

within the scope of the present invention. Moreover, one having ordinary skill in the art would recognize that natural clays may require processing so as to render them suitable for use in topical pharmaceutical compositions. These treatments are well within the skill of the art, and include removal of environmental or air-borne bacteria by sterilization. Also, it may be necessary to remove accessory minerals, such as quartz, by particle size separation techniques (e.g., separation of quartz and feldspar from the clay minerals by settling in water or by centrifugation according to Stokes Law), and cation exchange to change the chemical, sorptive and swelling properties of the clay. Well known sterilization treatment may include, for example, ultraviolet (uV) or heat sterilization. These would remove, render nonlethal, or inactivate potentially pathogenic organisms such as virus, bacterial spores or protozoan cysts.

[0017] Applicants anticipate that one skilled in the art will also recognize that an antibacterial effective amount of a reducing agent may be added to any natural clay or clay mineral, regardless as to whether or not that natural clay or clay mineral has natural bactericidal properties, so as to be certain that a composition containing that natural clay is suitable for the purpose intended herein. Prior to the present invention, applicants contend that there was no motivation to add a reducing agent to a clay or clay mineral (natural or synthetic) for the use described herein.

[0018] In addition, since Applicants' research has lead them to identify that it is the presence of a reducing agent in a natural clay that is responsible for its bactericidal activity, the present invention, therefore, also relates to a method of identifying a natural clay having bactericidal activity in its natural form. This method involves chemical and mineralogical analyses of clay in determining the presence of a reducing agent therein, or measurement of the oxidation-reduction potential of a clay slurry. Once identified, these naturally-bactericidal clays can be appropriately processed to render them suitable for topical pharmaceutical use. In the past, random clays would be evaluated for their "healing" (herein, antibacterial) properties; this method of evaluation was "hit-or-miss." With applicants' discovery as to what renders natural clays antibacterial, identifying clays having these properties has been rendered predictable. Specific motivation exists for further processing or modifying these clays to render them suitable for topical bactericidal pharmaceutical use. Modification of clays could occur, for instance, by adding a pH buffering agent such as CaCO_3 or NaHCO_3 to maintain a slightly acidic (pH 4.5-5) rather than strongly acidic (pH 2-3) environment.

[0019] Compositions within the scope of the present invention may be used to topically treat bacterial skin infections and diseases—including those caused by antibiotic-resistant bacteria, such as methicillin resistant *Staph. Aureus* (MRSA). Water, or other suitable pharmaceutically acceptable aqueous liquids (e.g., inert solution), are added to a composition in sufficient amounts to create a paste. It is the composition in this paste form that is topically applied to an infected area, for example, of the skin. The mechanism in which these bactericidal compositions operate is different from the mechanism of commonly used or commercially available antibiotics.

[0020] Data from Williams et al. 2008 included results for two types of French clays; they indicated that the Argiletz French green clay was not bactericidal against *E. coli*. By contrast, Argicur supplied green clay displayed antimicrobial properties and was found to be bactericidal against several

species of bacteria, including *E. coli* and *S. aureus*. One question was whether or not changing chemical conditions mediated by clays might be important in clay bacterial activity.

[0021] Our experimentation with these clay types upon several bacterial types such as *Salmonella*, *E. coli*, *Pseudomonas*, *Staphylococcus* and *Streptococcus*, suggested that clay type and degree of bactericidal activity depended upon reducing conditions, possibly mediated by FeS_2 (pyrite) or by other minerals with available reduced metals. Pyrite has been implicated in spontaneous production of chemical radicals; chemical radicals such as OH. and O_2^- , would be highly damaging to biomolecules such as sugars, fatty acids or proteins located on bacterial cell surfaces and within cells. Additionally, the Fe^{2+} from pyrite might produce intracellular Fenton-type reactions (described later herein). The reaction products could damage nucleic acids such as DNA or RNA or hamper cellular metabolic functions. Blue clay (a clay from Oregon that naturally contains about 10% pyrite) was determined to be bactericidal, but neither weathered Blue clay (Blue clay that had been oxidized naturally by weathering) nor Ormalite (a commercial name for a clay from a nearby deposit) were particularly bactericidal. Of note is that neither weathered Blue clay nor Ormalite were found to contain pyrite or other reducing agents.

[0022] Data from dialysis tube experiments (described later herein) indicated a clear dose-response among pyrite content, redox state and bactericidal activity. Wyoming smectite was chosen initially as an end member for montmorillonite clays since it is similar in composition to the smectite-rich Argicur clay. Whereas the Wyoming montmorillonite was only mildly bactericidal initially, the addition of pyrite (and finer grained pyrite created by grinding) increased bactericidal activity by 7- to 28-fold (against *E. coli* and *Staphylococcus*, respectively).

[0023] Two domestic clays, Pyroclay and Blue clay, were found to be bactericidal, and each contained 3 to 10% by weight pyrite. These were both somewhat reducing when mixed with water. By contrast, Blue clay in which all of the pyrite had been removed by oxidation (weathered Blue), which was mineralogically similar to antibacterial Blue clay with respect to mineral content other than the presence of pyrite (Table 1) displayed nearly 10-fold greater viable cells. This suggests that bactericidal components contained within the clay could be diminished by chemical oxidation. A clay collected from nearby the Blue Clay formation (designated with the commercial name "Ormalite") did not contain pyrite and was not bactericidal.

[0024] It is recognized that the composition of these varied clays differ in more than pyrite content. For example, in an initial study by Williams et al, 2004 (GSA poster), studies of Pyroclay, Wyoming montmorillonite (Swy-1 from The Clay Mineral Society repository) and Argicur showed that only Argicur was antibacterial (i.e., little or no bacterial growth when the clay suspension was incubated with log-phase *E. coli*). By contrast, clays later confirmed as non-bactericidal (Wyoming montmorillonite and Argiletz) produced little effect upon bacterial growth when bacteria were incubated with clay suspension.

[0025] Applicants conducted experiments using Wyoming montmorillonite. These are set forth as Example 1, under Experimental Procedures and Data herein. The results are set forth in Table 4 and in FIGS. 2A, 5A and 5B.