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(54) Title: ANTIMICROBIAL CHEMICAL COMPOSITIONS

(57) Abstract: Antimicrobial chemical compositions comprise an aluminum phosphate (AlP) solid dispersed within a binding polymer, wherein one or more bioactive materials are disposed within AlP forming a bioactive-AlP complex. The complex may comprise the bioactive material chemically bonded with the AlP, physically combined with the AlP, or a combination of both. The complex may be formed according to precipitation, condensation and sol-gel methods of forming. The complex is engineered to provide a controlled delivery of the bioactive material or a constituent thereof upon exposure to moisture to give a desired level of antimicrobial resistance to a film or composite formed from the composition of at least about 30 μg/m2, and may also provide a desired degree of corrosion resistance through the release of passivating phosphate anion. Such antimicrobial chemical compositions provide an improved degree of active, long-term resistance to a broad range of micro-organisms when compared to known antimicrobial chemical compositions.

ANTIMICROBIAL CHEMICAL COMPOSITIONS

FIELD OF THE INVENTION

This invention relates to chemical compositions having antimicrobial properties and, more specifically, to chemical compositions that are specially formulated to include an aluminum phosphate complex comprising one or more antimicrobial agents, and methods for making the same.

BACKGROUND OF THE INVENTION

Chemical compositions formulated to include one or more antimicrobial agents to provide antimicrobial properties, e.g., provided in the form of a coating composition or the like for forming a film layer on an underlying substrate surface, are known in the art. Such antimicrobial chemical compositions make use of antimicrobial agents known to provide some degree of protection against unwanted micro-organisms.

Conventional antimicrobial chemical compositions known in the art, e.g., formulated products such as water-based paints and coatings, include biocides incorporated therein to preserve the liquid composition during storage from spoilage by micro-organisms. Antimicrobial protection is afforded from such conventional paints and coatings by the incorporation of agents that prevent defacement of the applied, dry film in service by mold and/or mildew growth.

While conventional antimicrobial chemical compositions are known to provide some protection against unwanted microorganisms, the protection afforded is somewhat limited in both the degree of its activity, and the length in time of its being able to offer a desired level of resistance to unwanted microorganisms. This is largely due to the nature of the formulation and the limited activity of the antimicrobial agent disposed therein, and the resulting inability to provide a highly-active and long-lasting resistance to unwanted microorganisms. Thus, while such conventional antimicrobial chemical compositions are capable of providing some degree of resistance to microorganisms, they are unable to provide a desired or needed level of microorganisms control sufficient to meet the demands of certain end-use applications.

There is an unmet need to provide active, long-term resistance to a broad range of bacteria, mold, mildew, and other harmful micro-organisms to prevent collateral effects of illness and/or product spoilage due to infection. Examples of target end-use applications where it is critical to prevent infection and product spoilage from surface contact in sensitive environments includes: hospitals and health care facilities; kitchens and food processing and storage areas; dairies; breweries; bathroom and rest room facilities; hotels; school, recreation, amusement, and sports facilities. While existing anti-microbial additives may provide some degree of anti-microbial action, their effectiveness in such formulated products as paints and coatings is limited by the amounts of material required to achieve anti-microbial action, which exceeds: (1) cost constraints for the formulated product; (2) usage limitations relative to non-target toxicity; (3) the practical limits for incorporation in the formulated product; and (4) which may be limited by the mechanism for delivery to the surface of the article to be protected.

It is, therefore, desired that antimicrobial chemical compositions be formulated in a manner that provide a desired active, long-term resistance to a broad range of micro-organisms, including bacteria, mold, mildew, and other micro-biological species to prevent collateral effects of illness and product spoilage, when compared to known antimicrobial chemical compositions, thereby meeting the needs of certain end-use applications. It is desired that such antimicrobial chemical compositions be engineered in a manner facilitating the ability to effectively customize, adjust and/or tailor changes in the performance characteristics of the formulations for the purpose of effectively addressing the specific antimicrobial needs associated with different end-use applications. It is further desired that such antimicrobial chemical compositions be formulated from readily available materials, and/or be made by methods, that facilitate manufacturing the chemical compositions in a manner that does not require the use of exotic equipment, that is not unduly labor intensive, and that is economically feasible.

