systems, nanocomposites are a possible nanocarrier for API's to be delivered. Many nanocomposite-based drug delivery systems have been approved in clinical trials, some of which are still in the early stages of development. This capability has been used to the development of smart medication delivery systems, with smart polymer matrices releasing pharmaceuticals in reaction to environmental changes.

#### REFERENCES

- 1. Pfaendner, R. Nanocomposites: Industrial opportunity or challenge? *Polymer Degradation and Stability*, 2010; 95(3): 369–373. doi:10.1016/j.polymdegradstab.2009.11.019
- 2. Ohani, O. R., Phatak, A. A., & Chaudhari, P. D. Use of nanocomposites in drug delivery systems. *Pharma Times*, 2015; 47.
- 3. Palekar P. Shanbhag, Rane D., Nanocomposites: A Newer Technology in Drug Delivery Systems. Int. J. Pharm. Sci. Rev. Res., 2019; 56(2): 144-154.
- 4. Zhang, S., Sun, D., Fu, Y., & Du, H. Recent advances of superhard nanocomposite coatings: a review. *Surface and Coatings Technology*, 2003; *167*(2): 113–119. doi:10.1016/S0257-8972(02)00903-9.
- 5. Waseem. S. Khan1, Nawaf. N. Hamadneh2 and Khan A. *Polymer nanocomposites synthesis techniques, classification and properties* Science and applications of Tailored Nanostructures, 51.

- Dr. Charles Chikwendu Okpala, THE BENEFITS AND APPLICATIONS OF NANOCOMPOSITES Okpala, Int J Adv Engg Tech/Vol. V/Issue IV/Oct.-Dec., 2014/12-18.
- 7. Paravastu, V. K. K., Yarraguntla, S. R., & Suvvari, A. Role of nanocomposites in drug delivery. *GSC Biological and Pharmaceutical Sciences*, 2019; 8. doi:10.30574/gscbps.2019.8.3.0150.
- 8. Cardoso, S., da Silva, C. F., Severino, P., Silva, A. M., Souto, S. B., Zielińska, A., ... Souto, E. B. Genotoxicity assessment of metal-based nanocomposites applied in drug delivery. *Materials*, 2021; *14*. doi:10.3390/ma14216551.
- Vaia RA. Polymer nanocomposites open a new dimension for plastics and composites (No. AFRL-ML-WP-TP-2005-408). Air force research lab wright-patterson AFB oh materials and manufacturing directorate, 2002.
- 10. De Sousa Rodrigues, L. A., Figueiras, A., Veiga, F., de Freitas, R. M., Nunes, L. C. C., da Silva Filho, E. C., & da Silva Leite, C. M. The systems containing clays and clay minerals from modified drug release: A review. *Colloids and Surfaces B: Biointerfaces*, 2013; 103. doi:10.1016/j.colsurfb.2012.10.0680.
- 11. Iliescu, R. I., Andronescu, E., Voicu, G., Ficai, A., & Covaliu, C. I. Hybrid materials based on montmorillonite and citostatic drugs: Preparation and characterization. *Applied Clay Science*, 2011; 52. doi:10.1016/j.clay.2011.01.031.
- 12. Suresh R., Borkar SN., Sawant VA., Shende VS., Dimble Sk., Nanoclay drug delivery system. Int. J Pharm. Sci. and Nanotech, 2010; 3: 901-904.
- 13. Pavlidou, S., & Papaspyrides, C. D. A review on polymer-layered silicate nanocomposites. *Progress in Polymer Science (Oxford)*, 2008; 33. doi:10.1016/j.progpolymsci.2008.07.008.
- 14. Patel, H. A., Somani, R. S., Bajaj, H. C., & Jasra, R. V. Nanoclays for polymer nanocomposites, paints, inks, greases and cosmetics formulations, drug delivery vehicle and waste water treatment. *Bulletin of Materials Science*, 2006; 29. doi:10.1007/BF02704606.
- 15. Naslain, R., Langlais, F., & Fedou, R. THE CVI-PROCESSING OF CERAMIC MATRIX COMPOSITES. Le Journal de Physique Colloques, 1989; 50. doi:10.1051/jphyscol:1989526.
- 16. Simon, R. A. Progress in processing and performance of porous-matrix oxide/oxide composites. *International Journal of Applied Ceramic Technology*, 2005; 2. doi:10.1111/j.1744-7402.2005.02016.x

