Clay and non-clay minerals in the pharmaceutical industry
Part I. Excipients and medical applications

M. Isabel Carretero a,*, Manuel Pozo b

Abstract

Minerals are widely used in the pharmaceutical industry as lubricants, desiccants, disintegrants, diluents, binders, pigments and opacifiers, as well as emulsifying, thickening, isotonic agents, and anticaking agents, and flavour correctors and carriers of active ingredients.

A variety of minerals are used as excipients in pharmaceutical preparations because they have certain desirable physical and physico-chemical properties, such as high adsorption capacity, specific surface area, swelling capacity, and reactivity to acids. Other important properties are water solubility and dispersivity, hygroscopicity, unctuosity, thixotropy, slightly alkaline reaction (pH), plasticity, opacity, and colour. Clearly such minerals must not be toxic to humans. The following minerals are commonly used as excipients: oxides (rutile, zincite, periclase, hematite, maghemite, magnetite), hydroxides (goethite), carbonates (calcite, magnesite), sulfates (gypsum, anhydrite), chlorides (halite, sylvite), phosphates (hydroxyapatite), and phyllosilicates (palgorysite, sepiolite, kaolinite, talc, montmorillonite, saponite and hectorite). More recently, some tectosilicates (zeolites) also feature in pharmaceutical preparations.

Minerals also enjoy the following medical/health applications: a) contrast diagnostic techniques, b) production of dental cements and dental molds in odontology, c) immobilization of limbs and fractures or dental and craniofacial surgical procedures in traumatology, d) bone grafts or construction of orbital implants, and e) spas and aesthetic centers. Examples of such minerals are oxides (zincite, magnemite and maghemite), sulphates (gypsum and barite), phosphates (hydroxyapatite) and phyllosilicates (clay minerals).

© 2009 Elsevier B.V. All rights reserved.

1. Introduction

Minerals are used in pharmaceutical preparations as either active ingredients (having therapeutic properties), or excipients. Whereas this paper deals with the use of minerals as excipients, a companion paper (next issue) reviews their use as active ingredients. Excipients are more or less inert minerals that determine the consistency, form, and volume of the pharmaceutical preparations. Some excipients have organoleptic properties (e.g., colour), induce liberation of the active ingredient within the organism, or facilitate the elaboration and conservation of the pharmaceutical preparation. Minerals also enjoy diagnostic, odontological, and traumatological applications, and are used in spas and aesthetic centers for therapeutic proposes (Fig. 1).

Although the market volume for pharmaceutical minerals is small, the added value is substantial, since the price of pharmaceutical grade minerals may be up to ten times that of the same minerals dedicated to other uses. This is because pharmaceutical minerals must meet the strict chemical, physical, and toxicological specifications set out in the European or United States Pharmacopoeia (López Galindo et al., 2007). Purification treatments, such as particle size fractionation, thermal treatment, and acid activation, improve the physical and physico-chemical properties of the minerals in question.

The majority of crystalline substances, used as either active ingredients or excipients, are synthetic analogues of the naturally occurring minerals (Carretero and Pozo; next issue). The few natural minerals that feature in pharmaceutical applications are there because they are abundant and inexpensive (e.g., calcite, halite, gypsum), or because their synthesis is complicated and costly (e.g., clay minerals).

The papers published until now related with minerals used in pharmaceutical industry show that besides being non-toxic to humans, some pharmaceutical minerals should have a high adsorption capacity, specific surface area, and swelling capacity as well as thixotropic and colloidal properties (Galan et al., 1985; Veniale, 1992; Bolger, 1995; Veniale, 1997; Carretero, 2002; Love, 2004; López Galindo and Viseras, 2004; Carretero et al., 2006; Droy-Lefaix and Tateo, 2006; Carretero and Pozo, 2007; Lefort et al., 2007; Viseras et al., 2007). No comprehensive review, however, is available on the all physical and physico-chemical properties of minerals that are used in the pharmaceutical industry.

