# Hot Topics in Pharmacognosy: To "Escape" or Not to "Eskape"

*By Dr. David Newman*

Our title's play on terminology is deliberate. "ESKAPE" when capitalized, is the acronym given by clinical microbiologists and infectious disease physicians to the coterie of resistant microbes better known as *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter* species. With the recent news about colistin-resistant microbes that are also resistant to carbapenems appearing in the continental U.S., the search for antibiotics that can control these agents needs to move into full gear.

In a recent publication in the online journal *Frontiers in Microbiology*, Tiwari and colleagues reviewed compounds from herbal sources that had activity against *A. baumannii* and other pathogens. This article listed some interesting compounds that demonstrated activity, tended to be from Ayurvedic sources, and ranged from well-known compounds such as curcumin, eugenol, berberine, and thymol, etc., to paeonol.[1]

In the same time frame however, there were three very interesting papers published, dealing with various aspects of this problem. Though not the first, the perspective by Fisher and Mobashery[2] gives the background and costs of discovery for new antibiotics, whether from natural products or synthesis; this sets the stage for the other two papers. In the first, Fleeman et al., demonstrated nicely how using quite simple molecules based mainly on guanidine substitution on known classes of antibiotics, led to very interesting molecules with *in vivo* activity in relevant murine models.[3] Then in the second, Grace et al. demonstrated the effect that cationic polymers with a low degree of polymerization had on certain pathogens.[4]

One may now ask, "Where is the pharmacognosy at this stage?" It comes along from two very interesting and recent papers, and an earlier paper, that cover an area not usually considered under this term. These papers are from studies of the use of clays by both Canadian indigenous peoples and in the treatment of Buruli ulcers. Buruli ulcers are caused by a toxin expressed by *Mycobacterium ulcerans*, and the only effective treatment is excision of the wound. In 2004, a group at the United States Geological Survey reported on the utility of clays as treatments,[5] further elaborated on by Haydel et al in 2008, demonstrating that clay minerals had significant in vitro activities against sensitive and resistant microbes.[6]

The story languished for a few years until Dr. Julian Davies at the University of British Columbia, Vancouver, Canada, was asked to look at the properties of a clay known as "Kisameet Clay (KC)." This material had been used for centuries by the local First Nations (Heiltsuk) peoples, appeared to have excellent therapeutic properties, and seemed to be different on mineralogical investigation from the other local clay deposits. It was known from published and unpublished investigations that KC has significant populations of microbes (1,000-3,000 taxa) including *Actinobacteria*, and may have a resident "reservoir" of bioactive compounds. However, investigation of the properties of 1% aqueous extracts of KC demonstrated very significant activities against a wide variety of resistant ESKAPE microbes with no resistance shown as yet. In vivo studies have not yet been performed or reported, but there are anecdotal data of the Heiltsuk using such extracts

*continued on page 10*

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*continued from page 9*

for treatment without reports of toxicity. The two recent papers covering these responses are available from mBio and should be read by people interested in this topic.[7,8]

Thus, pharmacognosy is not just the study of plants and their associated "organisms," nor the study of marine invertebrates and others, but also may have significant inorganic or bio-inorganic chemistry involved. ■

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