- 17. Hussain, F., Hojjati, M., Okamoto, M., & Gorga, R. E. Review article: Polymer-matrix nanocomposites, processing, manufacturing, and application: An overview. *Journal of Composite Materials*, 2006; 40. doi:10.1177/0021998306067321.
- Gopi Krishna, M., Praveen Kumar, K., Naga Swapna, M., Babu Rao, J., & Bhargava, N.
  R. M. R. Metal-metal Composites-An Innovative Way For Multiple Strengthening.
  Materials Today: Proceedings, 2017; 4(8): 8085–8095. doi:10.1016/j.matpr.2017.07.148.
- 19. Behrens, S., & Appel, I. Magnetic nanocomposites. *Current Opinion in Biotechnology*, 2016; *39*: 89–96. doi:10.1016/j.copbio.2016.02.005.
- 20. Malaki, M., Xu, W., Kasar, A. K., Menezes, P. L., Dieringa, H., Varma, R. S., & Gupta, M. Advanced metal matrix nanocomposites. *Metals*, 2019; 9. doi:10.3390/met9030330.
- 21. Qiao, J. Elastomeric nano-particle and its applications in polymer modifications. Advanced Industrial and Engineering Polymer Research, 2020; 3(2): 47–59. doi:10.1016/j.aiepr.2020.02.002.
- 22. Das, S., Ghosh, B., & Sarkar, K. Nanocellulose as sustainable biomaterials for drug delivery. *Sensors International*, 2022; *3*. doi:10.1016/j.sintl.2021.100135.
- 23. Massoud M., Wenwu Xu, Kasar A, Metals, Advanced metal matrix nanocomposites, 2019; 9, doi: 10.3390/met9030330.
- 24. Sivanesan, I., Gopal, J., Muthu, M., Shin, J., Mari, S., & Oh, J. Green synthesized Chitosan/Chitosan Nanoforms/Nanocomposites for drug delivery applications. *Polymers*, 2021; *13*. doi:10.3390/polym13142256.
- 25. McCarthy, P. C., Zhang, Y., & Abebe, F. Review recent applications of dual-stimuli responsive chitosan hydrogel nanocomposites as drug delivery tools. *Molecules*, 2021; 26. doi:10.3390/molecules26164735.
- 26. Niezabitowska, E., Smith, J., Prestly, M. R., Akhtar, R., Aulock, F. W. V., Lavallée, Y., ... Mcdonald, T. O. Facile production of nanocomposites of carbon nanotubes and polycaprolactone with high aspect ratios with potential applications in drug delivery. *RSC Advances*, 2018; 8. doi:10.1039/c7ra13553j.
- 27. Zhang, G., Li, X., Liao, Q., Liu, Y., Xi, K., Huang, W., & Jia, X. Water-dispersible PEG-curcumin/amine-functionalized covalent organic framework nanocomposites as smart carriers for in vivo drug delivery. *Nature Communications*, 2018; 9. doi:10.1038/s41467-018-04910-5.
- 28. Hu, Y., & Niemeyer, C. M. Designer DNA-silica/carbon nanotube nanocomposites for traceable and targeted drug delivery. *Journal of Materials Chemistry B*, 2020; 8. doi:10.1039/c9tb02861g.

29. Salahuddin, N., Abdelwahab, M., Gaber, M., & Elneanaey, S. Synthesis and Design of Norfloxacin drug delivery system based on PLA/TiO2 nanocomposites: Antibacterial and antitumor activities. *Materials Science and Engineering C*, 2020; *108*. doi:10.1016/j.msec.2019.110337.