Smectite Clays for Solid Dosage Forms

Smectite clays have a long history of use as excipients in pharmaceutical formulations. In liquids, they are used primarily as suspension stabilizers and emulsion stabilizers. In ointments and suppositories they are used to control drug release. In solid dosage forms they are traditionally used as binders and disintegrants for wet granulations and, in micronized form, for direct compression tablets. Smectite clays are also used in solid dosage forms as components of drug delivery systems, an application of increasing interest because these entirely natural excipients provide a unique combination of physicochemical properties for drug-clay interaction, including cation exchange, anion exchange, hydrogen bonding, high surface area and intercalation.

SMECTITE CLAYS FOR PHARMACEUTICALS

Smectite is the mineralogical term for a group of trilayer clays which include the commercially significant varieties montmorillonite, hectorite and saponite. At one time this group was referred to generically as montmorillonite clay. The group name was changed to smectite clay to avoid confusion with the mineralogically distinct montmorillonite member, but the generic use of the term montmorillonite has persisted among some researchers in the pharmaceutical industry. Smectites are also, by tradition, referred to by the geological term bentonite. Bentonite is an ore or product with substantial smectite content, most often the mineral montmorillonite.

In the United States, pharmaceutical grade smectite clays must conform to the specifications of one of three National Formulary monographs:

Magnesium Aluminum Silicate NF – combinations of montmorillonite and saponite that are purified by water-washing processes and controlled for viscosity, pH, acid demand, moisture, heavy metals and microbiological content.

Purified Bentonite NF – montmorillonite that is purified by water-washing processes and controlled for viscosity, pH, acid demand, moisture, heavy metals and microbiological content.

Bentonite NF – montmorillonite that is milled ore or that is purified by water-washing processes and controlled for gel formation, swelling power, pH, moisture, +200 mesh grit, heavy metals and microbiological content.

R.T. Vanderbilt Company offers several **VEEGUM®** Magnesium Aluminum Silicate water-purified natural clay products that conform to compendial requirements and have a long history of use as excipients:

	Compendia	Mineralogy	Form
VEEGUM	Magnesium Aluminum Silicate NF, Type IA Aluminium Magnesium Silicate EP	montmorillonite + saponite	fine granules
VEEGUM F	Magnesium Aluminum Silicate NF, Type IB Aluminium Magnesium Silicate EP	montmorillonite + saponite	micronized powder
VEEGUM HV	Magnesium Aluminum Silicate NF, Type IC Aluminium Magnesium Silicate EP	montmorillonite + saponite	fine granules
VEEGUM K	Magnesium Aluminum Silicate NF, Type IIA Aluminium Magnesium Silicate EP	montmorillonite + saponite	fine granules
VEEGUM HS	Purified Bentonite NF	montmorillonite	fine granules

SMECTITE CLAY PHYSICOCHEMICAL PROPERTIES

Smectite clays have characteristic layered structures, as a result of which individual crystals have a flake or platelet shape. They contain a continuous alumina or magnesia octahedral layer that is bound on both sides by a continuous silica layer. The silica layer is composed of tetrahedra with three shared oxygens, forming linked rings with hexagonal openings. When the predominant octahedral cation is Al^{3+}, as in the aluminum silicate montmorillonite, charge balancing within the clay lattice requires that only two of every three octahedral positions be filled, and the clay is described as dioctahedral. If Mg^{2+} predominates, as in the magnesium silicates saponite and hectorite, all octahedral positions must be filled, and the clay is called trioctahedral. A single smectite clay platelet is 0.96 nanometer thick and up to several hundred nanometers across.

