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Clay minerals and their beneficial effects upon human health. A review

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Abstract

This work examines the beneficial effects for human health of clay minerals, describing their use in pharmaceutical formulations, spas and aesthetic medicine. Their therapeutic action as active principles in pharmaceutical formulations orally administered (gastrointestinal protectors, laxatives, antidiarrhoeaics) or for topical applications (dermatological protectors and cosmetics) is described. Their use as excipients and their influence in the bioavailability of the organic active principle is also described, both in the liberation process and in its possible degradation effect. Among their uses in spas, clay minerals therapeutic activity, in geotherapy, pelotherapy and paramuds is commented upon. Moreover, the applications of the clay minerals in aesthetic medicine (to clean and moisturise the skin and to combat compact lipodystrophies, acne and cellulite) are also described. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

The use of minerals for medicinal purposes is almost as old as mankind itself. Minerals have been used for curative ends since Prehistory. There are indications that *Homo Erectus* and *H. Neanderthalensis* used ochres mixed with water and different types of muds in order to cure wounds, soothe irritations, as a method of cleansing the skin, etc. This might have been due to their mimicking animals, many of which instinctively use minerals for the above purposes. The use of medicinal earths in Mesopotamia and Ancient Egypt has also been proven. The use of Nubian earth as an anti-inflammatory or the use of mud materials for mummification of cadavers can be cited as examples (Bech, 1987; Robertson, 1996; Veniale, 1997). In the Ancient Greek period, mud materials (Lemnos Earth) were used as antiseptic cataplasms to cure skin afflictions, as cicatrisers or as a cure for snake bites. Both Hippocrates and Aristotle, among others, produced classifications of medicinal earths. Most of these materials are clays, given different names depending on their origins or on the differences in their mineralogical composition and properties. For example, *Terra Samia*, *T. Sigillata*, *T. Lemnia*, *T. Cimolia*, *T. Sonóptica*, *T. Eretria*, *T. Negra*, etc. (Bech, 1996; Giammatteo et al., 1997). Furthermore, Cleopatra, Queen of Egypt, used muds from the Dead Sea for cosmetic purposes and Marco Polo describes how in his travels he saw Muslim pilgrims cure fevers by the ingestion of "pink earth" (Veniale, 1996).

The first written reference known to exist upon the use of "stones" and a description of their curative

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powers dates from Roman times, 60 BC, and is in Dioscorides' "De Materia Medica". This book also has a final section dealing with minerals and chemical substances used in Pharmacy. Moreover, in his "Natural History" Pliny the Elder describes the use of clays, especially those to be found around Naples (volcanic muds) for stomach and intestinal ailments. During the Middle Ages Avicena and Averroes in the 9th and 10th Centuries classified and encouraged the use of medicinal muds, and Galeno, Arabic doctor, used clays for the malaria, (Bech, 1987; Veniale, 1999). Later, "Lapidarios", works which partially dealt with the use of minerals from a therapeutic perspective, would appear, among which figures the famous "Lapidarios" of the Spanish King, Alfonso the Wise (1250). The first "Lapidario", which has been completely kept, is a translation into Spanish by Yhuda Mosca and Garci Pérez from the Abolays' arabic book which Abolays himself had previously translated from Chaldean into Arabic although its original source is not known (Brey Mariño, 1982).

During the Renaissance *Pharmacopoeia* appeared. These were texts, which classify, among other drugs, the different minerals for medicinal uses and regulations upon the same, such as official codes, which had to be obligatorily followed in order to produce medicines. Their appearance coincided with the first mineralogical classifications. In the 17th Century, the first Scientific Academies were founded and one aspect of their work was to document the advances of Mineralogy with respect to medico-pharmaceutical matters, thus producing various entries in the pharmacopoeias. The development of Crystallography and Mineralogy in the 18th and early 19th Centuries was of great importance in increasing the knowledge of the raw mineral materials used in pharmacy and cosmetics. However, the development of the Chemistry in the early 20th Century, which enabled numerous minerals to be obtained through synthesis, had a negative effect upon the use of minerals for therapeutic uses, due to the use of "synthetic mineral-like" (Bech, 1987; Galán et al., 1985).

