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Adaptive function of soil consumption: an *in vitro* study modeling the human stomach and small intestine

Nathaniel J. Dominy[1,*], Estelle Davoust[2] and Mans Minekus[3]

[1]*Department of Ecology and Evolution, University of Chicago, 1101 East 57th Street, Chicago, IL 60637, USA,* [2]*Université d'Auvergne, 28 place Henri Dunant, 63300 Clermont-Ferrand, France* and [3]*TNO Nutrition and Food Research Institute, PO Box 360, NL-3700 AJ Zeist, The Netherlands*

*Author for correspondence (e-mail: njdominy@uchicago.edu)

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Summary

Despite occurring in a wide variety of taxa, deliberate soil consumption (geophagy) is a poorly understood behavior. In humans, geophagy is sometimes considered aberrant or a sign of metabolic dysfunction. However, geophagy is normally assigned an adaptive function in nonhuman primates and various other organisms. One hypothesis submits that clay-rich soil adsorbs intestinal insults, namely plant metabolites or diarrhoea-causing enterotoxins. Here we test the capacity of kaolin, a commonly ingested clay, to adsorb quinine (an alkaloid) and two types of tannin (digestion-inhibitors). Trials were conducted *in vitro* using the TNO Intestinal Model, a device that closely simulates digestion by the human stomach and small intestine. Kaolin reduced the bioavailability of each compound by ≤30%. However, because we could not replicate clay–epithelial adhesion and reduced motility, these results may underestimate adsorption *in vivo*. We also show that kaolin fails to render calcium oxalate soluble. We conclude that gastrointestinal adsorption is the most plausible function of human geophagy. Adaptive advantages include greater exploitation of marginal plant foods and reduced energetic costs of diarrhoea, factors that could account for the high frequency of geophagy in children and pregnant women across the tropics.

Movies available on-line

Key words: geophagy, pica, diet, tannin, alkaloid, human.

Introduction

Deliberate consumption of soil (geophagy) is a conspicuous though poorly understood behavior. In humans, the practice is variously regarded as a global health issue or an anthropological idiosyncrasy; indeed, it is widely viewed as an aberrant behavior or a symptom of metabolic dysfunction (Simon, 1998). Paradoxically, geophagy is usually considered an adaptive behavior in nonhuman primates and a wide diversity of mammals (Klaus and Schmid, 1998; Krishnamani and Mahaney, 2000). For humans, adaptive benefits must eclipse the costs of ingesting geohelminths (Saathoff et al., 2002) and soil-based toxins, such as lead, copper and potassium (to a hyperkalemic extent) (Simon, 1998). Despite such costs, an adaptive function is probable given its persistence in human history. Geophagy was first reported by Aristotle and further described by Dioscorides and Avicenna in 40 BC and 1000 AD, respectively (Halstead, 1968; Danford, 1982). Among the functions suggested for vertebrates (Gilardi et al., 1999), two are most plausible for humans: (1) mineral nutrient supplementation, particularly with respect to Ca, Cl, Na and Fe; and (2) adsorption of intestinal insults, such as plant secondary metabolites and diarrhoea-causing enterotoxins.

Mineral nutrient supplementation is the historical and intuitive basis for geophagy (Jones and Hanson, 1985; Kreulen, 1985). Indeed, sodium acquisition reportedly explains the phenomenon in organisms ranging from butterflies to babirusas (Arms et al., 1974; Clayton and MacDonald, 1999). In humans, however, investigators have largely discounted the hypothesis that geophagy is a physiological response to a need for nutrients, such as iron. The tendency to infer that anemia elicits soil consumption (Abrahams, 1997) is confounded by the fact that geophagy often leads to, rather than corrects, iron, zinc, or potassium deficiencies (Severance et al., 1988; Reid, 1992). The phenomenon is exacerbated when clays with high cation-exchange capacities are ingested. Moreover, mineral nutrients are usually sufficient in an animal's routine diet (Hladik and Gueguen, 1974; Gilardi et al., 1999); and, among primates, elements are similar between unconsumed soils and those consumed selectively and repeatedly (Izawa, 1993; Mahaney et al., 1995; Müller et al., 1997; Bolton et al., 1998). Furthermore, in soils consumed by chimpanzees, only Fe was present in high concentrations (range 6–17%; Mahaney et al., 1997). However, available Fe was only partially soluble in conditions modeling the chimpanzee stomach (oxalic acid at pH 2.0), indicating it was an improbable cue. Finally, it is

