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Bentonite, Band-aids, and Borborygmi

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Abstract

The practice of eating clay for gastrointestinal ailments and applying clay topically as band-aids for skin infections is as old as mankind. Bentonites in particular have been used in traditional medicines, where their function has been established empirically. With modern techniques for nanoscale investigations, we are now exploring the interactions of clay minerals and human pathogens to learn the lessons that Mother Nature has used for healing. The vast surface area and chemical variability of hydrothermally altered bentonites may provide a natural pharmacy of antibacterial agents.

Keywords

healing clay; geophagy; pelotherapy; antibacterial; microbiology; health

HEALING CLAYS

The healing practices of ancient cultures, as well as of modern society, have depended on clay minerals to treat a variety of topical and internal maladies, and natural clays with adsorptive and absorptive properties have been exploited in cosmetics and pharmaceuticals. Traditionally, clay is mixed with water to form a gel or paste that can be applied externally for cosmetic purposes or skin protection (Carretero et al. 2006). High cation exchange capacity and extremely fine particle size explain why these minerals are used topically as band-aids to absorb secretions, toxins, and contaminants. Clays also cleanse and refresh the skin and aid in the healing of blemishes. The driving force behind the therapeutic use of bentonite (TERMINOLOGY BOX) for digestive and gastrointestinal maladies that cause borborygmi—the stomach rumblings caused by gas moving through the intestines—is the attractive power of clay-particle surfaces (Carretero et al. 2006). Negatively charged surfaces attract positively charged substances, and like a sponge, some clay minerals absorb substances between the layers of their crystal structure. Cation exchange can take up or release toxins or nutrients (e.g. Ca, Fe) that may be used by bacteria. While the absorption of water and

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organic compounds is the most common attribute of clays for healing, the geochemical processes leading to the antibacterial properties of clays have received less attention (Williams et al. 2008).

The high cation exchange capacity of various clay minerals has been targeted as a platform for creating inorganic antibacterial materials by replacing their native ions with known antibacterial ions, such as silver, copper, and zinc (Ohashi et al. 1998). During therapeutic use of these clays, the absorbed ions are gradually released for long-term effectiveness. Thus far, silver-loaded clays have been pursued most aggressively, but could there be chemical schemes to increase the effectiveness of clays used for medicinal purposes? This article reviews the common uses of clays for human health and new avenues of research for methods to control bacterial populations.

TRADITIONAL CLAYS IN HUMAN HEALTH

Geophagy

The deliberate consumption of earth for medicinal or spiritual healing, geophagy, is a practice that provides a direct connection between human health and Earth's rocks and minerals. Intermediaries in the food chain are eliminated, thus providing direct access to potentially beneficial or harmful elements and compounds associated with the ingested materials. Many colloquial expressions and scientific terms are used for edible clay, including beidellitic montmorillonite, chalk, clay dirt, white dirt, clay tablets, colloidal minerals, *panito del señor*, *Terra sigillata*, and white mud (Reinbacher 2003). The beneficial uses of clay (bolus alba) for bacteriostasis, sterilization, membrane coating, adsorption of toxins, and the clearing of the alimentary canal were recorded historically in pharmacopoeiae until the 1850s (Robertson 1996). In modern society there is much skepticism, and many believe that geophagy is evidence of aberrant behavior (Grigsby et al. 1999). However, geophagy is a social practice that has been observed in cultures worldwide (Ferrell et al. 1985).

Although geophagy is well documented, mineralogical studies are rare; montmorillonite, kaolinite, and halloysite are reported to be the clay minerals most commonly consumed. The mineral properties so far associated with health effects include small particle size, large surface area, particle shape, surface charge, abundance of macro- and trace-nutrient elements, variable sorption properties, and abundance of admixed carbonates and oxyhydroxides. Wilson (2003) listed several reasons for geophagy: "Detoxification, or at least enhancement of the palatability of foodstuffs containing undesirable components; alleviation of gastrointestinal upsets such as diarrhea; mineral supplementation, particularly Fe and Ca, and as an antacid to relieve excess acidity in the digestive tract." In general terms, smectites (including montmorillonite) are thought to be more reactive than kaolins (i.e. kaolinite) in the gastrointestinal tract. A special issue of *Applied Clay Science* (Carretero and Lagaly 2007) was dedicated to the health effects of clay minerals, largely related to those of geophagy and pelotherapy.

