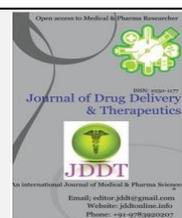


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Review Article

## A review on Nanocomposite Drug Delivery

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### ABSTRACT

Low aqueous solubility is the major problem come across the formulation development of new chemical entities as well as for the generic development. Supplementary than 40% New Chemical Entities developed in pharmaceutical industry are practically insoluble in water. Hence, there is a need for boosting the solubility and dissolution of such drugs. Enhancement of the solubility and dissolution of the practically insoluble drug was achieved by forming nanocomposites. Nanocomposites are formed by using synthetic polymers such as gelatin, chitosan, polyvinyl pyrrolidone, carboxymethyl cellulose, etc. Selection of polymers was based on their surfactant and wetting properties. To check the solubility enhancement of drugs solubility studies is carried out. Nanocomposites are characterized by Fourier transform infrared spectroscopy, differential scanning calorimetry, X-ray diffraction studies, scanning electron microscopy and transmission electron microscopy. As the concentration of polymer in the composite increased the solubility and dissolution of poorly water soluble drug were enhanced. In end, new technology require substances showing novel properties and/or progressed performance in comparison to conventionally processed additives. In this context, nanocomposites are appropriate materials to meet the emerging needs bobbing up from medical and technologic advances.

**Keywords:** nanocomposites, polymers, synthesis.

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### INTRODUCTION

At gift, solubility of drug is most hard factors inside the formulation development. Hence greater knowledge concerning dissolution and absorption of low aqueous soluble drug could be very vital to formulate extra soluble and bio available drug. Drug effectiveness may be seriously constrained by means of negative aqueous solubility and most of the medicine also show facet results due to their terrible solubility. By increasing solubility we growth efficiency and decrease side outcomes of positive pills. Drugs having negative water solubility are related to the sluggish drug absorption and subsequently inadequate or exceptional bioavailability. Today approximately forty % of the new pills are poorly water soluble. The poorly aqueous solubility of drug in the gastrointestinal fluid frequently causes inadequate bioavailability. The drug having poor aqueous solubility require high dose to reach therapeutic plasma awareness.<sup>1-4</sup> Nanoparticles are getting appealing drug delivery gadget because of their useful homes which include small size, excessive surface to quantity ratio, and accelerated tumor penetration. Properties of nanosized fabric which include conductivity, mechanical, and optical residences are distinct than bulk cloth even though composition of material is same.<sup>5-7</sup> The physical, chemical

and biological houses of nano substances range from the homes of character atoms and molecules or bulk be counted. By developing nano particles, it's far feasible to control the fundamental houses of substances inclusive of their melting temperature, magnetic residences, fee capability and even their shade without changing the materials' chemical compositions.<sup>8</sup> Synthetic polymers are organized from petrochemicals take very long time to degrade and for this reason poisonous. This disadvantage can be triumph over the use of biodegradable polymer. These polymers degraded by way of microorganism and enzyme. Biodegradable polymer can be herbal or synthetic origin. Natural biopolymers consist of chitosan, collagen, silk, and protein. Synthetic biopolymers are polylactic acid (PLA), polyglycolic acid, poly-l-lactic acid, and poly e-caprolactone. In previous couple of years, use of artificial degradable polymer as drug shipping machine has extended. Recently, use of biopolymers together with polysaccharides, proteins, lipids, and their blends has been extended as packaging materials because of their biodegradability, sustainability, and availability. Biopolymer offers obvious movie and coating that provide oxygen barrier and mechanical houses. Biodegradable polymers are used in various fields which include drug transport, gene therapy, tissue engineering, and plastic enterprise.<sup>1</sup> In the case of nanocomposite substances

can be categorized, in keeping with their matrix substances, in 3 distinct categories:

1. Ceramic Matrix Nanocomposites (CMNC);
2. Metal Matrix Nanocomposites (MMNC) and
3. Polymer Matrix Nanocomposites (PMNC).<sup>9</sup>

### HISTORY OF NANOCOMPOSTES

Nanocomposites had been studied for almost 50 years, but few references address the importance of how the organoclay is processed into the plastic of preference. Nanocomposites have been first referenced as early as 1950, and polyamide nanocomposites had been said as early as 1976. However, it became not till Toyota researchers started out an in depth exam of polymer/layered silicate clay mineral composites that nanocomposites have become greater widely studied in both instructional and industrial laboratories. Acquarulo & O'Neil (2002) in their work discovered that inside the early 1980s that Toyota's Central Research and Development Laboratories started working with polymer-layered silicate-clay mineral composites and that the period turned into whilst the technology began to be studied extra broadly. The clay mineral this is producing the maximum interest for use in nanocomposites is montmorillonite, generically called nanoclay, and from time to time known as bentonite. According to Briell (2004) bentonite "is natural clay this is maximum typically formed via the in situ alteration of volcanic ash or via the hydrothermal alteration of volcanic rocks" This clay is broadly to be had and relatively inexpensive, thus becoming the maximum extensively used clay in nanocomposite applications. In his look at, Azonano (2009) defined that the true begin of polymer nanocomposites history turned into in 1990 whilst "Toyota first used clay/nylon-6 nanocomposites for Toyota automobile if you want to produce timing belt covers." He pointed out that once that different car software became applied, which encompass:

- Mitsubishi's GDI cover clay/nylon-6 nanocomposites engines; and
- General Motors clay/polyolefin nanocomposites step assistant GMC Safari and Chevrolet Astro vans.