notable that dissolved salts in some soils may render calcium oxalate soluble (Kreulen, 1985). To our knowledge, this hypothesis has never been tested despite the importance of Ca to vertebrate reproduction. In plants, Ca exists principally as oxalate crystals (Finley, 1999; Prychid and Rudall, 1999), which readily cross intestinal epithelia (Hatch and Freel, 1995). It is perhaps significant that primates incurring high reproductive costs consume soil despite considerable risk of predation (Heymann and Hartmann, 1991).

The clay fraction of ingested soils could also protect the gastrointestinal epithelium by cross-linking with glycoproteins in the intestinal mucosa (Rateau et al., 1982; Moré et al., 1987). Because toxins and tannins cross or afflict the epithelium (Mitjavila et al., 1977; Gee and Johnson, 1988), the adsorption of such dietary compounds is the leading hypothesis for geophagy in some animals (Gilardi et al., 1999; Setz et al., 1999; Wakibara et al., 2001). Clays with high cation-exchange properties also adsorb diarrhoea-causing enterotoxins (Said et al., 1980; Brouillard and Rateau, 1989). Accordingly, Kaopectate® and Smecta® are common commercial products featuring, respectively, kaolinite and smectite, clays that assuage diarrhoea in monkeys and humans (Beck et al., 1977; Leber, 1988; Guarino et al., 2002). Compellingly, humans report consuming soil expressly to relieve diarrhoea, and kaolinite is usually, but not always, the principle clay fraction ingested by humans and nonhuman primates (Vermeer and Ferrell, 1985; Aufreiter et al., 1997; Mahaney et al., 1997, 2000; Knezevich, 1998). Of course, both adsorptive functions are not mutually exclusive. Indeed, they may be linked. Practitioners of geophagy are often socially disadvantaged cultural and ethnic groups living in the tropics (Abrahams and Parsons, 1996; Simon, 1998). Under such conditions, geophagy may facilitate exploitation of marginal plant foods and concomitantly reduce the energetic costs of diarrhoea. Given the selective benefits to pregnant women and children, it is unsurprising that they are the principal consumers of soil (Wiley and Katz, 1998). In fact, humans use clay explicitly to render tanniniferous acorns and alkaloid-rich potatoes edible (Johns, 1986; Johns and Duquette, 1991a,b).

Although the incidence of geophagy is decreasing (Parry-Jones and Parry-Jones, 1992), the practice remains common in many cultures. For example, a single Nigerian village produces 500 tons of soil yearly for consumption across West Africa (Vermeer and Ferrell, 1985). Moreover, children consume considerable quantities of soil regardless of geography and socio-economic status. Ingestion varies from the incidental to the incredible, ranging from 75 mg day^{-1} in Amherst, USA (Stanek and Calabrese, 1995) to 650 g reported *in vivo* in a single Gambian boy (Collinson et al., 2001). Accordingly, understanding and quantifying the adsorptive capacity of clay continues to be important. To date, modeling of dietary compound adsorption by clays has been investigated only in Amazonian parrots (Gilardi et al., 1999). Here we model the human gastrointestinal system and test the capacity of kaolin to adsorb a toxin (quinine) and tannins, both condensed (quebracho) and soluble (tannic acid). Furthermore, we evaluate the solubility of calcium oxalate in the presence of kaolin.

Materials and methods

Intestinal modeling

The TNO intestinal model (TIM) provides a unique opportunity to simulate the adsorption of dietary compounds during *in vitro* digestion (Minekus et al., 1995, 1999). Briefly, the model consists of four successive compartments (Fig. 1), simulating the stomach, duodenum, jejunum and ileum. After inserting kaolin and/or test compounds into the gastric compartment, gastric solutions are added while the pH is measured and controlled according to a predetermined curve. The compartments consist of two connected glass units with flexible interior walls. Water to control temperature is pumped from a water bath through the space between the jacket and flexible wall. The flexure of the walls is adjusted by varying water pressure. Alternate flexing of the walls mixes the chyme in each compartment. Computer-controlled peristaltic valve pumps control meal transit through individual compartments. Secretions of 4% porcine bile extract (Sigma, St Louis, USA) and 10% pancreatin (Pancrex V; Paines and Birne, Greenford, UK) enter the duodenal compartment. The duodenal pH is measured and controlled with $NaHCO_3$. Water and digestive products are absorbed from the jejunal and ileal compartments by pumping dialysis liquid through hollow-fiber devices with a molecular mass limited to ca. 5000 kDa. A filter prevents retention of larger particles in the hollow fiber devices. Ileal delivery is collected in a vessel.

