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ORIGINAL PAPER

Healing and edible clays: a review of basic concepts, benefits and risks

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Abstract The use of clay by humans for medicinal and wellness purposes is most probably as old as mankind. Within minerals, due to its ubiquitous occurrence in nature and easy availability, clay was the first to be used and is still used worldwide. Healing clays have been traditionally used by man for therapeutic, nutritional and skin care purposes, but they could impart some important health and skin care risks. For instance, clay particles could adsorb and make available for elimination or excretion any potential toxic elements or toxins being ingested or produced, but they could adsorb and make available for incorporation, through ingestion or through dermal absorption, toxic elements, e.g. heavy metals. Edible clays, a particular case of healing clays, have been traditionally used by man for nutritional and therapeutic purposes. Geophagy, the deliberate soil eating, earth eating, clay eating and pica (medical condition or eating disorder shown by individuals addicted to eat earth substances), has been observed in all parts of the world since antiquity, reflecting cultural practice, religious belief and physiological needs, be they nutritional (dietary supplementation) or as a remedy for disease. This paper pretends to review historical data, basic concepts and functions, as well as benefits and risks of the use of healing clays, in general, for therapeutic and cosmetic purposes, and of edible clays, in particular, for therapeutic purposes.

Keywords Healing clay · Edible clay · Mud therapy · Peloid therapy · Health benefits and risks

Introduction

Clay, a quite ubiquitous geomaterial, has been used by humans since before recorded history to accomplish basic but fundamental healthcare purposes. The *clay plates of Nippur*, Mesopotamia, which date back to about 2500 BC, contain reference to the use of clays for therapeutic purposes, including the treatment of wounds and the inhibition of haemorrhages. Also, the famous *Papyrus Ebers* dated about 1600 BC describes the treatment of some diseases using clay-based medicines. Since then, from Ancient Greece, Roman times, medieval times, renaissance times to contemporary times, there exist reports on the therapeutic, nutritional and cosmetic uses of clay and clay-based products.

In Ancient Greece, Hippocrates (460–377 BC) regarded as the Father or Founder of Medicine released interesting information about *medicinal earths or terras* in his book "On Airs, Waters, and Places". The so-called *medicinal terras* or *medicinal earths* from the volcanic Greek islands, Lemnos,

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Chios, Samos, Milos and Kimolos were particularly famous. The *lemnian earth*, in particular, believed to have supernatural healing properties, after being extracted in an annual ceremony, was rolled into small cylinders or tablets, each of which was then stamped with the image of the goddess Artemis, becoming known as *terra sigillata*. According to Robertson (1986), it constitutes one of the early examples in history of the trade-marked therapeutic agents that were distributed over most of the Western world.

Aristotle (384–322 BC) made the first reference to the deliberate eating by humans of earth, soil or clay for therapeutic and religious purposes. Theophrastus (c.373/368–288/284 BC), a disciple of Aristotle, who developed an empirical approach to natural history, in his book "On Stones", the first scientific publication dealing with stones, industrial minerals and artificial products derived thereof mentioned four types of *earths*: Melos or Milos earth, Kimolos earth, Samo earth and Tunphaic earth, all considered important from an applied or "industrial" point of view. We know now that the first three *earths* referred to are clays and the fourth is gypsum. The *kimolian earth*, known today as calcium montmorillonite, occurs in two varieties, white and red, both extracted in the island of Kimolos.

The *Armenian bole*, also known as *bolus armenus*, was another famous healing clay native of Armenia. Historically this fine, soft, reddish clay was used as an astringent prescribed against diarrhoea, dysentery, haemorrhage, etc. The *Armenian bole* deserved references by Theophrastus, Dioscorides (c.41–90 AD) and Pliny the Elder (23–79 AD). *Bole* with other origins has been and is still used under the name "*Armenian bole*", as is the case of clay used as pigment, as a ground for oil painting and gilding (application of gold leaf over carven wooden pieces, common for instance in church's retables or altarpieces) and for bookbinding.

In Roman times, Dioscorides author of the book "*De Materia Medica*" (precursor of modern Pharmacopoeias) mentions an *earth* from Lemnos named *morochthos*, a white clay used in medicine to stanch blood and treat wounds. Also, Pliny the Elder author of the book "*Naturalis Historia*" described the use of clay, some of volcanic origin occurring nearby Naples, especially for stomach and intestinal ailments.

Galeno (131–201), a Greek doctor, describes the *medicinal terras* being used, for instance, for gastrointestinal affections and indicates their therapeutic properties, their organoleptical characteristics and properties, and how to recognize them.

During the Middle Ages, the Arabian physician Avicena (980–1037) and Averroes (1126–1198) encouraged the use of medicinal mud and have classified various types of mud. Avicena whose name corresponds to the Latin transcription of the Arabian name Ibn-Sînâ, in his book "*El Canon*", reports twelve types of clay, some for internal and other for external applications. He mentions that certain clays if ingested could cause obstructions of the digestive tube and that other clays were beneficial for rheumatic pathologies involving articulations or joints, for antipoison treatment, etc.

Later the Arabian physician Ibn al-Baitar (1197–1248) discloses cases of both therapeutic and cosmetic uses of clay-based materials. Also, Giovanni Dondi in his book "*Tractatus de fontibus calidis agri patavini*" (1388) recommended the topical application of mud to treat subcutaneous affections.

Paracelsus (1493–1541) has used minerals for the preparation of drugs and created a branch of Chemistry named Iatrochemistry that preceded the actual Pharmacology, aimed at the study and use of chemical substances for therapeutic purposes.

Along Renaissance Georgius Agricola in his book "*De re metallica*" (1556) reports the use of medicinal clay, and Andrea Bacci in his book "*De Thermis*" (1571) recommended the use of *fango* (thermal mud) in rheumatic pathologies, ulcers and oedemas. Also, along the Renaissance were issued the first texts of the so-called *Pharmacopoeias*, namely the *Pharmacopeia of Valence* (1601) and the *Pharmacopeia Londinensis* (1618). Besides drugs, these texts classify and describe regulations of various minerals used for medicinal purposes.

During the eighteenth, nineteenth and twentieth centuries, the use of clay-based materials for therapeutic purposes, the so-called *mud* for *mud therapy*, and later the so-called *peloid* for *peloid therapy*, both under the form of *mud packs* or *peloid packs*, were thoroughly used in European Thermal Resorts, particularly in France, Germany and Italy. For instance, in France, Dax, Balaruc and Aix-les-Bains were famous and representative resorts where *medicinal mud* was very much employed.

The health benefits of *clays* are very well documented in several relatively recent scientific articles: Bech (1987, 1996), Robertson (1986, 1996), Novelli (1996, 1998, 2000), Reinbacher (1999, 2003), Viseras and López-Galindo (1999), Veniale (1996, 1998, 1999), Carretero (2002) and Veniale et al. (2004). More recently yet, other authors such as Veniale et al. (2007), Gomes and Silva (2007), Tateo et al. (2006, 2009), Carretero and Pozo (2007), Viseras et al. (2007), Gomes et al. (2009), Rautureau et al. (2010), Kikouama and Baldé (2010), Fioravanti et al. (2010), De Vos (2010), Carretero et al. (2006, 2013), Gomes et al. (2013), Peiró and Tejero (2014), Williams and Hillier (2014) and Gomes (2015). All these articles disclose interesting information about properties, applications and functions on human health of *clay*, *clay minerals* and *clay-based products*.

There are several types of *clay* and within them the so-called *healing clay* and *edible clay* had been used and are still being used, by man for therapeutic, nutritional and cosmetic purposes. *Edible clay* is a particular type of *healing clay* which use is limited to internal application through ingestion, for instance, of cookies made of clay/animal fat or of clay/potable water dispersion/suspension. Conceptually *healing clay* besides the oral use for internal health benefits of the digestive tract can also be used in external or topical applications under the form of clay/mineral water paste called *mud* or *peloid* for the treatment of muscle-skeletal and dermatological disorders.

In both *healing clay* and *edible clay*, *clay minerals* which are hydrous phyllosilicates of very small particle size exhibiting either planar or non-planar structures are the fundamental clay constituents characterized by particular crystallochemical properties, the unique globally negative electric charge being the most important one, since it is responsible for the reversible fixation or adsorption of chemical elements and compounds (particularly polar compounds), the electric charge value being variable within clay mineral species (for instance, it is significantly higher in *montmorillonite*, the most naturally occurring mineral species of the *smectite group*, than in *kaolinite*, the most naturally occurring mineral species of the *kaolin–serpentine group*).

With regard to clay/human body interaction, clay particles could adsorb and make available for incorporation through ingestion, both bioessential and toxic elements (e.g. heavy metals); also they could adsorb and make available for elimination or excretion any potential toxic elements or toxins which had been ingested or metabolically produced.

On the one hand, the internal use of *edible clay* is particularly reckoned as a potential means for: dietary supplementation of the mineral nutrients necessary for the synthesis of new tissues; combating iron deficiency or anaemia; detoxification of noxious or unpalatable compounds present in the diet; and relief of abdominal pains (heartburn) with accompanying vomiting.

On the other hand, the ingestion of *edible clay* can cause health risks, such as constipation as well as reduction in the adsorption capacity of bioessential chemical elements, such as Fe, Zn, Mg, Ca and Se, or of bioactive pharmaceutical compounds existing, for instance, in *drugs* if almost simultaneously taken with the *clay*. Also some metals and metalloids, such as Pb Hg, Cd, Cr, Sb, Ba, U, As and Se, could be present in the *edible clay* in such concentrations that could make it toxic and poisonous, particularly due to their easy assimilation and bioaccumulation (the gradual build up over time of a chemical element or compound in a living organism).

Toxicity much depends on for how long and frequent is the intake of *edible clay* and, naturally, of the nature of the chemical species (oxidation states) and bioavailability of the metals and metalloids referred to.

Davies et al. (2008), Brand et al. (2010), Ekosse and Jumbam (2010) and Jumbam (2013) discuss the possible effects on human health of the chemical composition, particularly of heavy metals, caused by geophagic materials. Al-Rmaldi et al. (2010) report the health risk of geophagic practices by pregnant Bangladeshi women living both in Bangladesh and in UK, since they are exposed to high concentrations of As, Pb, Cd and Mn when they eat baked clay named Sikor (also purchased from shops in UK), and in regard to As in Bagladesh the As of the clay is accumulated with the As from contaminated drinking water. The authors also mention how important would be the evaluation of the bioavailability of As and other toxic elements as well as the clinical evaluation of the adverse effects. Also recently Bonglaisin et al. (2011) discuss the potential hazardous effects of intake of Pb, Cd and Hg related to kaolin eating after analysing geophagic kaolin samples from Cameroon and Nigeria sold in open markets, and finding in them relatively high concentrations of those highly toxic heavy metals.

Samples of the famous *Eko clay* were analysed. Villagers outside of Uzalla, in Nigeria, mine blocks of kaolinitic clay from a depth of 30–90 cm from the surface, then sun-dry and smoke those blocks transforming them into a substance called *eko* that is sold in local markets. *Omumu clay* is other local *edible clay* highly traded in open markets and consumed in Nigeria by pregnant women to manage nausea. More recently yet Lar et al. (2014) and Owumi and Oyelere (2015) have chemically analysed these geophagic clays since they are potential sources of heavy metals with health implications in women and children who consume them.

Gomes et al. (2009) in a study of *edible clays* sold in open and public markets and consumed in the islands of Cape Verde' archipelago besides high contents of Cr, Cu, Pb, Mo, Zn, V, U, Th have identified too high contents of rare earth elements (for instance, Ce—1356 ppm; La—562 ppm). Such clays particularly rich in the clay minerals smectite and illite are the weathering products of phonolite, alkaline extrusive volcanic rock with occurrences in the island of Boavista of the same archipelago.

Functioning as drugs, the natural geophagic materials that correspond to *edible clays* should be chemically safe for consumers. The European Medicines Agency (EMEA), in 2008, for the oral exposure of pharmaceutical drugs, had established the upper limits for permitted daily exposure (PDE) relatively to essential trace minerals such as Cr, Mo, Ni, V, Cu, Mn, Zn and Fe. In regard to heavy metals, the International Conference on Harmonization (ICH) Q3D had established, in 2013, the technical requirements (guidelines) for registration of pharmaceuticals for human use and classified the most potentially toxic elements (heavy metals included) into three classes: class 1 (As, Cd, Hg, Pb); class 2 (Co, Ni, Ag, Au, V, Ir); and class 3 (Ba, Cr, Cu, Li, Mo, Sb, Sn), based on their PDE and likelihood of occurrence in the drug products.

In general, the chemical composition of the geophagic materials described in the previous paragraph shows contents in those elements much higher than the ones established as upper limits. Naturally not all *edible clays* are equal, some being more chemically and microbiologically safer than others. Also whenever clay water dispersion or "argillic water" or "clay water" is ingested, the water quality is another important requisite, and it should be chemically and microbiologically safe. WHO (2011) and EU (2011) established the guidelines or standards for drinking water quality.

Also a matter of concern is the presence of potentially toxic metals and metalloids in *healing muds* also called *natural peloids* (maturated in situ), as well as in artificial peloids (maturated in an artificial environment) also called *peloids s.s* (*stricto* sensu) or just *peloids* of either medical or cosmetic grade that had been reported by various authors such as Mascolo et al. (1999), Tateo et al. (2009), Gomes et al. (2009), Khlaifat et al. (2010), Carretero et al. (2010), Ngole et al. (2010), Rebelo et al. (2011), Quintela et al. (2012) and Sánchez-Espejo et al. (2014).

Clay-based natural or more or less manipulated products are used either orally or topically for therapeutic and cosmetic purposes, reason why they could be considered natural remedies and pharmaceuticals. Hence, their sanitary safety, both chemical and microbiological, needs to be monitored to ensure compliance with general medical and pharmaceutical legal regulations in force. On this subject, no specific legislation exists for *edible clay* and *healing mud/peloid*, products that could be included into the concept of ethnopharmaceutics (Heinrich and Pieroni 2011), and as so their compliance with the guidelines proposed in pharmacopoeias (EP 7.0 2011; USP 36-NF 31 2013) should be taken into account.

Natural peloids as well as artificial peloids of either medical or cosmetic grade could be applied directly onto the skin, as *mud packs* or *peloid packs*, for instance, on joints (of knee and hand) or on backbone regions. Just before its application that, as a rule, lasts 20–30 min, both *healing mud* and *medical* or *therapeutic peloid* could be heated up to about 45 °C, and the heat promoting the opening of skin pores facilitates the transdermal absorption of both beneficial and hazardous substances contained in the peloid. Immediately before application, *mud* or *peloid compresses* could also be warmed up to about 45–50 °C using a microwave oven.

Potentially toxic elements (heavy metals included) are always present in variable contents both in the so-called *natural peloid* and in the *peloid s.s* (*stricto* sensu). As said above, there is a lack of normative regulation for the quality and safety of the raw materials that constitute both natural peloid and *peloid* *s.s* or just *peloid*. In fact, in general, in regard to quality criteria and regulations, there are no effective chemical constraints for both peloid types used for therapeutic applications. On the contrary for cosmetic products (in which *cosmetic peloids* could be included), there are highly restrictive chemical constraints, situation well exemplified in the European Directive (76/768/ECC) stating that elements such as Hg, Cd, Pb, Sb, As and Se should not be present, or in case of being present only extremely low contents (around 1 ppm) should be admitted.