However, Nanocomposites were used commercially considering the fact that Toyota brought the first polymer/clay auto elements as the capacity packages go past automotive enterprise. One of the maximum promising is drink packaging application thinking about improved barrier homes of polymer clay nanocomposites. It is easy to recognize the industrial and technical importance of this subject. Recently, advances inside the capacity to represent, produce and control nanometer-scale substances have brought about their extended use as fillers in new varieties of nanocomposites.<sup>10</sup>

### What are Nanomaterials?

Nanomaterials have at the least one outside size in the size range from approximately 1-100 nanometers and nanoparticles are items with all 3 outside dimensions at the nanoscale. These nanoparticles are either evidently happening obtained from volcanic ash, soot from forestres and so on. Or they're byproducts of combustion processes (e.G., welding, diesel engines). These materials are physically and chemically heterogeneous and regularly referred as extremely fine particles. Often, the conduct of nanomaterials may also depend more on floor region than particle composition itself. Relative-floor vicinity is one of the most important factors that enhance its reactivity, power and electrical properties. These nano-scale debris, tubes, rods, or

fibres are being utilized in healthcare, electronics, cosmetics, textiles, records era and environmental safety. The properties of nanomaterials aren't constantly well-characterized. Important physical and chemical residences of nanomaterials are as follows:

1. Physical properties encompass:

☒ Size, form, particular surface region and ratio of width & peak

☒ Size distribution

☒ Surface smoothness

☒ Structure consisting of crystal structure and any crystal defects

☒ Dissolvability

2. Chemical houses encompass:

☒ Molecular structure

☒ Composition, such as purity and recognized impurities or components

☒ State (stable, liquid or fuel)

☒ Surface chemistry

☒ Attraction to water molecules or oils and fat

Nanomaterials can be metals, ceramics, polymeric substances, or composite substances with a huge range of homes and possible packages. These encompass particularly tiny digital gadgets, miniature batteries to biomedical programs, packaging films, awesome absorbents, additives of armor and components of motors. Nanotechnology may be used to design pharmaceuticals that can goal specific organs or cells within the frame which includes cancer cells and enhance the therapeutic effectiveness. Nanomaterials can also be delivered to cement, fabric and different substances to cause them to more potent and yet lighter. Their size makes them extraordinarily beneficial in electronics and they also can be used in environmental remediation or clean-up by way of binding with and neutralizing toxins. Engineered nanoparticles are produced and designed with very specific properties associated with form, length, floor residences and chemistry. These nanoparticles may be produced experimentally by using laser ablation, HiPCO (excessive-pressure carbon monoxide), arc discharge and chemical vapour deposition (CVD) strategies. These substances have precise optical, magnetic, electrical and different houses and have made exceptional affects in electronics, medication and other sectors. Engineered nanomaterials include nanocrystals, which can be composed of a quantum dot surrounded by using semiconductor materials, nano-scale silver, dendrimers (repetitively branched molecules) and fullerenes (carbon molecules in the form of a hole sphere, ellipsoid or tube). However, even as engineered nanomaterials offer amazing benefits, their ability consequences on human fitness and the surroundings aren't widely recognized. Nano-sized debris can enter the human body through inhalation and ingestion and via the skin. Fibrous nanomaterials made from carbon have proven to set off inflammation within the lungs just like asbestos.<sup>8,11,12</sup>

### POLYMERS

The selection of a polymer as a composite depends at the mechanical chemical characters, hydrophobic/hydrophilic stability, chemical stability, biocompatibility, and chemical functionalities. Among many polymers, PDMS, PANI, PVB, PVP, PMMA, PVDF, PE, CMC, alginate, and chitosan may be

taken into consideration handy for environmental applications. These polymers may be employed as polymeric matrices for filtration, water remediation, disinfection, and many others. In environmental remediation, because of no longer only their chemical and bodily homes, however also their synergistic effect among polymers and the opposite element of the composites. In this phase, recent advances within the preparation of nanocomposites the usage of a diffusion of polymers are very well discussed.

### 1. Poly(dimethylsiloxane) (PDMS)

PDMS is an inert, risk-free, nonflammable, and enormously flexible, broadly used polymer, that's used in sponge shape for remediation programs. PDMS sponges are replicated from sugar templates and do now not want any complicated synthesis tactics or system. Besides, they can be used for selective absorption of oil due to their hydrophobic/oleophilic homes, thanks to their molecular shape. Additionally, the sponge form of PDMS can be became any shape in air or beverages with none damage, so it is able to absorb oils and natural solvents then remove them, and it's far usable repeatedly. Moreover, absorption potential of the sponge can be adjusted with the aid of numerous quantities of sugar carbohydrate debris within the shape. Hence, comfort houses of the PDMS sponge are vital to remediate poisonous chemicals from oil spills and cast off organic pollution from water.