Edible earths are marketed in a variety of ways. Clay tablets sold in the market of Esquipulas, Guatemala, are embossed with Indian and Christian symbols (Fig. 2A), and this "bread of Christ" is distributed throughout Latin America (Hunter et al. 1989). In Nigerian markets, clay is sold in spindle form, as discs, and as rough blocks that may be raw or smoked (Vermeer and Ferrell 1985). Georgia kaolin (Fig. 2B) can be found as a "non-food item" in small grocery stores throughout central Georgia, USA. The holistic health benefits of commercial bentonites reported to contain Ca-montmorillonite are extolled by numerous commercial providers. Worldwide, the choice of geophagical materials is dictated by local

custom, and the clay mineral content and percentage of clay-sized particles in the samples vary widely.

Consequences for Human Health—The most severe risk of eating clay is a total blockage of the lower intestine, which can only be remedied by surgery (Padilla and Torre 2006). Eating clay can also result in nutrient deficiencies. Other complications are detrimental effects on the teeth and gums and on the digestive system, nutrient excesses, poisoning, and parasitic invasions. Reports on the health effects of geophagy are conflicting. For example, consumption of some clays causes high levels of potassium in the blood, while eating others promotes low potassium (Abraham 2005). Although clay mineral analyses were not reported, potassium contribution from an illite or adsorption by smectite could readily explain the difference. Even when clays are known to influence nutrition adversely, follow-up mineralogical investigations are rarely undertaken.

Kaolinite is the most commonly used geophagic clay mineral (Wilson 2003), especially in tropical areas. In other parts of the world, geophagists consume smectite and mixed clay mineral assemblages such as those illustrated by the X-ray powder diffraction (XRD) patterns in Figure 3. XRD is used by clay mineralogists to identify mineral composition because clay particles are so small that their optical properties are difficult to measure with an optical microscope. XRD uses monochromatic X-radiation that interacts with crystalline structures to produce unique diffraction patterns. Sample MX1 (Fig. 3), from capsules bought in a Mexican market, produces an XRD pattern similar to a smectite-rich commercial bentonite from Wyoming; MX1 also contains clinoptilolite, feldspars, quartz, and opalcristobalite as accessory minerals, suggesting that it originated as an alteration product of volcanic ash. Other samples (Fig. 3) exhibit smectite peaks with different heights and widths, indicative of changes in the quantity and crystallinity of the smectites used for medicinal purposes. Smectites are often associated with soluble Fe or Ca and a variety of macro- and micronutrients. Each of these clays produces different effects when ingested.

Box 1 DEFINITIONS

Clay Terminology Much of the popular literature on clays in human health is riddled with inaccuracies and confusion about clay mineralogy. Therefore, we outline some basic terminology as a foundation for effective communication. **Clay** is material with very fine particle size (<2.0 µm in diameter). It often describes a mixture of predominantly clay-sized hydrous phyllosilicates (**clay minerals**) and variable amounts of very fine-grained quartz, feldspars, carbonates, iron oxyhydroxides, and organic matter. Clay- and silt-sized material, when moistened with water, makes **mud**, which is called a **peloid** in therapeutic applications. **Soil** is partially composed of clay-sized minerals and organic matter (humus); it forms on the Earth's surface and, by definition, it must be able to support plant life (Voroney 2006). **Bentonite**, a rock composed chiefly of clay minerals, is one of the most common deposits of clay-sized particles. The term refers to smectite-rich materials formed from a weathered layer of volcanic ash or silicate glass (Christidis and Huff 2009 this issue). The type of smectite depends on the composition of the volcanic glass and the time–temperature history of hydrothermal waters that circulate through the deposits (Christidis 1998). While **smectites** are commonly used as “healing clays,” it is often assumed that the smectite is **montmorillonite**, which is simply one mineral in the smectite group. Natural clay deposits are rarely pure; most contain mixtures of a variety of minerals from the various clay mineral groups (e.g. smectite, illite, kaolinite, chlorite) and varying amounts of other, nonclay minerals.