SUMMARY OF THE INVENTION

Antimicrobial chemical compositions as described herein generally comprise an aluminum phosphate (AlP) solid that is dispersed within a binding polymer. One or more bioactive materials are disposed within or combined with the AlP to form a bioactive-AlP complex. A feature of the complex is that it is specifically engineered such that, when the composition is provided in the form of a dried film or composite, it

provides a controlled delivery of a bioactive constituent (derived from the bioactive material upon exposure to moisture) to the film or composite surface to provide a desired level of antimicrobial resistance. The AlP used to form the complex may be in amorphous form, in crystalline form, or in a combination thereof. In an example embodiment, the AlP comprises amorphous AlP.

The bioactive material or a bioactive constituent derived therefrom, used to form the complex may either be chemically bonded with, e.g., provided in the backbone of, the AlP polymer, or may be physically incorporated, enmeshed, encapsulated, or intertwined with the AlP polymer, depending on the particular method used to make the complex. The bioactive material can be organic and/or can be a metal salt or oxide such as those including silver salts, copper salts, zinc salts, calcium salts, and combinations thereof, and/or can be a metal ion such as those including silver, copper, zinc, calcium, and combinations thereof. Additionally, the bioactive material may comprise one or more metal oxides, which may include and are not limited to oxides of zinc, copper, magnesium, barium, calcium and combinations thereof, and which may add to the antimicrobial effectiveness and/or light stability of the bioactive material. Further, the bioactive material may be complexed before being combined to form the bioactive-AlP complex, which may add to the color or light stability of the bioactive material. In an example, where the bioactive material comprises a metal salt such as silver nitrate, the metal salt can be complexed with a ligand such as ammonia, imidazole, substituted imidazole, and combinations thereof before the complexed metal salt is combined with other ingredients used to form the bioactive-AlP complex. Binding polymers used to form the composition can include polyurethanes, polyesters, solvent-based epoxies, solventless epoxies, water-borne epoxies, epoxy copolymers, acrylics, acrylic copolymers, silicones, silicone copolymers, polysiloxanes, polysiloxane copolymers, alkyds and combinations thereof.

In an example embodiment, the AlP is engineered to provide a controlled delivery of the bioactive constituent when the chemical composition is in a cured form, e.g., in the form of a coating film or a composite structure, of from about 5 to 1,000 ppm, preferably about 10 to 900 ppm, and most preferably from about 15 to 800 ppm. In an example embodiment, it is desired to provide at controlled delivery of at least 100 ppm or greater of the bioactive constituent. The amount of the bioactive material, e.g., Ag, in

the complex may be in the range of from about 1 to 10 percent by weight, preferably from about 2 to 8 percent by weight, and more preferably from about 3 to 6 percent by weight based on the total weight of the complex. The ratio of phosphate to aluminum in the complex is in the range of from about 0.5:1 to 1.5:1. The bioactive-AlP complex in the chemical composition comprises from about 0.1 to 2 percent of the dry film weight, or 20 to 1,000 ppmw of bioactive constituent, e.g., Ag in the paint. In a preferred embodiment, an effective leaching rate, that is, amount of bioactive constituent, e.g., Ag, released on the surface of a cured coating or cured composite comprising the bioactive-AlP complex is at least about 30 $\mu g/m^2$, and is preferably about 36.9$\mu g/m^2$ or >2$\mu g/L$ in a rinse for bioactivity.

In an example embodiment, the antimicrobial chemical composition may also provide a desired degree of corrosion resistance, e.g., when formulated as a coating for use with metallic substrates. In such embodiment, the AlP is formulated to provide, in addition to the controlled release/delivery of bioactive constituent, a controlled delivery of passivating anion such as phosphate anion upon exposure to moisture. In an example embodiment, such antimicrobial chemical composition may provide a controlled delivery of phosphate anion of greater than about 100 ppm.

Antimicrobial chemical compositions as described herein are made by first forming the bioactive-AlP complex, which comprises forming an AlP by combining a desired aluminum source, with a desired phosphate source under suitable reaction conditions, e.g., in an aqueous solution at suitable pH and suitable temperature, to form the AlP. The bioactive material is added to the AlP during and/or after the step of forming the AlP so that the bioactive material is dispersed or combined with the AlP, thereby forming the bioactive-AlP complex. If desired, further AlP can be added to the bioactive-AlP complex before combining the complex with the binding polymer.

According to one example method of making, the bioactive material is added to the AlP after it has been formed, in which case the resulting bioactive-AlP complex comprises the bioactive material physically incorporated, enmeshed, encapsulated, or intertwined with the AlP polymer. According to another example method of making, the bioactive material is added to the AlP during formation of the AlP, in which case the resulting bioactive-AlP complex is formed in-situ with the ALP and comprises a

bioactive constituent of the bioactive material chemically bonded to the AlP polymer, e.g., as part of the ALP polymer backbone.