Mud therapy and *peloid therapy*, both under the comprehensive name *pelotherapy*, are reckoned as being potential efficient means to treat muscular-skeletal affections due to the action of a double process: *thermotherapy* and *chemotherapy*.

As aforesaid, *mud* and *peloid* are particularly distinguished because *mud* also called *natural peloid* or *primary peloid* is maturated in a natural environment, whereas *secondary peloid* or *artificial peloid* or *peloid s.s* (*stricto* sensu) or yet simply *peloid* is maturated in an artificial environment, for instance inside *spa* facilities.

Microbiological control for sanitary safety, particularly of pathogenic microorganisms, is essential along the processes of preparation, storage, application and reuse of both *mud* and *peloid*. Naturally, *mud* and *peloid* with origin in sedimentary deposits, due to the possibility of bearing higher contents of organic matter, are more susceptible to microbiological contamination comparatively to *mud* and *peloid* with origin in volcanic deposits.

Dermal absorption is the natural pathway for microbial infection due to *mud* or *peloid* topical application; hence, the skin areas under treatment should be healthy, i.e. without "*entrance doors*". A particular concern in regard to the presence in *mud* and *peloid* of potentially hazardous microorganisms (bacteria and fungi) has been reported by various authors such as Mpuchane et al. (2010), Bisi-Johnson et al. (2010, 2013) and Okunlola and Owoyemi (2011).

In the European Union, there are no uniform rules for the microbiological specifications of *muds* and *peloids*, despite the concern shown by the European Spas Association (ESA). In its General Assembly held in 2006 in the Thermal Resort São Pedro do Sul, in Portugal, ESA had considered and proposed quality criteria for *spring medicinal waters* and *thermal peloids* but has not quantitatively defined the minimum requirements or guidelines, both chemical and microbiological, for both *spring medicinal water* and *healing mud/peloid* used in balneology (the study and therapeutic use of *mineral medicinal waters* and of *healing mud/peloid*). If *medical peloids* are considered equivalent to remedies or medicines, they should not contain pathogenic microorganisms such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Candida albicans*, *Escherichia coli* and *faecal coliforms*, within others.

In regard to the pathogenic germs of anthropogenic origin *E. coli* and *Coliform bacteria* that could be present in the liquid phase extracted from *mud/peloid,* ESA established the guide value of 100 CFU (Colony-Forming Units)/100 ml and the limit of 2000 CFU/100 ml for *E. coli*, and the guide value of 500 CFU/100 ml and the limit of 10,000 CFU/100 ml for *Coliform bacteria*.

Also in regard to microbial quality and quantity, the normative limits proposed by European legislation (EP 7.0 2011) could be applied to clay-based natural products used for therapeutic purposes, such as *edible clays* and *peloids*. The limit for total aerobic microbial count is 10^3 CFU/g in "non-sterile substances for pharmaceutical use", and for "non-sterile oral dosage forms containing raw-materials of natural (animal, vegetal or mineral) origin", the limit is 10^4 CFU/g. The pathogen microorganisms *E. coli*, *P. aeruginosa*, *Salmonella* spp. and *S. aureus* should be absent.

Both negative and positive effects on human health of healing and edible clays are matter of concern and study of the emerging scientific field of Medical Geology that assesses the complex relationships between geoenvironmental factors and their impacts (beneficial or toxic) on humans and looks at the understanding of the mobility (through natural and anthropogenic processes), bioavailability, bioaccessibility, exposure and transfer mechanisms and processes to humans of geogenic metals and metalloids as well as their ecotoxicological impacts and health effects.

According to Davies et al. (2004) and Skinner (2007), the intake and incorporation of geogenic elements could follow three processes: dermal absorption via mud baths or bathing in geothermal water; ingestion of water, food and soil/clay (either intended—geophagy or unintended); and inhalation of atmospheric dust and aerosols.

Medical Geology is a transdisciplinary scientific field that requires an integrated involvement and cooperation of specialists in geology, mineralogy, geochemistry, hydrochemistry, environment, toxicology, epidemiology and public health.

One review dealing essentially with basic concepts as well as with benefits and risks of using *healing clay* and *edible clay* for health and skin care will be hereunder disclosed.

Basic concepts

To start with some inconsistencies persist in the literature with regard to nomenclature, definition and classification involving the geomaterials and processes dealt with in the present paper. Therefore, a review of several basic concepts is hereunder put forward.

Targets, concepts, principles, methods, historical evolution, interactions with other sciences, systems and implications on society are common fundamentals to any science. Concepts, in particular, can be expressed differently by people from different educational background and experience; also, concepts can evolve over times.

Clay

A naturally occurring geomaterial composed primarily of fine-grained minerals—the so-called *clay minerals* being the fundamental constituents—which is generally plastic at appropriate water content and will harden on drying or firing. Also any clay has its own *clay fraction* for which conventionally some disciplines set a maximum size for clay particles: pedology <2 µm; geology, sedimentology and geoengineering <4 µm; colloid science <1 µm.

As a rule, besides *clay minerals* clay could contain the so-called *associated minerals* (silicates such as quartz and feldspar, carbonates such as calcite, oxides and hydrated oxides of iron and aluminium such as hematite, goethite and gibbsite), X-ray amorphous materials such as organic matter, inorganic X-ray quasi-amorphous materials such as opal A and ferrihydrite, and amorphous iron hydroxides.

There are several types of clay based on geological, technological and commercial arguments: primary or residual clay, secondary or sedimentary clay, special clay (ball clay, bentonite, kaolin, fuller's earth, fibrous clay and flint or hard clay), common clay (pottery clay, heavy clay), refractory clay, nanoclay, activated clay, etc.

Bentonite, kaolin, fibrous clay (sepiolite and palygorskite) and nanoclay are the clay types with more interest for medicinal, pharmaceutical and cosmetic applications.

Special clays relatively to *common clays* are characterized, as a rule, by the following aspects: smaller number and size of the mineral deposits, simpler composition although requiring more complex and expensive processing, and higher commercial value of the manufactured products.

Clay is a major constituent of the so-called *healing clays* and *edible clays*, and within the *healing clays*, it is also a major constituent of most *natural peloids* and *peloids s.s* hereunder described, particularly of the so-called *essentially inorganic peloids*, all of them used for therapeutic and/or cosmetic purposes, and applied either in the natural environment, or inside specialized *spas*.

Clay mineral

Fine-grained hydrous phyllosilicate, of planar or non-planar structure which could impart plasticity (if the right amount of water is added) and hardening (if dried or fired) to the clay in which it occurs.

About seventy species of clay minerals are actually known, species which are distinguished by their crystallochemical specificities and that are usually gathered in groups, such as serpentine–kaolin; talc–pyrophyllite; and smectite, true or flexible mica, vermiculite and chlorite (Guggenheim et al. 2006).

Kaolinite, halloysite, montmorillonite, beidellite, talc, sepiolite and palygorskite are the clay minerals mostly used for medicinal, pharmaceutical and cosmetic applications both as active substances and as excipients.

Geophagy (or Geophagia)

It is defined as the deliberate eating by man and animals of clay or clay soil. This practice that is justified in many cultures by therapeutic, nutritional and/or religious reasons goes back to prehistoric times and is widespread across the world; clayey soil or clay ingestion is an ancestral practice still current in several regions of all continents, reflecting cultural practice, religious belief and physiological needs (nutritional or therapeutic).

On this subject, the reading of papers by Woywodt and Kiss (2002), Wilson (2003), Abrahams (2005, 2010), Young (2011) and Lambert et al. (2013) is recommended.

Soil or clay ingestion known as geophagy is a behaviour commonly observed among peoples on all continents (Laufer 1930; Hunter 1973; Vermeer and Frate 1979; Hunter and De Kleime 1984; Johns and Duquette 1991; Reid 1992; Abrahams and Parsons 1996; Aufreiter et al. 1997; Grigsby et al. 1999; Mahaney et al. 2000; Tateo et al. 2001; Saathoff et al. 2002; Nchito et al. 2004).

According to Ferrell (2008), the direct consumption of the so-called edible earths for medicinal and spiritual purposes occurs worldwide and is deeply rooted in the so-called folk medicine and religion. The last situation is well represented in Chimayo, New Mexico, where close to the sanctuary clay is extracted from a pit and ingested, for spiritual healing, by the peregrines. Also according to Sheppard (1998) and Galzigna et al. (1999a, b), the practitioners of geophagy can consume about 30–50 g/day, and more women (particularly during pregnancy believed to help in relieving nausea and emesis and during lactation) than men are engaged in geophagic practice.

Geophagy is often associated with the eating disorder called *pica* that could be hazardous because the individual addicted to earth substances does not distinguish the safe ones from the hazardous ones that can contain toxic chemical elements or compounds and/or pathogenic microorganisms (bacteria and fungi). Kutalek et al. (2010) and Ozumba and Ozumba (2002) report microbial contamination caused by *pica*. The practice of geophagia has been associated with health or developmental problems: iron (Fe) deficiency (Danford 1982), mechanical bowel disorder (Key et al. 1982) and nutrition dwarfism (Prasad et al. 1961).

The habit of eating clay soil, especially among pregnant women, is still a common practice in many countries, particularly in Africa, such as Tanzania, Nigeria, Guinea, Senegal, Cape Verde, Ivory Coast, Zambia, Ghana, Kenya, Swaziland and South Africa, in America, such as Haiti, Peru, Panama, Guatemala, Mexico and USA (in southern rural areas), in Asia, such as Indonesia, India and China, and in Oceania. The reasons for clay soil ingestion are still not scientifically supported despite a quite a significant number of researchers have studied such popular practice: Woywodt and Kiss (2002), Izugbara (2003), Hooda et al. (2004), Kikouama et al. (2009a, b), Brand et al. (2010), Abrahams (2010), Davies (2010) and Ekosse and Jumbam (2010).

The determination of both essential and toxic elements present in the clay soil commonly consumed by pregnant women, in order to assess safety, has been recently carried out, for example, in Tanzania by Mwalongo and Mohamed (2013) and Nyanza et al. (2014) and in Nigeria by Lar et al. (2014), Igeoma et al. (2014) and Owumi and Oyelere (2015).

Kikouama and Baldé (2010) to compensate eventual dietary deficiencies in Fe and Zn have designed clay-containing pellets bearing certain Fe and Zn amounts; such pellets were able to be retained for few hours by flotation in the highly acidic stomach cavity in order to favour and optimize the controlled release and gastrointestinal absorption of those essential trace elements.

Edible clay

Clay is deliberately ingested by man as cookies (Fig. 1) or as clay/potable water dispersions; it can act as source of mineral micronutrients and as protective material against pathogens and toxins (detoxification of noxious or unpalatable compounds present in diet), or it can act as antacid for gastric acidity compensation (Wilson 2003; Abrahams 2005; Gomes et al. 2009; Ferrell 2008; Kikouama et al. 2009a; Kikouama and Baldé 2010; Young 2011).

Healing clay

Clay that once identified and characterized by its healing properties is used by man for internal or oral applications under the form of cookies or clay/water dispersion; under the form of *mud* clay or other clay bearing geomaterials could be also used for external or topical applications (*mud therapy* and *peloid therapy*); *edible clay* is a particular type of *healing clay* just used for oral applications.

Mud

From a sedimentological point of view, *mud* is a geologic field term for any soft silt–clay mixture with more than 50% of its size fraction smaller than 63 μm and that is plastic when wet. As a popular term, *mud* is

Fig. 1 Woman at Port-au-Prince, Haiti, exposing for sale cookies made of clay, salt and animal fat, which are particularly consumed by pregnant women as dietetic supplement. In Haiti, food is scarce and expensive (in National Geographic, PT, November 2008, no. 92, 88–91)

also a non-consolidate fine-grained sticky or slimy sediment of any origin. *Mud* may also be clay or carbonate-rich sediment that normally contains some silt-sized components and organic material.

As healing natural material, *mud* can be defined as a semisolid mixture of mineral matter and organic matter with mineral water in variable amounts. Occasionally, *mud* properties are relevant for healing purposes depending upon its origin and composition, and based on these two arguments several typologies and designations could be attributed to *mud: bioglea mud* or *biofilm mud* (called *barégine* in France and *muffe* in Italy); *estuary mud*; *lagoon mud; freshwater lake mud; gyttja* or *"nekron" mud; peat mud; river mud; salinas* or *salt pan mud; salt lake mud; sapropel mud; sea* or *marine mud; thermal spring mud;* and *volcanic mud*.

The names of the very singular *natural sediments* from which *healing muds* are derived change with the idioms of the countries derived or not from the Latin, as follows: *argilla, limus, lutum, lamae, caeum* (in Latin); *argila*, *barro*, *greda*, *lama*, *lodo*, *limo*, *vasa*, *silte*, *sapropel*, *turfa, biofilme* (in Portuguese); *arcilla*, *barro*, *greda*, *cieno*, *lama*, *lodo*, *fango*, *limo*, *vasa, silte*, *sapropelli*, *turba*, *bioglea* (in Spanish); *argile*, *boue*, *glaise*, *fange*, *liman, limon*, *silt*, *vase*, *sapropeli*, *tourbe*, *muffe, mousse, barégine, bioglée, gyttja* (in French); *argille*, *fango*, *limi*, *muffe*, *torbe* (in Italian); *clay*, *mud*, *mire*, *slime*, *ooze*, *loam*, *silt*, *sapropel*, *turf*, *moor*, *peat, biofilm* or *bioglea, gyttja* (in English); *ton*, *schlick*, *schlamm*, *torf* (in German); *and tîn*, *hama* (in Arab).

The designation *thermal mud* is attributed to *mud* with origin and deposition related to thermal springs.

Mud therapy

The topical use of natural muddy sediment under the form of mud paste for therapeutic and/or cosmetic purposes, mostly on an empiric way and without medical counselling and surveillance, such natural muddy sediment that has been maturated in the geologic site where it occurs is simply called *healing mud* or *natural peloid*.

The use of *mud* for healthcare purposes goes back to prehistory. Egyptians have used muddy sediments from the river Nilo, under the form of topical applications, to treat disorders of the feminine genital system and to treat skin burns. Romans were the first to recommend *mud baths* for therapeutic purposes, mud having origin in deposits occurring at the bottom of seas, lakes and rivers (case of Danube) as well as in peat from marshlands.

In France, before Roman occupation, mud baths were practiced in the so-called thermal stations of Dax (Aquitaine), Balaruc (Hérault) and Saint Amand (Nord), and after Roman occupation these and other stations were much developed becoming quite prosperous. The barbarian invasions in Europe significantly diminished the prosperity of the thermal stations, and only in Middle Ages the balneal activity could be recuperated.

Since Renaissance (final of fifteenth century) in Italy, the thermalism and the use of *warm mud* became popular, particularly in resorts located in the Euganean basin, in Italy, famous for thermal springs and *thermal muds* locally called *fangos*. Many documents exist reporting the application of *warm mud* washed out with thermal water when mud application was finished.

In Europe, several countries such as Germany, Italy, Romania, Hungary, Greece, Spain and Russia have used *mud* for therapeutic purposes before and after Roman occupation, and they are still using it. Soon public conscience of eventual sanitary risks related to malpractices of hygiene leads to the replacement of collective mud baths for individual mud baths, and the replacement of general mud baths

Fig. 2 Mud application (sea water being the liquid phase) to treat rheumatic disorders at Parede's beach (on the *left*) and for skin care purposes at the Porto de Mós's beach (on the *right*)

(involving almost all body) for local mud baths (involving parts of the body such as leg and arm).