The major structural feature of minerals in the smectite group is an aluminosilicate layer formed from sandwiching a single (Al, Mg, Fe) octahedral sheet between two sheets of (Al, Si) tetrahedra (referred to as a **2:1 layer**; Fig. 1). Isomorphous substitution of cations

in the 2:1 layers creates surfaces with a permanent negative charge, producing variable surface properties. Hydrated and anhydrous ions and molecules may be attracted to the surface and can be readily exchanged with external solutions or chemical components of bacterial cell envelopes. Ions in the interlayer region of the mineral structure are generally less mobile than those on the surface. Broken bonds at the edge of the 2:1 layer may be protonated or hydroxylated, depending on the pH of the fluid in contact. The aluminosilicate layers may be stacked or dispersed as individual layers, and surface area may approach the theoretical limit, $800 \text{ m}^2 \text{ g}^{-1}$.

Microbial Terminology In modern medicine, antibacterial, antimicrobial, and chemotherapeutic agents are terms used to describe chemical agents effective at treating infectious diseases. Most of these agents are **antibiotics**, which are low molecular weight by-products of microorganisms that kill or inhibit the growth of other microorganisms. *Antibiotic* is often incorrectly used to describe antibacterial or chemotherapeutic agents that are synthetically manufactured or modified by chemical processes, independent of microbial activity, to optimize their activity. Although the antibacterial clay minerals discussed herein are natural, if they are not produced by microorganisms, then they are not considered antibiotics. The majority of known antimicrobial materials function by affecting cell wall properties: inhibiting protein and nucleic acid synthesis, disrupting membrane structure and function, and inhibiting key enzymes essential for various microbial metabolic pathways.

Antibacterial agents can be either bacteriostatic or bactericidal. A **bacteriostatic agent** reversibly inhibits microbial growth, so microorganisms resume growth when it is removed. Elimination of the infection depends on the host's resistance and immune response. When administered at sufficient levels, a **bactericidal agent** kills the targeted bacterial pathogen. However, an antimicrobial agent that is bactericidal for one species may be bacteriostatic for another. Moreover, various antibacterial agents vary considerably in their range of effectiveness. A narrow-spectrum antibacterial agent is effective against a limited number of pathogens, usually Gram-positive or Gram-negative bacteria, but not both. A broad-spectrum antimicrobial agent is generally effective at destroying or inhibiting the growth of a wide range of Gram-positive and Gram-negative bacteria.

Complete chemical analyses of bentonites and other clays reveal a veritable smorgasbord of elements representing nearly the entire periodic table. Elemental abundance and potential bioavailability depend on the minerals present and the geologic history of the materials. Total chemical analysis has recently been augmented by techniques that mimic the extractability of elements in the human body. Abraham (2005) used 0.1 M HCl to assess dietary Fe supplementation in the gastric tract and found that one geophagical soil released considerable iron, but others did not. Laboratory-based aqua regia extractions from urban soils from Uppsala, Sweden, confirmed that ingestion could provide excessive Cd, Pb, and As (Ljung et al. 2006). Similarly, aqueous extractions of elements from therapeutic clays revealed elevated levels of Na, Si, Ca, K, Mg, Fe, Al, Mn, V, Mo, Sb, and As (Tateo et al. 2006). Comparison of the results with drinking water standards indicated that elemental abundances often exceed maximum contamination limits. Each natural clay sample requires individual consideration to determine if it provides nutrients or releases toxins. Smith et al. (2000) expanded the simulated digestion procedure to account for changes in Eh and pH. They used a mixture of pepsin and organic acids in 1% HCl adjusted to pH 2 to demonstrate that some smectite-poor clays could provide a major portion of the recommended daily allowance of Fe, whereas other smectite-rich clays could not. An extraction with 0.1 M HCl from clays consumed by women in Belize showed that significant concentrations of Ca, Mg,

K, Fe, Cu, and Zn were bioavailable and could account for 5–18% of their recommended daily allowance (Hunter and DeKleine 1984).

The potential risk of consuming the elements obtained by extraction from clay samples (Fig. 3) can be assessed by normalizing the quantities to the recommended reference dose (Environmental Protection Agency; IRIS database). Dose limits, multiplied by 80 kg to convert them to the body weight of an average adult, were then divided by the daily intake (~50 g of clay; Ferrell et al. 1985) to produce a daily reference dose ratio (RDR). A value of one indicates that the intake is equal to the recommended dose (Ferrell 2008); higher ratios exceed the recommended daily intake (Fig. 4).