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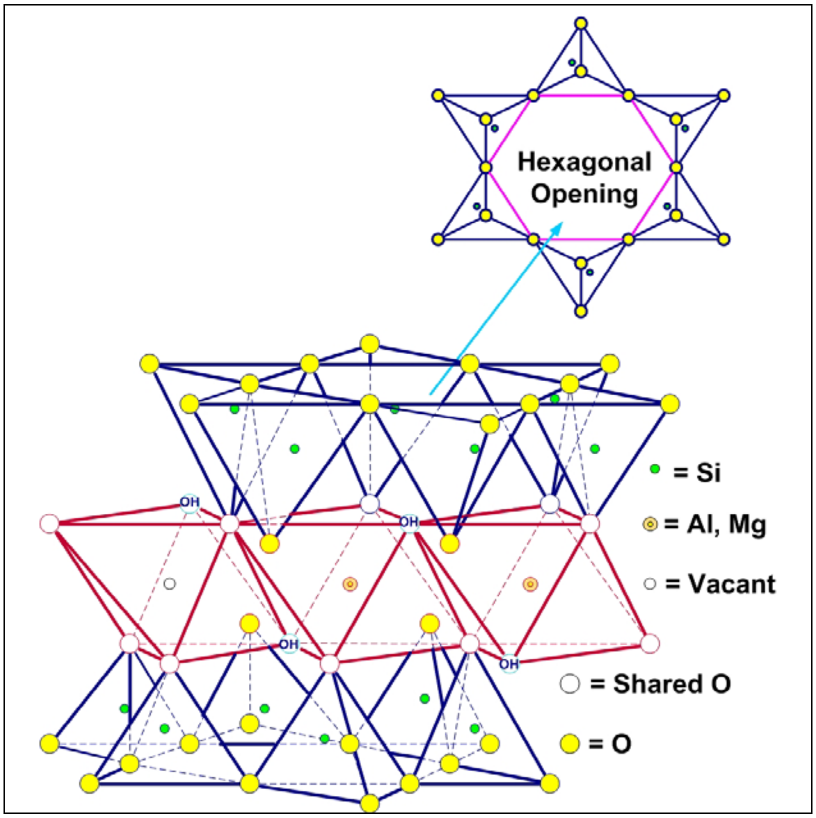
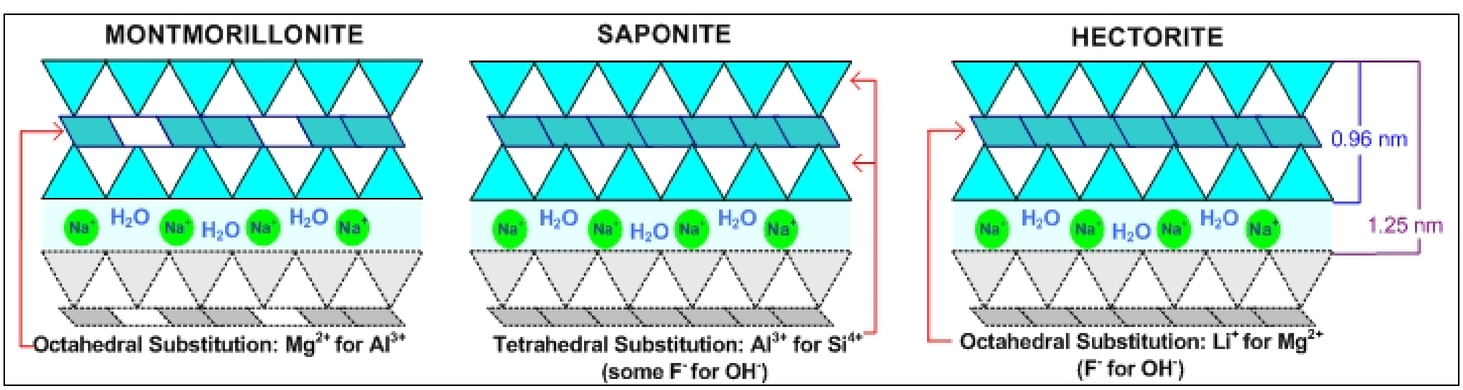
The smectite clays are characterized by metal ion substitutions within their lattice structures, so that they are electrically unbalanced. Substitutions within the crystal lattice result in negatively charged platelet faces. Lattice discontinuities account for a very slight positive charge on platelet edges. The net platelet charge is negative.