Good example of *mud therapy* is the traditional practice in certain natural sites of the littoral Atlantic of Portugal, more precisely at the beaches named Consolação, Parede, Meco, Porto de Mós, involving the empiric use of *mud*, more precisely of clay pastes made by mixing marly clay extracted from the nearby cliff with sweater, for the treatment of rheumatic and skin affections (Gomes 2002; Cardoso-Gomes and Gomes 2015). Figure 2 shows *mud application* at the beach of Parede (near of Lisbon) and at the beach of Porto de Mós (in Algarve). Also, *mud baths* are taking place in the discontinued salt pan named Barquinha, in Castro Marim (in Algarve), using the *saline mud* deposited at the bottom of the salt pan.

Peloid

The name *peloid* corresponds to the name *péloïde* proposed in 1933 by Judd Lewis, President of the International Standard Measurements Committee, to encompass all the diverse names of natural sediments to which therapeutic properties were attributed, names naturally varied from country to country. For essentially inorganic natural sediments deposited around springs, the names *boue*, *fango*, *schlamm*, *lama* and *barro* are employed in France, Italy, Germany, Portugal and Spain, respectively.

The name *peloid* is derived from the Greek word "πξλος" spelled "pelòs", meaning "mud", and from the name *peloid* the terms *peloid therapy* and *pelotherapy* (in short) were derived. The *peloid* designation was definitively adopted at the Conference of the ISMH (International Society of Medical Hydrology) held in Wiesbaden, Germany, in 1938.

Peloid is defined as "natural product (natural sediment) composed of a mixture of mineral water (sea water and lake water included) with organic or inorganic matter that results from either geologic or biologic processes or yet from both processes, and is utilized for therapeutic purposes under the form of packs, compresses or baths". This is the official *International Definition of Peloid* that was approved in the IV^{ème} ISMH Conference held in 1949, in Dax, France. Dax is the first and principal thermal town in France being frequented by about 55,000 patients/year.

The famous *peloid* of Dax (named Terdax®) is produced by mixing the "limon" (clay–rich sediment) extracted from the Adour river with the hyperthermal (39–44 °C) calcic and sodic chlorinated-sulphated natural mineral water that emerges from a local thermal spring, and submitting the mixture to maturation inside an hermetic container during 21 days. Also, the official *International Classification of Peloids* (the original, in French, is shown in Table 1) was established and approved at the same ISMH Conference based on: origin of the solid component, chemical nature and temperature of mineral water, and maturation conditions.

Before and after 1949, various authors have proposed definitions and classifications for *peloids*, since concepts and classifications can change with

Table 1 Original *International Classification de Péloïdes* (Dax 1949)

Dénomination des Péloïdes	Origine	Eau Minéral		Conditions de maturation
		Nature chimique	Température	
Boues (Fanghi, Muds, Schlamm)	A predominance inorganique (minérale)	Sulfureuse, sulfatée, chlorurée, bromurée, iodurée	Hyperthermale *au griffon* Homéothermale (36–38 °C) *au griffon* Hypothermale *au griffon*	a) In situ (sur le *griffon* des sources) b) *en bassin*
Limons	*Id.*	Eau de mer ou de lac salé	Hyperthermale *au bassin*	In situ
Tourbes (Torbe, Peats, Moor)	A prédominance organique	Alcaline, carbonatée, ferrugineuse, sulfureuse eau de mer	Hyperthermale *au griffon* Homéothermale *au griffon* Hypothermale *au griffon* Hypothermale *au bassin*	a) ouverte b) couverte
Muffe (Mousses, barégines)	*Id.*	Sulfureuse	Hyperthermale *au griffon*	In situ
Bioglées autres que le muffe (Algues, etc.)	*Id.*	Eaux minérales autres que les eaux sulfureuses	Hyperthermale *au griffon* Homéothermale *au griffon* Hypothermale *au griffon*	*Id.*
Sapropeli	mixte	Alcaline, ferrugineuse, sulfureuse	Hypothermale *au bassin*	*Id.*
Gyttja	*Id.*	Eau de mer	*Id.*	*Id.*

Limons—muddy sediments predominantly inorganic, such as loam, slime and ooze that are deposited by sea, lake or river waters; Muffe—muddy organic sediment rich in filamentous bacteria, known as bioglea or biofilm, that is formed on dependence of sulphurous mineral water; Bioglées—muddy organic-rich sediment known as bioglea or biofilm, that is formed on dependence of non sulphurous mineral water; (sur le *griffon* des sources)—(on the spring of sources)

time, situation justified by the progressive scientific evolution. Porlezza (1965) reports the various definitions of *peloid* being proposed in the time interval 1933–1952. Gomes et al. (2013) show the historical evolution of *peloid definition* and of *peloids classification* too, and the authors have proposed a new definition of *peloid* as follows:

> Peloid is a maturated mud or muddy dispersion with healing and/or cosmetic properties, composed of a complex mixture of fine-grained natural materials of geologic and/or biologic origins, mineral water or sea water, and commonly organic compounds from biological metabolic activity.

Maturation, an essential but complex and multifactorial process (depending on maturation time, stirring method, temperature and light exposure) provides matter exchanges till the physical, chemical and biochemical and equilibrium between *peloid* solid, liquid and gas phases could be attained. Maturation could be also a creative process particularly in the case of thermal mud bearing organic matter and thermophilic microorganisms, since along the process changes in the initial microflora and the production of anti-inflammatory compounds (sulphoglycolipids) could take place (Galzigna et al. 1995, 1996, 1998, 1999a b; Tolomio et al. 1999, 2002, 2004).

Peloid therapy

The topical use of natural muddy sediment under the form of mud paste for therapeutic and/or cosmetic purposes, under medical counselling and surveillance, sediment that besides maturation in the occurrence site has undergone later manipulation and maturation in the artificial environment existing inside the *spas* of both Thermal Resorts and Thalassotherapy Centers. Such artificialized natural muddy sediment is simply called *peloid s.s* or just *peloid*. In France, in 2005, in a total of 94 thermal stations 73 used *maturated muds* or *peloids* for therapeutic and cosmetic purposes (Francois et al. 2005).

Pelotherapy

Term of comprehensive meaning used for the topical application of either *mud* or *natural peloid,* or of *peloid s.s* or just *peloid,* with therapeutic or cosmetic purposes (see Figs. 3, 4).

Pelotherapy is applied all over the Europe, particularly in Thermal, Thalassotherapy and Rehabilitation Centres, to treat specific rheumatologic and dermatological pathologies. Maraver (2006), Gomes et al. (2013) and Horno (2014) report in a synthetic way relevant data concerned with the historical evolution of *pelotherapy*. *Mud* or *natural peloid* can be applied, either outdoors (at or nearby the occurrence site) or indoors of nearby or faraway *spas* where it could get the designation *therapeutic mud* or even *peloid* if the original *mud* had undergone some manipulation involving refining and beneficiation, situation exemplified in the case of the Dead Sea sulphur-containing mud enriched in magnesium salts known and commercialized worldwide due to its therapeutic and cosmetic properties (Harari 2012a, b).

Fangotherapy

It is a particular type of *pelotherapy* that involves the use of *fango* name of Italian origin attributed to muddy *natural peloids* deposited from thermal springs as happens in the case of the Euganean volcanic region, in Italy, where important Thermal Resorts exist, such as Montecatini, Abano and Battaglia. Such *natural peloids* become *artificial peloids*, or *peloids s.s*, or just *peloids,* after undergoing manipulation and maturation (process that lasts weeks or months and is needed to achieve the physicochemical equilibrium between *peloid* solid, liquid and gas phases) inside the *spas*.

Natural peloid

In general, it is a natural muddy sedimentary geomaterial of marine, fluvial, estuarine, lacustrine or volcanic origin and of complex composition consisting of a mixture of solid, liquid and gas phases, each one containing diverse and specific components. Depending upon *natural peloid* origin and composition, the *peloid* liquid phase could represent around 30% to 90% of the *peloid* weight, the lowest values corresponding to *peloids* rich in mineral matter and the highest values corresponding to *peloids* rich in organic matter.

Based on origin, *natural peloids* can be classified into two groups: *primary peloids* or *virgin peloids* if the solid component has been mechanically transported as particulate dispersed material in the mineral water of a spring, and thereafter it is deposited, and *secondary peloids* if the solid component and the mineral water come from different sources (Veniale 1998). Also based on origin, the designations *eu-peloids* and *parapeloids* have been used for *natural peloids* and *artificial peloids*, respectively.

Based on global composition, more precisely on the quantitative ratio inorganic/organic components, Gomes and Silva (2010) classified *natural peloids* into three main groups: *essentially inorganic peloids* (mud, fango); *essentially organic peloids* (peat and biofilm); and *mixed inorganic–organic peloids* (sapropel, gyttja). Also based on their mineral and chemical composition, *natural peloids* can be classified into three groups: *phyllopeloids* (characterized by significant content of phylossilicates represented by clay minerals); *organo-peloids* (characterized by significant participation of organic matter); and *sulpho-peloids* (characterized by significant participation of sulphur existing both in organic matter and in mineral waters, under the forms of S, H_2S or metal sulphides (Pozo et al. 2010). If yet based upon their application and function *natural peloids* can be classified into two groups: *therapeutic peloids* or *medical peloids* and *cosmetic peloids* (Gomes et al. 2013).

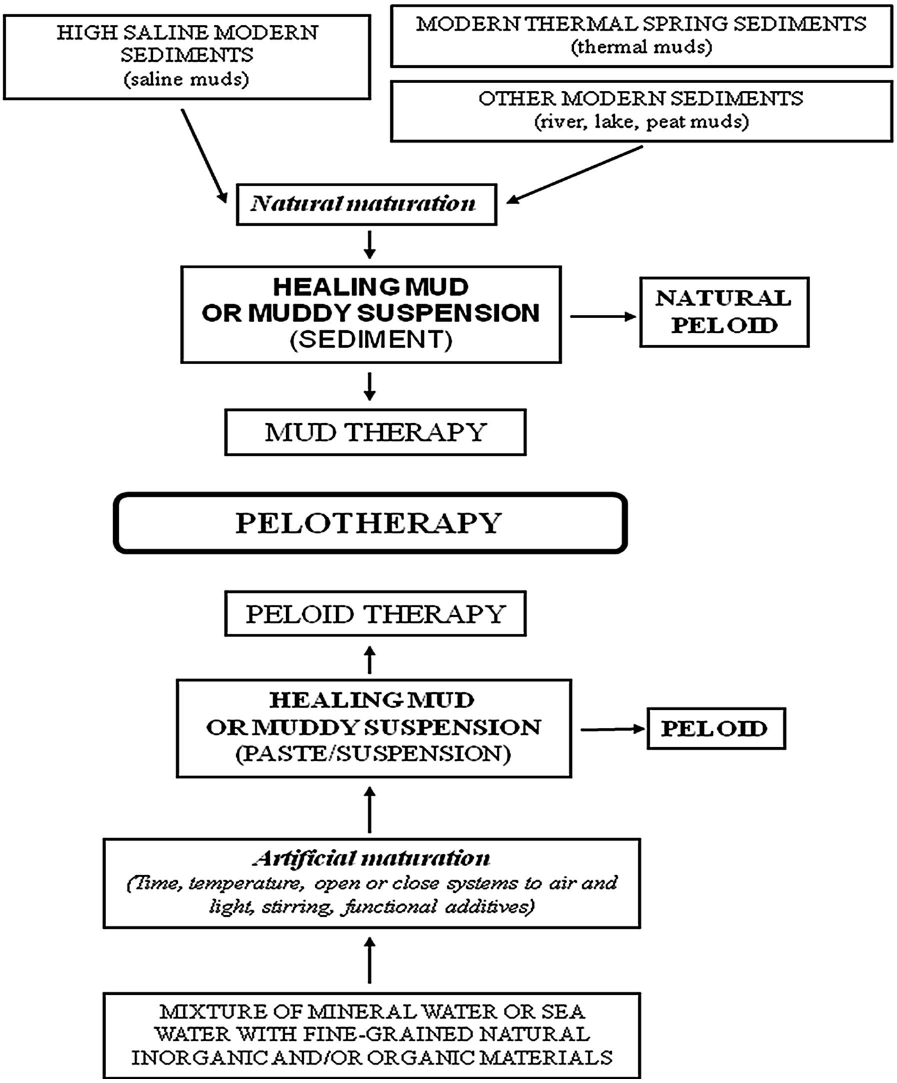

Fig. 3 Concepts of *mud* or *natural peloid*, *mud therapy*, *peloid*, *peloid therapy* and *pelotherapy*. *Source*: Gomes et al. (2013)

The classifications referred to could be applied as well as to *artificialized* or *artificial peloids* (derived from *natural peloids* but undergoing manipulation and maturation inside *spa* facilities).

In terms of health safety, *natural peloids* and even *artificial peloids* or *peloids s.s* could be hazardous due to the difficult control of their chemical and microbiological constituents that could cause potential health risks. As important as the chemical safety is the sanitary safety.

In what microbiological risks are concerned besides its *autochthonous or natural* microflora, *natural peloids* could have an *allochthonous microflora* of great importance as they may include undesirable pathogen microorganisms, most of anthropogenic origin.

Recently, Gerencsér (2014) has assessed the microbiological risk of five *natural peloids* occurring in the Carpathian Basin which are certified and marketed in Hungary, country where balneology is of paramount importance. The famous Héviz' *peloid* registered as "Neydharting" *peloid* was one of the *natural peloids* being studied and classified as peat due to its high organic matter content, and in it the average total plate count was estimated at 2794 colonies/g, the average *Clostridium* count was estimated at 800 colonies/g, and the faecal contamination was not confirmed.

Certain pathogenic bacteria for man could be present in *natural peloids* and even in *peloids s.s*, currently used as *mud packs* and *peloid packs* or

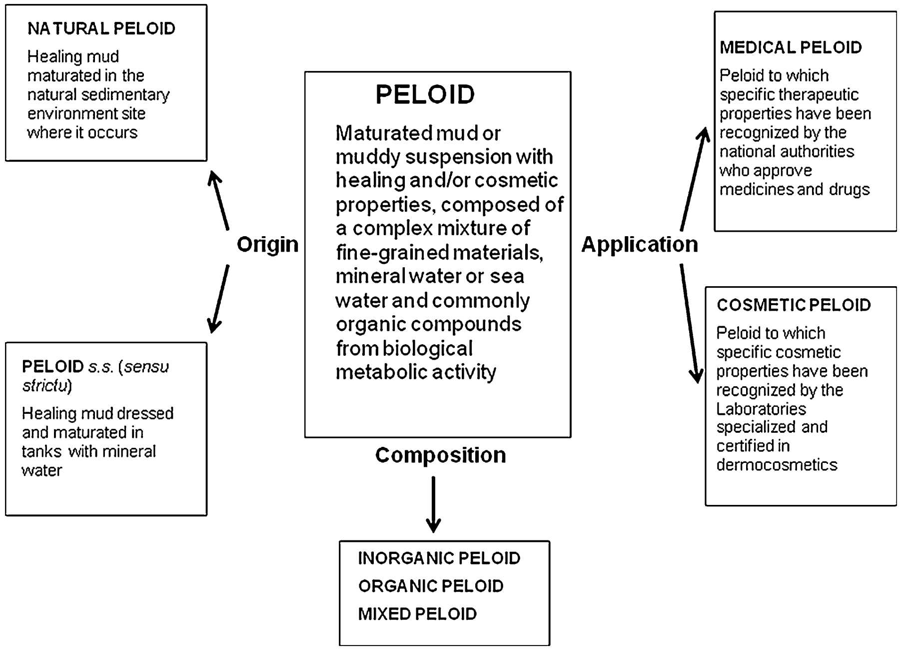

Fig. 4 Concepts of *natural peloid*, *peloid s.s*, *peloid*, *medical peloid* and *cosmetic peloid*. *Source*: Gomes et al. (2013)

cataplasms due to its direct contact with the skin are potentially more hazardous than compresses. Within bacteria, *Clostridium perfringens*, *Clostridium botulinum, Clostridium tetani, P. aeruginosa*, *S. aureus*, *E. coli* and *C. albicans* are pathogenic species that could be present in both *natural peloids* and *artificial peloids*. In the last type of *peloids*, the microbial source could be either the mineral water (thermal or not thermal) or the clay, or both. In what clay is concerned the mostly used clays (kaolin and bentonite) in pharmaceutical formulations, the Pharmacopeias (EP 4th edition and USP 29) establish the maximum of 10^3 CFU/g for microbial content.