### 2. Polyaniline (PANI)

PANI exists in diverse paperwork which has one-of-a-kind chemical and bodily homes. Three systems of PANI are leucoemeraldine (LEB), emeraldine (EB) and pernigraniline (PB), which might be related through their synthesis techniques. The different physicochemical homes create diverse application regions for PANI, including organic electrodes, sensors, and actuators. PANI is hired to take away chromium(VI) (Cr(VI)) because large particular surface vicinity, low value, and simpler manufacturing residences make conductive polymer PANI advanced. On the alternative hand, Cr(VI)-removing studies are challenging, and recognize of reactions among Cr(VI) and PANI has an vital function in environmental remediation. As a result, PANI-magnetite nanocomposites were fabricated to analyze the reaction mechanism among PANI and Cr(VI). In any other research direction, the composite of PANI and TiO<sub>2</sub> used for removal of Cr(VI) from polluted water changed into very efficient and rapid.

### 3. Poly(hydroxybutyrate) (PHB)

Poly(three-hydroxybutyrate) (PHB) is diagnosed as a certainly taking place p-hydroxyacid (a linear polyester). This green fabric has attracted attention inside the enterprise as a a hundred% biodegradable plastic for marine, agricultural, and scientific applications, and it is able to be made out of herbal sources. Degradation of PHB in soil and other environments inside a few weeks has been indicated. Although PHB isn't normally used due to its excessive-fee, unlike artificial materials which includes polypropylene (PP), it is desired because of its biodegradability. Therefore, recent research have centered on generating decrease value PHB by inspecting diverse methods together with bacterial pressure development, greater green fermentation/recovery methods, and the use of renewable resources. In addition, its bodily residences had been amplified by means of mixing with metal oxides (together with TiO<sub>2</sub>) to get rid of methylene blue from the surroundings.

### 4. Poly(vinyl pyrrolidone) (PVP)

PVP is a extensively desired, water soluble polymer, thanks to its physicochemical homes which includes mechanical balance, chemically inertness, right optical transparency, and binding and adhesive traits when utilized in colloidal suspensions. PVP also are used as a pigment dispersant, bonding agent, and suspension stabilizer. Because PVP has a saturated carbon chain, its nanocomposites own chemical balance and mechanical resistance. Furthermore, the polar nature of pyrrolidone residue lets in advanced retention of polar molecular and ionic species in its polymeric shape. This function allows disposing of polar contaminants such as bromate from water.

### 5. Poly(methyl methacrylate) (PMMA)

PMMA is generally chosen for coaching of PNCs for environmental remediation because of its fantastic functions for example dimensional balance, optical readability, and compatibility with ceramics. For environmental remediation, PMMA may be combined with magnetic nanoparticles to beautify its balance and dispersibility. In addition, the other properties that make this cloth acceptable are nontoxicity, easy producibility, and occasional price. Therefore, PMMA-lined nZVI debris is favorable for the environment, because of properties of each component. Furthermore, PMMA is insoluble, but it can swell in some organic solvents, together with TCE. Also, the glass-transition temperature (T<sub>g</sub>) of PMMA is decrease than the alternative sorts of polymers, and coffee T<sub>g</sub> presents fairly more clean investigation of the morphology of the composite.

### 6. Poly(vinylidene fluoride) (PVDF)

PVDF is a good material for a membrane thanks to its thermal balance, mechanical power, chemical resistance, and hydrophobicity, in contrast to different commercial polymers. In general, membranes made with PVDF are hired in ultrafiltration and microfiltration tactics. In addition, PVDF is being utilized in membrane contactor and membrane distillation applications. Nowadays, massive progress has been made within the green fabrication of PVDF membranes for the aforementioned applications, and remediation of wastewater. Hydrophobicity of PVDF isn't as excessive as polypropylene (PP) and polytetrafluoroethylene (PTFE), but is surprisingly extra hydrophobic. The right thermal balance of PVDF is some other suited belongings for industrial programs as a membrane cloth. PVDF can be described as a natural polymer, which makes it handy for biomedical and separation applications. PVDF is a semicrystalline polymer that normally incorporates 59.4wt% fluorine and 3wt% hydrogen and its chemical structure. Generally, polymer crystallinity and the morphology of membranes are important elements to determine the mechanical homes. PVDF is thermally more solid compared with some other hydrocarbon polymer, attributable to the excessive electronegativity of fluorine atoms, which give the strong CdF bonding and greater strong structure. Although PVDF can not stay stable at excessive reaction temperatures.<sup>8</sup>

### 7. Polyethylene (PE)

PE is a polymer with an amorphous crystalline shape, and is received by means of the polymerization of ethylene fuel, which is used in the encapsulation method for environmental remediation. PE encapsulation contributes to remediation whilst used as a stabilizer. PE has instead low flammability price, that's given as 1 (mild) by means of the National Fire Protection Association; additionally, flash-ignition temperatures and self-ignition temperatures are reported as 409°C and 430°C for PE. On the opposite hand,

PE might also lose its plasticity and end up breakable underneath ultraviolet situations. In mild of the those houses of PE, studies has shown that the PE/TiO<sub>2</sub> polymer nanocomposite, that is synthesized by using immobilizing TiO<sub>2</sub> powder on a foamed PE sheet, is capable of decomposing a ramification of natural substances, such as natural dye and methylene blue, and is handy for wastewater treatment.