At present, the minerals which are used for therapeutic purposes are basically clay minerals, given the difficulty and the cost involved in synthesising them industrially. An exception is a synthetic equivalent of hectorite named "Laponite S" provided by Laporte (NL) which is used as a gelifying material in cosmetic. Clay minerals are used in pharmaceutical formulations (as active principles or excipients), in spas and in aesthetic medicine.

2. The use of clay minerals in pharmaceutical formulations

The use of clay minerals in pharmaceutical formulations have been described by some authors (Bech, 1987; Bolger, 1995; Cornejo, 1990; Del Pozo, 1978, 1979; Galán et al., 1985; Gámiz et al., 1992; López Galindo and Viseras, 2000; Veniale, 1997; Viseras and López Galindo, 1999), and collected in Pharmacopeias (AA.VV., 1995, 1996, 1997a,b, 1998a,b).

Clay minerals used in pharmaceutical formulations are: smectites, palygorskite, kaolinite and talc. These minerals can act as active principles or excipients. The properties for which they are used in pharmaceutical formulations are fundamentally: a high specific area and sorptive capacity, rheological properties, chemical inertness and low or null toxicity for the patient.

There are some investigations about the possible use of sepiolite, as active principle or excipient, in pharmaceutical formulations (Cornejo et al., 1983; Del Hoyo et al., 1998; Forteza et al., 1988; Hermosin et al., 1981; López Galindo and Viseras, 2000; Viseras and López Galindo, 1999); but, until now, there are no commercial medicine which include sepiolite in its composition.

2.1. Use as active principles

Depending on the therapeutic activity for which the clay minerals are being used, they can be orally or topically administered to the patient.

2.1.1. Oral applications

2.1.1.1. Gastrointestinal protectors. The clay minerals which are used as gastrointestinal protectors are palygorskite and kaolinite. Their therapeutic action is based on their high specific area and sorption capacity. They adhere to the gastric and intestinal mucous membrane and protect them and can absorb toxins, bacteria and even viruses. They do, however, have the disadvantage that they also eliminate enzymes and other necessary nutritive elements, which makes their prolonged use inadvisable. They are administered to the patient in pill form, suspensions or powders, and are finally eliminated in the faeces due to the fact that these minerals are not absorbed by the intestinal tract and that they are not easily soluble in aqueous media, although the ambient acids may partially dissolve them. In general the smectites, with their high level of adsorption and high specific area, are not used as gastrointestinal protectors due to the fact that they are destroyed when they come into contact with the stomach's hydrochloric acid (pH 2) and/or that of the bowel (pH 6), if they arrive there protected by capsules. Nevertheless, a Na-Beidellite is used as a stomach buffer under the label "Beidelix".

2.1.1.2. Osmotic oral laxatives. Orally administered laxatives are those laxatives whose active principles' main effect is to encourage defecation. They can act by osmosis, by irritating the small bowel or the colon–rectum. The clay minerals used, sodium smectites, act by osmosis. The therapeutic action is not produced by the mineral per se but by the interlayered Na^+ which spreads through the stomach's fluids until it reaches the small bowel, producing an increase in the osmotic pressure of the intestinal contents. Under such conditions, water passes from the blood plasma through the bowel wall to re-establish the osmotic balance. This in turn produces a considerable increase in the volume of the bowel's contents, which stimulates the propulsive motor activity of the smooth intestinal muscle. This effect continues in the colon–rectum, producing liquid faeces. These laxatives are usually administered as suspensions. Excretion is mainly via the faeces when they provoke defecation. Between 15% and 20% of the Na^+ is absorbed, crossing the intestinal wall into the blood plasma, to be eliminated later by the kidneys or by perspiration.

2.1.1.3. Antidiarrhoeaics. Diarrhoea is either an acute or chronic pathological state characterised by an increase in the fluidity of the faeces and the frequency of their evacuation. Its causes are highly variable: bacterial infections, food poisoning, defective intestinal absorption, allergic states, etc. Treatment must be focused upon eliminating its cause, but in the symptomatic treatment of acute diarrhoea, compounds that eliminate the symptoms without combating the underlying cause can be used.