In an example, a bioactive-aluminum phosphate complex is made by combining an aluminum source (such as aluminum hydroxide in amorphous and/or in crystalline form) with a phosphate source (such as phosphoric acid) in the presence of a bioactive material to form a reaction mixture. The bioactive material can be provided as a separate ingredient or in a premixed form in combination with one or both of the aluminum source and the phosphate source. One or both of the aluminum source and phosphate source can be provided in the form of an aqueous solution. The reaction mixture is allowed to undergo reaction (e.g., at room temperature) to form a bioactive-aluminum phosphate complex, wherein the bioactive material is bonded with the aluminum phosphate. In an example, the bioactive material can be silver nitrate that may be complexed with imidazole or ammonia, and/or that may be combined with an oxide of zinc and/or copper. The so-formed bioactive-aluminum phosphate complex is combined with a desired polymer binder to form the antimicrobial chemical composition as disclosed herein.

Antimicrobial chemical compositions as described herein are specifically engineered to provide active, long-term resistance to a broad range of micro-organisms, including bacteria, mold, mildew, and other micro-biological species to prevent collateral effects of illness and product spoilage, when compared to known antimicrobial chemical compositions, thereby meeting the needs of certain formulated end-use applications, wherein such applications include paints, coatings, adhesives, composites, cements, plastics and the like. These antimicrobial chemical compositions are made from readily available materials and/or by methods that facilitate manufacturing in a manner avoiding exotic equipment, which is not unduly labor intensive, and that is economically feasible.

DETAILED DESCRIPTION

Antimicrobial chemical compositions as described herein generally comprise an aluminum phosphate (AlP) that is dispersed within a binding polymer that forms the bulk matrix of the composition. One or more bioactive materials are disposed within the aluminum phosphate, thereby forming a bioactive-AlP complex, and the aluminum phosphate is specifically engineered to provide controlled delivery or release of a bioactive constituent derived from the bioactive material upon exposure to moisture. Such antimicrobial chemical compositions are made by a number of methods described herein, and can be formulated for use as paints, coatings, adhesives, composites, cements, plastics, and the like.

Aluminum phosphates useful in this regard include amorphous aluminum phosphates, crystalline aluminum phosphate, and combinations thereof. Example aluminum phosphates useful in this regard are amorphous aluminum phosphates (AAlPs), and preferred AAlPs are amorphous aluminum orthophosphates. While the use of AAlPs is desired because AAlPs have been shown to have certain characteristic properties, making them well suited for use as a carrier to the bioactive material, crystalline AlPs and combinations of amorphous and crystalline AlPs are also understood to be useful in this regard and within the scope of the antimicrobial chemical compositions as disclosed herein.

In an example embodiment, the amorphous aluminum orthophosphates are amorphous aluminum hydroxy phosphates. Amorphous aluminum hydroxy phosphates provide uniform dispersion properties within the composition and the dispersion remains stable throughout the shelf-life of the formulation. The hydroxyl content of the amorphous aluminum hydroxy phosphate provides matrix stability by providing hydrogen bonds with suitable groups of the binding polymer of the formulation, e.g., such as carboxyl groups, amino groups, hydroxyl groups, acid groups and the like. This feature is unique to the amorphous aluminum hydroxy phosphate, and is not present in crystalline or other types of amorphous phosphates, and for this reason help to provide uniform dispersion properties

AlPs used to form antimicrobial chemical compositions disclosed herein are specially designed to have a high level of compatibility with a variety of different binding polymers or binding polymer systems useful for formulating such end-use applications, thereby providing a high degree of flexibility and choice in formulating such compositions to meet the needs and conditions of a variety of end-use applications in a number of different end-use industries.

Controlled delivery and/or release of the bioactive constituent within the chemical composition is largely dependent on the diffusion rate of the bioactive constituent through the bulk matrix of the composition, whether in the form of a coating or a composite. The diffusion rate of the bioactive constituent is dependent on the structural features of the bulk matrix that control bioactive constituent and water transport. These features include, but are not limited to, cross-link density, pigment to volume ratio (PVC), nature of the bioactive material carrier, hydrophilicity of components, and the polarity of the components.

Antimicrobial chemical compositions as disclosed herein use AlP as the bioactive carrier material, which AlP is engineered to provide a controlled diffusion of both moisture to the bioactive material contained therein, and a diffusion or delivery or release of the bioactive constituent to the surface of a coating or composite comprising such AlP, for purposes of providing a desired degree of antimicrobial resistance. Accordingly, the bioactive material is incorporated into the AlP, which has been specifically made to moderate and control the solubility of the bioactive constituent, and to control the diffusion of the dissolved bioactive constituent through the composition film or composite bulk matrix.