### 8. Alginate

Alginate is a polysaccharide produced by means of a few algae or microorganisms. Commonly used industrial alginate is normally extracted from brown algae (Phaeophyceae). It is a linear binary copolymer together with connected 1,4-β-D-mannuronic acid (M) and 1,4-β-L-guluronic acid (G). Alginate is generally utilized in biomedicine, inclusive of wound recovery, tissue engineering, and biosensor packages as in the form of hydrogel. The advantage of using alginate for encapsulation is the high porosity furnished with the aid of the open lattice structure of the gel. The bodily properties of alginate exchange with the sequence of M and G corporations and the molecular weight of the polymer. It has some precise properties that make it convenient for environmental remediation programs along with nontoxicity, biocompatibility, chelating capacity, and hydrophilicity. Calcium-alginate is an surest composite for its use in environmental programs because it is secure, biodegradable, and partially soluble in water. The porous nature of Calcium-alginate lets in solutes to diffuse and come in touch with the entrapped nano-scale FeO, which in turn provide an positive polymer composite candidate for environmental remediation.

### 9. Carboxymethyl cellulose (CMC)

CMC is typically used in its sodium salt form (cellulose gum), which is vital as an business spinoff. The most normally used water soluble CMC salts are sodium, potassium, and ammonium salts. Among these, the sodium carboxymethyl cellulose is the maximum common salt used as an emulsifying agent in numerous commercial programs. CMC presents steric stabilization that famous a larger repulsion pressure than electrostatic repulsion. Hence, it could assist to stabilize FeO nanoparticles thru carboxyl companies. CMC/FeO polymer nanocomposites may be given as an instance for Cr(VI) elimination. Water-soluble CMC acts as stabilizer in the course of the instruction of the FeO nanoparticles, in regards to their physical stability and chemical reactivity for reductive removal of Cr(VI) from water.

### 10. Chitosan

Chitosan is a clearly happening biopolymer derived from absolutely or partially deacetylated chitin. Chitosan has superior homes, which make it handy to use in environmental remediation which include the ability to coordinate with steel, biodegradability, antimicrobial pastime, and nontoxicity. Hence, it exists in numerous software areas along with meals, agriculture, pharmacy, and environmental remediation. Additionally, polycationic and chelating homes of chitosan closer to diverse natural and inorganic compounds make it beneficial for biofabrication and controlled freeing formulations (CRFs) of chemical compounds. These physicochemical and biological homes were attracted within the subject of environmental remediation. On the other hand, bulk chitosan polymer is insoluble in water and has notably low biostimulant moves that limit its potential in numerous environments.<sup>[13]</sup>

## PROPERTIES OF NANOCOMPOSITES

Nano-composites have won a lot interest recently. Significant efforts are underway to control the nano-structures via modern artificial methods. The residences of nano-composite substances rely now not most effective at the properties in their individual mother and father but also on their morphology and interfacial characteristics. The physical, chemical and organic homes of nano materials differ from the homes of character atoms and molecules or bulk depend. By creating nano particles, it's miles viable to manipulate the fundamental houses of materials, which includes their melting temperature, magnetic residences, rate potential and even their colour without changing the substances' chemical compositions. Nano-debris and nano-layers have very high surface-to-volume and factor ratios and this makes them ideal for use in polymeric materials. Such structures integrate the quality residences of each component to own better mechanical & superconducting houses for advanced programs. The homes of nano-composite substances depend now not best at the residences of their man or woman dad and mom however additionally on their morphology and interfacial characteristics. Some nanocomposite substances will be a thousand instances harder than the majority element. The trendy class of nanocomposite natural/inorganic materials is a quick developing place of studies. The inorganic additives can be 3-dimensional framework systems such as zeolites, two dimensional layered materials consisting of clays, metal oxides, metallic phosphates, chalcogenides, and even onedimensional and zero-dimensional materials together with (Mo<sub>3</sub>Se<sub>3</sub>)<sub>n</sub> chains and clusters. Thus, nanocomposites promise new packages in many fields which include mechanically reinforced light-weight additives, non-linear optics, battery cathodes, nano-wires, sensors and different systems. Inorganic layered materials exist in lots of varieties. They possess properly defined, ordered intralamellar area doubtlessly on hand through foreign species. This ability allows them to behave as matrices for polymers yielding hybrid nano-composites. Lamellar nanocomposites represent an extreme case of a composite in which interface interactions among the two stages are maximized. By engineering the polymer-host interactions, nanocomposites could be produced with the wide range of residences. Lamellar nano-composites may be divided into wonderful instructions viz. Intercalated and exfoliated. In the former, the polymer chains are alternately gift with the inorganic layers in a fixed compositional ratio and feature a properly-described number of polymer layers inside the intralamellar space. In exfoliated nano-composites, the quantity of polymer chains between the layers is sort of constantly variable and the layers stand >a hundred Å apart. The intercalated nano-composites are beneficial for digital and fee transport residences. On the other hand, exfoliated nano-composites possess advanced mechanical residences. For instance, the electronics enterprise makes use of materials which have excessive dielectric constants and which can be additionally flexible, easy to procedure, and sturdy. Finding unmarried aspect materials owning some of these homes is tough. The maximum commonly used ceramic substances with high dielectric steady are discovered to be brittle and are processed at high temperatures, even as polymer substances, which can be very clean to manner have low dielectric constants. Composite substances having micron-scale ferroelectric ceramic debris because the filler in liquid crystal polymer, fluoropolymer, or thermoplastic polymer matrices do no longer own best processing traits and are hard to form into the thin uniform movies used for lots microelectronics programs. Here comes the need of utilising nanocomposite materials having a wide variety of

