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Nano-Clay as Polymer Porosity Reducer: A Review

Mohit Batra*[1], Swati Gotam[1], Poonam Dadarwal[2], Rahul Nainwani[1] and Manoj Sharma[1]

*[1] Department of Pharmaceutics, Mahatma Gandhi College of Pharmaceutical Sciences, Sitapura, Jaipur, India.

[2] Department of Pharmaceutics, Maharashi Arvind College of Pharmaceutical Sciences, Mansarover, Jaipur, India

Abstract: Nanotechnology is the rapidly growing area of science. The term "nanotechnology" is now commonly used to refer to the creation of new objects with nanoscale dimensions between 1.0 and 100.0 nm. Nanotechnology having an impact on drug delivery. Now, researchers are starting to use NANO-CLAY particles in the field of drug delivery. Clay minerals are widely used materials in drug Products like as excipients and active agents. Nano-clay drug delivery system are widely used for those drugs which requires the slow release rate. Because nano-clay material reduce the polymer porosity. They are also useful in geology, agriculture, construction, engineering, process industries, and environmental applications. Organic surfactants modified clay minerals are usually used as adsorbents for hydrophobic organic contaminants remediation.

Keywords: Nanotechnology, Slow release rate, Nano-clay and Polymer Porosity.

Introduction

Natural Clays are inexpensive materials, Clay is a naturally occurring aluminium silicate composed primarily of fine-grained minerals and various clays or clays minerals are catalysts of Fenton-like reactions. Its promote decontamination of soils, groundwaters, sediments, and industrial effluents and they also participate in formulations used for topical application in both dermopharmacy and dermocosmetics (Garrido EG. et al., 2010), (Gomes CD. et al. 2008).Clay minerals may be administered either orally as antacids, gastrointestinal protectors, antidiarrhoeaics, osmotic oral laxatives, homeostatics, direct emetics, antianemics and mineral supplements, or parenterally as antianemics and homeostatics. They may also be used topically as antiseptics, disinfectants, dermatological protectors, anti-inflammatories, local anesthetics and keratolytic reducers (Carretero MI. et al., 2010). Clays were prepared based on halloysite, kaolinite and bentonite and used for nitrate adsorption, which are significant for providing mechanism for the adsorption of anionic contaminants from waste water (Xi Y. et al., 2009).

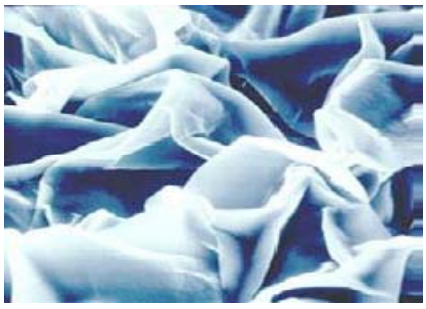

Figure 1: SEM view of clay .

Clay minerals are widely utilized in many facets of our society (Murray HH., 2000). There are four main groups of clay minerals:

Kaolinite group - includes kaolinite, dickite, nacrite, and halloysite; formed by the decomposition of orthoclase feldspar (e.g. in granite); kaolin is the principal constituent in china clay.

Illite group- also includes hydrous micas, phengite, brammalite, celadonite, and glauconite (a green clay sand); formed by the decomposition of some micas and feldspars; predominant in marine clays and shales.

Vermiculite

Smectite group- also includes montmorillonite, bentonite, nontronite, hectorite, saponite and sauconite; formed by the alteration of mafic igneous rocks rich in Ca and Mg; weak linkage by cations (e.g. Na+, Ca++) results in high swelling/shrinking potential (De Paiva LB. et al., 2008).

Nanoclay can be obtained by simply the ion exchange reaction of hydrophilic clay with an organic cation such as an alkyl ammonium or phosphonium ion (Jahromi SG. et al.,2009).
Nano clay have the following minerals and these minerals and their modified forms can be effectively used in modify drug delivery systems (Viseras C. et al., 2010).