Microbiological study of *natural peloids* and *artificial peloids* or *peloids s.s* comprises the determination of indicators such as total plate count (number of colonies that will grow within 48 h at the temperature of 37 °C and are determined in 1 g of *mud* or *peloid*) and total coliforms count (also determined in 1 g of *mud/peloid*) that could indicate faecal contamination.

Within the European countries, with exception of certain regions of Germany and France there are not quality standards or guidelines for *muds* or *peloids* utilized for therapeutic purposes. In Germany, the guidelines are as follows: mesophilic heterotrophic microorganisms determined at 20 °C $< 10^7$ CFU (colony-forming units)/g; mesophilic heterotrophic microorganisms determined at 36 °C $< 10^7$ CFU/g; *Ps. aeruginosa*—0 CFU/g; yeasts and fungi $<10^4$ CFU/g; coliforms $<10^4$ CFU/g; *E. coli* $<10^2$ CFU/g; *S. aureus*—0 CFU/g; 5.5 < pH < 9.5.

Outside of Europe, in Cuba, a country where *natural peloids* and *peloids* have a paramount importance for therapeutic and cosmetic purposes, the sanitary control of these materials has deserved high concern, reason why a regulation (Norma Cubana de Peloides 1998) was established containing references to *peloids* chemical and microbiological specifications.

Comparatively to *natural peloids*, the hereunder referred to *designed and engineered peloids* which are a particular type of *artificial peloids* could be sanitary much safer, in terms of hazardous chemicals and pathogen microorganisms, because each individual main component (mineral water and clay) could be previously analysed, and adequate control could be carried out during each stage of the *peloid* preparation.

Artificial peloid

It is a *natural peloid* that after being extracted from the natural occurrence site had undergone manipulation and maturation inside *spas* in previously established conditions hoping that the eventual changes on its physical, chemical and biochemical properties could improve the therapeutic benefits of the *artificialized* or *artificial peloid*. The artificialization process could be still more developed in case the final product, although equally based on natural components, is *designed* and *engineered* inside specialized manufacturing units, indoors or outdoors the application units, i.e. the *spas*.

Mud therapy based on the use for therapeutic or skin care purposes of *mud* or *natural peloid* (maturated and applied at or near the natural site of occurrence) is progressively losing applied interest in favour of *peloid therapy* based on *artificial peloids* or *peloids s.s* (*stricto* sensu) manipulated (refined and beneficiated) and maturated to be used inside *spas*, due to the following facts:

1. The access to *natural peloids* is becoming more and more difficult due to environmental restrictions (the deposits are, as a rule, located inside *environmental protected areas*);
2. The geologic sites where *natural peloids* occur are *open systems highly vulnerable to anthropogenic contamination particularly due to pathogen microorganisms*; the vulnerability could be due also to potential toxic inorganic and organic compounds resulting from nearby urban, agricultural and industrial activities; the situations referred to would make either very difficult or unfeasible the sanitary control and safety of *natural peloids*;
3. The use of *natural peloids* could be hazardous has happens with mud deposited by acidic volcanic waters which are characterized by very low pH (2–3) naturally aggressive to the skin and that usually bear relatively high contents of *heavy metals*;
4. The complexity of *natural peloids* composition and characteristics makes difficult not only the identification of the *healing active principles*, but also the understanding of the *healing mechanism of action and process*, and the control of both *composition* and *sanitary state* too.

As a matter of fact, the four aforesaid facts justify the increasingly interest for *peloid therapy* based on *artificial peloids* or *peloids s.s* (*stricto* sensu), particularly on those called *designed and engineered peloids.*

Designed and engineered peloid

It is a particular type of *artificial peloid* and *secondary peloid* that can be either produced inside specialized manufacture units with the objective of its trading for application in *spas*, or produced inside the *spa* facilities where it is applied. In both cases, the products could be designed and manipulated to comply with both therapeutic and cosmetic anticipated goals and functions too.

Designed and engineered peloids easily can be manufactured using, for instance, specific mixtures of one almost monomineral and commercial clay (e.g. kaolin or bentonite), preferably of pharmaceutical grade, with one specific mineral water (e.g. sea water and salt lake water) or natural mineral water (e.g. spring thermal water), that after undergoing manipulation and maturation could be beneficiated (for instance through the incorporation of *healing functionally active additives*, either natural or synthetic, characterized by analgesic, anti-inflammatory, antioxidation, anticellulite, antipsoriasis, antiacne, etc., properties).

Natural mineral water is defined as a bacteriologically acceptable mineral water of relatively deep circulation into the earth's crust that shows specific physical and chemical properties which are stable at the source; these properties may bring about therapeutic benefits or simply favourable health benefits; the emergence or source of this type of water can be natural (spring) or related to a deep water well; generally natural mineral waters used for therapeutic purposes emerge as natural thermal springs within the territories of Thermal Resorts.

Figure 5 shows the flow sheet we have adopted for the preparation of *designed and engineered peloids*.

Due to their simple composition, controlled processing and evaluation *designed and engineered peloids* of both medical and cosmetic typologies easily can be periodically submitted to both chemical composition control (identification and quantification of inorganic or mineral and of organic constituents) and sanitary control (identification and quantification of pathogenic microorganisms).

Chemical control, for example in what heavy metals are concerned, should comply with specifications disclosed in European Pharmacopeia (2002), US Pharmacopeia (2006) and Health Canada (2009).

Decontamination of pathogen microorganisms could be achieved either by heating at 160 °C for at least 1 h (process that could cause irreversible changes in the *peloid* system) or by exposure to gamma radiation (Viseras et al. 2007). Favero et al. (2016) report an effective method for decontamination of the clay raw material (e.g. kaolin or bentonite) used in the

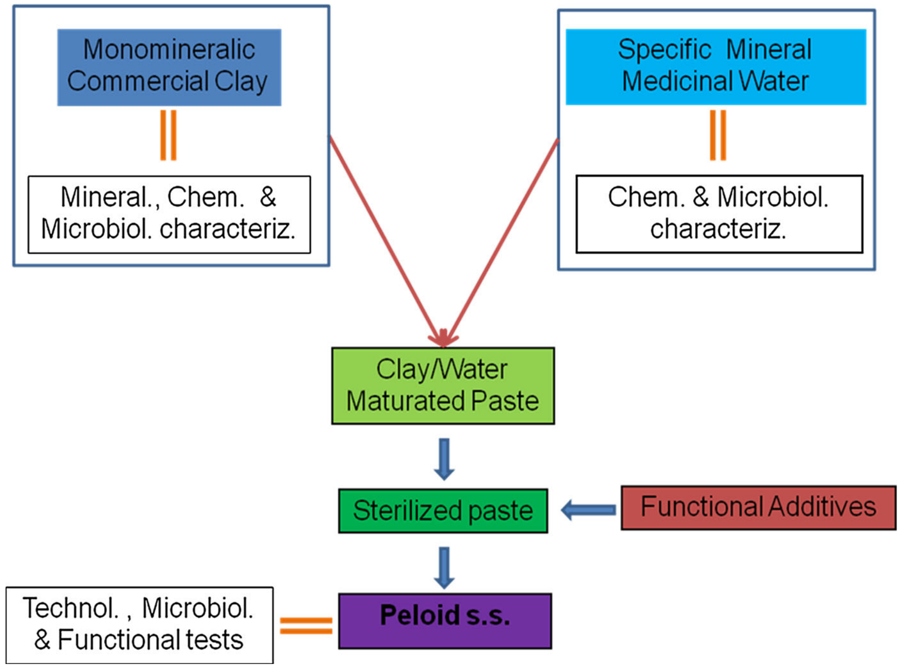

Fig. 5 Flow sheet of the preparation of *designed and engineered peloids* (Gomes et al. 2015)

preparation of *cosmetic peloids* which are very much demanding in sanitary terms [specifications disclosed, for instance, in US Pharmacopeia (2006) and in British Pharmacopeia (2008)], in case pathogen microbial contamination is found in the clay. In Europe, the Scientific Committee on Consumer Safety (SCCS) of the European Commission has reviewed and approved at its 17th plenary meeting of 11 December 2012 the regulations for testing and safety evaluation of cosmetic substances which are compiled in the document "Notes of Guidance for Testing of Cosmetic Ingredients and their Safety Evaluation" (8th revision).

The *designed and engineered peloids* are distinguished from the hereunder referred to *extemporaneous peloids* since they require a short-term maturation not longer than 1–2 weeks, time required to get a sufficient physical, chemical and eventual biochemical equilibrium between all the *peloid* constituents.

Extemporaneous peloid

It is a healing mud that is prepared at the local and time of use, blending one common or one special clay (kaolin or bentonite), or algae with natural mineral water or with sea water without undergoing maturation; it is not a real *peloid s.s* because the maturation does not occur. Meijide et al. (2010) and Arribas et al. (2010) have studied and assessed the effects on the mechanical and functional characteristics of skin from the application of *extemporaneous peloids* based on bentonite mixed with both sulphurous thermal water and sea water, as well as the clinical effects (expressed by scaling off and inflammation) on *psoriasis*.

Paramud or parapeloid or parafango

It is a product that is the result of the intimate blend, for instance, of bentonitic or illitic clay with paraffin. As a matter of fact, *paramud* or *parapeloid* or *parafango* really is not a type of *peloid*, otherwise it is a *peloid succedaneum*; it is applied, either as cataplasms or as compresses, and always hot (not above 50 °C) in physiotherapy.

Peloids action, function and benefits

As a rule, both *natural peloids* and *peloids s.s* are 3-phase systems consisting of: one *solid phase* (inorganic, organic or mixed inorganic/organic); one *liquid phase* (thermal spring, river, lake or sea water); and one *gas phase* (H_2S, CO_2, NH_4, CH_4, Rn). Also, as a rule, and in quantitative terms, the gas phase is irrelevant, but it could be therapeutically relevant. According to Burguera et al. (2012) and Fioravanti et al. (2013), H_2S, either formed from organic matter decomposition (situation common in mud of salt pans), or existing in solution in sulphurous water (chemical type quite frequent within thermal mineral waters), would act as an anti-inflammatory and antioxidant agent in human osteoarthritic articular chondrocytes. Also, according to Yamaoka et al. (2004) and Falkenback et al. (2005), radon (Rn) therapy is known to be effective against pain-related rheumatic diseases such as osteoarthritis which is commonly treated with *peloids*.

The inorganic component is mainly composed of a fine-grained sediment called clay, itself a very complex system that consists of *clay minerals* (as a rule, 2 or 3 species) and *non-clay minerals* (as a rule, 3 or 4 species). The organic component could be more complex and is surely less studied than the inorganic component; it could contain several eventually beneficial active hydrophilic and lipophilic compounds.

Peloids are used under *medical counselling and accompanying* in Health Resort Medicine or Spa Therapy Centers. The health benefits of *peloids* are being attributed to a combination of actions, and within these, the *thermal actions* and the *chemical actions* are currently the most emphasized.

Clinical evidence based on epidemiological studies which are reported in specialized literature emphasizes the benefits of *mud therapy* and *peloid therapy* on degenerative and inflammatory rheumatism taking advantage of *peloids* analgesic, anti-inflammatory, antioxidant and antimicrobian actions.

Several authors have emphasized the benefits of *peloid properties* and *peloid therapeutic functions*: Veniale (1996, 1997, 1999), Carretero (2002), Carretero et al. (2006, 2013), Maraver (2013), Tefner (2014), Maraver et al. (2015), Roques (2015), Fioravanti et al. (2014), Fioravanti and Chelesschi (2015), Meijide et al. (2014, 2015) and Gomes (2015). Also, there is evidence of the positive effects of *peloids* on dermatological affections, especially on psoriasis, acne and seborrhoea, as well as on skin care functions (cleansing, degreasing, exfoliating, hydrating, tonifying and reaffirming). Several authors have emphasized the benefits of *peloid properties* and *peloid dermatological and aesthetic functions*: Carabelli et al. (1998), Arribas et al. (2012), Baschini et al. (2010), Meijide et al. (2014) and Garcia (2014).

Clay/clay minerals and human health

Both therapeutic and cosmetic uses of clay and clay minerals (hydrous phyllosilicates) have been reported by several authors such as Bech (1987), Viseras and López-Galindo (1999), Veniale (1999), Reinbacher (2003), Gomes and Silva (2007), Carretero (2002), Carretero et al. (2006, 2013), Viseras et al. (2007), Gomes and Silva (2010), Rautureau et al. (2010), De Vos (2010), Young (2011), Gomes (2013), Gomes et al. (2013), Meijide et al. (2014), Williams and Hillier (2014), Gomes et al. (2015) and Mattioli et al. (2016).

Clays such as kaolin, bentonite, palygorskite, sepiolite and talc are reported in Pharmacopoeias. Therefore, being considered medicines they could participate in pharmaceutical formulations as active principles and/or as excipients (Viseras and López-Galindo 1999; Lopez-Galindo and Viseras 2004; Lopez-Galindo et al. 2007; Viseras et al. 2007, 2010). In particular, the use of bentonite and kaolin in human health has been the object of significant research (Novelli 1996, 1998, 2000; Cara et al. 2000; Viseras et al. 2006; Williams et al. 2009; Williams and Hiller 2014; Casás et al. 2011; Carretero et al. 2013).

Clays and clay minerals may enter the human body by inhalation, ingestion or dermal absorption.