The RDR for Na exceeded 1.0 for 22 of the 23 samples in the study (Fig. 4), and median RDRs for Cr, Sb, and As were also >1.0, suggesting that their intake could be a concern. Maximum values for Mn, Ba, Cd, V, and Se were very close to, or greater than, 1.0, while the median RDR for these elements was between 1.0 and 0.1. Mo and Be showed the lowest median ratios. The range obtained from one clay type often overlapped that from another. Although the extracted quantities differed by several orders of magnitude, their potential impact on human health is similar. The RDR takes into account factors related to elemental abundance and dietary requirements, but it does not account for chemical speciation, which could significantly influence bioavailability.

Physiologically Based Extraction Techniques—Five laboratory protocols were assessed to determine the bioavailability of Cd, Pb, and As in three soils (Oomen et al. 2002). Extraction results were highly variable, depending on the nature of the extraction (static or dynamic), extractant composition and concentration, ionic strength, fluid to solid ratio, temperature, pH, Eh, and reaction time. In many cases, the bioavailability of these potential toxins was less than 50%. Thus, a certified soil and standard testing protocol based on physiological extraction techniques was recommended for bioavailability assessment.

Another approach to assessing the effects of soil ingestion on human nutrition (Hooda et al. 2004) examined uptake from mixing pH 2 solutions containing 50%, 80%, and 100% of the recommended daily allowance of the essential nutrients Ca, Mg, Fe, Zn, Mn, and Cu with five soils of variable mineral content. After initial reaction, the solutions were filtered and the residues were reacted with similar solutions at pH 10. In some soils, an initial increase of nutrient concentration in the acid solution was followed by a decrease in the alkaline solution, demonstrating that geophagy “can potentially reduce the absorption of already bioavailable nutrients, particularly micronutrients such as Fe, Cu, and Zn” (Hooda et al. 2004). The results supported the common observation that geophagy can sometimes enhance nutrient deficiencies while, in other cases, clay consumption can provide nutrients.

Geophagy and human health are becoming more firmly linked because more Earth scientists and medical practitioners are aware that the practice is common. People around the world are deliberately or inadvertently ingesting clay minerals and the compounds adsorbed on them. Some of the health effects are obvious while others are not. Unraveling the benefits or problems of geophagy will require cooperative efforts that use advanced soil surveying, mineralogical characterization, clinical and in vitro experiments supported by procedures mimicking human digestive processes, and appropriate experimental and statistical designs.

Pelotherapy

Pelotherapy is the therapeutic application of mud (peloids), such as is used in spa baths, to treat rheumatic disorders, osteoarthritis, gynecological infections, sciatica, skin diseases, and other ailments that might benefit from increased blood circulation, heat, and adsorption of toxins (Carretero et al. 2006). The pelotherapeutic clay is usually rich in smectite of

bentonitic origin. Smectitic clay expands on hydration and provides a smooth, slippery texture to the mud. The mineral's heat capacity is increased because of water in the interlayer, so smectitic muds enhance skin heating, perspiration, and blood circulation (Ferrand and Yvon 1991). Clay often contains organic matter (peat or humic materials), and it is mixed with natural mineral or salt water and “matured” or equilibrated over several months. The water composition is adjusted to enhance exchange of selected elements into the clay structure, so that when the mud is topically applied, these elements are released for transmission through the skin.

The transport of chemicals from the clay to the body is a complex process that involves absorption and diffusion through skin, sweat ducts, and hair follicles (Cygan et al. 2002). There are no blood vessels in the epidermis (upper skin layer), so chemical transport to the blood occurs through sweat glands and hair follicles anchored in the vascular part of the dermis (lower skin layer). Clearly the surface area of smectite-rich clays in contact with the skin provides an efficient interface for chemical exchange. Future research will require the interdisciplinary approach of geochemistry and medicine for understanding the delivery of nutrients and drug exchange between the human body and clays.

ANTIBACTERIAL CLAYS

Some bentonites offer distinct antibacterial properties. The effectiveness of Fe-rich clays for healing severe skin infections has recently been documented, drawing attention from the medical community (Haydel et al. 2008). French green clays, sold as “healing clays” were used to treat a necrotic mycobacterial skin infection called Buruli ulcer (Williams et al. 2008). Microbiological testing of French green clays from two different suppliers showed that one sample enhanced the growth of common human pathogens while the other killed or inhibited the growth of the broad spectrum of bacteria tested (Haydel et al. 2008). This motivated testing of bentonites from around the world and resulted in the identification of several clays with bactericidal effects on a broad spectrum of human pathogens. Antibacterial effects might result from physical interaction (i.e. penetration or tearing of the cell) and/or chemical interaction of the clay with bacteria (i.e. poisoning or nutrient deprivation).

