

## Attacking MRSA with Metals from Antibacterial Clays



In the race to protect society from infectious microbes, the bugs are outrunning us. The need for new therapeutic agents is acute, given the emergence of novel pathogens as well as old foes bearing heightened antibiotic resistance.

Shelley Haydel, a researcher at Arizona State University's Biodesign Institute has a new approach to developing effective, topical antibacterial agents — one that draws on a naturally occurring substance recognized since antiquity for its medicinal properties: clay.

In research appearing in the journal *PLOS ONE*, Haydel and her graduate student, Caitlin Otto, lay out the case for clay, demonstrating that certain varieties of clay have the ability to aggressively kill a range of pathogens including *E. coli* and methicillin-resistant *Staphylococcus aureus* (MRSA) — a stubborn, highly contagious, and dangerous pathogen that has lately been the scourge of many hospitals and is a common cause of skin infections in the community. Their study further indicates that, rather than the physical particles of the clays, particular metal ions attached to the clay are likely responsible for its potent antibacterial properties.

"While some natural clays, which have absorptive properties similar to sponges, have been used topically for centuries, scientific studies investigating the antibacterial mechanisms represent a relatively new area of research," Haydel says. "With this study, we have demonstrated that the antibacterial activity of these natural clays is not dependent on the physical clay particles, but rather the abiotic, microbicidal activities of specific metal ions desorbed from the clay surface. While we are still working on mechanism of action studies, determining that specific metal ions influenced antibacterial activity was critical in leading us in the appropriate scientific directions."

Medical use of clay has a storied history. As early as 5000 years ago, clay was listed in the ancient tablets of Nippur as a wound-healing medicament. Around 1600 BC, the Ebers Papyrus—recognized as the world's oldest medical text—recommended clay for ailments including diarrhea, dysentery, tapeworm, hookworm, wounds, and abscesses. Clays came into common use in the 19th century as topical treatments for surgical wounds, demonstrating their beneficial effects for pain management, inflammation, putrefaction, and healing processes.

In their current study, Otto and Haydel examined four clay samples and their respective aqueous mineral extracts or leachates and determined that the clays exhibited different *in vitro* antibacterial activities against *E. coli* and MRSA. Mineralogically, the samples were nearly identical with 52 percent clay and 48 percent non-clay minerals, but the composition of metal ions released from the mineral surfaces varied considerably across the samples. The tests, using aqueous mineral leachates of the four clay samples, uncovered a variety of elements in varying concentrations. Based on previous studies, the research team focused on five metal ions—iron (Fe), copper (Cu), cobalt (Co), nickel (Ni), and zinc (Zn).

When non-antibacterial clays with low concentrations of these five critical metal ions were supplemented with higher amounts and the pH was matched with that of antibacterial clays, the new formulation displayed killing ability against *E. coli* and MRSA. The result pointed to the presence of metal ions in sufficient concentration as the antibacterial agent in the clay. Further tests narrowed the field of antibacterial candidates, establishing Fe<sup>+2</sup>, Cu<sup>+2</sup>, and Zn<sup>+2</sup> ions as contributing antibacterial agents.

While the pH level was found to play a mediating role, the lethal effect of the clays could not be attributed exclusively to pH, absent the influence of metal ions. Metal speciation modeling and statistical analysis of the results indicated that Cu<sup>+2</sup>, Co<sup>+2</sup>, Ni<sup>+2</sup>, and Zn<sup>+2</sup> are effective against *E. coli*, while Cu<sup>+2</sup>, Co<sup>+2</sup>, and Zn<sup>+2</sup> are effective against MRSA. Intriguingly, the study found that the metal ion toxicity of a given clay sample is not always proportional to the total ion concentration. Toxicity instead is critically dependent on a variety of other factors including pH, ion solubility, osmotic strength, and temperature. The tests undertaken helped to evaluate the interplay of these factors in determining both the antibacterial effectiveness and toxicity of the samples.

Haydel notes that physical and chemical properties of minerals contained in clays together contribute to healing properties. Minerals contained in clay mixtures have a negative surface charge that allows the free exchange of compounds from the environment, including bacteria, viruses, proteins, nucleic acids, and cations. Kaolinite, talc, and smectite clay minerals are highly absorptive. Due to their ability to adhere to the skin,

clays offer mechanical protection similar to a bandage, sealing out external physical or chemical agents, as well as absorptive properties which assist in removing devitalized tissue, particulate matter, or foreign materials from a wound.

Haydel is optimistic about the potential for medicinal clays to play a greater therapeutic role, particularly against the growing threat of topical and antibiotic-resistant infections:

"We have demonstrated that mineralogically-identical clays exhibit chemical variability which correlates with variability in antibacterial activity. Since clays can contain toxic metals, such as arsenic, cadmium, lead, and mercury, safety precautions must be in place to minimize exposure to toxic ions. Efforts must be taken to standardize the composition and antibacterial efficacy of clays if they are to be used therapeutically and prophylactically."

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