1. **Montmorillonite**
   Montmorillonite consists of ~ 1 nm thick aluminosilicate layers surface-substituted with metal cations and stacked in ~ 10 μm-sized multilayer stacks. Depending on surface modification of the clay layers, montmorillonite can be dispersed in a polymer matrix to form polymer-clay nanocomposite. Within the nanocomposite individual nm-thick clay layers become fully separated to form plate-like nanoparticles with very high (nm × μm) aspect ratio. Sigma-Aldrich, in collaboration with the Nanocor Corporation, offers a range of montmorillonite nanoclay products with different organic modifications optimized to be compatible with various polymer systems (He H. et al., 2009).

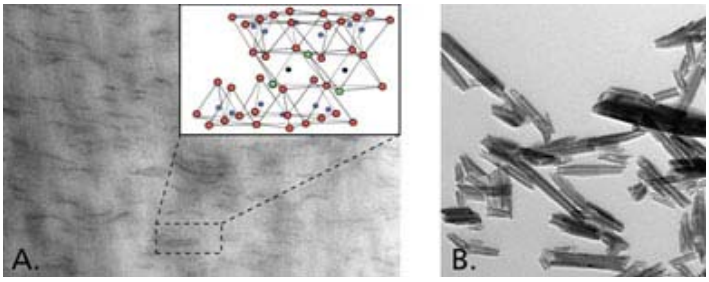

Figure 2: A. TEM micrograph of nylon-clay nanocomposite showing nm-thick platelets of montmorillonite clay fully dispersed in the polymer matrix. Inset shows schematic of montmorillonite aluminosilicate layer structure.
B. TEM micrograph of halloysite clay nanotubes.

Montmorillonite exists as nanoscale particles which are agglomerated due to surface attraction of one particle to another. When the attractive force is minimized using surface treatment, each particle can disperse to its naturally occurring nanoscale size.

Surface treatment

Montmorillonite particles are agglomerated to within a distance of about 3.5 Å. Surface treatment reduces particle-particle attraction, promoting an expansion of the distance to above 20 Å. At this distance the particles can be seprated further either by absorbing monomer into the gallery prior to polymerization or in the case of high polymer employing shearing force using an extrusion compounder.Depicts the case where dispersion occurs in the compounding operation. Complete dispersion is called "exfoliation." When Nanomers are exfoliated in a resin matrix, the result is nanocomposite (He H. et al., 2009).

2. **Hydrotalcite**
   Halloysite is a naturally occurring aluminosilicate nanotube. The two-layer halloysite tubes are chemically similar to kaoline and have average dimensions of 15 × 1000 nm comparable to carbon nanotubes. Halloysite tubes are hollow and can be used for controlled delivery and release of drugs as well as nanocomposite and rheology modification applications (De Paiva LB. et al., 2008).
3. **Octasilicate**
4. **Mica fluoride**
   In its fluride (0.4N NH_4F, 0.1N HCL, N HCl), Dioctahedral mica and Dioctahedral vermiculite minerals are present (Rich CI. et al. 1991).

Table 1: Nanoclays Properties (Jahromi SG. et al.,2009).

Treatment/Properties		Cloisite-15A	Nanofill-15
Organic Modifier		MT2ETOH(Methyl, tallow, bis-2-hydroxyethyl, quaternary ammonium)	Nanodisperse layered silicate longchain hydrocarbon
Base		Montmorillonite	Montmorillonite
Moisture		<2%	<3%
Weight Loss On Ignition		43%	35%
Anion		Chloride	Ammonium Chloride
Particle Size	Less than 10%	2µm	5 µm
	Less than 50%	6 µm	15 µm
	Less than 90%	13 µm	25 µm
Colour		Off white	Cream
Density, gm/cc		1.66	1.88
Plastic Index		88%	85%

Nano-clay(Layered Sillcate) and polymer intrection

Nano-clay particles enhance the polymer performance by the intraction to polymer. The interaction between layered silicates and polymers may produce two types of nanoscale composites (Figure 2), namely: intercalated nanocomposites, which result from penetration of polymer chains into the interlayer region of the clay, producing an ordered multilayer structure with alternating polymer/inorganic layers the clay layers delaminated and randomly dispersed in the polymer matrix (Hitzky RE. et al.,2006), (Okamoto M.,2009) and by the intrection of clay and polymer various properties are encanced. Ex. polysiloxane nanocomposites produced from poly(dimethylsiloxane) and organoclay mixtures have improved in tensile properties, thermal stability and resistance to swelling solvents (LeBaron PC. et al., 1999), (Gilman JW., 1999).