Physical Bactericide

The potential for clays to kill bacteria by physical means can be assessed by measuring the attractive and repulsive forces, which vary according to the minerals' surface energy, crystal size, and structure. Clays can be hydrophilic (attract water) or organophilic (attract organic substances). Organophilic smectites manufactured by inserting alkyl-ammonium compounds into the clay interlayer (Kostyniak et al. 2000) can behave as physical bactericides. The bacterial cell is attracted to the surface of the clay with such force that the cell membrane is torn, causing cytoplasmic leakage and cell death (i.e. lysis). In contrast, the two French green clays were hydrophilic. Scanning electron microscope (SEM) images of the contact between the French antibacterial clay and bacteria revealed no preferred orientation of the clay crystals around the bacteria that might cause suffocation or cell lysis. Furthermore, no mineral precipitates were found on the cell surfaces that might have impaired influx of nutrients or efflux of wastes (Williams et al. 2008). While a bactericide that works by physical processes is desirable for applications where contact between a cell and clay is possible (e.g. air filters, sewage systems, etc.), cell lysis resulting from physical contact with natural or modified clays makes its use on human tissue potentially harmful.

Chemical Bactericide

The natural antibacterial clays identified by Williams et al. (2008) kill by chemical exchange through aqueous media. Direct application of dry clay to *Escherichia coli* grown on solid agar showed no zone of inhibition for bacterial growth. However, when the clay was mixed with water to a consistency similar to that used for clay poultices (2–4 parts water to 1 part clay) and incubated for 24 hours with live bacteria at body temperature (37°C), a broad spectrum of bacteria was killed (Haydel et al. 2008). The interpretation is that chemical exchange either supplies a toxin that kills bacteria or deprives bacteria of nutrients essential for metabolism (e.g. K^+ preferentially absorbed by the clay).

As a test of various chemical-exchange hypotheses, bacteria growing actively in their growth media were exposed to a suspension of antibacterial clay inside dialysis tubing (Metge et al. 2007). Bactericidal activity was observed. Aqueous leachates were subsequently prepared by ultrasonifying a clay suspension in water for 24 hours. Tests of the *E. coli* exposed to leachate showed that the solution alone kills bacteria and therefore contains the antimicrobial agent(s). However, when the leachate ages (6 months or more), it loses the antibacterial effect. Either oxidation affects the antibacterial potency of the leachate, or a chemical reaction takes place that depletes the antibacterial product. It is likely that the presence of the clay is required to buffer the aqueous system to bactericidal conditions.

Antibacterial Clay Investigations

Microbiological Testing—The in vitro, broad-spectrum antimicrobial activity of clay minerals is now beginning to be tested for effectiveness in bacterial strains that are recommended as quality control strains for laboratory testing of antimicrobial agents by the U.S. Clinical and Laboratory Standards Institute (CLSI; formerly NCCLS) (Haydel et al. 2008). Before use, all clay mineral samples were sterilized by autoclaving at 121°C, 15 psi, for 1 hour. Bacteria–clay mineral suspensions (clay:water ratio of 1:2) were incubated at 37°C for 24 hours, and serial dilutions of all samples were grown on agar plates to determine bacterial viability. Minimal bactericidal concentrations were determined by the lowest concentration of a clay mineral suspension that kills $\geq 99.9\%$ of the bacterial population in a liquid medium. This approach could potentially validate clays for treating topical infections as a safe alternative to current antibiotics and antimicrobial products.

Mineralogical Testing—All of the clays tested for antibacterial activity contained smectite as the dominant mineral group, but the structure and composition of the smectites varied among the samples (Williams et al. 2008). The antibacterial clays have extremely small crystallite sizes, with diameters ranging from 20 to 200 nm. The small particles enhance the relative surface area and offer a tremendous potential for chemical exchange. The variability in the composition and concentration of the exchangeable trace elements in the expandable clays is likely a result of the composition of the hydrothermal fluids that produced the bentonite from the original ash layer.

