

## Researchers test antibacterial effects of healing clays

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Clay is most commonly associated with the sublime experience of the European spa where visitors have been masked, soaked and basted with this touted curative since the Romans ruled. If ASU geochemist Lynda Williams and microbiologist Shelley Haydel's research on the antibacterial properties of clays realizes its full potential, smectite clay could one day rise above cosmetic use to take its place comfortably with antibacterial behemoths like penicillin.

"We use maggots and leeches in hospitals, so why not clay?" Haydel poses. "I had a professor in graduate school say, 'Maybe perhaps once in your life, in your scientific career, you'll come across something that can change the world.' Sometimes I think: Is this it? Will this help some people?"

Theirs is an unusual research pairing. They are female scientists, each in the College of Liberal Arts and Sciences, yet pursuing different lines of scientific discovery. Williams is an associate research professor in the School of Earth and Science Exploration and studies clay mineralogy. Haydel is an assistant professor and expert in tuberculosis in the School of Life Sciences and with the Center for Infectious Disease and Vaccinology in the Biodesign Institute at Arizona State University.

"People are interested in natural cures and I think that there is a lot of nature that we don't understand yet," Williams says. "What if we discover a mechanism for controlling microbes that had never been discovered before? It is these avenues, at the boundaries of scientific

discovery, at the edges of my field and knowledge (and Shelley's), where such discoveries are made."

National Institutes of Health (NIH) program directors agreed. They awarded a \$438,970 grant over two years to Williams and Haydel for the study of clay mineral alternative treatment for Buruli ulcer. What makes this award even more interesting is the rarity for a geochemist to net a NIH grant.

## **National Center encourages alternative studies**

The National Center for Complementary and Alternative Medicine at NIH was established in 1998 for just this kind of study. One of the 27 Institutes making up NIH, the Center funds scientific research and technologies that examine herbal remedies, such as dandelion, green tea, valerian, and horse chestnut, and practices like acupuncture, Tai Chi, and Reiki that fall outside conventional medicines.

The ASU duo will examine the mechanisms that allow two clays mined in France to heal Buruli ulcer, a flesh-eating bacterial disease found primarily in central and western Africa. Buruli ulcer has been declared to be "an emerging public health threat" by the World Health Organization (WHO). Related to leprosy and tuberculosis, the *Mycobacterium ulcerans* produces a toxin, lesions, and destroys the fatty tissues under the skin.

"The toxin is immunosuppressant; the patients feel no pain and the body mounts no response to infection. It leads to disfigurement, isolation, not unlike that seen in leprosy," Haydel explains. "Traditional antibiotics can only make a difference at the very earliest stages of the disease, so treatments have, in the past, been largely confined to amputations or surgical excision of the infected sites."

This means if the clays are antibacterial in nature and the locus for that activity can be isolated, they may represent a new form of treatment, one that goes beyond the capacity of existing antibiotics. "And they could be produced and distributed cheaply," Williams notes.

## **Humanitarians answer Internet challenge**

So how did a clay mineralogist whose background is in low temperature geochemistry become involved with a health care project centered in the Ivory Coast? The scientific equivalent of an online dating or matchmaking service: "I answered a posting on the Clay Mineral Society's list serve placed by Thierry Brunet de Courssou. He was asking to have someone take high resolution scanning electron micrographs of the clays," Williams explains. "I confess that we all ignored him initially."

According to the Brunet de Courssou Web site, the family has been operating health clinics on the Ivory Coast and in New Guinea. For a decade, Madame Line Brunet de Courssou, Thierry's mother, had been importing two French clays to treat people with Buruli ulcer and was getting startling results, while her use of native clays had no effect. Williams reviewed the mother's work and notes that "Line Brunet de Courssou was a careful observer." However, Madame Brunet de Courssou was not a scientist. The mother, who is now deceased, approached the WHO in 2002 at its fifth advisory group meeting on Buruli ulcer, having documented more than 50 cases of successful healing with the clay treatments. WHO documents indicate that the organization was receptive, calling her results "impressive," yet, Williams notes, funding was denied for lack of scientific study.

Williams, from a family of physicians, says that it was really the second message that finally drew her to the project. "He said, 'I guess that no American scientists are interested in helping poor people in Africa.'"