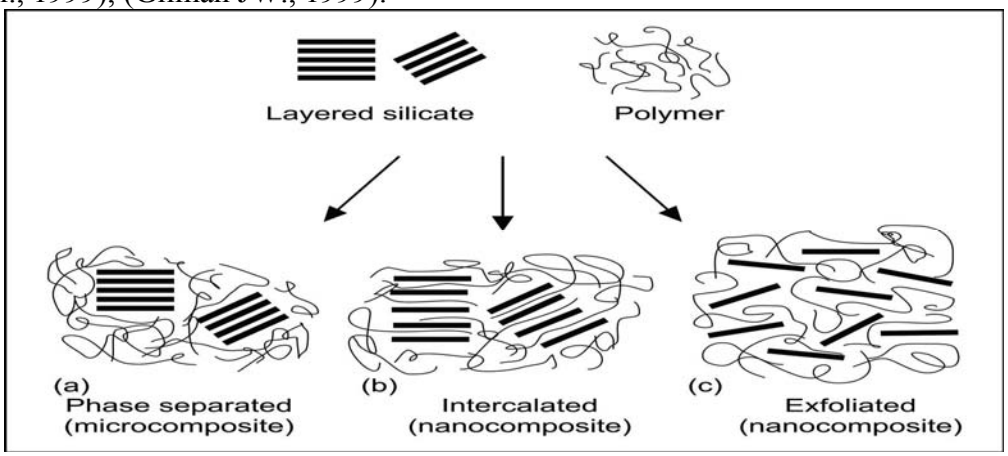

Figure 3: Types of composites from polymer-clay interactions (Bhat G. et al.,2008).

Mechanisms of clay – drug interactions

Clay minerals are naturally occurring inorganic cationic exchangers and so they may undergo ion exchange with basic drugs in solution. Smectites, especially montmorillonite and saponite, have been the more commonly studied because of their higher cation exchange capacity compared to other pharmaceutical silicates (such as talc, kaolin and fibrous clay minerals) Nevertheless; there are several mechanisms that may be involved in the interaction between clay minerals and organic molecules (Suresh R. et al.,2010).

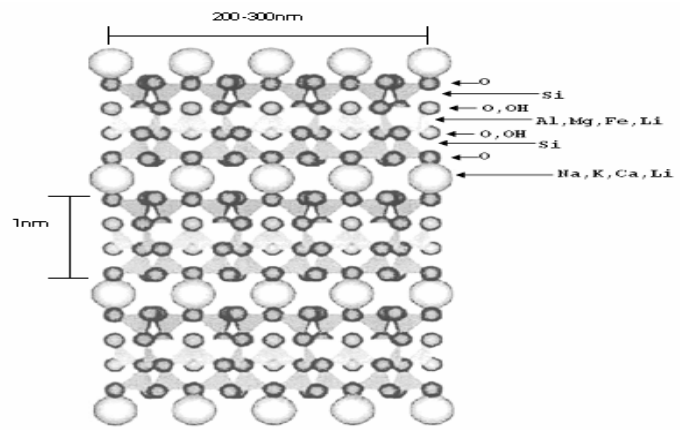

Figure 4: The structure of 2: 1 layered silicates treatment (Aguzzi C. et al. 2006).