The main properties of clays, attributed to clay minerals, that justify the healing effects of the so-called *healing clays* and *edible clays* are as follows: (1) ubiquitous geological occurrence of clay deposits at or near the earth's surface; (2) very small particle size (as a rule less than 2 μm) and particle shape (platy in most clay minerals, but fibrous, tubular and spherical in others), essential conditions to yield high specific surface area (SSA), good when they could enable, for instance, the coating of stomach and small intestine in order to alleviate nausea and indigestion, or the topical coating and adhesiveness of skin, or yet drug delivery, bad when they could to enable, for instance, toxicity associated with long-term inhalation; (3) low hardness and abrasiveness providing an agreeable sensation when the clay paste gets in touch with the skin and is spread on it; (4) great affinity to water, facilitating the formation of plastic pastes with adequate flowing, spreading and adhesiveness to the skin; (5) electric charge globally negative; (6) high adsorption/absorbing capacities allowing the adsorption and absorption of toxins, bacteria and viruses and their elimination from the skin, making efficient the use of certain *peloids* in the treatment of cutaneous affections such as, acne, seborrhoea, eczema, psoriasis, and allowing too the use of certain nanotubular clays, as is the case of halloysite, in controlled release of drug delivery; (7) clays of alkaline character can buffer the gastrointestinal acidic pH, whereas clays characterized by acid pH, if similar to the skin pH, avoid skin irritations; (8) high cation and anion exchange capacities promoting the reversible fixation and the exchange of chemical elements, for instance between the clay from facial masks and the skin, or the incorporation of the elements with medicinal interest; (9) exchangeable reduced elements, as is the case of Fe^{+2} and its oxidation, are responsible for the bactericide character of certain clays that become toxic to human pathogens; (10) high capacity of heat retention and low heat diffusiveness, important factors for coatings (*mud packs* or *peloid packs*) based on clay minerals since they can be applied warm or cool, depending on the nature of the affections to be treated; and (11) diversity of natural colours.

Due to these and other properties such as dispersivity, hygroscopicity, unctuosity, plasticity and thixotropy, chemical inertness and inconsiderable toxicity clays and clay minerals are widely used in the pharmaceutical industry as lubricants, desiccants, disintegrants, diluents, binders, pigments, opacifiers, as well as emulsifying, thickening, isotonic and anticaking agents. Also they could be used as flavour correctors and carriers of active ingredients.

Within the main curative properties of clays and clay minerals, the following should be enhanced: antacids, gastrointestinal protectors, antidiarrheaics, laxatives, homeostatics, emetics and antianemics.

Kaolinitic clays and smectitic clays are the most used *healing clays* and *edible clays* for therapeutic and cosmetic purposes. Kaolins are being considered effective as haemostatic wound dressings, and various forms of kaolin have been shown to be antibacterial, and being utilized too in drug delivery (Williams and Hillier 2014). Also, the bactericide character has been reported in the case of the so-called *French green clays* (Williams et al. 2004, 2008, 2011; Williams and Haydel 2010; Otto and Haydel 2013), being attributed to their specific mineralogical/chemical composition. In a very recent and interesting article, Photos-Jones et al. (2015) have tested the antibacterial properties attributed to the *Samian Earth*, a Greek traditional medicinal earth now identified as a boron/boric acid rich smectitic clay, whose medicinal properties (eye salve) were reported by Dioscorides (c.41–90 AD) in his book "De Materia Medica".

Kaolinite (shows platy morphology) and halloysite (can show, either platy or tubular or yet spherical morphology) are the main clay minerals that could be present in kaolins. Compared to platy kaolinite forms, halloysite tubular forms have higher specific surface areas and consequently greater potential to bind, in particular, cationic drugs, enabling the conditioning and control of their release rate. Halloysite nanotubes (with *c.* 50–70 nm of external diameter and *c.* 15 nm diameter lumen) are able to entrap and carry inside their lumen drug molecules that could be used in biomedical applications.

Smectite clays which are characterized by much higher surface areas and unit layer charges comparatively to kaolins have interlayer free and size variable spaces where drug molecules could be entrapped or encapsulated enabling its biomedical use as drug delivery systems. Within the clay mineral species constituting the smectite group, montmorillonite has been the most used species.

Smecta® and Beidelix are two drugs commercialized in Pharmacies, whose active substances are the clay minerals *diosmectite* (dioctahedral smectite of Al–Mg montmorilonite typology) and *beidellite* (also dioctahedral smectite but richer in Al), respectively. Under the form of powders, both drugs are ingested after being dispersed in potable water. The effectiveness of *beidellite* on colopathy has been clinically shown by Bigard and Gilbert (1990).

Edible clay: benefits and risks

Both benefits and risks of the use of *edible clay* are particularly well reported: Prasad et al. (1961), Key et al. (1982), Danford (1982), Hunter and De Kleime (1984), Vermeer and Ferrell (1985), Ziegler (1997), Aufreiter et al. (1997), Wiley and Katz (1998), Mahaney et al. (2000), Woywodt and Kiss (2002), Saathoff et al. (2002), Hooda et al. (2002, 2004), Kwong and Henry (2003), Izugbara (2003), Nchito et al. (2004), Tayie (2004), Trivedi et al. (2005), Abrahams et al. (2006), Tateo et al. (2006), Kikouama et al. (2009a, b), Abrahams (2010), Young (2010), Ekosse and Jumbam (2010), Kikouama and Baldé (2010), Njiru et al. (2011), Ekosse and Ngole (2012), Mwalongo and Mohamed (2013), Lambert et al. (2013), Nyanza et al. (2014) and Owumi and Oyelere (2015), some of them being briefly shown hereunder.

With regard to benefits, the authors emphasize a double effect: clay chemical composition enables the release of bioessential trace elements, such as iron, zinc, magnesium and calcium, whereas clay mineralogical composition enables its use in the treatment of digestive diseases. According to Young (2011), *edible clay* could provide a dietary supplement of the trace elements referred to as well as of other micronutrients. Also, according to Williams and Hillier (2014) an association between anaemia and geophagy has been recognized since Roman times.

Benefits

Gastroenterological diseases Diarrhoea, colitis, nausea, colopathy and ulcers.
Source of mineral nutrients Dietary supplementation: in case, for instance, of Fe, Zn and Mg deficiencies.

Risks

Microbiological contamination Pathogenic microorganisms, both present in the natural geomaterial and/or acquired during its manipulation, baking being not a sufficient process for their inactivity;
Contamination of toxic trace elements Pb, Cd, Hg, Al, As, etc. through enteric incorporation.
Constipation and reduction in the gastrointestinal absorption capacity of drugs simultaneously taken with the edible clay.

The determination of both essential and toxic elements present in the clay soil commonly consumed by pregnant women, in order to assess safety, has been recently carried out, for example, in Tanzania by Mwalongo and Mohamed (2013) and Nyanza et al. (2014) and in Nigeria by Lar et al. (2014), Igeoma et al. (2014) and Owumi and Oyelere (2015).

Kikouama and Baldé (2010) to compensate eventual dietary deficiencies in Fe and Zn have designed clay-containing pellets bearing certain Fe and Zn amounts; such pellets were able to be retained for few hours by flotation in the highly acidic stomach cavity in order to favour and optimize the controlled release and gastrointestinal absorption of those essential trace elements.

Healing clay: benefits and risks of topical uses

Benefits

Rheumatologic diseases Osteoarthritis (AO), back pain and fibromyalgia.
Dermatologic diseases Psoriasis, acne and seborrhoea.

Risks

Contamination of toxic trace elements Pb, Cd, Hg, Al, As, Sb, Zn, Cr, Cu, Ni, etc. could be incorporated through dermal absorption.
Contamination of microorganisms Pathogenic microorganisms could cause skin infection and other skin disorders; manipulation and maturation could favour the development of pathogenic microorganisms.

Microbiological study of *natural peloids* and *artificial peloids* or *peloids s.s* comprises the determination of indicators such as total plate count (number of colonies that will grow within 48 h at the temperature of 37 °C and are determined in 1 g of *mud* or *peloid*) and total coliforms count (also determined in 1 g of *mud/peloid*) that could indicate faecal contamination.

Decontamination of pathogen microorganisms could be achieved either by heating at 160 °C for at least 1 h (process that could cause irreversible changes in the *peloid* system) or by exposure to gamma radiation (Viseras et al. 2007). Favero et al. (2016) report an effective method for decontamination of the clay raw material (e.g. kaolin or bentonite) used in the preparation of *cosmetic peloids* which are very much demanding in sanitary terms [specifications disclosed, for instance, in US Pharmacopeia (2006) and in British Pharmacopeia (2008)], in case pathogen microbial contamination is found in the clay.

Mechanisms of action in the use of edible clay and healing clay

Edible clay

Protective action of the mucous membrane of the gastric wall and/or duodenum, since the covering or coating capacity of clay particles could avoid the action of chlorhydropeptic aggressive factors (Kikouama and Baldé 2010);

Buffer and antacid action neutralizing the stomach excessive acidity; kaolinitic and smectitic clays having basic pH values are the most effective;

Releasing action in the stomach acidic medium of micronutrients (bioessential minerals), able to supplement the diet of deprived people (Kikouama 2009a, b);

Restoration action of the hydro-electrolytic balance due to clay adsorption/absorption and cation exchange capacities, reason why clay-based medicines, such as Smecta® and Beidelix, constituted by dioctahedral smectites (montmorilonite and beidellite) are widely used against diarrhoea, due to high sorption capacities of those clay minerals (Kikouama and Baldé 2010);

Reduction action of pathogenic microorganisms and toxins through their fixation and posterior removal by defecation.

Healing clay: healing mud/peloid

Thermotherapeutic action In the treatment of rheumatic diseases (particularly osteoarthritis), *therapeutic mud* and *peloid* are currently applied directly onto the skin of the affected areas after being warmed up to 42–45 °C, for periods of normally 20–30 min. Local vasodilatation and hyperaemia improve blood irrigation and circulation in the skin and underlying tissues; liberation of histamine and acetilcoline; and modification of serum levels of amino acids (Pastor 1998; Fernández-Lao et al. 2012; Sarsan et al. 2012; Maraver 2013; Tricás et al. 2014).

The thermotherapeutic action of both *therapeutic mud* and *peloid* provided by the heat very much depends upon the thermal properties of these materials, such as specific heat (the highest possible), heat capacity (the highest possible) and cooling rate (the lowest possible), which values depend upon the texture, the nature and quantity of the solid phase, as well as the nature and quantity of the liquid phase (Armijo 1991; Armijo et al. 2016). These authors found that for clay pastes with 60% water the cooling rate is slower for bentonite-based peloids than for kaolin-based peloids, different behaviour that in our opinion could be justified by particle size and distribution as well as by particle aggregation. Therefore, in terms of just thermotherapeutic action *bentonite-based designed and engineered peloids* are preferred to *kaolin-based designed and engineered peloids*.

Chemotherapeutic action Numerous studies have demonstrated that the anti-inflammatory, analgesic, chondroprotecting and immunological actions could be attributed to the chemical properties of both *therapeutic mud* and *peloid* (Carretero 2002; Carretero and Pozo 2007; Gomes and Silva 2007; Gomes 2013) and to the transdermal absorption of minerals (Tateo et al. 2009; Carretero et al. 2010) and organic substances (Maraver et al. 1987; Teixeira et al. 1996; Curri et al. 1997; Tolomio et al. 1999; Nissenbaum et al. 2002; Torrella 2006; Odabasi et al. 2008; Tserenpil et al. 2010; Kim et al. 2010; Suárez et al. 2011) having analgesic, anti-inflammatory, chondroprotecting and immunological action (Roques 2004; Carretero et al. 2010; Tateo and Summa 2007, 2009; Beer et al. 2003, 2013), mostly resulting from the maturation process (Galzigna et al. 1996, 1999a, b; Veniale et al. 2004; Carretero et al. 2007, Carretero 2008; Gámiz et al. 2008, 2009; Delgado et al. 2010; Fernández-González, 2010; Fernández-González et al. 2013; Fioravanti et al. 2011; Fioravanti and Chelesschi 2015).

The organic fraction of *therapeutic mud* and *peloid* has been less investigated than the inorganic fraction. In studies of *peat mud*, Beer et al. (2002, 2003) consider that the existing aqueous pharmacologically active and water-soluble (hydrophilic) substances, such as humic, fulmic and ulmic acid derivatives, could permeate human skin in quantities sufficient to cause biologic effects. Odabasi et al. (2007) consider that *peat mud* beneficial chemical effects could be attributed not only to organic hydrophilic substances, but also to lipophilic low molecular weight substances derived from fatty acids such as palmitic acid, linoleic acid, oleic acid, stearic acid, lauric acid and phthalic acid, and the authors have consider too that the subject requires more investigation.

Also in terms of just chemotherapeutic action, *bentonite-based designed and engineered peloids* are preferred to *kaolin-based designed and engineered peloids*, since both chemical and surface properties of smectite (the basic constituent of bentonite), such as electric charge, ion exchange and adsorption, are favourable comparatively to same properties of kaolinite (the basic constituent of kaolin).

There is sufficient clinical evidence from specialized literature confirming, at least, the short-term benefits of peloids which are being attributed to a combination of the factors earlier discussed. Whereas both thermal and chemical factors are considered the most effective ones, while the first is generally well established and attributed to the solid phase (clay), there is little evidence relatively to the second factor, although one might expect that minerals and organic substances dissolved in the liquid phase (mineral water) of the peloid could interact and provide dermal absorption during the peloid application. On the one hand, the solid phase of the *peloid paste* favours the maintenance of *peloid heat* along *peloid application* as well as the contact and eventual dermal absorption of chemical elements and molecules reversibly fixed at clay minerals surfaces by ion exchange. On the other hand, minerals and organic substances dissolved in the liquid phase of the *peloid paste* become able for dermal absorption along all time (around 20 min) of peloid application. However, the hydrofobicity of the skin barrier formed by the epidermis *stratum corneum* (SC) layer does not facilitate the percutaneous penetration of hydrophilic substances, minerals and polar organic compounds (Gomes 2015). Mineral salts, trace elements and organic polar compounds carried in solution in the hydrophilic mineral water cannot easily penetrate the skin (Bolzinger et al. 2012).

Recent and very interesting research is looking at transdermal delivery systems attractive for both topical and systemic therapeutics. The so-called skin permeation enhancers (such as, surfactants, natural oils, hydrocarbons and fatty acids) which are being looked at by several researchers (Naik et al. 1995; Tanojo et al. 1999; Lim et al. 2014; Pandey et al. 2014) can improve the penetration of bioessential substances by perturbing the barrier function of the *stratum corneum*.

To favour skin permeation, immediately before *peloid* application, skin cleansing, gumming exfoliation and hydration are recommended. According to Araújo et al. (2015) to overcome such hindrance, the cosmeceutical/cosmetics industry is innovating and developing studies involving nanobiotechnology to create and encapsulate effective functional molecules in nanocarrier systems, namely liposomes, polymeric and solid lipid nanoparticles, and nanoemulsions, which are considered fundamental to increase the skin permeation/penetration to minerals and organics carried in solution in mineral water.

However, the *peloid solid substances* can modify the properties of the liquid phase through the passage into solution of the water-soluble compounds existing in those substances and of the reversibly fixed chemical elements existing at the surfaces of the fine-grained particles of both clay minerals and organic matter.

The simple composition and easy manipulation of *designed and engineered peloids*, and the easy incorporation into their formulations of amphiphilic organic compounds (containing polar water-soluble chemical groups and water insoluble chemical groups) could overcome such hindrance.