Testing of different size fractions for several antibacterial clays revealed that the finer fractions (<200 nm) were antibacterial while coarser fractions were not (Haydel et al. 2008). In natural sedimentary clay deposits, these nano-size fractions are typically dominated by newly crystallized (authigenic) clay minerals, not detrital minerals from distal sources. The bactericidal effect was eliminated by cation exchange (K^+ or NH_4^+ saturation), which removes exchangeable ions and molecules. Comparison of the aqueous leachates and exchange solutions from antibacterial clays identified so far did not reveal a single element that was above the minimum inhibitory concentration for the bacteria tested (Williams et al. 2008). Orders of magnitude differences in certain soluble elements (e.g. Na, Mn, As, Mo,

Ag, and U) were observed, but their concentrations in the exchange solutions were not distinguishable from the compositions of leachates that were not bactericidal. These data point to the importance of chemical speciation of the elements absorbed and released by clays, which is largely controlled by the ionic strength, pH, and oxidation state of the aqueous solution. Furthermore, dissolved species might react in combination to produce toxic conditions for bacteria.

Chemical exchange between the clay and bacterial populations is difficult to define because there is often undetectable change in dissolved-element concentration before and after interaction and because it is not possible to separate the bacteria from the clay to analyze them separately. Identification of elements taken up by the bacteria are best examined by ultrasensitive, in situ imaging techniques, such as secondary ion mass spectrometry (NanoSIMS). However, technique development is required to avoid chemical alteration of bacteria during cell fixation and analysis.

As a simple means to identify where antibacterial agents may reside in the clay structure, the clays were progressively heated to dehydrate and dehydroxylate the 2:1 layer silicate. Heating to 200°C removed water and associated volatile elements from the clay interlayer and on the exterior surfaces. Heating to 550°C removed organic compounds from consideration in the antibacterial process and mostly dehydroxylated the clays, thus volatilizing species such as P, S, and Hg possibly bound to the hydroxyl groups. The French green clays, when progressively heated, remained antibacterial until 900°C, when they completely broke down to oxides (Haydel et al. 2008).

Chemical effects to be considered in future investigations should focus on pH- and Eh-controlled interactions of clay-associated solutions and bacteria. A large clay-induced pH or Eh gradient imposed by antibacterial clay could impair metabolic function in even the most adaptive bacteria. The antibacterial clays identified tend to buffer associated solutions to highly acidic or alkaline pH values (<4 or >10). Reactive oxygen species are another frontier for investigating the possible inhibitors to bacterial survival. For example, Fenton-mediated reactions drive the oxidation of mineral-bound Fe²⁺ to generate hydroxyl radicals (Schoonen et al. 2006) that can damage cells. Furthermore, during active infections, it is important to consider the complexity of host–pathogen interactions, which are largely influenced by in vivo chemistry, in addition to the chemical interactions identified in vitro (Sahai et al. 2006).

CONCLUDING REMARKS

Humans have developed medical uses for natural clays largely through trial and error. From topical application of clay as band-aids to geophagical consumption that reduces borborygmi and intestinal ailments, anecdotal accounts of therapeutic clays are known. However, there is a scarcity of scientific evidence to define the mechanisms by which clays kill bacteria or otherwise promote human and animal health. Analysis of the chemical interactions occurring at the clay mineral–bacteria interface is a promising avenue of research that is well developed in the environmental sciences (Konhauser 2007), and investigations into the medical benefits of antibacterial clays are a logical extension. Similar approaches, with emphasis on clay mineralogy and the bioavailability of nutrients and toxins that exchange with biological systems, will further elucidate both the beneficial and harmful effects of clays in health.

Although natural clays can be mineralogically similar, they may have quite different effects on microbial populations, ranging from growth enhancement to complete bactericidal activity. The discovery that natural geological minerals harbor antibacterial properties provides impetus for exploring bentonites and other Earth materials for novel therapeutic compounds. In comparison with antibiotics, inorganic antimicrobial minerals are

considerably more stable and heat resistant, making their use particularly advantageous. Identification of the combinatorial chemistry of solutions buffered by natural, potentially bioactive mineral resources could result in the discovery of new antibacterial agents to fight existing antibiotic-resistant infections and diseases for which there are no known therapeutic agents.