substances mixed on the nanometer scale. By optimized fabrication system and controlled nano-sized second segment dispersion, thermal balance and mechanical residences including adhesion resistance, flexural electricity, longevity & hardness can be more suitable which can end result into progressed nano-dispersion. The possibilities of producing materials with tailor-made physical & digital houses at low value may want to bring about thrilling programs starting from drug delivery to corrosion prevention to electronic/car elements to industrial system and several others. Nanocomposites are substances that comprise nanosized particles right into a matrix of standard material. The end result of the addition of nanoparticles is a drastic development in houses that could encompass mechanical energy, durability and electrical or thermal conductivity. The effectiveness of the nanoparticles is such that the quantity of material added is normally most effective between 0.5 and 5% by way of weight. Typically, nanocomposites are clay, polymer or carbon, or a aggregate of these substances with nanoparticle constructing blocks. They have an exceedingly excessive floor to extent ratio which dramatically modifications their properties when in comparison with their bulk sized equivalents. It also adjustments the way in which the nanoparticles bond with the majority cloth. The end result is that the composite can be frequently improved with appreciate to the issue parts. Some nanocomposite materials have been proven to be a thousand times more difficult than the bulk component substances.

Nanocomposites can dramatically enhance properties like:

- Mechanical residences which include energy, modulus and dimensional balance.
- Electrical conductivity.
- Decreased gas, water and hydrocarbon permeability.
- Flame retardancy.
- Thermal balance.
- Chemical resistance.<sup>[10]</sup>

## METHODS TO GENERATE NANOCOMPOSITES

Methods which can be used for the coaching of nanoparticles can be used to prepare nanocomposite with some change.

### 1. Emulsion/solvent evaporation

It is primarily based at the formation of emulsion and then evaporation of solvent. Evaporation of solvent and excessive pressure stirring outcomes in precipitate formation in nanoform. It is suitable for hydrophobic pills. Both drug and polymer are dissolved in common natural solvent to make oil phase. Water segment is made up with water soluble polymer. Oil section is then dispersed in aqueous phase with non-stop stirring or sonication to shape oil in water emulsion. Then, solvent is authorized to evaporate to shape drug-loaded nanocomposite particles. In oil in oil emulsion, both phases are oil. In this method, oil phase and aqueous section are decided on relying on solubility of drug and polymer. Paclitaxel-loaded PLGA/MMT nanocomposite by using this technique the usage of dichloromethane (DCM) as solvent. 5 mg paclitaxel and a hundred and ten mg PLGA had been dissolved in DCM to put together clean answer of oil section. Aqueous answer is prepared with 2% w/v PVA and various amounts of MMT (0, 0.046%, and 0.092% w/v). Oil segment is then emulsified inside the aqueous segment with sonication for one hundred twenty s. The formed emulsion was allowed to evaporate overnight at room temperature to harden the debris.

### 2. Emulsification solvent diffusion

This technique is based on emulsification then diffusion of solvent to outer section to form nanocomposite particle precipitate. Diffusion of solvent is due to its solubility in outer phase. Diffusion of solvent and excessive pressure stirring outcomes in precipitate formation in nanoform. Polymers are dissolved in numerous solvents based totally on solubility and swelling nature of polymers. Then, inner natural oil segment is emulsified in outer aqueous section with keeps stirring or homogenization to form nanocomposite particle. The organized PLA/MMT nanobiocomposite emulsion via emulsification solvent diffusion approach. PLA solution and MMT dispersion have been one by one prepared in ethyl acetate solvent. The PLA solution, clay dispersion, and lauryl alcohol have been then blended and used as an oil section. The aqueous segment is prepared with surfactants and PVA in distilled water. Oil segment is dispersed in the aqueous phase with homogenization and then magnetic stirring.