Most pharmaceutical formulations that act efficiently against diarrhoea work by reducing the quantity of liquid that reaches the colon–rectum from the small bowel, either by reducing the speed of passage through the bowel which encourages the absorption of water and electrolytes or by the active principle itself absorbing part of the water present. In this case, it is advisable that absorbent minerals be used to eliminate the excess water in the faeces, rendering them more compact. Absorbent minerals are also recommended if excess gases are present in the digestive tract since not only do the minerals protect the bowel and eliminate excess water, but they can also absorb gases. The clay minerals used as antidiarrhoeaics are kaolinite and palygorskite due to their high capacity of water absorption. Calcium smectites are also occasionally used, minerals that act as laxatives due to the astringent action of the Ca^{+2} ion which forms non-soluble hydrated phosphates which give rise to the formation of pulvulerunt faeces that are difficult to evacuate and provoke constipation. The minerals used as antidiarrhoeaics are orally administered either as pills or powders. Excretion is completely via the faeces. In the case of calcium smectites, part of the Ca^{+2} might be absorbed in the bowel. A part of this absorbed Ca^{+2} will be eliminated by the kidney, the non-absorbed part will be excreted in the faeces.

2.1.2. Topical applications

Topically administered pharmaceutical formulations are those medicines applied to the body's exterior, on a limited portion of the same. Clay minerals are applied topically as dermatological protectors or for cosmetic reasons.

2.1.2.1. Dermatological protectors. Dermatological protectors are generally powders, creams and ointments to protect the skin against external agents and occasionally agents exuded by the skin itself or excreted liquids. Clay minerals used as dermatological protectors are kaolinite, talc and smectites which due to their absorbent power, are substances capable of adhering to the skin forming a film which protects it mechanically against external physical or chemical agents. Moreover, by absorbing the skin's secretions, they also have a refreshing action, creating a large surface for their evaporation which in turn promotes a gentle antiseptic action as it creates a water-poor medium, unfavourable for the development of bacteria. This latter action is reinforced by these minerals' capacity to absorb dissolved and suspended substances, such as greases, toxins and even bacteria and viruses. The use of palygorskite as a dermatological protector is not advisable and they practically do not appear in any pharmaceutical formulation due to the present existing doubts concerning their possible carcinogenic effect if inhaled, although some authors maintain that these minerals are neither toxic nor dangerous (McConnochie et al., 1993; Santaren and Alvarez, 1994; Governa et al., 1995).

2.1.2.2. Cosmetics. Clay minerals are used as active principles in cosmetics, in face masks, due to their high adsorbency level of substances such as greases, toxins, etc. Therefore, they are recommended for inflammatory processes such as boils, acne, ulcers, etc. They are also used in creams, powders, emulsions, etc., as antiperspirants and to give the skin opacity, remove shine and cover blemishes. Clay minerals such as kaolinite, smectites, talc and palygorskite are used, although use of the last two is recommended only in liquid preparations (creams, emulsions, etc.).

2.2. Use as excipients

Excipients are substances introduced into certain pharmaceutical formulations in order to: (a) improve its organoleptic characteristics such as taste, smell and colour, or its physical–chemical properties such as viscosity, (b) facilitate the pharmaceutical formulation's preparation, and (c) promote the pharmaceutical formulation's disintegration when it is orally administered in the form of pills, capsules, etc.

The clay minerals used as excipients are palygorskite, smectites, kaolinite and talc. These minerals are used as: (a) lubricants to ease the manufacture of pills (talc), (b) agents to aid disintegration, due to their ability to increase in volume in the presence of water (smectites), or the dispersion of fibres (palygorskite), which favour the liberation of the drug of the pharmaceutical formulation when it arrives in the stomach, (c) inert bases for cosmetics (palygorskite, kaolinite, smectites, talc), and (d) as emulsifying, polar gel and thickening agents because of their colloidal characteristics (palygorskite, smectites) and to avoid the segregation of the pharmaceutical formulation's components and the formation of a sediment which is difficult to redistribute.