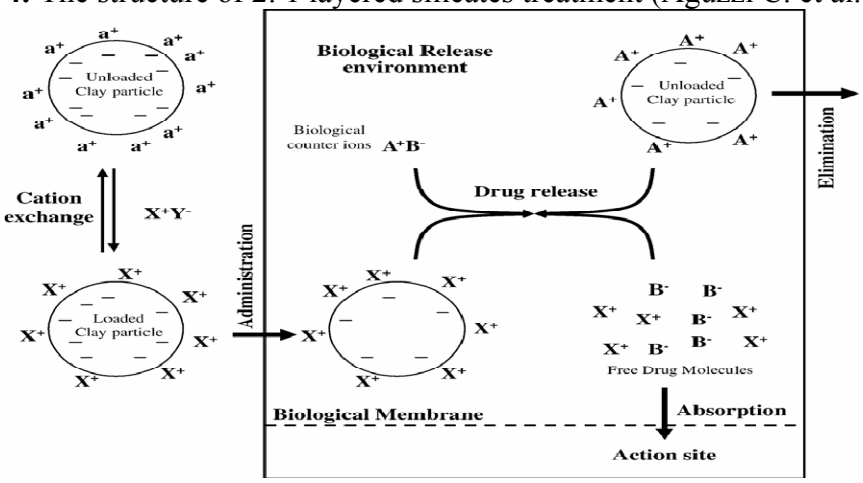

Figure 5: Idealization of clay–drug complexation and in vivo drug release mechanisms. {clay mineral surface charge (−); compensating cations (a+); cationic drug (X+); drug associated anions (Y−); in vivo counter ions (A+); anions associated with the counter ions (B−)} (Aguzzi C. et al. 2006).

Table 2: Interactions between clay minerals and organic compounds (Suresh R. et al.,2010).

Mechanism	Mineral examples	Organic functional groups involved
Hydrophobic interaction (vander Waals)	Any clay with neutral sites (e.g., kaolinite, smectites)	Uncharged, non polar (e.g. aromatic, alkyl C)
Hydrogen bonding	Any clay with oxygen surfaces (e.g.kaolinite)	Amines, carbonyl, carboxyl, phenyhydroxyl, heterocycle N)
Protonation	Aluminosilicate edge sites, Fe and Al ,oxides, allophane, imogolite	Amines, heterocycle N, Carbonyl, Carboxylate
Ligand exchange	Aluminosilicate edge sites, Fe and Al ,oxides, allophane, imogolite Smectite, vermiculite, illite	Carboxylate, Phenolate
Cation exchange (permanent charge sites)	Aluminosilicate edge sites, Fe and Al, oxides, allophane, imogolite	Amines, ring NH, heterocyclic- N
PH Dependent charge sites (Anion exchange usually, cation exchange rarely)	Smectite, vermiculite, illite	Carboxylate for anion exchange, amines, ring NH, heterocyclic N for cation exchange.
Cation bridging		Carboxylate, amines, Carbonyl,
Water bridging		Alcoholic – OH

Preparation of clay–drug complexe

Clay particles are dispersed in aqueous drug solutions, dispersions are allowed to equilibrate for a suitable time, and finally solid phases are recovered and dried.

- To "entrap" bioactive molecules by inducing coagulation in nanoclay dispersions.
- Dry method (specifically helpful for poorly soluble molecules) was also reported, consisting in grinding the clay and the drug together or putting them in contact at the melting temperature of the drug (Suresh R. et al.,2010).