### 3. Solution intercalation

This technique is in general used for layered silicates as nanofiller which might be to be intercalated inside the polymer matrix. Principle involves diffusion of the polymer chain in the galleries among silicate layers. In this technique, solvent is selected such that polymer is soluble in solvent at the same time as inorganic nanofiller simply swells. Polymer is dissolved in solvent, and then, inorganic nanofiller is introduced in answer with stirring. Usually, fillers are allowed to swell before addition in polymer matrix. This leads to intercalation of polymer into silicate to form nanobiocomposite.

### 4. Melt intercalation

This method operates at the same precept as that of answer intercalation, however right here, heat is used in place of solvent for intercalation of polymers into the silicate. In this method, the combination of polymer and layered silicate are heated until the softening factor of polymer executed. Then, it's far mixed with high shear charge. This leads to intercalation of matrix into silicate layered. Instruments such as unmarried screw extruder and double screw extruder are used for soften intercalation. It is beneficial over solution intercalation in phrases of the absence of organic solvents and ease of industrial techniques. Polymer chain diffuses within the galleries between silicate layers. Depending on diploma of penetration of polymer chain into the silicate, nanobiocomposite can be of two types, i.e., intercalated and exfoliated. Poly (butylene adipate-co-terephthalate) - MMT nanobiocomposite via soften intercalation technique using interbatch mixer, counter rotating mixer at one hundred 60°C for 15 min for 50 rpm then 120°C for 20 min for a hundred rpm.

### 5. Double emulsion solvent evaporation

In this method, two polymers selected are dissolved in oil phase and aqueous section relying on their solubility. Then, water in oil emulsion is ready with stirring. The resulting emulsion is then brought to external section that's aqueous phase with stabilizer like PVA; then, machine is stirred to evaporate solvent at room temperature. The writer prepared calcium phosphate (Cap)/ poly(hydroxyl butyrate-co-hydroxyl valarate) (PHBV) nanobiocomposite through stable in oil in water (solid-in-oil-in-water [s/o/w]) emulsion the usage of solvent evaporation method. W/O emulsion turned into made via aqueous answer of bovine serum albumin (BSA) and natural solution of PHBV in chloroform using homogenizer. The resulting emulsion changed into introduced in PVA aqueous method to shape w/o/w

emulsion. Then, aggregate changed into magnetically stirred to evaporate solvent. PHBV-BSA microspheres had been filtered, freeze-dried. Modified s/o/w emulsion solvent evaporation approach become used to produce BSA-loaded Ca-P/PHBV nanocomposite microspheres. Ca-P nanoparticles had been dispersed inside the PHBV-chloroform answer using ultrasonication and homogenization to shape a s/o nanosuspension and it's far dispersed within the internal water phase (the aqueous BSA solution), observed by the same method for PHBV-BSA microsphere preparation.

### 6. Electrospinning

This method is used to prepare nanobiocomposite fiber. The equipment encompasses flat tip needle, excessive voltage strength deliver, pump, and accomplishing collector plate. Mixture of polymer is prepared in organic solvents together with dimethyl formamide (DMF) and chloroform. Then, it is loaded on electrospun needle and the high voltage implemented to form composite fiber. The writer organized PLA/carbonated calcium-poor hydroxyapatite (CDHA) bionanocomposites fibers by using this approach. In brief, PLA pellets have been dissolved in chloroform; CDHA precipitate turned into brought to PLA technique to shape aggregate followed by way of DMF addition with continuous stirring for 4 hr. This mixture is then loaded into the electrospun equipment and injected via the needle to form fibers. Fibers are then dried in fume hood.

### 7. Ultrasonication

Here, conversion of material into nanosize is because of high-frequency ultrasound waves. Usually, on this technique, polymers are brought in solvent (normally ethanol), and the combination is then ultrasonicated to achieve nanobiocomposite. The last solvent is removed. The frequency of irradiation, time for irradiation, and power deliver are variable which controls length and morphology of nanobiocomposite. The creator organized poly(ester-imide)s (PEA) ZnO nanobiocomposite by ultrasonication approach. They used PEA as a matrix and modified ZnO nanoparticles (modification by way of the silane coupling agent, i.E.,  $\gamma$ -methacryloxypropyltri-methoxysilane). PEA dispersion is made in ethanol the use of ice-water ultrasonic tub. Followed with the aid of addition of different proportion of modified ZnO nanoparticle in PEA suspension and aggregate became ultrasonicated for 4 h. Then, solvent was eliminated, and nanobiocomposite was dried.

## CHARACTERIZATION OF NANOCOMPOSITES

### Morphological characterization

Following techniques are used for morphological characterization.

#### 1. XRD (X-ray Diffraction) techniques

XRD interpretation operates on precept of positive interference shaped by way of X-ray (monochromatic) and crystalline pattern. Bragg's law is used to provide an explanation for constructive interference. Here, XRD is used to decide shape, crystalline, and amorphous nature of nanofiller, drug, and polymer. It is also used to decide segment separation of nanofiller and polymer. Intercalation of layered silicate with polymer can be diagnosed that is exfoliated or intercalated.