Gastric environment

Before introducing the substance to be digested, 10 ml of gastric electrolyte solution ($CaCl_2$ 0.22 g l^{-1}, KCl 2.2 g l^{-1}, NaCl 5 g l^{-1} and $NaHCO_3$ 1.5 g l^{-1} adjusted to 500 ml with water) with 500 kU l^{-1} pepsinogen (Sigma) and rhizopus lipase (Amano, Nagoya, Japan) were introduced into the gastric compartment and adjusted to pH 1.5 with 1 mol l^{-1} HCl. Gastric solutions were secreted at 0.5 ml min^{-1} and pH was controlled according to a pre-set profile by secreting 1 mol l^{-1} HCl or water.

Small intestine environment

Secretions of $NaHCO_3$ or water at 0.25 ml^{-1} min^{-1} maintained pH in the small intestine at 6.5. Pancreatic output was simulated by secreting 10% pancreatin in small intestinal electrolyte solution ($CaCl_2$ 0.22 g l^{-1}, KCl 2.2 g l^{-1}, NaCl 5 g l^{-1}) at 0.25 ml min^{-1}. Biliary output was simulated by secreting 4% bile solution at 0.5 ml min^{-1}. Before the experiment, the duodenal compartment was filled with 1 g trypsin (Bovine Pancreas Type III; Sigma), 15 ml of 4% bile solution, and 7 ml 10% pancreatin solution. Jejunal and ileal compartments were filled with 100 ml of small intestinal electrolyte solution and pumped through the hollow fiber at a rate of 10 ml min^{-1}.