It is likely that no single mechanism or reaction pathway is uniquely responsible for the observed bactericidal activity of bentonite. Progress requires identifying general themes displayed by the interactions between problematic human pathogens (i.e. antibiotic-resistant pathogens) and natural clay minerals that exhibit antibacterial behavior. The new focus on medical mineralogy, and bentonites in particular, will progress because novel *in vitro* and *in vivo* experiments with clay minerals have much to offer for improving human health. Modern techniques for measuring interfacial forces (i.e. atomic force microscopy) and for mineralogical and chemical imaging (i.e. high-resolution electron microscopies and ion imaging) at the nanoscale provide some tools necessary to advance knowledge in this field.

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REFERENCES

- Abraham, PW. Geophagy and the involuntary ingestion of soil.. In: Selinus, O., editor. *Essentials of Medical Geology*. Vol. 17. Elsevier Academic Press; Chapter: 2005. p. 435-458.
- Carretero MI, Lagaly G. Clays and health: An introduction. *Applied Clay Science* 2007;36:1-3.
- Carretero, MI.; Gomes, CSF.; Tateo, F. *Developments in Clay Science 1*. Elsevier; Amsterdam: 2006. Clays and human health. In: Bergaya F, Theng BKG, Lagaly G (eds) *Handbook of Clay Science.*; p. 717-741.
- Christidis GE. Comparative study of the mobility of major and trace elements during alteration of an andesite and a rhyolite to bentonite, in the islands of Milos and Kimolos, Aegean, Greece. *Clays and Clay Minerals* 1998;46:379-399.
- Christidis GE, Huff WD. Geological aspects and genesis of bentonites. *Elements* 2009;5:93-98.
- Cygan RT, Ho CK, Weiss CJ. Linking the Geosciences to Emerging Bio-engineering Technologies. Sandia National Laboratories Report SAND2002-3690 2002:59.
- Ferrand T, Yvon J. Thermal properties of clay pastes for pelotherapy. *Applied Clay Science* 1991;6:21-38.
- Ferrell RE. Medicinal clay and spiritual healing. *Clays and Clay Minerals* 2008;56:751-760.
- Ferrell, RE.; Vermeer, DE.; LeBlanc, WS. Trace Substances in Environmental Health XIX. University of Missouri; 1985. Chemical and mineralogical composition of geophagical materials.; p. 47-55.
- Giese, RF.; van Oss, CJ. *Colloid and Surface Properties of Clays and Related Minerals*. Marcel Dekker; New York: 2002. p. 295
- Grigsby KR, Thyer BA, Waller RJ, Johnston GA Jr. Chalk eating in middle Georgia: A culture-bound syndrome of pica? *Southern Medical Journal* 1999;92:190-192. [PubMed: 10071665]
- Haydel SE, Remenih CM, Williams LB. Broad-spectrum *in vitro* antibacterial activities of clay minerals against antibiotic-susceptible and antibiotic-resistant bacterial pathogens. *Journal of Antimicrobial Chemotherapy* 2008;61:353-361. [PubMed: 18070832]
- Hooda PS, Henry CJK, Seyoum TA, Armstrong LDM, Fowler MB. The potential impact of soil ingestion on human mineral nutrition. *Science of the Total Environment* 2004;333:75-87. [PubMed: 15364520]