The use of clay minerals and non-silicate minerals as excipients in pharmaceutical formulations has been described by many authors.
2. Physico-chemical and physical properties of minerals used in the pharmaceutical industry

The most important physico-chemical properties of minerals used in pharmaceutical industry are surface reactivity (adsorption, cation exchange, swelling), rheology, acid-absorbing capacity, and solubility (HCl, H_2O). Because of their small particle size, large specific surface area, and peculiar charge characteristics, clays and clay minerals have interesting surface properties. Fig. 2a shows the external specific surface areas of representative clay minerals, measured by adsorption of N_2 gas at 78 K, and applying the Brunauer–Emmett–Teller (BET) equation. Fig. 2b gives the total (external and interlayer space) specific surface areas of different clay minerals and metal (hydr)oxides, measured by adsorption of polar organic compounds.

Clay minerals exhibit ion exchange behavior, as do zeolites, colloidial metal (hydr)oxides, and natural organic matter (humic substances). The CEC values for a range of clay minerals are shown in Fig. 3.

The ability of smectites, notably Na^+–montmorillonite, to swell in water in two phases has been well documented (van Olphen, 1977; Madsen and Müller-Vonmoos, 1989).

The rheological properties (e.g., dispersion, swelling, viscosity) of minerals are important to many industrial and pharmaceutical applications, while the mechanical properties (e.g., plasticity) of clays determine their usefulness in health-related applications (e.g. peltotherapy).

The rheology of clay mineral dispersions has been reviewed by Güven and Pollastro (1992). Of special interest are the flow behaviour and stability of clay dispersions, and the time-dependent deformation of clays in a solid or semi-solid state. By dispersing clay mineral particles in water, the viscosity of the medium (water) is greatly increased. Thus, when excipients are prepared in a liquid or semi-solid form, both dispersing and anticaking agents are used to prevent drastic changes in dispersion properties.

Dilute smectite dispersions (smectite content <1% w/v) generally show Newtonian flow behaviour (Vali and Bachman, 1988; Lagaly, 2006). At concentrations >1% w/v, the flow behaviour of smectite dispersions becomes non-Newtonian, while the apparent viscosity increases exponentially with clay concentration. The flow of smectite dispersions is also influenced by the pH and ionic strength of the medium, as do the rate and mechanism of coagulation. Gelation represents an advanced stage of coagulation. Increasing time gels may regain their fluidity on applying mechanical stress (stirring or shearing). This process is known as thixotropy (Mewis, 1979). As the name suggests, ‘antithixotropy’ (rheopexy) is the reverse of thixotropy. A rheopexic dispersion shows a gradual rise in viscosity as time increases, and eventually transforms irreversibly into a gel state.
The viscosity and flow behaviour of smectite dispersions are of paramount importance to using this clay mineral in many industrial products, including pharmaceutical formulations. In reviewing the colloidal and rheological properties of bentonite (montmorillonite) suspensions, Luckham and Rossi (1999) have emphasized that layer silicate gels are sensitive to the addition of electrolytes. The influence of Fe$^{3+}$ ions on the colloidal behaviour of montmorillonite has been studied by Ma and Pierre (1999). They concluded that both Fe$^{3+}$ and its hydrolysis products, acting as counterions, could neutralise the electric double layer charge around the clay mineral particles, causing the suspension to coagulate. The effect of ion type and ionic strength on the sol–gel transition of Na–montmorillonite dispersions has been studied by Abend and Lagaly (2000).

According to Alvarez (1984), sepiolite is able to give stable suspensions of high viscosity at relatively low solid concentrations. Sepiolite suspensions show non-Newtonian flow behaviour. Under low shear stress conditions, the gel shows a rheopexic behaviour (increase of viscosity with time) but becomes thixotropic when the shear stress is increased. At high pH (>9) and ionic strength, sepiolite suspensions coagulate and show pseudoplastic flow behaviour. When dispersed in water, fibrous clay minerals (e.g., sepiolite) form a three-dimensional structure composed of interconnecting fibres (Simonton et al., 1988). The fibrous gels retain their stability in the presence of high concentrations of electrolytes, making them ideal for pharmaceutical applications (Eriksson et al., 1990). In assessing the effects of shear history on the rheology of lamellar and fibrous clay mineral dispersions, Viseras et al. (1999) found that the degree of dispersion and the structural changes resulting from differences in particle shape significantly affected rheological properties.