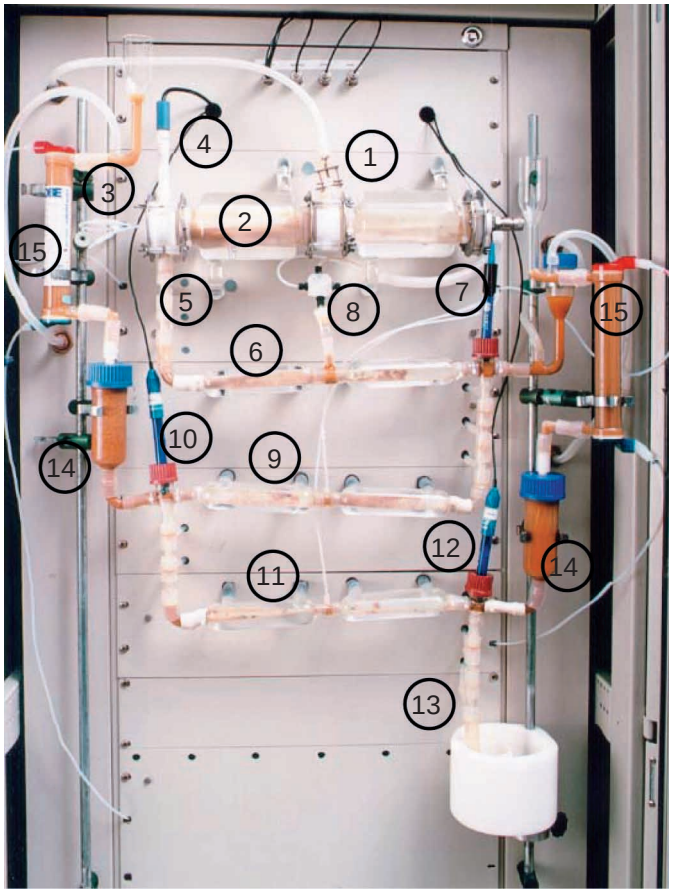

Fig. 1. The TNO intestinal model (TIM). (1) The gastric compartment, comprising two glass units with interior flexible walls, surrounded by water at 37°C; (2) the persitaltic movements of the gastric wall are simulated; (3) secretion of gastric acid, electrolytes and enzymes (pepsinogen/pepsine, lipase); (4) pH electrode to control gastric pH; (5) simulated pyloric sphincter, regulating the delivery of gastric contents into the duodenum; (6) duodenal compartment with simulated peristaltic movements (see Supplemental data); (7) pH electrode to control the duodenal pH by the secretion of bicarbonate; (8) secretion of duodenal electrolytes, bile and pancreatic enzymes; (9) jejunal compartment with simulation of the peristaltic movements (see Supplemental data); (10) pH electrode to control the jejunal pH value by the secretion of bicarbonate; (11) ileal compartment with simulation of the peristaltic movements; (12) pH electrode to control the ileal pH value by the secretion of bicarbonate; (13) simulated ileo-caecal valve, regulating the delivery of ileal contents into the large intestine, mimicking the intestinal passage; (14) prefilter system; and (15) semipermeable membrane unit (hollow fibers) for absorption of digested products and water.

Digestion trials

We used kaolin (Sigma) and four test compounds: calcium oxalate (Farco, Beijing, China), crude quebracho (a condensed tannin from the bark of *Schinopsis balansae*; gift of Dr A. E. Hagerman), tannic acid (a soluble tannin; Riedel de Haën, Seelze, Germany), and quinine (an alkaloid, Sigma). Digestion trials and control trials (without kaolin) were executed in duplicate with a meal volume of 300 ml. For experimental trails we chose 10 g kaolin. Although this amount exceeds the US Environmental Protection Agency's 200 mg day^{-1} risk-assessment level for involuntary soil ingestion (Stanek and Calabrese, 1995), it is within the daily range of human consumption reported by Simon (1998). For example, children in western Kenya consume an average of 28 g of soil daily, ranging from 8 to 108 g (Geissler et al., 1997).

Because humans and chimpanzees share a similar gastrointestinal system (Lambert, 1998), we chose 1 g tannic acid and 3.3 g quebracho (40% of which is condensed tannin; A. E. Hagerman, personal communication) to approximate a dietary intake of 1% tannin in both humans and chimpanzees (Hladik, 1977; Narasinga Rao and Prabhavathi, 1982; Reynolds et al., 1998). We chose 1 g calcium oxalate to simulate a modest meal of 100 g spinach (US Department of Agriculture, Agricultural Research Service 2001, *USDA Nutrient Database for Standard Reference, Release 14.* http://www.nal.usda.gov/fnic/foodcomp). Finally, we chose 1 g quinine as a dosage toxic enough to induce human cinchonism (Bateman and Dyson, 1986).

Sampling and analyses

Digestion was simulated during duplicate 5 h experiments. Ileal delivery was collected after 2, 4 and 5 h. The mass of the samples was measured to determine fresh matter emptying. Samples were stored at 4°C. Similarly, the bottles with dialysis fluid were replaced every 2 h and samples were collected and stored at 4°C. At the end of the experiment the contents of the gastric and intestinal compartments were collected and stored at 4°C.

We measured levels of absorbed calcium directly using a Ca^{2+}-selective electrode (Orion; Beverly, USA). Levels of condensed tannin (crude quebracho) were measured with the Folin–Denis assay (200 µl sample + 100 µl $NaHCO_3$ + 100 µl Folin–Denis reagent + 1.6 ml H_2O) at 790 nm on an LKB spectrophotometer (Pharmacia LKB Biotechnology, Uppsala, Sweden) after 30 min. For tannic acid, the assay was adjusted (200 µl sample + 200 µl Folin–Denis Reagent + 1.6 ml $NaHCO_3$) and absorption measured at 760 nm. Quinine was measured by adding 100 µl of sample with 1900 µl Dragendorff's reagent and measuring absorption at 595 nm. All measurements were referenced to 5-point standard curves.

Results

Kaolin significantly reduced the bioavailability of quebracho, tannic acid and quinine, with mean adsorption ranging from 21.5 to 29.5% of the bioavailable fraction (Fig. 2). Adsorption was greatest in the small intestine, where pH was maintained at 6.5. Kaolin did not improve calcium absorption: Ca delivery (262±37 µg g^{-1}) was equivalent to the input (300 µg g^{-1}) of control trials. Surprisingly, delivery in the presence of kaolin (356±33 µg g^{-1}) exceeded input by a mean of 19% (range: 8–30%) (Fig. 2D).