#### 2. FTIR (Fourier Transform Infrared Spectroscopy)

Each practical organization indicates some constant resonance frequency throughout infrared irradiation that is to stumble on this useful group. It is used to determine

changes in nanobiocomposite in terms of useful organization. Chemical modifications occurred all through composite practise by way of distinct polymers and drug can be without problems detected. It also identifies unknown metal in pattern, great, and consistency of pattern and quantity of element in combination. It is used to determine chemical composition of intermediate and received particle.

### 3. TEM (Transmission Electron Microscopy)

Here, electrons are transmitted through an ultrathin sample, these electrons have interaction with the pattern at some stage in passing. An image is formed from the interplay of the electrons all through transmission that is detected and magnified. TEM is used to come across pleasant about internal structure, various defects, and area distribution of various levels. It provides facts about state of dispersion of nanofiller in polymer matrix. Nature of intercalation of layered silicate with polymer may be diagnosed, i.E., exfoliated or intercalated.

### 4. Atomic force microscopy

Images are fashioned by means of measuring the bodily interplay among a sharp AFM tip and the sample. It provides three dimensional snap shots of a particle and group of debris. Surface morphologies including surface roughness, surface forces, and size range of the nanoparticles are decided. Information together with mechanical, chemical, and adhesive homes of floor can be obtained.

### 5. SEM (Scanning Electron Microscopy)

Accelerated electrons are allowed to incident on pattern, 3-dimensional pics are formed by secondary electrons and backscattered electrons. It gives facts approximately morphology of unmarried polymer, drug, and nanobiocomposite. It affords statistics approximately country of dispersion of nanofiller in polymer matrix. Surface fracture and aggregation of particles in nanobiocomposite may be easily detected.

### Thermal evaluation

#### 1. TGA (Thermal Gravimetric Analysis)

It is used to degree alternate in weight of sample as temperature or time changes. Change in weight loss between single polymer and composite may be compared. It indicates physical adjustments including melting which do now not involves weight loss in addition to chemical changes along with combustion which involves weight reduction. The weight of the sample is plotted towards time or temperature which shows thermal adjustments in the material which includes loss of solvent, water of hydration in inorganic substances, and in the end decomposition of the material.

#### 2. DSC (Differential Scanning Calorimetry)

This method is used to discover nature of crystallization, exothermic, and endothermic response. In endothermic reactions, e.G., stable pattern melts to a liquid; it requires more warmth flowing to the sample to growth its temperature on the equal fee because the reference due to the fact pattern absorbs warmth to transform into liquid nation, consequently extra warmth is require to raise temperature of pattern compared to reference. Reverse is the case with endothermic reaction which happens during crystallization. It offers information about thermal stability of natural polymer and nanobiocomposite by way of melting factor.

### 3. Magnetization

It is specifically utilized in characterization of magnetic nanobiocomposite. It offers facts about magnetic power of nanobiocomposite, i.e., what are the adjustments befell in magnetic property of material after making composite. It checks the response of external magnetic field on nanobiocomposite. It also recommend about impact of temperature on magnetic assets. The strategies used are vibrating sample magnetometer (VSM) and SQUID. VSM operates on Faraday's law of induction, i.e., changing magnetic discipline produce electric present day which can be measured. Initially, pattern is located in consistent magnetic subject to bring about magnetization. Magnetic discipline is created around sample by magnetic dipole second then sample is vibrated. This creates exchange in magnetic area and, in turn, modifications electric discipline. It suggests magnetic behaviour and magnetic power of substances.

### 4. In vitro drug launch

In this examine distinct varieties of equipment and methods are used relying on formula. Wang et al. Prepared sodium alginate hydroxyapatite nanobiocomposite. They used intelligent dissolution apparatus stirred at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$  temperature. The launch of magnetic hydrogel nanobiocomposite drug launch by means of pyrocatechol violet dye as version drug. Nanda et al. used dissolution tester equipped with 6 paddles at 100 rpm for the discharge of anticancer drug paclitaxel. Feng et al. used 10 ml phosphate buffer answer in capped centrifuge tube for drug release from paclitaxel-loaded PLGA-MMT nanobiocomposite.<sup>5</sup>

## CHARACTERIZATION OF POLYMERS

### 1. Swelling index (SI)

SI of polymers changed into calculated to check the swelling pressure. Accurately weighed 10 g of polymers changed into transferred to a hundred ml measuring cylinder. The initial quantity engaged by way of polymer became widely recognized. Distilled water turned into brought inside the cylinder as much as a hundred ml, and the open give up of cylinder become sealed with an aluminum foil. Measuring cylinder became kept aside for 24 h and quantity of swelled polymer changed into stated. The SI of polymer was calculated by the following method:

$$\text{SI} = \frac{\text{Hf} - \text{Hi}}{\text{Hi}} \times 100$$

Where, SI: Swelling index; Hi: Initial peak of powder; Hf: Final top of powder after 24 h.