Clay bodies become plastic after taking up a certain amount of water (Grim, 1962). The difference between the Atterberg liquid and plastic limits is referred to as the plasticity index. Values for the plastic limit, liquid limit, and plasticity index for the main clay minerals are shown in Fig. 4a. The corresponding bivariate graph (liquid limit vs plasticity index) is given in Fig. 4b.

Calcium carbonates, notably calcite, and clay minerals have a high acid-absorbing capacity. The addition of HCl to calcite in a neutralization reaction gives rise to calcium chloride and releases CO$_2$. Clay minerals have the capacity to neutralise acidity by adsorbing H$^+$ ions from the external (acidic) medium.

Among the many physical properties of minerals, only the mechanical (hardness, plasticity), thermal (heat capacity, specific heat) and optical (colour, opacity, refractive index, reflectance) attributes are relevant for pharmaceutical purposes and will be described here. For more details about physical properties of minerals see Klein and Hurlbut (1993).

The heat capacity of a mineral is the amount of heat required to change its temperature by one degree. A more useful quantity is the specific heat (cp) which is the amount of heat required to change the temperature of one unit of mass by one degree. The relationship between cp and water content for a number of clay minerals is given in Fig. 5. Minerals that can take up water molecules into their interlayer spaces (montmorillonite, saponite) or channels (sepiolite) have a higher cp value than those that lack these structural features (Ferrand and Yvon, 1991; Legido et al., 2007). The thermal properties of minerals are especially important to their use as thermal muds and peloids in balneotherapy and pelotherapy (Cara et al., 2000; Veniale et al., 2004).

The astringency of some minerals is important in relation to their behaviour toward living organisms. Astringent substances can cause tissues to contract or shrink, and secretions to dry up. The activity of minerals is to coagulate superficial tissue layers into a crust.

Fig. 6 shows a diagram of the main physical and physico-chemical properties of clay and non-clay minerals.

### 3. Minerals as excipients in pharmaceutical preparations

Excipients are used in pharmaceutical preparations to: (a) enhance their organoleptic characteristics, such as flavour (flavour correctors) and colour (pigments); (b) improve their physico-chemical properties, such as viscosity of the active ingredient (emulsifying, thickening and anticausting agents); (c) facilitate their elaboration (lubricants, diluents, binders, isotonic agents) or conservation (desiccants, opacifiers), and (d) facilitate liberation of the active ingredient within the organism (disintegrants, carrier-releasers).

A wide range and variety of minerals are used as excipients in pharmaceutical preparations, including oxides (rutile, zincite, periclase, hematite, maghemite, magnetite), hydroxides (goethite), carbonates (calcite, magnesite), sulphates (gypsum, anhydrite), chlorides (halite, sylvite), phosphates (hydroxyapatite), phyllosilicates (smectites, palygorskite, sepiolite, kaolinite and talc) and recently
tectosilicates (zeolites). Within the smectite group, montmorillonite, saponite, and hectorite are the most widely used species (Table 1).

Besides being non-toxic to humans, the above-mentioned minerals have certain structural and physico-chemical properties that make them suitable for use as excipients, in pharmaceutical preparations: (1) high adsorption capacity and specific surface area for use as carriers and releasers of active ingredients and flavour correctors; (2) propensity to take up water and decompose in acid media, for use as disintegrants and desiccants; (3) uncoticusness for use as lubricants; (4) thixotropic and colloidal properties for use as emulsifying, thickening and anticaking agents; (5) slight alkaline reaction (pH) and plasticity for use as diluents and binders; (6) Solubility in water, giving solutions with an osmotic pressure similar to that of corporal liquids, for use as isotonic agents; and (7) opaqueness and colour for use as opacifiers and pigments (Table 2).