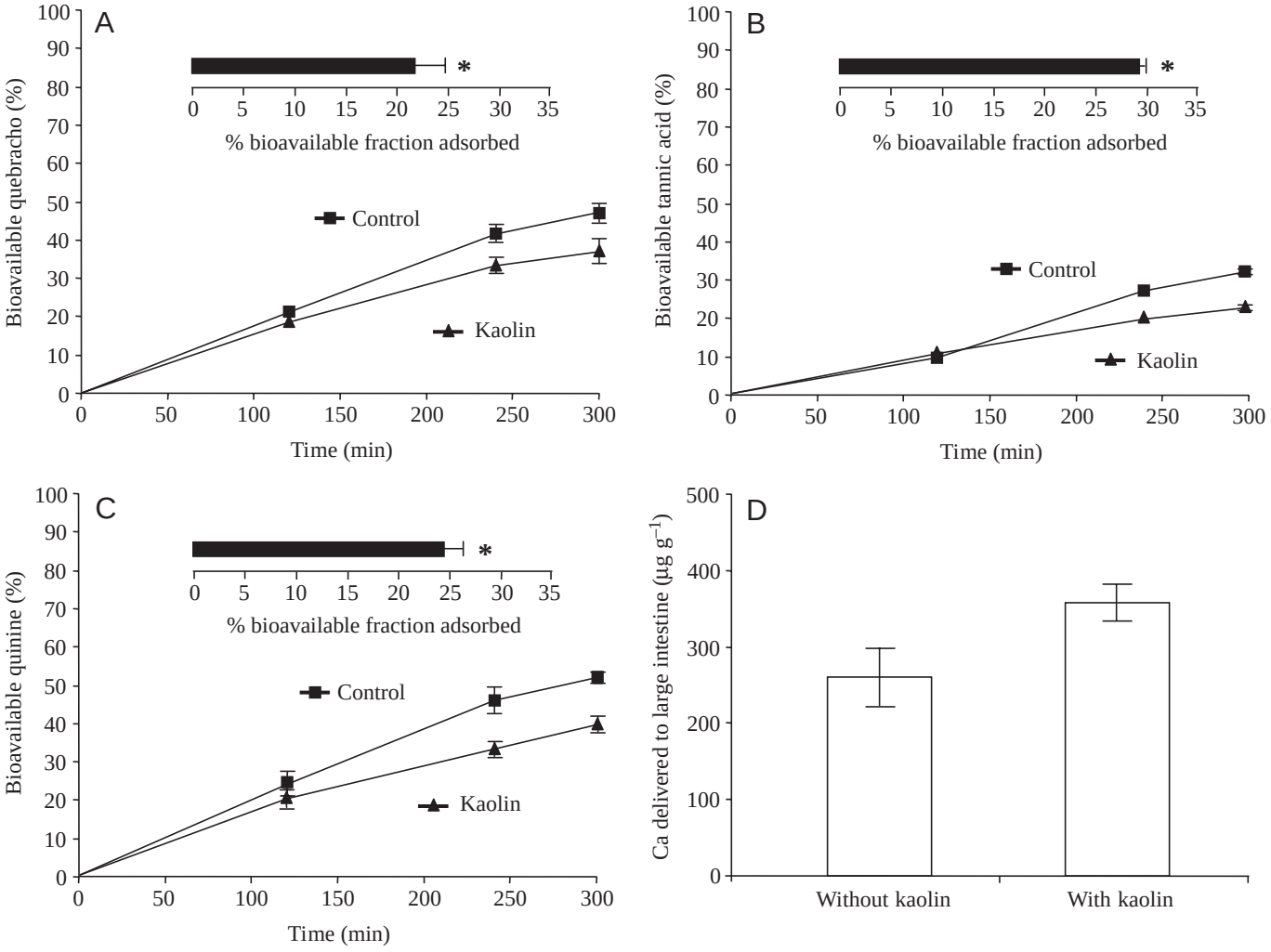

Fig. 2. Bioavailable quebracho (A), tannic acid (B), and quinine (C) during *in vitro* digestion with kaolin and without (control). Kaolin adsorbed a significant percentage (*P<0.05) of the bioavailable fraction of each compound studied except for calcium oxalate, which was insoluble. In fact, kaolin increased Ca precipitation, with Ca delivery exceeding the comminuted input: two-tailed t-test, t=2.6, P<0.02 (D). Values are means ± 1 S.D.