A characteristic/parameter of the AlP discovered to have an influence over the diffusion of moisture and delivery of the bioactive constituent is the porosity of the AlP molecule. A feature of AlP complexes as disclosed herein is the ability to engineer the morphology and the porosity of such complexes by choice of synthesis method. As used herein, the term "engineered porosity" is defined as the volume of space existing within a solid material consisting of particle voids, interstitial space between particles in particle aggregates, and interstitial space between aggregates in agglomerates. Mercury

porosimetry is used to characterize the porosity properties of solids and pigments. Key measurements include:

1. Total intrusion volume (ml/g) - measures the overall space in the sample into which mercury can be absorbed as a function of pressure.
2. Total pore area (m^2/g) - converts volume to area and defines how much area is occupied by the total intrusion volume.
3. Average pore volume ($4V/A=\mu$) - shows the distribution of volume by area, i.e., how much volume on the average goes into different pore sizes.
4. BET (m^2/g) - is the measure of total surface area accessible to nitrogen gas under test conditions. BET and porosity correlate.

AlP complexes comprising a metal salt or metal ion, e.g., such as silver, as the bioactive material and formed by sol-gel method (as described in better detail below) result in the formation of nano-sized primary particles incorporated into aggregates of very-high surface area and porosity. An advantage of having such high surface area and porosity is that it ensures optimum diffusion contact with water and subsequent release of the silver ion in the film formed by the binding polymer bulk matrix, thereby promoting uniform distribution of the complex throughout the film or composite, and promoting a relatively rapid release of the bioactive material from the complex upon contact with water.

AlP complexes comprising a metal salt or metal ion, e.g., such as silver, as the bioactive material and prepared by the sol-gel method have BET surface areas ranging from about 100 and 250 m^2/g, and preferably between about 125 and 200 m^2/g, and most preferably between about 140 and 160 m^2/g. Such AlP complexes have a total intrusion volume of between about 1 and 2 mL/g, and preferably between about 1.3 and 1.8 mL/g. Such AlP complexes have an average pore volume of from about 0.02 to 0.06 μm, and preferably between about 0.04 and 0.05 μm.

In contrast, AlP complexes comprising a metal salt or metal ion, e.g., such as silver, as the bioactive material and formed by precipitation or condensation method (as described in better detail below) result in the formation of nano-sized primary particles incorporated into aggregates of relatively low surface area and low porosity. An

advantage of having low surface area and porosity is that it ensures reduced degree of diffusion contact with water and subsequent release of the silver ion in the film or composite formed by the binding polymer bulk matrix, thereby promoting uniform distribution of the complex throughout the film or composite, and promoting a relatively slow release of the bioactive material from the AlP complex upon contact with water.

AlP complexes comprising a metal salt or metal ion, e.g., such as silver, as the bioactive material and prepared by precipitation or condensation method have BET surface areas ranging from about 2 to 10 m^2/g, total intrusion volumes ranging from about 0.5 to 0.9 mL/g, and have average pore volumes ranging from about 0.4 to 0.6 μm.

Thus, a feature of AlPs useful for making antimicrobial chemical compositions is that they have an engineered porosity calculated to provide the desired rates of moisture diffusion and delivery of bioactive constituent that promotes a desired degree of activity and antimicrobial resistance when placed in an end-use application.

Thus, the desired porosity of the AlP is understood to vary depending on the certain requirements called for by each different end-use application. However, it is generally desired that the porosity of the AlP be not so great so as to rapidly extinguish the bioactive constituent upon exposure to moisture, e.g., be highly active but provide a greatly reduced effective service life. The loading of the bioactive material and/or the type of bioactive material that is used will also influence the activity and effective service life. Accordingly, the porosity of the AlP reflects a balance or compromise between a desired degree of antimicrobial activity and a desired effective service life for a given amount or general loading range of a given bioactive material.

The porosity of the AlP is engineered during the process of making the AlP and/or during post formation processing, e.g., drying and/or other heat treatment, as described in greater detail below.

AlPs as disclosed herein, in addition to serving as the bioactive material carrier to provide desired controlled delivery/release of the bioactive constituent, provide anticorrosion protection through the delivery of phosphate anion when exposed to moisture. Accordingly, for those end-use applications calling for both antimicrobial and

anticorrosion properties, e.g., in the case where the composition is formulated for use as a coating on a metal substrate, the AlP can also be engineered to provide a controlled delivery of the phosphate anion to provide a desired degree of corrosion protection through passivation to a metal substrate.