As pointed out by several investigators (Cornejo, 1990; Carretero, 2002; Aguzzi et al., 2007; and references therein), mineral excipients should be able to adsorb or absorb diverse organic compounds, or decompose the compounds when drug and mineral interact. This process has a determining influence on the bioavailability of the active (organic) ingredient. This interaction takes place during elaboration and storage of the pharmaceutical preparations containing mineral excipients. Sometimes this interaction also occurs in the patient’s gastrointestinal tract as in the case of simultaneous oral administration of several pharmaceutical preparations, although only some of them contain minerals. This possibility, however, must be kept in mind when doctors prescribe medications because of the potential risk to human health. Since the drug–excipient interaction affects bioavailability, the process should be studied prior to launching new pharmaceutical specialties, and also when their formulation is changed.

The influence of mineral excipients on bioavailability of the organic drug may be described in terms of stability and liberation. The effect of mineral excipients on drug stability is harmful or not desired. For example, montmorillonite induces the degradation of adsorbed digoxine, a cardiovascular tonic (Porubcan et al., 1979) and dexamethasone, an anti-inflammatory drug (Fortea et al., 1989). Similarly, hydrocortisone and dexametasonone are degraded when adsorbed to palygorskite and sepiolite (Cornejo et al., 1983; Fortea et al., 1988). Being basic, periclase and brucite can react with acidic compounds in the solid state to form salts, such as Mg(ibuprofen)$_2$, or cause the degradation of alkaline-labile drugs (Tugrul et al., 1989). Periclase can also have a negative impact on the solid-state chemical stability of drugs, such as diazepam (Jain and Kakkar, 1992a). Magnesite is incompatible with phenobarbital sodium (Peterson et al., 1993), diazepam solution at pH ≥ 5 (Jain and Kakkar, 1992b) and lansoprazole (Tabata et al., 1994), while calcium-rich minerals (calcite, gypsum or hydroxyapatite) interfere with the bioavailability of tetracycline antibiotics (Weiner and Bernstein, 1989). All calcium-rich minerals are also incompatible with indomethacin, aspirin, aspartame, ampicillin, cephalixin and erythromycin (Eerikäinen et al., 1991; Landin et al., 1994). Titanium dioxide, used as pigment, can catalyze the photolysis of certain active substances (drugs), such as famotidine (Kakinoki et al., 2004).

On the other hand, the effect of mineral excipients on drug liberation may be either beneficial or harmful, depending on the mineral–drug interaction, and whether or not this interaction is used for therapeutic purposes. Clay minerals generally have an influence on the liberation of antibiotics (e.g., amoxicilin, tetracyclines, erythromycin, ampicillin, cyclamycin), analgesics (e.g., paracetamol), anxiolytics (e.g., diazepam), amphetamines, solar protectors, and antihistamines (McGinity and Lach, 1977; Porubcan et al., 1978; Iwuagwu and Aloko, 1992; Ayarne and Sultana, 1993; Del Hoyo et al., 1998). Periclase and brucite, however, can adsorb various drugs such as antihistamines, antibiotics (especially tetracyclines), salicylates, atropine sulfate, hyoscymine hydrobromide, paracetamol, chloroquine (Khalil et al., 1976; Singh and Mital, 1979; Iwuagwu and Aloko, 1992), or form a complex with polymers (e.g., Eudragit RS) as a result of which drug liberation is retarded (Racz et al., 1996). Periclase and brucite can also reduce the bioavailability of some anticonvulsant (e.g., phenytoin) and antiarhythmic agents (Remon et al., 1983). Carbonates (e.g., magnesite) increase the dissolution of acetazolamide formulations at pH 1.12 (Hashim and El-Din, 1989) and modify the pharmacokinetics of halofantrine by increasing the time to reach maximum plasma concentration but reducing maximum plasma concentration (Aidelojoe et al., 1998).

The different roles that mineral excipients play in pharmaceutical preparations, are summarized below, with special emphasis on the physical and physico-chemical properties of the minerals.

### 3.1. Lubricants

In making tablets it is often necessary to add a lubricant to the pharmaceutical preparation in order to facilitate tablet elaboration. Talc is widely used as a lubricant because it is soft and unctuous. Being uncharged, the layers of this 2:1 type clay mineral are held together by weak van der Waals forces, allowing them to slide past each other. The
lubricating action of talc prevents adhesion of the powder to the compression pistons, facilitating preparation compaction and tablet formation.