Discussion

Although soil consumption is sometimes viewed as an aberrant behavior, it has persisted in human history to the extent that it is now a fashionable palliative (Knishinski, 1998). Here we provide some experimental support for this view. We show that under controlled conditions modeling the human stomach and small intestine, kaolin adsorbed ≤30% of the bioavailable fraction of three commonly ingested chemical compounds. However, modeling clay adhesion to the gastrointestinal epithelium was not possible with the silicon tubing of TIM. Accordingly, adsorption may be considerably greater *in vivo*, where the interface between clay and epithelial mucosa is prolonged by reduced motility (Gilardi et al., 1999). Although we could not replicate this effect, we show that conditions in the small intestine are propitious for cytoprotection.

Furthermore, we show that calcium oxalate is insoluble in the presence of ingested kaolin; however, dissolved salts in natural clay licks may improve solubility to some extent (Kreulen, 1985). This possibility deserves further study. Moreover, the causal link between increased Ca precipitation and kaolin is unclear, although the range reported here is consistent with the results of von Unruh et al. (2003), in which calcium oxalate precipitated 2.2–18.5% (±4.0–7.9%) of ingested Ca.

Our results support hypotheses advocating an adsorptive function of ingested clay. For pregnant women the advantages of reduced toxicity and digestion-inhibition are clear. By adhering to gastrointestinal epithelia, clays may not only improve digestive efficiency, but also reduce fetal exposure to toxins tolerated by the mother (Profet, 1992). Similarly, economically disadvantaged children living in the tropics are also frequent consumers of soil. They are particularly susceptible to undernourishment and diarrhoeal dehydration, conditions that may be exacerbated by a reliance on marginal plant foods rich in tannins and toxins (Johns, 1990). It is notable that howling monkeys are geophagous when they

consume foliage, which is often toxic (De Souza et al., 2002). Both adsorption and cytoprotection mechanisms offer adaptive advantages.

Similar effects are attributed to charcoal, which is prescribed commonly in cases of child poisoning (Levy, 1982). In fact, murine models indicate that charcoal is more effective than kaolin at adsorbing endotoxins (Ditter et al., 1983), which could explain why some primates consume charcoal regularly (Cooney and Struhsaker, 1997; Struhsaker et al., 1997). However, the adsorptive properties of clay or charcoal can also produce negative effects. For example, Tsakala et al. (1990) reported that a traditional anti-diarrhoeal soil from the Republic of Congo (mouboumou) adsorbed ≤60% of bioavailable chloroquine. The compromising effect of anti-diarrhoeal soils on common antimalarial treatments deserves further study. Furthermore, we show that consuming kaolin-rich soils together with calcium oxalate-rich leaves could precipitate ≤30% of available Ca. Nevertheless, given its prominence in human history, the adaptive benefits of geophagy would appear to surpass these potential costs, as well as those of ingesting geohelminths, lead and other potentially harmful elements (e.g. Gelfand et al., 1975).

Finally, although we did not study the importance of mineral supplementation, it is an unlikely cause of geophagy in parrots, humans and nonhuman primates (Reid, 1992; Mahaney et al., 1997; Gilardi et al., 1999; Krishnamani and Mahaney, 2000). However, for large herbivores, mineral supplementation could be an important factor (Klaus et al., 1998; Abrahams, 1999; Milewski, 2000; Holdo et al., 2002). Accordingly, the adaptive function of soil consumption could be multifactorial, with none of the mechanisms being mutually exclusive (Wilson, 2003). We conclude that human geophagy is a likely mechanism for maintaining gastrointestinal health. Our results are consistent with this view as kaolin reduced the bioavailability of three dietary compounds by ≤30%. Thus, the tendency of the medical literature to view geophagy as aberrant behavior or a symptom of metabolic dysfunction is probably unwarranted in most cases.

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