2.3. The influence of the minerals used as excipients in the bioavailability of the active principle

Although all excipients are considered to be inert, research carried out during the last 25 years has proved that when clay minerals are used, interaction might exist between the drug and the mineral (White and Hem, 1983; Sánchez Martín et al., 1988; Cornejo, 1990). This interaction can occur either in the pharmaceutical formulation itself or in the gastrointestinal tract, even though they are administered in different pharmaceutical formulations, given the clay minerals' superficial reactivity. These interaction phenomena can have a decisive influence on active principle's bioavailability, resulting in a greater activity of the drug and in other cases, in no activity, with the consequent health risk to the patient's health.

Clay minerals used as excipients can have an influence on two highly important aspects in the drug's bioavailability: its liberation and its stability.

2.3.1. Influence on the liberation process

The interaction between the drug and its excipient can retard the drug's release and therefore its absorption, lowering its levels in the blood. This phenomenon, which can be observed in in vitro studies, will produce undesirable effects if, in order for the drug to be effective, therapeutic levels are required immediately in the blood, as in the case of antihistamines. The effect, however, can be beneficial when the slow, controlled desorption of the drug has a positive effect upon its therapeutic action, in the case, for example of amphetamines and antibiotics. Studies carried out on the concentration of orally administered amphetamine sulphate in urine indicate that its excretion is much less when it is absorbed in montmorillonite which maintains blood levels 14 h later, something which does not occur when it is administered on its own (McGinity and Lach, 1977). Another example is the antibiotic clindamycin, a weak base which, at pH 2, is in a protonate form and, via a physical surface adsorption, forms a complex with montmorillonite. So, protonate clindamycin form will be highly adsorbed by the clay in the stomach. When the clay–drug leaves the stomach and passes onto the bowel, its pH slowly rises and it forms an acid–base equilibrium, which will give rise to the neutral clindamycin form. As the drug is physically adsorbed in the clay by ionic forces, it is desorbed slowly in the bowel, where the majority of drugs are absorbed, when it changes into a neutral form. Therefore, the absorption of clindamycin is favoured when it is administered with montmorillonite and its therapeutic action is prolonged (Porubcan et al., 1978).

The beneficial effect of retarding the liberation of a drug united to a clay mineral can also be achieved by increasing the ionic force on coming into contact with the intestinal fluid, if administered orally, or with the skin if administered topically. Therefore, some minerals, such as talc and kaolinite, which are used as dermatological protectors and adsorbents, can carry superficially adsorbed antibiotic, analgesic or antihistaminic which are released on contact with damp skin.

Another example of the liberation advantages where an interaction exists between the drug and mineral is that of water-resistant sun screens. Sepiolite and smectites have the ability to form complexes with organic compounds which absorb ultra-violet radiation thus enabling them to be used in sun screens with protection factors (Del Hoyo et al., 1998; Vicente et al., 1989). Absorption/desorption studies carried out, have demonstrated that the level of absorption is good and that even systems containing low drug levels have a great ultraviolet radiation absorption capacity. The adsorption of *N*-methyl-8-hydroxy quinoline methyl sulphate on smectite makes the active principle's desorption in salt water slower, which means that the active principle remains on the skin longer during bathing (Vicente et al., 1989).

2.3.2. Influence in the drug's degradation

The phenomena of interaction between a drug and a mineral excipient can accelerate the drug's degradation, thus losing its therapeutic activity. This has been demonstrated in numerous research works carried out in recent years (Porubcan et al., 1979; Hermosin et al., 1981; Cornejo et al., 1983; Forteza et al., 1988, 1989). It has been proven, for example, that dexamethasone, an anti-inflammatory, degrades in the presence of palygorskite and sepiolite although this degradation is more rapid in the presence of the former, because of the Fe of palygorskite catalyses the degradation reaction. The same result has been obtained for other anti-inflammatories such as hydrocortisone.

The degradation of a drug can occur in the presence of a clay mineral, even though the two are not administered in the same pharmaceutical formulation. The mineral's surface carries a negative charge, which means that while it is in the stomach it will absorb protons. If a drug which degrades in the presence of protons coincides in the stomach with a clay mineral, it will degrade more rapidly than if the mineral were not there. This is the case with digoxin, a cardiovascular tonic that degrades by hydrolysis, catalysed by acids, in the presence of montmorillonite. Studies undertaken have demonstrated that the drug degrades more rapidly in the presence of montmorillonite than when it is dissolved alone. At pH 2, digoxin degrades 20% in 1 h while in the presence of montmorillonite it degrades completely in the same time (the time of gastric residence), a fact to be taken into account when administering it (Porubcan et al., 1979).