- Hunter JM, DeKleine R. Geophagy in Central America. *Geographical Review* 1984;74:157–169. [PubMed: 11614511]
- Hunter JM, Horst OH, Thomas RN. Religious geophagy as a cottage industry: The holy clay tablet of Esquipulas, Guatemala. *National Geographic Research* 1989;5:281–295.
- Konhauser, K. *Introduction to Geomicrobiology*. Blackwell Publishing; Oxford: 2007. p. 425
- Kostyniak, PJ.; Giese, RF.; Costanzo, PM.; Syracuse, JA. Antimicrobial compositions. 2000. US Patent 6015816
- Ljung K, Selinus O, Otabbung E, Berglund M. Metal and arsenic distribution in soil particle sizes relevant to soil ingestion by children. *Applied Geochemistry* 2006;21:1613–1624.
- Metge, DM.; Harvey, RW.; Eberl, DD.; Williams, LB. Geological Society of America Abstracts with Programs. Denver, CO: 2007. Bactericidal properties of clays used for treatment of Buruli ulcer—an emerging public health threat.. Abstract 130928
- Ohashi F, Oya A, Duclaux L, Beguin F. Structural model calculation of antimicrobial and antifungal agents derived from clay minerals. *Applied Clay Science* 1998;12:435–445.
- Oomen AG, 11 coauthors. Comparison of five in vitro digestion methods to study the bioaccessibility of soil contaminants. *Environmental Science & Technology* 2002;36:3326–3334. [PubMed: 12188361]
- Padilla FV, de la Torre AM. La pica: retrado de una entidad clinica poco conocida. *Nutricion Hospitalaria* 2006;21:557–566. [PubMed: 17044601]
- Reinbacher WR. Healing Earths: The Third Leg of Medicine 2003:244. ISBN 1-4033-5090-5.
- Robertson RHS. Cadavers, choleras, and clays. *Mineralogical Society Bulletin* 1996;113:3–7.
- Sahai N, Schoonen MAA. Medical Mineralogy and Geochemistry. *Reviews in Mineralogy & Geochemistry* 64, Mineralogical Society of America, Chantilly, VA 2006:332.
- Schoonen, MAA.; Cohn, CA.; Roemer, E.; Laffers, R.; Simon, SR.; O'Riordan, T. Mineral-induced formation of reactive oxygen species.. In: Sahai, N.; Schoonen, MAA., editors. *Medical Mineralogy and Geochemistry. Reviews in Mineralogy & Geochemistry* 64, Mineralogical Society of America. Chantilly, VA: 2006. p. 179–221.
- Smith B, Rawlins BG, Cordeiro MJAR, Hutchins MG, Tiberindwa JG, Serunjogi L, Tomkins AM. The bioaccessibility of essential and potentially toxic trace elements in tropical soils from Mukono District, Uganda. *Journal of the Geological Society* 2000;157:885–891.
- Tateo F, Summa V, Giannossi ML, Ferrero G. Healing clays: Mineralogical and geochemical constraints on the preparation of clay–water suspension “argillic water”. *Applied Clay Science* 2006;33:181–194.
- Vermeer DE, Ferrell RE Jr. Nigerian geophagical clay: A traditional antidiarrheal pharmaceutical. *Science* 1985;227:634–636. [PubMed: 3969552]
- Voroney, RP. *The Soil Habitat in Soil Microbiology, Ecology, and Biochemistry*. Academic Press; 2006. p. 552
- Williams LB, Haydel SE, Giese RF Jr, Eberl DD. Chemical and mineralogical characteristics of French green clays used for healing. *Clays and Clay Minerals* 2008;56:437–452. [PubMed: 19079803]
- Wilson MJ. Clay mineralogical and related characteristics of geophagic materials. *Journal of Chemical Ecology* 2003;29:1525–1547. [PubMed: 12921434]

Figure 1.

Schematic structure of a 2:1 layer expandable clay such as those found in bentonite (modified from Giese and van Oss 2002). Two layers of cations bound to 4 oxygens (tetrahedra) sandwich cations bound to 6 oxygens (octahedra) to make a silicate layer. These layers are weakly bound in stacks, with water and interlayer cations between the layers. The large blue spheres represent hydrated cations, and the small red spheres stand for hydrogen ions.

Figure 2. Commercially available geophagic materials. (A) 5 cm wide clay tablet embossed with a religious design, from Esquipulas, Guatemala. (B) Edible kaolinite sold in markets near Athens, Georgia. MODIFIED FROM FERRELL 2008

Figure 3.

XRD patterns ($\text{Cu K}\alpha$ radiation) from smectite and X-ray amorphous clays typically consumed by geophagists. The top pattern represents a smectite-rich sample with well-structured crystallites. The three bottom samples contain abundant X-ray amorphous compounds. Diagnostic peaks are labeled: S – smectite; I – illite; K – kaolinite; Q – quartz; QI – quartz, illite, and smectite; Cp – clinoptilolite; Cc – calcite; Oc – disordered silica; and G – goethite. Samples were collected from Mexico (MX1 and MX2), Togo (TOG), New Mexico, USA (NM1 and NM2); Guatemala (GT1 and GT2); and Indonesia (INO). MODIFIED

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Figure 4.

Reference dose ratios (RDR) for extracts from 50 g of smectite- and kaolinite-rich geophagic materials by 0.12 N HCl compared to the EPA Daily Reference Dose. Values above 1 exceed the recommended daily dose for an 80 kg adult. Maximum (square), median (dash), and minimum (circle) values are shown. The boxes enclose values between the first and third quartiles. MODIFIED FROM FERRELL 2008