### 2. Viscosity determination

Viscosity of polymer was determined through taking 1 g of each polymer and dispersed in 100 ml distilled water (1% w/v). The viscosity of resultant dispersion turned into measured by means of viscometer (Brookfield DV-E, Brookfield Engineering Laboratories, Inc., Middleboro, MA, USA) using spindle 3 at one hundred rpm.

### 3. Foaming index

The foaming index become calculated to test the surfactant assets of polymer. Accurately weighed 1 g of polymer was transferred in 250 ml measuring cylinder containing 100 ml distilled water to make dispersion. Resultant dispersion changed into vigorously shaken for 2 mins. The foaming index of polymer changed into calculated with the aid of the following equation:

$$\text{Foaming index} = \text{Hf} - \text{Hi}$$

Where, Hf is the peak of solution of gum after shaking and Hi is the peak of solution of gum before shaking.<sup>[14]</sup>

## APPLICATION IN DRUG DELIVERY

### 1. Control release

The nanocomposite of hydrogel with magnetic debris may be utilized in pulsatile drug delivery machine. Remote manipulate launch of drug is designed via magnetic nanocomposite of N-isopropylacrylamide (NIPAAm). Iron oxide is used as far flung heating tool, and NIPAAm is a temperature sensitive hydrogel. Alternating high-frequency magnetic subject leads to heat technology in nanocomposite which forces the swelling transition of the hydrogel. It became observed that drug launch decreases with boom in temperature. Nanobiocomposite of sodium alginate/hydroxyapatite demonstrates manage launch of diclofenac drug. Prepared nanocomposite beads will be used inside the production of oral pharmaceutical formulations. Nanocomposite prolonged the discharge of diclofenac drug for eight h more compared with the neat sodium alginate hydrogel beads. Control launch of drug discovered in glycolic acid-g-chitosan-gold-nanoflower nanocomposite. The nanohybrid scaffolds had been discovered to be stable toward the pH of the medium. The prepared nanohybrid scaffolds are biocompatible. This nanocomposite showed control drug release price in the buffer answer (pH 7.4). Therefore, gold nanoflowers are the viable additive for the glycolic acid grafted chitosan-primarily based machine, for drug transport.

### 2. Sustained release

A coaching for spinal cord injury organized efficaciously inside the shape of sustained launch nanobiocomposite containing hyaluronan and methylcellulose hydrogel with PLGA nanoparticle, it was found to be secure and biocompatible. It was verified that this coaching is nicely tolerated in intrathecal area of injured rats for 28 days and showing no growth in irritation, scarring, or cavity extent relative to controls and no impact on locomotor capabilities.

### 3. Anticancer

Nanobiocomposite organized with PLGA-MMT with paclitaxel drug for oral delivery of anticancer. Paclitaxel is anticancer drug cannot accept orally due to low absorption through GIT and first-bypass effect. PLGA-MMT nanocomposite demonstrated increased GIT absorption and boom cell uptake through CaCo-2 and HT-29 cells. The drug release take a look at confirmed an initial burst accompanied via a slow, sustained release, which become now not considerably suffering from the MMT component. The observation indicates that nanobiocomposite of hydroxyapatite-chitosan with celecoxib drug is powerful and safe car for colon most cancers drug delivery. It become discovered that nanocomposite debris conquer aspect effect shown by way of loose celecoxib and also nanocomposite showed stronger anticancer pastime than free celecoxib.

### 4. Antianemic

Ferroarabinogalactan (A nanobiocomposite) prepared from nanodispersion of iron oxide in arabinogalactan matrix showed decorate antianemic hobby. Arabinogalactan is received from Siberian larch (*Larix sibirica*) posses antianemic activity. It has been shown that this composite produces a hemopoiesis stimulator and iron stabilizing impact; this is due to synergistic effect of iron nanoparticle and arabinogalactan.

## 5. Antibacterial and antifungal

The powerful and secure centered antibacterial and antifungal drug transport may be completed by magnetic nanocomposite of iron oxide and silver nanoparticles. At the discovered minimal inhibition concentrations, nanocomposite did not exhibit acute cytotoxicity in opposition to mice embryonal fibroblasts. The synergistic effect of magnetic residences of iron oxide nanoparticles and antimicrobial assets of silver nanoparticle thus show these nanocomposites for use in antibacterial and antifungal programs as a centered drug delivery.<sup>5</sup>

## CONCLUSION

Solubility is a maximum essential parameter for the oral bio availability of poorly soluble drugs. Dissolution of drug is the rate determining step for oral absorption of the poorly water soluble drug, which can in the end have an effect on the in vivo absorption of drug. Because of solubility problem of many drugs the bio availability of these drugs is affected. More than forty percent of New Chemical Entities advanced in pharmaceutical industry are almost insoluble in water. Solubility enhancement of those drugs stays one of the most challenging features of drug improvement. A range of devices have been developed through the years to enhance the drug solubility and dissolution of the drugs. Nanocomposites is best approach for the solubility enhancement of poorly water soluble drug. Various methods discussed above are used for the preparation of nanocomposites. The various methods discussed have been successful in the laboratory as well as the scale-up.

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