Conclusions

1. *Medicinal uses of clay*, for instance as gastrointestinal ailments, nutritional supplementation and wound dressings, have been recorded since the Antiquity; presently, there is an extensive record of data concerned with worldwide practices and investigation;
2. *Healing clays* could be used internally or orally, either as previously prepared cookies sucked or crunched, or yet as beverage of clay water dispersions (*argillic water*); such *healing clays* are called *edible clays*, and they could provide benefits or risks to human health; risks are known attributing to geophagic practices situations of heavy metals poisoning, bowels blockage and microbial contamination; much has been investigated about the physical, physicochemical and chemical properties of *edible clays*, but little is still known about their real medical effects and consequences;
3. *Healing clays* also could be used externally or topically in the form of semisolid pastes, called *mud* and *peloid*, inside the *spas* of Thermal Resorts and Thalassotherapy Centres;
4. Much research is still required in order to discuss and confirm the effective *mechanisms of action*

and the health benefits of *healing clays* when used under the form of general or local *mud baths* or under the form of *mud packs* or yet *peloid packs*; experience has shown that when *peloid packs* are utilized, for instance, in the treatment of musculoskeletal disorders (e.g. knee osteoarthritis), randomized, controlled and double-blind studies are recommended; the benefits (a significant number of studies point out, at least, to short-term effective positive effects) are attributed, in general, to the combination of thermal and chemical actions, although the agents, mechanisms and processes for transdermal absorption enhancement and optimization still require more research.

References

Abrahams, P. W. (2005). Geophagy and the involuntary ingestion of soils. In O. Selinu, B. Alloway, A. A. Centeno, R. B. Finkelman, R. Fuge, U. Lindh, et al. (Eds.), *Essentials of medical geology* (pp. 435–458). Amsterdam: Elsevier.

Abrahams, P. W. (2010). ''Earth eaters'': Ancient and modern perspectives on human geophagy. In E. R. Landa & C. Feller (Eds.), *Soil and culture* (pp. 369–398). Dordrecht: Springer **(Chapter 23)**.

Abrahams, P. W., Follansbee, M. H., Hunt, A., Smith, B., & Wragg, J. (2006). Iron nutrition and possible lead toxicity: An appraisal of geophagy undertaken by pregnant women of UK Asian communities. *Applied Geochemistry, 21,* 98–108.

Abrahams, P. W., & Parsons, J. A. (1996). Geophagy in the tropics: A literature review. *Geographical Journal, 162,* 63–72.

Al-Rmaldi, S. W., Jenkins, R. O., Watts, M. J., & Haris, P. I. (2010). Risk of human exposure to arsenic and other toxic elements from geophagy: Trace element analysis of baked clay using inductively coupled plasma mass spectrometry. *Environmental Health, 9*, 79. http://www.ehjournal.net/content/9/1/79.

Araújo, A. R. T. S., Paiva, T., Ribeiro, M. P., & Coutinho, P. (2015). Innovation in thermalism: An example in Beira Interior Region of Portugal, chapter 11. In M. Peris-Ortiz & J. Álvarez-Garcia (Eds.), *Health and wellness tourism: Emergence of a new market segment* (pp. 165–180). Berlin: Springer.

Armijo, F. (1991). Propriedades térmicas de los peloides. *Boletin de la Sociedad Española de Hidrologia Médica, 6*(3), 151–158.

Armijo, F., Maraver, F., Pozo, M., Carretero, M. I., Armigo, O., Fernandez-Torán, M. A., et al. (2016). Thermal behaviour of clays and clay-water mixtures for pelotherapy. *Applied Clay Science, 126,* 50–56.

Arribas, M., Meijide, R., & Mourelle, M. L. (2010). Evolución de la psoriasis tratada con peloides y água mineromedicinal de La Toja. In F. Maraver & M. I. Carretero (Eds.), *Libro de Resúmenes del II Congreso Iberoamericano de Peloides* (p. 75). Madrid: C.E.R.S-A.

Arribas, M., Meijide, R., & Mourelle, M. L. (2012). Long term effects of psoriasis treatment with mineral water and peloids of la Toja. *Balnea, Medical Hydrology and Balneology, Environment Aspects, 6,* 289–290.

Aufreiter, S., Hancock, R. G., Mahaney, W. C., Stamolic-Robb, A., & Sanmugadas, K. (1997). Geochemistry and mineralogy of soils eaten by humans. *International Journal of Food Sciences and Nutrition, 48,* 293–305.

Baschini, M. T., Pettinari, G. R., Vallés, J. M., Aguzzi, C., Cerezo, P., López-Galindo, A., et al. (2010). Suitability of natural sulphur-rich muds from Copahue (Argentina) for use as semisolid health care products. *Applied Clay Science, 49,* 205–212.

Bech, J. (1987). *Les terres medicinals*. Barcelona: Discurs per Reial Acadèmia de Farmàcia de Barcelona, Reial Acadèmia de Farmàcia de Barcelona-CIRIT (Generalitat de Catalunya).

Bech, J. (1996). Aspectos históricos y técnicos de las arcillas de uso medicinal, IX Simp. Grupo Especializado de Cristalografia La Cristalografia y la Industria Farmacéutica, Reales Soc. Esp. Fisica y Quimica (Ed.), Granada (pp. 15–17).

Beer, A. M., Fetaj, S., & Lange, U. (2013). Peloid therapy: An overview of the empirical status an d evidence of mud therapy. *Zeitschrift fur Rheumatologie, 72,* 581–589.

Beer, A. M., Junginger, H. E., Lukanov, J., & Sagorchev, P. (2003). Evaluation of the permeation of peat substances through human skin in vitro. *International Journal of Pharmaceutics, 253*(1–2), 169–175.

Beer, A. M., Lukanov, J., & Sagorchev, P. (2002). Isolation of biologically active fractions from the water-soluble components of fulvic and ulmic acids from peat. *Phytomedicine, 9,* 653–666.

Bigard, M. A., & Gilbert, C. (1990). Étude en double aveugle de l' effet du Beidelix sur la surproduction de gaz intestinaux induite par un repas riche en flatulents. *Médicine et Chirugie Digestives, 19,* 317–319.

Bisi-Johnson, M. A., Obi, C. L., & Ekosse, G. E. (2010). Microbiological and health related perspectives of geofagia: An overview. *African Journal of Biotechnology, 9*(19), 5784–5791.

Bisi-Johnson, M. A., Oyelade, H. A., Adediran, K. A., & Akinola, S. A. (2013). Microbial evaluation of geophagic and cosmetic clays from southern and western Nigeria: Potential natural nanomaterials. *International Journal of Environmental Chemical, Ecological, Geological and Geophysical Engineering, 7*(12), 832–835.

Bolzinger, M. A., Briançon, S., Pelletier, J., & Chevalier, Y. (2012). Penetration of drugs through skin, a complex rate-controlling membrane. *Current Opinion in Colloid & Interface Science, 17*(3), 156–165.

Bonglaisin, J. N., Mbofung, C. M. F., & Lantum, D. N. (2011). Intake of lead, cadmium and mercury in kaolin-eating: A quality control. *Journal of Medical Sciences, 11*(7), 267–273.

Brand, C. E., de Jager, L., & Ekosse, G. E. (2010). Possible health effects associated with human geophagic practice: An overview. *SA Medical Technology*, *23*(1), 11–13.
British Pharmacopeia. (2008). In Her Majesty's Stationery Office (Ed.), (10,952 pp). London: Health Ministers.
Burguera, E. F., Vela-Anero, A., & Magalhães, J. (2012). Effect of hydrogen sulfide sources on inflammation and catabolic markers on interleukin 1β-stimulated human articular chondrocytes. *Osteoarthritis Cartilage, 22,* 1026–1035.
Cara, S., Carcangiu, G., Padalino, G., Palomba, M., & Tamanini, M. (2000). The bentonites in pelotherapy: Thermal properties of clay pastes from Sardinia (Italy). *Applied Clay Science, 16,* 125–132.
Carabelli, A., De Bernardi Valserra, G., De Bernardi Valserra, M., Tripodi, S., Belloti, E., Pozzi, R., et al. (1998). Effect of thermal mud baths on normal, dry and seborrheic skin. *Clinica Terapeutica, 149*(4), 271–275.
Cardoso-Gomes, J., & Gomes, C. S. F. (2015). Mud used for therapeutic and skin care purposes at the beach of Porto de Mós, Algarve, Portugal. *Balnea, 10,* 355–356.
Carretero, M. I. (2002). Clay minerals and their beneficial effects upon human health: A review. *Applied Clay Science, 21,* 155–163.
Carretero, M. I. (2008). Efecto de la maduración sobre las arcillas empleadas en peloterapia. In J. L. Legido & M. L. Mourelle (Eds.), *Investigaciones en el ámbito Iberoamericano sobre Peloides Termales* (pp. 95–108). Vigo: Universidad Vigo.
Carretero, M. I., Gomes, C. S. F., & Tateo, F. (2006). Clays and human health. In F. Bergaya, B. K. G. Theng & G. Lagaly (Eds.), *Handbook of clay science. Developments in clay science* (Vol. 1, pp. 717–741).
Carretero, M. I., Gomes, C., & Tateo, F. (2013). Clays, drugs and human health. In F. Bergaya & G. Lagaly (Eds.), *Handbook of clay science* (pp. 711–764). Amsterdam: Elsevier.
Carretero, M. I., & Pozo, M. (2007). *Mineralogia Aplicada: Salud y Medio Ambiente* (p. 464). Madrid: Thomson.
Carretero, M. I., Pozo, M., Martin-Rubi, J. A., Pozo, E., & Maraver, F. (2010). Mobility of elements in interaction between artificial sweat and peloids used in Spanish spa. *Applied Clay Science, 48*(3), 506–515.
Carretero, M. I., Pozo, M., Sánchez, C., Garcia, F. J., Medina, J. A., & Bernabé, J. M. (2007). Comparison of saponite and montmorillonite behaviour during static and stirring maturation with sea water for pelotherapy. *Applied Clay Science, 36*(1–3), 161–173.
Casás, L. M., Legido, J. L., Pozo, M., Mourelle, L., Plantier, F., & Bessieres, D. (2011). Specific heat of mixtures of bentonitic clay with sea water or distilled water for their use in thermotherapy. *Thermochimica Acta, 524,* 68–73.
Curri, S. B., Bombardelli, E., & Grossi, F. (1997). Observations on organic components of thermal mud: Morphohistochemical and biochemical studies on lipid components of mud of the Terme dei Papi (Laghetto del Bagnaccio, Viterbo), Chemical bases of the interpretation of biological and therapeutic actions of thermal mud. *Clinica Terapeutica, 148,* 637–654.
Danford, D. E. (1982). Pica and nutrition. *Annals Reviews of Nutrition, 2,* 303–322.
Davies, T. C. (2010). Medical geology in Africa. In O. Selinus, R. B. Finkelman, & J. Centeno (Eds.), *Medical geology—A regional synthesis* (1st ed., pp. 199–219). Amsterdam: Springer **(Chapter 8)**.
Davies, B., Bowman, C., Davies, T., & Selinus, O. (2004). *Medical geology: Perspectives and prospects. Essentials of Medical Geology*. Amsterdam: Elsevier.
Davies, T. C., Lar, U. A., Solomon, A. O., & Abraham, P. W. (2008). Mineralogy and geochemistry of geophagic materials consumed in Jos-Plateau State of Nigeria. *Paper presentation at international conference South Africa*.
De Vos, P. (2010). European material medica in historical texts: Longevity of a tradition and implications for future use. *Journal of Ethnopharmacology, 176,* 10–17.
Delgado, R., Fernández-González, M. V., Gámiz, E., Martín-García, J. M., & Delgado, G. (2010). Evolución de la ultramicofábrica de los peloides en el proceso de maduración. In F. Maraver & M. I. Carretero (Eds.), *Libro de resúmenes del II Congreso Iberoamericano de Peloides* (pp. 41–42). Madrid: CERSA.
Ekosse, G. E., & Jumbam, D. N. (2010). Geophagic clays: Their mineralogy, chemistry and possible human health effects. *African Journal of Biotechnology, 9*(40), 6755–6767.
Ekosse, G. E., & Ngole, V. M. (2012). Mineralogy, geochemistry and provenance of geophagic soils from Swaziland. *Applied Clay Science, 57,* 25–31.
EMEA—European Medicines Agency. (2008). *Guidelines on the specification limits for residual metal catalysts or metal reagents*. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003586.pdf. Accessed Mar 2016.
EU. (2011). The drinking water directive (DWD). *Council Directive 98/83/EC*.
European Commission SCCS/1501/12. (2012). *Notes of guidance for testing of cosmetic ingredients and their safety evaluation* (8th revision). Scientific Committee on Consumer Safety (SCCS).
European Community Directive 76/768/ECC. (1976). On the approximation of laws of the member states relating to cosmetic products.
European Pharmacopeia (4th ed.). (2002). European pharmacopeia convention, Strasbourg.
European Pharmacopeia (7th ed.). (2011). Directorate for the quality of medicines of the council of Europe, Strasbourg.
Falkenback, A., Kovacs, J., Franke, A., et al. (2005). Radon therapy for the treatment of rheumatic diseases: A review and meta-analysis of controlled clinical trials. *Rheumatology International, 25,* 205–210.
Favero, J. S., Parisotto-Peterle, J., Weiss-Angeli, V., Brandalise, R. N., Gomes, L. B., Bergmann, C. P., et al. (2016). Physical and chemical characterization and method for the decontamination of clays for application in cosmetics. *Applied Clay Science*. doi:10.1016/j.clay.2016.02.022.
Fernández-González, M. V. (2010). Proceso de maduración de peloides con fase líquida de las principales aguas minerales y mineromedicinales de la provincia de Granada. Ph.D. thesis, Universidad Granada.
Fernández-González, M. V., Martín-García, J. M., Delgado, G., Párraga, J., & Delgado, R. (2013). A study of the chemical, mineralogical and physicochemical properties of peloids prepared with two medicinal mineral waters from Lanjarón

Spa (Granada, Spain). *Applied Clay Science, 80–81,* 107–116.

Fernández-Lao, C., Cantarero, I., Garcia, J. F., & Arroyo, M. (2012). Termoterapia. In M. Albornoz & J. Meroño (Eds.), *Procedimientos generales de fisioterapia* (pp. 53–65). Barcelona: Elsevier.

Ferrell, R. E. (2008). Medicinal clay and spiritual healing. *Clays and Clay Minerals, 56,* 751–760.

Fioravanti, A., Cantarini, L., Guidelli, G. M., & Galeazzi, M. (2011). Mechanisms of action of spa therapies in rheumatic diseases: What scientific evidence is there? *Rheumatology International, 31*(1), 1–8.

Fioravanti, A., & Chelesschi, S. (2015). Mechanisms of action of balneotherapy in rheumatic diseases. *Balnea, 10,* 43–56.

Fioravanti, A., Iacoponi, F., Bellisai, B., Cantarini, L., & Galeazzi, M. (2010). Short- and long-term effects of spa therapy in knee osteoarthritis. *American Journal of Physical Medicine and Rehabilitation, 89*(2), 125–132.

Fioravanti, A., Lamboglia, A., & Pascarelli, N. A. (2013). Thermal water of Vetriolo, Trentino, inhibits the negative effect of interleukin 1β on nitric oxide production and apoptosis in human osteoarthritic chondrocytes. *Journal of Biological Regulators and Homeostatic Agents, 27,* 891–902.

Fioravanti, A., Tenti, S., Giannitti, C., Fortunati, N. A., & Galeazzi, M. (2014). Short- and long-term effects of mud-bath treatment on hand osteoarthritis: A randomized clinical trial. *International Journal of Biometeorology, 58*(1), 79–86.