### 3.2. Desiccants

Desiccants are used to keep pharmaceutical preparations dry, and assist their conservation. Desiccants also prevent disintegration or crumbling of both tablets and granules. Being hygroscopic, anhydrite and periclase are suitable desiccants for pharmaceutical preparations (Table 2), although anhydrite incorporation is not recommended for formulations that are administered orally.

### 3.3. Disintegrants

When pharmaceutical preparations are administered in the form of tablets, the active ingredient (drug) is liberated as the tablet disintegrates in the patient's stomach. Smectite, palygorskite, sepiolite, calcite, and magnesite are commonly used as disintegrants (Table 2). Smectite favours liberation of the active ingredient because its particles can swell in water and readily decompose in the acidic medium of the stomach (pH ~2). Palygorskite and sepiolite favour tablet disintegration because their fibres are dispersible in water, while calcite and magnesite disintegrate at pH ~2 releasing CO₂.

### 3.4. Diluents and binders

By diluting the concentration of the active organic ingredient, diluents facilitate administration of the drug to the patient at a milligram or milliliter dose.
A wide range of minerals (smectites, palygorskite, sepiolite, kaolinite, talc, gypsum, hydroxyapatite, periclase, calcite, magnesite) can be used as diluents in pharmaceutical preparations because they are non-toxic to humans, and are plastic when moist. Addition of a diluent or binder also facilitates the compaction of tablets and granules. Some mineral diluents and binders, such as periclase, calcite, and magnesite, are added to increase the pH in the stomach (Patel et al., 2003). Some lamellar (smectite) and fibrous (sepiolite) clay minerals are particularly useful as stabilisers because of their thixotropic properties (Viseras et al., 1999).

Smectites and kaolinite are also useful diluents for cosmetics. Similarly, palygorskite and sepiolite have been used as excipients in cosmetics. However, the use of these fibrous minerals in solid preparations has been called in question because of their possible carcinogenic effect when inhaled (Guthrie and Mossman, 1993; Wagner et al., 1998; Carretero et al., 2006).

3.5. Pigments and opacifiers

Pigments are used to improve the organoleptic properties of the medication. This applies to preparations with an unpleasant colour, and/or show chromatic heterogeneity, and hence is difficult to administer, especially by oral means. Pigments also give a distinctive appearance to pharmaceutical preparations. This is useful to patients who are on simultaneous multiple medications because they can identify a given preparation by its colour. Using different colours for different strengths of the same drug can also help eliminate errors. In addition, pigments offer opacity to preparations, and hence can contribute to their stability when the active ingredients are sensitive to sunlight. Pigments are mainly used in tablet coatings, hard/soft gelatin capsules, oral liquids, and topical creams or ointments.

Coloured minerals such as zincite, calcite, rutile, hematite, magnetite, maghemite and goethite are widely used as pigments (Table 2). Iron oxides may be yellow, red, brown, or black depending on particle size and shape, and the amount of combined water. White zincite is commonly used as a pigment, opacifier, and coating of tablets. Natural rutile is red, brown-reddish, or black. However, the synthetic analogue is white, and known as ‘colouring E172’ in the pharmaceutical industry. Because of its high refractive index (n = 2.70) synthetic rutile confers a high opacity to the product. This property is desirable for the preparation of sunscreen lotions (Carretero & Pozo, next issue). On the other hand, calcite is not often used as a pigment although it is a well-known opacifier.

3.6. Emulsifying, thickening, and anticaking agents

These agents are used in liquid pharmaceutical preparations for oral or topical administration in order to avoid segregation of the components, and prevent formation of a sediment that may be difficult to resuspend (syrups, suspensions, gels, etc.).

Because of their colloidal characteristics and thixotropic properties smectite palygorskite, sepiolite, kaolinite, and talc are widely used as emulsifying, thickening and anticaking agents. The rheological behaviour of kaolinite is strongly influenced by particle morphology and surface charge (Lagaly, 1989; Yuan and Murray, 1997). In the case of smectite, the particles can interact in an ‘edge-to-face’ and ‘face-to-face’ fashion to form a rigid system (van Olphen, 1977). In suspensions of palygorskite and sepiolite, the fibres can form a three-dimensional interconnected structure that is stable even in presence of high concentrations of electrolytes (Alvarez, 1984).