Clays and their modification

Clays are naturally occurring minerals with variability in their constitution depending on their groups and sources. The clays used for the preparation of nanoclays belong to smectite group clays which are also known as 2 :1 phyllosilicates, the most common of which are montmorillonite {Si4[Al1×67Mg0×33]O10(OH)2×*n*H2O×X0×33 = Na, K or Ca} and hectorite {Si4[Mg2×7Li0×3]O10(OH)2×X0×4 = Na}, where octahedral site is isomorphically substituted. Other smectite group clays are beidillite {[Si3×67Al0×33]Al2 O10(OH)2×*n*H2O× X0×33 = Na, K or Ca}, nontronite {[Si3×67Al0×33]Fe2O10(OH)2× X0×33 = Na, K or Ca} and saponite {[Si3×67Al0×33] Mg3O10(OH)2×X0×33 = Na, K or Ca} in which tetrahedral site is isomorphically substituted. Crystal lattice of smectite group clay consists of a two-dimensional, 1 nm thick layers which are made up of two tetrahedral sheets of silica (SiO2) fused to an edge-shaped octahedral sheet of alumina. The lateral dimensions of these layers vary from 30 nm to several microns depending on the particular silicate. Stacking of the layers leads to a regular Van der Waals gap between them called the interlayer or gallery. Isomorphic substitution within the layer by Mg2+, Fe3+/Fe2+ or Al3+ generates negative charges that are normally counterbalanced by hydrated alkali or alkaline earth cations (Na+, K+, Ca+, etc) residing in the interlayer as shown in schematic 1. Because of the relatively weak forces existing between the layers (due to the layered structure), intercalation of various molecules, and even polymer, is facile (Mousty C., 2004).

The clay platelets are truly nano-particulate. In the context of nanocomposites, it is important to note that the molecular weight of the platelets (*ca.* 1×3 ´ 108 Dalton) is considerably greater than that of typical commercial polymers, a feature which is often misrepresented in schematic diagrams of clay-based nanocomposites. In addition, platelets are not totally rigid, but have a degree of flexibility. The clays often have very high surface areas, up to hundreds of m2/g of clay. The clays are also characterized by their cation exchange capacities, which can vary widely and depends on source and type of clay. The purity of the clay can affect the final nanocomposite properties; due to this it is very important to have montmorillonite with minimum impurities of crystalline silica (quartz), amorphous silica, calcite, kaolin etc. The technique mainly used for purification of clays includes hydrocyclone, centrifugation, sedimentation method and chemical treatment. Clays are inexpensive materials, which can be modified by ion exchange, metal/ metal complex impregnation, pillaring and acid treatment to develop catalysts with desired functionality (Patel HA. et al., 2005), (Liu P., 2007).

Particulate delivery systems based on clay minerals

Microparticles recently patented modulated release microparticulates for administration of macromolecules into lungs, containing silicates (e.g., amorphous silica, bentonite, attapulgite, kaolin and talc) as the encapsulating agents both for protecting the active substance and modulating release into the body. Pharmaceutical nanoparticles are often made of organic polymers (biodegradable or not) but inorganic systems are receiving much attention in the pharmaceutical field. In particular, clay minerals can provide spontaneous submicron dispersions in aqueous media, resulting in low cost and biocompatible systems with large surface area and high inclusion capacity. Polymer/clay nanocomposites are a new class of hybrid systems in which inorganic or organo-clay nanoparticles (often montmorillonites) are

dispersed in a polymer matrix. They have some interesting advantages compared to the pure polymer, such as enhanced mechanical and rheological properties. These benefits along with the good intercalation capacity offered by the clay mineral particles have been used to develop new controlled release systems, as documented by a number of patents. Polymer/layered silicate nanocomposites have attracted great interest, both in industry and in academia, because they often exhibit remarkable improvement in materials properties at very low clay content (3–6 wt %), when compared with virgin polymer or conventional composites. Three methods have been developed to produce polymer/ layered silicate nanocomposites: in situ polymerization in which a polymer precursor or monomer are inserted in between clay layers and then expanding the layered silicate platelets into the matrix by polymerization. This method has the advantage of producing well-exfoliated nanocomposites and have been applied to a wide range of polymeric systems; solution-induced intercalation method involves solvents to swell and disperse clays into a polymer solution and melt processing method applies intercalation and exfoliation of layered silicates in polymeric matrices during melt In addition to these three major processing methods, other fabrication techniques have also been developed. These include solid intercalation covulcanization and the sol–gel method. The structure of polymer/layered silicates composites has typically been established using wide angle X-ray diffraction analysis and transmission electron micrographic observation (Suresh R. et al.,2010) (Choy JH. et al., 2007).