Francois, G., Micollier, A., & Rouvie, I. (2005). *Les Boues Thermales* (p. 29). Atelier Santé Environmental: ENSP (École Nationale de la Santé Publique), Rennes.

Galzigna, L., Bettero, A., & Bellometti, S. (1999a). La maturation de la boue thermale et sa mesure. Première partie. *La Presse Thermale et Climatique, 136*(1), 23–26.

Galzigna, L., Bettero, A., & Bellometti, S. (1999b). La maturation de la boue thermale et sa mesure. Deuxième partie. *La Presse Thermale et Climatique, 136*(1), 27–30.

Galzigna, L., Ceschi-Berrini, C., Moschin, E., & Tolomio, C. (1998). Thermal mud-pack as anti-inflammatory treatment. *Biomedicine & Pharmacotherapy, 52,* 408–409.

Galzigna, L., Lalli, A., Moretto, C., & Bettero, A. (1995). Maturation of thermal mud controlled conditions and identification of an anti-inflammatory fraction. *Journal of Physical and Rehabilitation Medicine, 5,* 196–199.

Galzigna, L., Moretto, C., & Lalli, A. (1996). Physical and biochemical changes of thermal mud after maturation. *Biomedicine & Pharmacotherapy, 50*(6–7), 306–308.

Gámiz, E., Fernández-González, M. V., Párraga, J., & Delgado, R. (2008). Maduración de peloides. Influencia sobre la fase mineral. In J. L. Legido & M. L. Mourelle (Eds.), *Investigaciones en el ámbito Iberoamericano sobre Peloides Termales* (pp. 191–203). Vigo: Universidad Vigo.

Gámiz, E., Martín-García, J. M., Fernández-González, M. V., Delgado, G., & Delgado, R. (2009). Influence of water type and maduration time on the propieties of kaolinite-saponite peloids. *Applied Clay Science, 46*(1), 117–123.

Garcia, P.T. (2014). Peloterapia en Cosmética y Medicina Estética. In A. H. Torres (Ed.), *Peloterapia: Aplicaciones médicas y cosméticas de fangos termales. Fundación para la investigación e innovación en Hidrologia Médica y Balneoterapia "Bílbilis"* (pp. 185–207). Madrid. ISBN: 978-84-616-8551-6

Gerencsér, G. (2014). Experimental balneology: The biological effects of medicinal water and mud samples from the Carpathian Basin. Ph.D. thesis, University of Pécs, Faculty of Health Sciences, Hungary.

Gomes, C. S. F. (2002). Argilas: Aplicações na Indústria. In O Liberal (Ed.), Câmara de Lobos, Região Autónoma. da Madeira, 338 pp.

Gomes, C. S. F. (2013). Naturotherapies based on minerals. *Geomaterials, 3,* 1–14.

Gomes, C. S. F. (2015). In pelotherapy what is more important, the peloid solid phase or the peloid liquid phase? *Balnea, 10,* 125–142.

Gomes, C. S. F., Carretero, M. I., Pozo, M., Maraver, F., Cantista, P., Armijo, F., et al. (2013). Peloids and pelotherapy: Historical evolution, classification and glossary. *Applied Clay Science, 75–76,* 28–38.

Gomes, C. S. F., Hernandez, R., & Sequeira, M. C. (2009). Characterization of clays used for medicinal purposes in the Archipelago of Cape Verde. *Geochimica Brasiliensis, 22*(3), 315–331.

Gomes, C. S. F., & Silva, J. B. P. (2007). Minerals and clay minerals in medical geology. *Applied Clay Science, 36,* 4–21.

Gomes, C. S. F., & Silva, J. B. P. (2010). A geological approach to the typology and nomenclature of the essentially inorganic peloids. In F. Maraver & M. I. Carretero (Eds.), *Libro de Resúmenes del II Congreso Iberoamericano de Peloides, Lanjarón* (pp. 12–13). Madrid: C.E.R.S-A.

Gomes, C. S. F., Silva, J. B. P., & Gomes, J. H. C. (2015). Natural peloids versus designed and engineered peloids. *Boletín/Sociedad Española de Hidrología Médica, 30*(1), 15–36.

Grigsby, R. K., Thyer, B. A., Waller, R. J., & Johnston, G. A., Jr. (1999). Chalk eating in middle Georgia: A culture-bound syndrome of pica? *South Medical Journal, 92,* 190–192.

Guggenheim, S., Adams, J. M., Bain, D. C., Bergaya, F., Brigatti, M. F., Drits, V. A., et al. (2006). Summary of recommendations of nomenclature committees relevant to clay mineralogy: Report of the Association Internationale pour l'Étude des Argiles (AIPEA) Nomenclature Committee for 2006. *Clays and Clay Minerals, 54,* 761–772.

Harari, M. (2012a). Climatotherapy of skin diseases at the Dead Sea: An update. *Anales de Hidrología Médica, 5*(1), 39–51.

Harari, M. (2012b). Beauty is not only skin deep: The Dead Sea features and cosmetics. *Anales de Hidrología Médica, 5*(1), 75–88.

Health Canada. (2009). *Draft guidance on heavy metal impurities and cosmetics*. http://www.hc-sc.gc.ca/cps-spc/legislation/consultation/cosmet/metal-metaux-consult-eng.php. Accessed Mar 2016.

Heinrich, M., & Pieroni, A. (2011). Ethnopharmakologie der Albaner Süditaliens. *Zeitschrft Fürphytotherapie, 22,* 236–240.

Hooda, P. S., Henry, C. J. K., Seyoum, T. A., Armstrong, L. D. M., & Fowler, M. B. (2002). The potential impact of geophagia on the bioavailability of iron, zinc and calcium in human nutrition. *Environmental Geochemistry and Health, 24,* 305–319.

Hooda, P. S., Henry, C. J. K., Seyoum, T. A., Armstrong, L. D. M., & Fowler, M. B. (2004). The potential impact of soil ingestion on human mineral nutrition. *Science of Total Environment, 333,* 75–87.

Horno, M. A. P. (2014). Historia de la Peloterapia. In A. H. Torres (Ed.), *Peloterapia: Aplicaciones médicas y cosméticas de fangos termales. Fundación para la investigación e innovación en Hidrologia Médica y Balneoterapia "Bílbilis"* (pp. 47–53). Madrid. ISBN: 978-84-616-8551-6.

Hunter, J. M. (1973). Geophagy in Africa and United States: A culture-nutrition hypothesis. *Geographical Review, 63,* 170–195.

Hunter, J. M., & De Kleime, R. (1984). Geophagy in central America. *Geographical Review, 74,* 157–169.

ICH—International Conference on Harmonization Q3D. (2013). *Guideline for elemental impurities*. http://www.ich.org/products/guidelines/quality/quality-single/article/impurities-guideline-for-metal-impurities.html. Accessed 16 Apr 2016.

Igeoma, K. H., Onyoche, O. E., Uju, O. V., & Chukwuene, I. F. (2014). Assessment of heavy metals in edible clays sold in Onitsha metropolis of Anambra State, Nigeria. *British Journal of Applied Science & Technology, 4*(14), 2114–2124.

Izugbara, C. O. (2003). The cultural context of geophagy among pregnant and lactating Ngwa women of southeastern Nigeria. *The African Anthropologist, 10*(2), 180–199.

Johns, T., & Duquette, M. (1991). Detoxification and mineral supplementation as functions of geophagy. *American Journal of Clinical Nutrition, 53,* 448–456.

Jumbam, N. D. (2013). Geophagic materials: The possible effects of their chemical composition on human health. *Transactions of the Royal Society of South Africa, 68,* 177–182.

Key, T. C., Jr., Horger, E. O., III, & Miller, J. M. (1982). Geophagia as a cause of maternal death. *Obstetrics & Gynaecology, 60,* 525–526.

Khlaifat, A., Al-Khashman, O., & Qutob, H. (2010). Physical and chemical characterization of Dead Sea mud. *Materials Characterization, 61,* 564–568.

Kikouama, O. J. R., & Baldé, L. (2010). From edible clay to clay-containing formulation for optimization of the oral delivery of some trace elements: A review. *International Journal of Food Science and Nutrition, 61*(8), 1–21.

Kikouama, O. J. R., Konan, K. L., Katty, A., Bonnet, J. P., Baldé, L., & Yagoubi, N. (2009a). Physicochemical characterization of edible clays and release of trace elements. *Applied Clay Science, 43*(1), 135–141.

Kikouama, O. J. R., Le Cornec, F., Bouttier, S., Launay, A., Baldé, L., & Yagoubi, N. (2009b). Evaluation of trace elements released by edible clays in physicochemically simulated physiological media. *International Journal of Food Sciences and Nutrition, 60*(2), 130–142.

Kim, J. H., Lee, J., Lee, H. B., Shin, J. H., & Kim, E. K. (2010). Water-retentive and anti-inflammatory properties of organic and inorganic substances from Korean sea mud. *Natural Products Communications, 5*(3), 395–398.

Kutalek, R., Wewalka, G., Gundacker, C., Auer, H., Wilson, J., Haliza, D., et al. (2010). Geophagy and potential health implications: Geohelminths, microbes and heavy metals. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 104*(12), 787–795.

Kwong, A. M., & Henry, J. (2003). Why is geophagy treated like dirt? *Deviant behaviour, 24,* 353–371. doi:10.1080/713840222.l.

Lambert, V., Boukhari, R., Misslin-Tritsch, C., & Carles, G. (2013). La géophagie: Advances dans la comprehension de ses causes et consequences. *La Revue de Médicine Interne, 34,* 94–98.

Lar, U. A., Agene, J. I., & Umar, A. I. (2014). Geophagic clay materials from Nigeria: A potential source of heavy metals and human health implications in mostly women and children who practice it. *Environmental Geochemistry and Health*. doi:10.1007/s10653-014-9653-0.

Laufer, B. (1930). Geophagy. Field Museum of natural History, Publication 280. Ph.D. thesis Anthropology Series (Vol. 18, pp. 99–198).

Lim, D. G., Jeong, W.-W., Kim, N. A., Lim, J. Y., Lee, S.-H., Shim, W. S., et al. (2014). Effect of the glyceryl monooleate-based lyotropic phases on skin permeation using in vitro diffusion and skin imaging. *Asian Journal of Pharmaceutical Science, 9,* 324–329.

Lopez-Galindo, A., & Viseras, C. (2004). Pharmaceutical and cosmetic application of clays. In F. Wypych & K. G. Satyanarayana (Eds.), *Clay surfaces: Fundamentals and applications* (pp. 267–289). Amsterdam: Elsevier.

Lopez-Galindo, A., Viseras, C., & Cerezo, P. (2007). Compositional, technical and safety specifications of clays to be used as pharmaceutical and cosmetic products. *Applied Clay Science, 36,* 51–63.

Mahaney, W. C., Milner, M. W., Mulyono, H. S., Hancock, R. G. V., Aufreiter, S., Reich, M., et al. (2000). Mineral and chemical analyses of soils eaten by humans in Indonesia. *International Journal of Environmental Health Research, 10,* 93–109.

Maraver, F. (2006). Antecedentes históricos de la Peloterapia. *Anales de Hidrlogia Médica, 1,* 17–42.

Maraver, F. (2013). Mechanisms of action of pelotherapy: State of the art. In J. Nunes, C. Gomes, & J. Silva (Eds.), *Livro de Actas do III Congresso Iberoamericano de Peloides* (pp. 9–18). São Miguel, Açores: Ponta Delgada.

Maraver, F., Fernandez-Torán, M. A., Corvillo, I., Morer, C., Váquez, I., Aguillera, L., et al. (2015). Peloterapia: Una Revisión. *Medicina Naturista, 9*(1), 38–46.

Mascolo, N., Summa, V., & Tateo, F. (1999). Characterization of toxic elements in clays for human healing. *Applied Clay Science, 15,* 481–500.

Mattioli, M., Giardini, L., Roselli, C., & Desideri, D. (2016). Mineralogical characterization of commercial clays used in cosmetics and possible risk for health. *Applied Clay Science, 119,* 449–454.

Meijide, R., Burguera, E. F., & Vela-Anero, A. (2015). Peloterapia y Artrosis. *Balnea, 10,* 289–300.

Meijide, R., Mourelle, M. L., Vela-Anero, A., López, E. M., Burguera, E. F., & Pérez, C. G. (2014). Aplicación a pacientes: Peloterapia en patologias dermatológicas. In A. H. Torres (Ed.), *Peloterapia: Aplicaciones médicas y cosméticas de fangos termales. Fundación para la Investigación y Innovación en Hidrologia Médica y Balneoterapia "Bílbilis"* (pp. 169–183). Madrid. ISBN: 978-84-616-8551-6.

Meijide, R., Salgado, T., Lianes, A., Legido, J. L., Mourelle, M. L., & Gómez, C. (2010). Evaluación de los câmbios en la piel trás la aplicación de peloides mediante métodos de bioengenharia cutânea. In F. Maraver & M. I. Carretero (Eds.), *Libro de Resúmenes del II Congreso Iberoamericano de Peloides* (pp. 48–49). Madrid: C.E.R.S.-A.

Mpuchane, S. F., Ekosse, G. E., Gashe, B. A., Morobe, I., & Coetzee, S. H. (2010). Microbiological characterization of southern African medicinal and cosmetic clays. *International Journal of Environmental Health Research, 20*(1), 27–41.

Mwalongo, D., & Mohamed, N. K. (2013). Determination of essential and toxic elements in clay soil commonly consumed by pregnant women in Tanzania. *Radiation Physics and Chemistry, 91,* 15–18.

Naik, A., Pechtold, L., Potts, R., & Guy, R. (1995). Mechanism of oleic acid-induced skin penetration enhancement in vivo in humans. *Journal of Controlled Release, 37,* 299–306.

Nchito, M., Geissler, P. W., Mubila, L., Friis, H., & Olsen, A. (2004). Effects of iron and multimicronutrient supplementation on geophagy: A two-by-two factorial study among Zambian schoolchildren in Lusaka. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 98,* 218–227.

Ngole, V. M., Ekosse, G. E., Jager, L., & Songca, S. P. (2010). Physicochemical characteristics of geophagic clayey soils from South Africa and Swaziland. *African Journal of Biotechnology, 9*(36), 5929–5930.

Nissenbaum, A., Rullköetter, J., & Yechieli, Y. (2002). Are the curative properties of ‘black mud’ from the Dead Sea due to the presence of bitumen (asphalt) or other types of organic matter? *Environmental Geochemistry and Health, 24*(4), 327–335.

Njiru, H., Elchalal, U., & Paltiel, O. (2011). Geophagy during pregnancy in Africa: A literature review. *Obstetrical & Gynecological Survey, 2011*(66), 452–459.

Norma Cubana de Peloides. (1998). *Oficina Nacional de Normalización (NC) Calle E No. 261 Vedado*. Cuba: Ciudad de la Habana.

Novelli, G. (1996). Applicazion medicali e Igieniche delle bentoniti. In F. Veniale (Ed.), *Atti Conv. “Argille Curative”, Gruppo Italiano AIPEA, Salice Terme (PV)*, Tipografia Trabella, Milano.

Novelli, G. (1998). Applicazioni Cosmetiche e Medicaliu delle argille smectiche. *Cosmetic News, 122,* 350–357.

Novelli, G. (2000). Bentonite: A clay over the centuries. *Incontri Scentifici, V Corso di Formazione “Metodi di Analisi di Materiali Argillosi*”. Gruppo Itaiano AIPEA (pp. 263–304).