He guessed wrong. Armed with 100 grams of green powder (clay high in reduced iron), Williams not only took the micrographs of the minerals, she went a step further and examined their crystal structure and chemical compositions. She recruited Haydel to the project before the microbiologist arrived at ASU in 2005. Haydel brought more than 13 years of experience with pathogenic bacteria, in particular tuberculosis, to the project. Within two months of Haydel's arrival, they submitted the grant proposal to the NIH.

"I approached this work from the viewpoint of a clinical microbiologist," Haydel says. "I ordered bacterial strains that pharmaceutical companies use to test their antimicrobials."

Haydel and Williams tested both of the French clays that Brunet de Courssou had been importing. One completely inhibited pathogenic *Escherichia coli*, *Salmonella typhimurium*, *Pseudomonas aeruginosa* (often a problem as an opportunistic infection in burn wards) and *Mycobacterium marinum* (related to *Mycobacterium ulcerans*, which causes Buruli ulcer disease). The clay was also found to partially inhibit the growth of pathogenic *Staphylococcus aureus*, including a multi-drug resistant variety. "The other clay actually helps the bacteria to grow," Haydel adds.

What makes one clay kill bacteria, and the other promote growth? And why do most clays tested have no effect? Research like that being done by Williams and Haydel can answer such questions. "Clay can be as variable as the bacteria we are studying. There is a lot to be learned yet," Williams notes.

## **Clay's properties fuel interest**

Williams' career fascination with clay started when she was a mineral exploration geologist looking for ore deposits. She worked with 'the

father of clay mineralogy,' Bob Reynolds, at Dartmouth College. Later, as a research associate at Louisiana State University, a colleague was studying geophasia – eating clay, a behavior seen in animals and people, since the time of the aborigines.

"In the South Appalachian Mountains, poor women would eat the local clay to help soothe nausea and stomach ailments, particularly during pregnancy. The clay was rich in kaolinite. (Kaolinite is the major ingredient in the over the counter remedy Kaopectate). But one day, they ran out of clay and moved over to another mountain and people began dying. We wanted to know why."

The key to clay's variable nature seems to be its structure. "Clay is a mineral; it has a crystalline structure that is both flexible and fluid," Williams says. She likens them to very thin, two-nanometer-thick slices of bread in a "peanut butter and jelly sandwich." The "bread" is composed of three regions, two silicate layers with tetrahedral rings bounding an octahedral core. The "peanut butter" is the charged cations, for example, potassium, that stick to the negatively charged tetrahedral ring surface. And the jelly? Organic compounds or other species of any or no charge are possible. This interlayer, as the peanut butter and jelly are termed, can vary in width and composition depending on the kinds of waters and elements present when it was formed. It is this interlayer where much of the elemental variability between clays can be found. And the interlayer surface area is huge (greater than 100 square meters per gram of clay – bigger than a football field). As a result, surface chemical reactions from these sites have an enormous impact on the geochemistry of the local environment.

Williams is passionate about her subject: "Clays are as individual in character as people are in personality. They can be as old as Precambrian time (probably older, since meteorites contain clay minerals from other celestial bodies) or as young as I can make them in my lab in a few

hours. They form when the chemistry, temperature and pressure conditions are right. In the case of the two French clays we are testing, their chemical structures are almost identical, but the different trace element chemistry of the interlayer records an older geologic condition, from a time when the antimicrobial property was likely inherited."

Crystal structure, the interlayer, the way other materials, metals, ions bind to clays, the absorptive characteristics of clays, all could potentially play a role in the antibacterial activity they find in the one French clay. And, while preliminary results suggest that the antibacterial activity is associated with the interlayer, crystal size and structure also seem to play a role.

It is a mystery that engages both research partners: "It's fascinating," Haydel says. "Here we are bridging geology, microbiology, cell biology – transdisciplinary sciences, exactly what (ASU President) Michael Crow has been promoting. A year ago, I'd look at the clay and say, 'well that's dirt.' Now I know a little something about clay structure; Lynda knows a little bit about microbiology. Alone, we each would have had to study for years; together we are partnering these disciplines with synergy that really works."

Source: Arizona State University

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