Nano-clay as drug vehicle

The continuous development of new controlled drug delivery systems is driven by the need to maximize therapeutic activity while minimizing negative side effects. One class of drug delivery vehicle that has received more attention in recent years is layered materials which can accommodate polar organic compounds between their layers and form a variety of intercalated compounds. Because the release of drugs in drug-intercalated layered materials is potentially controllable, these new materials have a great potential as a delivery host in the pharmaceutical field. Calcium montmorillonite has also been used extensively in the treatment of pain, open wounds, colitis, diarrhea, hemorrhoids, stomach ulcers, intestinal problems, acne, anemia, and a variety of other health issues. Not only does montmorillonite cure minor problems such as diarrhea and constipation through local application, it also acts on all organs as well (Vaia et al., 1996).

Yuancai and Si-Shen described the novel poly (D,L-lactide-co glycolide) /montmorillonite nanoparticle drug delivery system, formulating the drug carrier from a material, which can also have therapeutic effects, either synergistic with or capable to mediate the side effects of the encapsulated drug. Paclitaxel (anticancer drug)-loaded poly (D,L-lactide-co-glycolide)/montmorillonite nanoparticles were prepared by the emulsion /solvent evaporation method and was tested for *in vitro* drug release. The initial burst of 22% on the first day can be observed for sample. After that, the release of paclitaxel was at a slow constant rate. In three weeks, about 36% drug was released with a slightly reduced initial burst and speed release. The adsorption and desorption of organic molecules and surfactants on layered silicates indicates that these materials can be used for drug delivery. The release of buformin from buformin/ montmorillonite complex and pure buformin hydrochloride in artificial intestinal juice over 360 min. Buformin/montmorillonite complex released 70% of buformin with lower rate as compared to pure compound in 360 min. Medical devices such as a drug delivery patch, implantable or insertable medical device comprise of polymer carrier (as matrix) and drug intercalated layered silicates (as reinforcement) provides controlled release of therapeutic agent to damaged cell of a patient. In addition to surface unmodified and modified montmorillonite, layered double hydroxides are also used as drug carrier in

various applications. Intercalation of fenbufen in a layered double hydroxide followed by coating with Eudragit® S 100 gives a composite material which shows controlled release of the drug under *in vitro* conditions which model the passage of a material through the gastrointestinal tract . Intercalations of anti-inflammatory drug in layered double hydroxide have the advantage of gradual release over a longer period of time . Gene therapy is gaining growing attention for the treatment of genetic deficiencies and life-threatening diseases. For the efficient introduction of foreign DNA into cells, a carrier system is required. Recently, it has been successfully demonstrated that novel layered double hydroxide could form a nanohybrid by intercalating with bimolecular anion such as mononucleotides, DNA which shows that antisense oligonucleotide molecules packaged in the layered double hydroxide can enter cells, presumably through phagocytosis or endocytosis. The leukemia cells were used to explore the layered double hydroxide's potential as gene carriers (Carretero MI. et al. 2002), (Patel HA. et al., 2005).

Clay miner also used to improve drug dissolution rate

Improving dissolution of poorly water-soluble drugs remains one of the more important challenges for pharmaceutical technologists. Among the several approaches applied the surface adsorption of drug is one interesting approach. Molecules onto finely divided solids greatly increase the surface area available to the dissolution medium. Smectites were found to effectively enhance the in vitro dissolution rate of nonionic and acidic insoluble drugs. Drug release from the clay surface is promoted by the weak bonding between them and concomitantly drug wettability is enhanced due to the hydrophilic properties of the clay. Phenytoinmontmorillonite adsorbates were able to improve the bioavailability of the drug in humans in comparison with phenytoin sodium capsules (Ruskin R. et al.,2004) (Lopez A. et al., 2007).

Conclusion

Significant progress in the development of clay nocomposites has been made over the past fifteen years. The advantage and limitations of these technology have become clear. The Nano-clay drug delivery system holds a bright future in various pharmaceutical applications and diagnostic in the coming years as they have unique features. Nano-Clay have the great potential as compared to polymers and other nanotechnological drug delivery system like dendrimer, carbon nano tube, liposomes and neosomes etc. for drug delivery applications.

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