Halite and sylvite can also serve as emulsifying, thickening, and anticaking agents because the Na⁺ and K⁺ ions can control micelle size (McDonald and Richardson, 1981). By altering the ionic strength of the formulation, these minerals can also control the viscosity of polymer dispersions (Okor, 1993). For example, the addition of NaCl to aqueous spray-coating solutions of hydroxypropyl cellulose or hydropropelllose suppresses the agglomeration of crystalline cellulose particles (Yuasa et al., 1997).

3.7. Flavour correctors

These substances are used in pharmaceutical preparations to mask the unpleasant flavour or taste of certain active ingredients that must be administered orally. Because of their high adsorption capacity and large specific surface area, clay minerals as smectites, palygorskite and sepiolite are the principal minerals used as flavour correctors. Other minerals with lower adsorption properties (kaolinite and talc) are also used.

3.8. Isotonic agents

Liquid preparations of drugs must be isotonic with, and have the same osmotic pressure as, the intracellular fluid of the patient. A solution is isotonic with regard to a live cell when there is neither gain nor loss of water when the cell is in contact with the solution. The osmotic pressure of body fluids generally corresponds to a 0.9% w/v solution of sodium chloride. Thus, sodium chloride is used in a large variety of parenteral and non-parenteral pharmaceutical formulations to produce isotonic solutions. The high solubility of halite in water is an added advantage.

3.9. Carriers and releasers of active ingredients

The mineral–organic interaction can be used to control the release of active ingredients (drugs) with improved therapeutic properties. Here the minerals first serve as a carrier, and then as a releaser of the active ingredient (Cornejo, 1990; Aguzzi et al., 2007). Because of their large specific surface area and high adsorption capacity, smectites, palygorskite, sepiolite and zeolites are well suited to acting as drug carriers and releasers. Other clay minerals used are kaolinite and talc. The potential use of hydrotalcite and related minerals as carriers of anti-inflammatories, solar protectors, and drugs for cancer therapy has also been evaluated (Choy et al., 2007; Del Hoyo, 2007). Lin et al. (2002) have reported on the use of montmorillonite as a carrier of a drug (e.g., 5-fluorouracil) against colon cancer suitable for oral administration. These materials, however, have so far not been used in pharmaceutical preparations.

Pharmaceutical preparations, using minerals as carrier-releasers of active ingredients, can generally be administered orally to the patient. However some drugs (antibiotics, analgesics, and antiinflammatories) adsorbed on clay minerals phyllosilicates (e.g., talc, kaolinite) are applied topically (e.g., to the skin). For example, natural zeolites (clinoptilolite) are used successfully as carriers-releasers of zinc and erythromycin for topical application against acne (Cerri et al., 2004; Bonferoni et al., 2007).

4. Minerals for other medical uses

Besides serving as active ingredients (drugs) (Carretero & Pozo, next issue) or excipients, a number of oxides (zincite, magnetite, maghemite), sulphates (gypsum, barite), phosphates (hydroxyapatite), and phyllosilicates (clay minerals) have been used for other medical applications (Table 3).

Zincite, for example, is used in odontology for the production of dental cements. When mixed with phosphoric acid, zincite forms a hard material (composed mainly of zinc phosphate) suitable for use as a temporary dental filling agent (with addition of clove oil or eugenol). It should be borne in mind, however, that zincite may accelerate the growth of Aspergillus fumigatus, causing aspergillosis to develop in the jaw bone of some patients.