Lattice structure of montmorillonite, a dioctahedral smectite

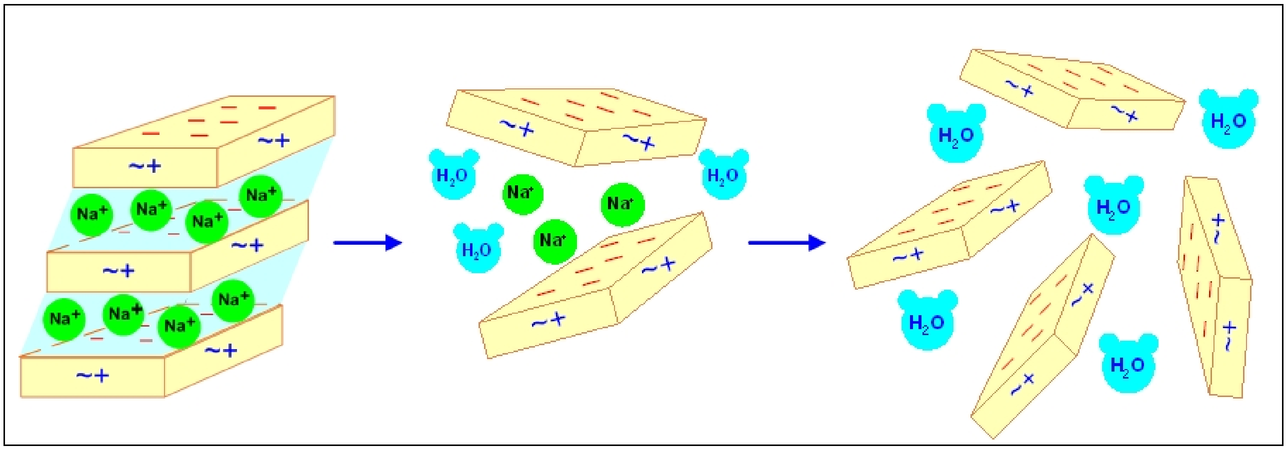
Montmorillonite is characterized by the substitution of a limited number of octahedral Al^{3+} with Mg^{2+}, which accounts for its negative charge. In pharmaceutical grade products, this is naturally balanced by Na^+ between the clay platelets, partially sunk in the hexagonal openings of the silica layer. Because the sodium ions are not structural they can be easily replaced by other positively charged atoms or molecules, and are called exchangeable cations. In addition to the charge balancing cations, a tightly held layer of oriented water, about 0.29 nanometers thick, occupies the space between individual flakes. This water requires temperatures well in excess of 100°C for removal. A macroscopic montmorillonite particle is composed of thousands of these sandwiched platelets with exchangeable cations and a layer of water between each.

The trioctahedral analogues of montmorillonite are saponite and hectorite. Saponite has limited substitution of tetrahedral Si^{4+} by Al^{3+}, while hectorite has limited substitution of octahedral Mg^{2+} by Li^+ and OH^- by F^-. As with montmorillonite, the resulting charge imbalance is naturally compensated for by exchangeable Na^+.



Primary lattice substitutions in smectite clays

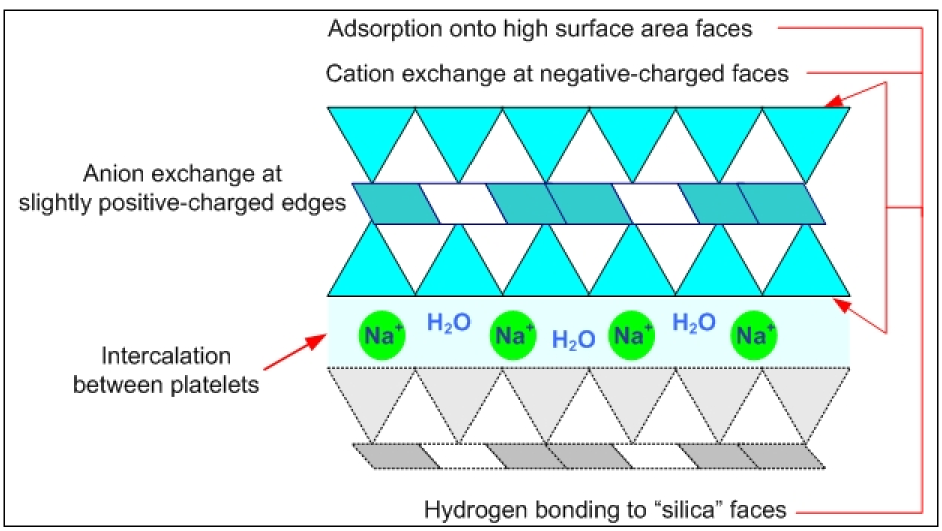
The binding effect of inter-platelet water and counterions makes mechanical delamination of smectite clays very difficult, but swelling by intercalation with polar liquids and solutions is quite easy. Likewise, in cases where the full surface area of the clay needs to be exposed and/or its rheological properties exploited, hydraulic delamination is relatively simple. When clay and water are mixed, water penetrates between the platelets, forcing them further apart. The cations begin to diffuse away from platelet faces. Diffusion (the movement of cations from between platelets out into the water) and osmosis (the movement of water into the space between platelets) then promote delamination until the platelets are completely separated.



Hydraulic delamination of smectite clay

The structure of smectite clays allows for several routes to drug-clay interaction or complexation:

- Cation exchange with cationic drugs. This produces a relatively strong drug-clay bond on platelet faces that is suitable, for example, to extend drug release.
- Weak anion exchange of anionic drugs at platelet edges.
- Hydrogen bonding at platelet faces.
- Intercalation between un-delaminated platelets, which may also involve cation exchange.
- Adsorption by solvent deposition onto the high surface area of the clay to increase the dissolution rate of poorly soluble drugs.



Drug-clay interactions

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