3. The use of clay minerals in spas

Clay minerals are widely used in spas. They are mixed with water (geotherapy), mixed with sea or salt lake water, or minero-medicinal water, and then matured (pelotherapy) or mixed with paraffin (paramuds). The clay minerals which are most used are smectites and kaolinite, although illite and palygorskite are also used. They are applied alone or more frequently as complex clay minerals muds. Calcite, quartz, feldspars, etc., sometimes are present as minor or trace minerals. The principal properties of these clay minerals which make them useful in spas are: their absorption/adsorption capacity, their high cation exchange capacity, plastic properties, rheological properties, grain size and cooling index (Bettero et al., 1999; Cara et al., 1999, 2000a,b; Ferrand and Yvon, 1991; Gorgoni et al., 1999; Jobstraibizer, 1999; Minguzzi et al., 1999; Sánchez et al., 2000a; Summa and Tateo, 1998; Yvon and Ferrand, 1996; Veniale, 1997; Veniale and Setti, 1996).

On the other hand, it is necessary to study the presence of toxic elements as As, Pb, Hg, Cd, Se, Sb, Cu, Zn, etc., in the clay–water mixed used in spas, about all, it is necessary to know their mobility for avoid possible intoxications. It is important to know if the potential toxic elements are readily exchangeable during the development of the therapy or if they are strongly, and how strongly, bounded to the mineral structures (Summa and Tateo, 1998, 1999).

3.1. Geotherapy

Geotherapy is the mixture of one or more clay minerals with water and its direct application upon the skin, forming a consistent layer of about 1 cm thick. The applications can take the form of cataplasms or mud baths, depending on the area of the body to be treated. Both are used to treat dermatological diseases (boils, acne, ulcers, abscess, seborrhoea, etc.) and to alleviate the pain caused by chronic rheumatic inflammations and sport traumatism (Benazzo and Todesca, 1999; Martín Díaz, 1998; Novelli, 1996; Torrescani, 1990).

3.1.1. Cataplasms

Cataplasms are used when the mud is applied to a small area of the body. In acute pathologies (inflamed or congested areas) the application temperature must be lower than body temperature (cold muds). In this case, the mixture of clays and water produces a cooling of the area under treatment and since the mixture is a good conductor of the heat given off by the inflammation, it acts as an anti-inflammatory agent. The mixtures can also be used cold in liquid retention problems. When treating chronic articulatory processes, the mud must be hot and replaced before it cools.

3.1.2. Mud baths

These are used when the area under treatment is extensive. The application is carried out by submerging part of the body (bathing the arms, hands or feet) or the whole body in a bowl or bath filled with a mixture of clays and water. The temperature of application (hot or cold) depends on the therapeutic aims.

3.2. Pelotherapy

The International Society of Medical Hydrology defines the term peloid as a natural product consisting of a mixture of sea–salt lake- or minero-medicinal water (liquid phase), with organic and inorganic material (solid phase) produced by biological action (humus) and geological action (clay minerals) which are applied topically as therapeutical agents in the from of cataplasms or baths, the treatment receiving the name of pelotherapy (Martín Díaz, 1998; Veniale, 1997). A peloid is therefore a therapeutic agent in which the inorganic component (clay minerals) has undergone a maturing process with saline water (sulphurous, with sulphates, chlorides, sodium bromide, etc.). During the maturing process, some of the clay minerals' properties, for example, its plasticity, capacity of absorption and cooling index (it cools more slowly) increase, while its grain size decreases. These modifications improve the properties required for use in spas (Veniale et al., 1999; Sánchez et al., 2000b).