Nyanza, E. C., Joseph, M., Premji, S. S., Thomas, D. S., & Mannion, C. (2014). Geophagy practices and the content of chemical elements in the soil eaten by pregnant women in artisanal and small scale gold mining communities in Tanzania. *BMC Pregnancy Childbirth, 14,* 144.

Odabasi, E., Gul, H., Macit, E., Turan, M., & Yildiz, O. (2007). Lipophilic components of different therapeutic mud species. *The Journal of Alternative and Complementary Medicine, 13*(10), 1115–1118.

Odabasi, E., Turan, M., Erdem, H., & Tekbas, F. (2008). Does mud pack treatment have any chemical effect? A randomized controlled clinical study. *Journal of Alternative Complementary Medicine, 14*(5), 559–565.

Okunlola, O. A., & Owoyemi, K. A. (2011). Compositional characteristics of geophagy in soils of Nigeria. In *1st Conference on clay and clay minerals: An innovative perspective on the role of clays and clay minerals and geophagia on economic development* (pp. 290–305). South Africa: Free State University Bloemfontein.

Otto, C. C., & Haydel, S. E. (2013). Exchangeable ions are responsible for the in vitro antibacterial properties of natural clay mixtures. *PLoS ONE, 8*(5), 1–9.

Owumi, S. E., & Oyelere, A. K. (2015). Determination of metal ion contents of two antiemetic clays used in geophagy. *Toxicology Reports, 2,* 928–932.

Ozumba, U. C., & Ozumba, N. (2002). Patterns of helminth infection in the human gut at the University of Nigeria Teaching Hospital, Enugu, Nigeria. *Journal of Health Science, 48,* 263–268.

Pandey, A., Mittal, A., Chauhan, N., & Alam, S. (2014). Role of surfactants as penetration enhancer in transdermal drug delivery. *Molecular Pharmaceutics & Organic Process Research, 2,* 2.

Pastor, J. M. (1998). Termoterapia superficial. In M. Martine, J. M. Pastor, & F. Sendra (Eds.), *Manual de Medicina Física* (pp. 91–104). Madrid: Harcourt Brace.

Peiró, P. S., & Tejero, S. S. (2014). Utilización terapeutica de la arcilla. In A. H. Torres (Ed.), *Peloterapia: Aplicaciones médicas y cosméticas de fangos termales. Fundación para la investigación e innovación en Hidrologia Médica y Balneoterapia “Bílbilis”* (pp. 279–288). Madrid. ISBN: 978-84-616-8551-6.

Photos-Jones, E., Keane, C., Jones, A. X., Stamatakis, M., Robertson, P., Hall, A. J., et al. (2015). Testing dioscorides’ medicinal clays for their antibacterial properties: The case of Samian Earth. *Journal of Archaeological Science, 57,* 257–267.

Porlezza, C. (1965). Considerazione sui fanghi terapeutici (peloidi). *Thermae II, 2–3,* 6–57.

Pozo, M., Carretero, M. I., Pozo, E., Martin Rubi, J. A., & Maraver, F. (2010). Caracterización mineralógica y química de peloides españoles y argentinos; Evaluación de elementos traza potencialmente tóxicos. In F. Maraver & M. I. Carretero (Eds.), *Libro de Resúmenes del II Congreso Iberoamericano de Peloides* (pp. 37–38). Granada: Balneario de Lanjaron.

Prasad, A. S., Halsted, J. A., & Nadimi, M. (1961). Syndrome of iron deficiency anemia, hepatosplenomegaly, hypogonadism, dwarfism and geophagia. *The American Journal of Medicine, 31,* 532–546.

Quintela, A., Terroso, D., Ferreira da Silva, E., & Rocha, F. (2012). Certification and quality criteria of peloids used for therapeutic purposes. *Clay Minerals, 47,* 441–451.

Rautureau, M., Liewig, N., Gomes, C. S. F., & Katouzian-Safadi, M. (2010). *Argiles et Santé: Propriétés et Thérapies*. Paris: Editions Médicales Internationales, Lavoisier. ISBN 978-2-7430-1202-1.

Rebelo, M., Viseras, C., Lopez-Galindo, A., Rocha, F., & Ferreira da Silva, E. (2011). Characterization of Portuguese geological materials to be used in medical hydrology. *Applied Clay Science, 51,* 258–266.

Reid, R. (1992). Cultural and medical perspectives on geophagia. *Medical Anthropology, 13,* 337–351.

Reinbacher, R. (1999). Brief history of clay in medicine. *Clay Minerals Society News, 11,* 22–23.

Reinbacher, R. (2003). *Healing earths: The third leg of medicine*. Bloomington: 1st Books Library.

Robertson, R. H. S. (1986). *Fuller's earth: A history*. Kent: Volturna Press.

Robertson, R. H. S. (1996). Cadavers, choleras and clays. *Bulletin Mineralogical Society, 113,* 3–7.

Roques, C. F. (2004). Mud therapy and health. In *Proceedings of the 3rd symposium on thermal muds in Europe*, Dax (pp. 75–77).

Roques, C. F. (2015). Mud therapy: Data for clinical evidence. *Balnea, 10,* 57–62.

Saathoff, E., Olsen, A., Kvalsvig, J. D., & Geissler, P. W. (2002). Geophagy and its association with geohelminth infections in rural school children from Northern KwaZulu Natal, South Africa. *Transactions of the Royal Society of Tropical Medicine and Hygiene, 96,* 485–490.

Sánchez-Espejo, R., Aguzzi, C., Cerezo, P., Salcedo, I., López-Galindo, A., & Viseras, C. (2014). Folk pharmaceutical formulations in western Mediterranean: Identification and safety of clays used in pelotherapy. *Journal of Ethnopharmacology, 155,* 810–814.

Sarsan, A., Akkaya, N., Ozgen, M., Yildiz, N., Atalay, N. S., & Ardic, F. (2012). Comparing the efficacy of mature mud pack and hot pack treatments for knee osteoarthritis. *Journal of Back and Musculoskeletal Rehabilitation, 25*(3), 193–199.

Sheppard, S. C. (1998). Geoghagy: Who eats the soils and where do possible contaminants go? *Environmental Geology, 33,* 109–114.

Skinner, H. C. W. (2007). Earth, source of health and hazards: An introduction to medical geology. *Annual Review of Earth and Planetary Sciences, 35,* 177–213.

Suárez, M., González, P., Domínguez, R., Bravo, A., Melián, C., Pérez, M., et al. (2011). Identification of organic compounds in San Diego de los Baños Peloid (Pinar del Río, Cuba). *Journal of Alternative and Complementary Medicine, 17*(2), 155–165.

Tanojo, H., Boelsma, E., Junginger, H., Ponec, M., & Boddé, H. (1999). In vivo human skin permeability enhancement by oleic acid: A laser Doppler velocimetry study. *Journal of Controlled Release, 58,* 97–104.

Tateo, F., Ravaglioli, A., Andreoli, C., Bonina, F., Coiro, V., Degetto, S., et al. (2009). The in vitro percutaneous migration of chemical elements from a thermal mud for healing use. *Applied Clay Science, 44,* 83–94.

Tateo, F., & Summa, V. (2007). Element mobility in clays for healing use. *Applied Clay Science*, *36*(1), 64–76.

Tateo, F., Summa, V., Bonelli, G. C., & Bentivenga, G. (2001). Mineralogy and geochemistry of herbalist's clays for internal use: Simulation of the digestive process. *Applied Clay Science, 20,* 97–109.

Tateo, F., Summa, V., Gianossi, M. L., & Ferraro, G. (2006). Healing clays: Mineralogical and geochemical constraints on the preparation of clay-water suspension ("argillic water"). *Applied Clay Science, 33,* 181–194.

Tayie, F. (2004). Pica: Motivating factors and health issues. *African Journal of Food, Agriculture, Nutrition and Development, 4*(1). http://www.bioline.org.br/request?nd04010.

Tefner, I. K. (2014). Effect of balneotherapy on musculoskeletal disorders with chronic pain. Ph.D. thesis, University of Szeged, Hungary.

Teixeira, F., Maraver, F., Crespo, P. V., & Campos, A. (1996). Estudo microanalítico da materia orgánica de águas sulfúreas portuguesas e espanholas. *Publicação do Instituto de Climatologia e Hidrologia da Universidade de Coimbra*, *34,* 1–5.

Tolomio, C., Appolonia, F., Moro, I., & Ceschi-Berrini, C. (2004). Thermophilic microalgae growth on diferente substrates and at different temperatures in experimental tanks in Abano Therme (Italy). *Algological Studies, 111,* 145–157.

Tolomio, C., Ceschi-Berrini, C., Appolonia, F., Galzigna, L., Masiero, L., Moro, I., et al. (2002). Diatoms in the termal mudo f Abano Therme, Italy (Maturation period). *Algological Studies, 105,* 11–27.

Tolomio, C., Ceschi-Berrini, C., Moschin, E., & Galzigna, L. (1999). Colonization by diatoms and antirheumatic activity of thermal mud. *Cell Biochemistry and Function, 17*(1), 29–33.

Torrella, F. (2006). La sulfuraria de Baños de Montemayor (Cáceres): Características morfológicas y funcionales de la comunidad microbiana constituyente. *Anales de Hidrologia Medica, 1,* 61–78.

Tricás, J. M., Fortún, M., Jiménez, S., & Estébanes, E. (2014). Fisioterapia: fundamentación fisioterápica de la utilización de peloides. In A. H. Torres (Ed.), *Peloterapia: Aplicaciones médicas y cosméticas de fangos termales. Fundación para la investigación e innovación en Hidrologia Médica y Balneoterapia "Bílbilis"* (pp. 251–260). Madrid. ISBN: 978-84-616-8551-6.

Trivedi, T. H., Daga, G. L., & Yeolekar, M. E. (2005). Geophagia leading to hypokalemic quadriparesis in a postpartum patient. *The Journal of the Association of Physicians of India, 53,* 205–207.

Tserenpil, Sh, Dolman, G., & Voronkov, M. G. (2010). Organic matters in healing muds from Mongolia. *Applied Clay Science, 49*(1–2), 55–63.

United States Pharmacopoeia 29-NF 24. (2006). US Pharmacopeial Convention, Rockville, MD.

United States Pharmacopoeia 36NF31. (2013). United States Pharmacopoeia 36 and National Formulary 31. US Pharmacopoeial Convention Rockville, MD.

Veniale, F. (1996). Argille Curative: Antefatti, Fatti e Misfatti. In *Atti Convegno "Argille curative"*. Salice Terme (PV, Italy) (pp. 26–28) Oct 1–11.

Veniale, F. (1997). Applicazioni e utilizzazioni medico-sanitarie di materiali argillosi (naturali e modificati). In N. Morandi & M. Dondi (Eds.), *Argille e Mineralli delle Argille. guida alla definizione di caratteristiche e proprietà per gli usi industriali, Corso di Specializzazione* (pp. 205–239). Rimini: Gruppo Italiano AIPEA.

Veniale, F. (1998). Applicazioni e utilizzazioni medico-sanitarie di materiali argillosi (naturali e modificati). *Corso di Specializzazione, Gruppo Italiano AIPEA* (pp. 1–40).

Veniale, F. (1999). Simposio ''Argille per fanghi peloidi termali e per trattamenti dermatologici e cosmetici''. Montecatini Terme, May 14–15, *Pisa, Italy. Gruppo Italiano AIPEA.*

Veniale, F., Barberis, E., Carcangiu, G., Morandi, N., Setti, M., Tamanini, M., et al. (2004). Formulation of muds for pelotherapy: Effects of "maturation" by different mineral waters. *Applied Clay Science, 25,* 135–148.

Veniale, F., Bettero, A., Jobstraibizer, P. G., & Setti, M. (2007). Thermal muds: Prespectives of innovation. *Applied Clay Science, 36,* 141–147.

Vermeer, D. E., & Ferrell, R. E., Jr. (1985). Nigerian geophagical clay: A traditional anti-diarrheal pharmaceutical. *Science, 227,* 634–636.

Vermeer, D. E., & Frate, D. A. (1979). Geophagia in rural Mississipi: Environmental and cultural contexts and nutritional implications. *American Journal of Clinical Nutrition, 32*(10), 2129–2135.

Viseras, C., Aguzzi, C., Cerezo, P., & Lopez-Galindo, A. (2007). Uses of clay minerals in semisolid health care and therapeutic products. *Applied Clay Science, 36,* 37–50.

Viseras, C., Cerezo, P., Sanchez, R., Salcedo, I., & Aguzzi, C. (2010). Current challenges in clay minerals for drug deliver. *Applied Clay Science, 48,* 291–295.

Viseras, C., Cultrone, G., Cerezo, P., Aguzzi, C., Baschini, M., Valle, J., et al. (2006). Characterization of northern Patagonian Bentonites for pharmaceutical use. *Applied Clay Science, 31,* 272–281.

Viseras, C., & López-Galindo, A. (1999). Pharmaceutical applications of some Spanish clays (sepiolite, palygorskite, bentonite): Some pre-formulation studies. *Applied Clay Science, 14,* 69–82.

WHO. (2011). *Guidelines for drinking water quality* (4th ed.). Geneva: WHO.

Wiley, A. S., & Katz, S. H. (1998). Geophagy in pregnancy: A test of a hypothesis. *Current Anthropology, 39,* 532–545.

Williams, L. B., & Haydel, S. E. (2010). Evaluation of the medicinal use of clay minerals as antibacterial agents. *International Geology Review, 52,* 745–770.

Williams, L. B., Haydel, S. E., & Ferrell, R. (2009). Bentonite, bandaids and borborygmi. *Elements, 5,* 99–104.

Williams, L. B., Haydel, S. E., Giese, R., & Eberl, D. D. (2008). Chemical and mineralogical characteristics of French green clays used for healing. *Clays and Clay Minerals, 56,* 437–452.

Williams, L. B., & Hillier, S. (2014). Kaolins and health: From first grade to first aid. *Elements, 10,* 207–211.

Williams, L. B., Holland, M., Eberl, D. D., & Brunet de Courrsou, L. (2004). Killer Clays! Natural antibacterial clay minerals. *Mineralogical Society Bulletin, 139,* 3–8.

Williams, L. B., Metge, D., Eberl, D. D., Harvey, R., Turner, A., Prapaipong, P., et al. (2011). What makes a natural clay antibacterial? *Environmental Science and Technology, 45,* 3768–3773.

Wilson, M. J. (2003). Clay mineralogical and related characteristics of geophagic materials. *Journal of Chemical Ecology, 29,* 1525–1547.

Woywodt, A., & Kiss, A. (2002). Geophagia: The history of earth-eating. *Journal of the Royal Society of Medicine, 95,* 143–146.

Yamaoka, K., Mitsunobu, F., Hanamoto, K., et al. (2004). Study on biologic effects of radon and thermal therapy on osteoarthritis. *The Journal of Pain, 5,* 20–25.

Young, S. L. (2010). Pica in pregnancy: New ideas about an old condition. *Annual Review of Nutrition, 30,* 403–422.

Young, S. L. (2011). *Craving earth* (p. 228). New York: Columbia University Press.

Ziegler, J. L. (1997). Geophagy: A vestige of paleonutrition. *Tropical Medicine & International Health, 2,* 609–611.