Besides serving as pigments in pharmaceutical preparations, magnetite and maghemite nanoparticles are used in contrast diagnostic techniques because of their magnetic properties.
<table>
<thead>
<tr>
<th>Mineral</th>
<th>Chemical formula</th>
<th>Physical and physico-chemical properties</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxides</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zincite</td>
<td>ZnO</td>
<td>Mixed with phosphoric acid it forms a hard material composed mainly of zinc phosphate. Production of dental cements, and in dental and craniofacial surgical procedures.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Magnetic properties</td>
<td>Contrast diagnostic techniques, and in gastro-intestinal tract.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Radial contrast in examining the gastrointestinal tract.</td>
<td>Bone grafts and orbital implants, Rheological properties.</td>
</tr>
<tr>
<td>Sulfates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barite</td>
<td>BaSO_4</td>
<td>High specific weight (4.49)</td>
<td>Insoluble in acids. Radiological contrast in examining the gastrointestinal tract. Barite is insoluble in acid media (e.g., the stomach) and is opaque to X-rays due to its great density (specific weight 4.49). As such, barite is used as a radiological contrast in examining the gastrointestinal tract. In this application the mineral should be free of carbonates, sulphides, and other barium compounds that are acid-soluble since the barium ion is very toxic. For the same reason, it should also be free of arsenic and heavy metals. Barite is used in forming moulds in dental and craniofacial procedures.</td>
</tr>
<tr>
<td>Saponite</td>
<td>MgAl_2(Si_3O_10)(OH)_2</td>
<td>High capacity for water sorption, cation exchange and heat-retention</td>
<td>High capacity for water sorption, cation exchange and heat-retention. Barite is used in forming moulds in dental and craniofacial procedures.</td>
</tr>
<tr>
<td>Montmorillonite</td>
<td>Al_2(Si_3Al_1)(OH)_8</td>
<td>High capacity for water sorption, cation exchange and heat-retention</td>
<td>High capacity for water sorption, cation exchange and heat-retention. Barite is used in forming moulds in dental and craniofacial procedures.</td>
</tr>
</tbody>
</table>

**Table 3**

Gypsum is used as plaster of Paris for the immobilization of limbs and fractures in traumatology, for the manufacture of dental molds in odontology, and in dental and craniofacial surgical procedures (Cho et al., 2002). To obtain plaster of Paris, gypsum is milled and then heated until 75% of the water has been eliminated. When the resultant bassanite (CaSO_4·1/2 H_2O) is mixed with water, it solidifies and hardens as it slowly takes up moisture.

Barite is insoluble in acid media (e.g., the stomach) and is opaque to X-rays due to its great density (specific weight 4.49). As such, barite is used as a radiological contrast in examining the gastrointestinal tract. In this application the mineral should be free of carbonates, sulphides, and other barium compounds that are acid-soluble since the barium ion is very toxic. For the same reason, it should also be free of arsenic and heavy metals.

Hydroxyapatite is used in bone grafts because it is similar to the apatite in bones. Hydroxyapatite, derived from marine corals, is also used in constructing orbital implants for use following surgical removal of the eye. Problems associated with its use as orbital implants have been described by Shields et al. (1994).

Talc is used as an esclerosant for the recognition of pleural spills and spontaneous and recurrent pneumothorax, that is, the presence of air or gas in the pleural cavity. The mineral is normally injected into the pleural cavity as a dilute suspension by means of an intercostal tube, or by thoracoscopy. Common secondary effects associated with using talc in this fashion, are pain and fever. At times local infection, emphysema, cardiovascular complications, and breathing failure can take place.

A number of clays (bentonite, kaolin, illite–smectite) are used in spas and aesthetic centers for therapeutic purposes on the basis of their softness, small particle size, rheological properties, and their high capacity for water adsorption, cation exchange and heat-retention (Veniale, 1996; Cara et al., 2000; Veniale et al., 2004; Carretero et al., 2006; Veniale et al., 2007; Carretero and Pozo, 2007). The clays are used after mixing with either natural or mineromedicinal water (geo-therapy), after ‘maturation’ with mineromedicinal water (pelo-therapy), or after mixing with paraffin (paramuds). The topical application of hot clays in the form of poultices is commonly practised in spas and aesthetic centers with therapeutic and cosmetic purposes.

**Acknowledgements**

We are grateful to Dr. Benny Theng for his detailed review of this manuscript, improving it by means of several comments, suggestions and advices. This work was funded by the Research Group RNM-349 of the Andalusia Board.

**References**