Generally in pelotherapy, the mixture of clays and water is applied hot (40–45 °C) for between 20 and 30 min in layers of between 1 and 2 cm, covering it with an impermeable material to conserve the heat. The heat is conducted via the skin to the subcutaneous areas and, after 10 min, it reaches the interior of the body, though at this point it is not only by conduction but also by convection via the bloodstream. The application of peloids produces a sensation of heat in the area being treated, vasodilatation, perspiration and the stimulation of cardiac and respiratory frequency. The greater the area under treatment, the greater are such effects. Peloids therefore have in general, a stimulatory, antiphlogistic, analgesic action and are indicated for chronic rheumatic processes, degenerative osteoarthrosis in any part of the body, dysendocrine arthropathies, spondilo-arthritis ankylopoietic, spondylosis, myalgias, nueralgias, etc. They are also recommended for the sequelae of osteo-articular injuries, fractures, dislocations; disorders following vasculopathies, dermatological diseases, etc. The application of peloids is contraindicated in the acute and sub-acute phases of rheumatic processes, discompensated cardiopathies, tuberculosis and renal or hepatic deficiencies (Barbieri, 1996; Benazzo and Todesca, 1999; Lotti and Ghersetich, 1999; Martín Díaz, 1998).

3.3. Paramuds

These are a mixture of paraffin and clay minerals. They are supplied in blocks or plaques that are heated and stirred in a specially designed vessels and are usually recycled from one patient to another. They are applied at high temperature (40–45 °C) in layers of approximately 1–5 cm thick which are then covered to avoid heat loss and are kept in place for between 20 and 30 min. Paramuds are used for the same therapeutic purposes as peloids (Martín Díaz, 1998).

4. The use of clay minerals in aesthetic medicine

Clay minerals are used in aesthetic medicine in cosmetic products, as active principles or excipients, and in geotherapy, pelotherapy and paramuds.

Geotherapy is mainly used for facial treatments, generally in the cold direct application on the skin (kaolinite or smectites mixed with water). To treat dermatological diseases as blackheads, spots, acne, seborrhoea, etc., it is recommended that the mixture of clays and water be applied hot as face masks due to the fact that this method promotes perspiration and sebaceous secretions which flow more easily in a fluid state, while it also opens the pylosebaceous orifices. Moreover, during the perspiration sodium, cloro, potassium and urea are eliminated, which activate the metabolic change and the excretion of catabolites (Lotti and Ghersetich, 1999; Martín Díaz, 1998). In aesthetic medicine, peloids are used for the same purposes as geotherapy, with the advantage that they may also contribute nutrients that they contain from the maturing process.

Paramuds are used to moisturise the skin since during their application the perspiration produced cannot evaporate due to the paramud's impermeability. This perspiration soaks into the upper layers of the epidermis, moisturising it from within. Moreover, after applying a paramud, the skin is in a hyper-porous state, which means that cosmetic substances will be easily absorbed by the corneous layer, reaching the epidermis' deepest layers. They are also used in aesthetic medicine to treat compact lipodystrophies in their initial state and which need preventive care but are not treatable by more aggressive treatments due to this early state of evolution. Moreover, it is recommended to retard the development process of cellulite, given the fact that they stimulate venous and lymphatic circulation in the application area and that they act as an anti-inflammatory (Martín Díaz, 1998).

5. Conclusions

Clay minerals are used for therapeutic purposes, with a beneficial effect on health, in pharmaceutical formulations, spas and aesthetic medicine. In pharmaceutical formulations, they are used as active principles orally administered (gastrointestinal protectors, osmotic oral laxatives, antidiarrhoeaics) or administered topically (dermatological protectors, cosmetics); and as excipients (lubricants, delivery systems, inert bases, emulsifiers), principally due to their high specific area and their absorption/adsorption capacity, rheology, chemical inertness and low or no toxicity for the patient. When clay minerals are used as excipients there might be an interaction between the drug and the mineral which influences the bioavailability of the active principle, both in its liberation process and its stability. In spas and aesthetic medicine, geotherapy, pelotherapy and paramuds are used due to their absorption/adsorption capacity, their cation exchange capacity, plastic properties, rheology, grain size and cooling index. They are used in spas to treat dermatological diseases and to alleviate the pain of chronic rheumatic inflammations. In aesthetic medicine, they are mainly used to clean and moisturise the skin and to combat compact lipodystrophies, acne and cellulite.

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