In an example embodiment, wherein such corrosion resistance is also desired, the AlP is engineered to release in the range of from about 50 to 500 ppm, and preferably 100 to 200 ppm of the passivating phosphate anion when present in a cured film or composite placed into an end-use application. The amount of passivating anion to be delivered depends on a number of different factors such as the loading or amount of the AlP used, the type of binding polymer that is used, the type of metallic substrate being protected, and the type of environment present in the end-use application. In a preferred embodiment, where the metallic substrate being protected comprises iron and the corrosion environment comprises water, oxygen, and other corrosive salts, the AlP is engineered to release approximately 160 ppm of the passivating phosphate anion.

Example binding polymers include those currently used for making known antimicrobial chemical compositions, and can be selected from the general group including water-borne polymers, solvent-borne polymers, hybrids and combinations thereof. Example water-borne polymers useful for making anticorrosion coating compositions include acrylic and acrylic copolymers, alkyd, epoxy, polyurethane, and silicone, and polysiloxane polymers. Example solvent-borne and/or non-aqueous polymers useful for making anticorrosion coating compositions include acrylic and acrylic copolymers, epoxy, polyurethane, silicone, polysiloxane, polyester, and alkyd. Preferred binding polymers include acrylic copolymer latex, alkyd, polyurethane and epoxy polymers.

In an example embodiment, antimicrobial chemical compositions comprise in the range of from about 15 to 75 weight percent, preferably in the range of from about 20 to 60 weight percent, and more preferably in the range of from about 20 to 35 weight percent of the binding polymer based on the total weight of the chemical composition when in a pre-cured or wet state. An antimicrobial chemical composition comprising less than about 15 percent by weight of the binding polymer may include a greater amount of the bioactive material (present as the bioactive-AlP complex) than necessary

to provide a desired degree of antimicrobial protection. An antimicrobial chemical composition comprising greater that about 75 percent by weight of the binding polymer may include an amount of the bioactive material (present as the bioactive-AlP complex) that is insufficient to provide a desired degree of antimicrobial resistance. While certain amounts of the binding polymer have been provided, it is to be understood that the exact amount of the binding polymer that is used to formulate antimicrobial chemical compositions will vary depending on such factors as the type of binding polymer used, the types and amounts of other materials used to form the chemical composition, the type and/or quantity of bioactive material that is used, and/or the particular end-use antimicrobial application.

Bioactive materials or agents useful in forming antimicrobial chemical compositions described herein can be selected from a variety of bioactive materials and/or species including, but not limited to: (1) antimicrobial additives comprising organic molecules that are either biocidal (kill microbes) or biostatic (inactivate microbes); (2) bio-pesticides, typically peptides that have biostatic or biocidal effects on microbes; (3) natural products that inhibit or prevent the growth of the target organisms naturally; (4) "friendly" bacteria that interfere with the growth and/or development of target microbes; (5) minerals and metals that release or produce antimicrobial species in response to certain environmental conditions; and (6) combinations thereof. Organic antimicrobial additives and metal-based biocides have most commonly been used to impart antimicrobial properties to formulated products.

Metal-based materials useful as bioactive materials or agents include metal ions and metal salts. Suitable metal ions include those selected from the group consisting of silver, copper, zinc, calcium, and combinations thereof. Suitable metal salts include salts of the above-identified metal ions. In an example embodiment, silver is a desired bioactive material because it has several advantages, provided that it can be made compatible with the formulation of the binding polymer in which is it incorporated, and provided that the silver can be maintained in an active state within the formulation for delivery to the surface upon exposure to moisture in a consistent and cost effective manner. Silver is advantageous over organic materials because it has higher degree of thermal stability, a lower level of toxicity to non-target organisms than typical organic biocides, and has a higher level of UV stability.

Silver ion (Ag^+) is bioactive, and in sufficient concentration kills a variety of microorganisms. Silver has proven anti-microbial activity and is known to be effective against certain antibiotic-resistant bacteria. It has broad spectrum anti-microbial activity and minimal toxicity toward mammalian cells. Silver is typically formulated or incorporated as an active ingredient in a carrier component (at concentration levels typically <5% by weight) such as glass, silica, or zeolite. The mechanism of action by which silver-based materials control micro-organisms involves the release of silver ion in response to ambient moisture. The silver ion is formed by contact with water, and the ion contacts the organism and interacts with multiple binding sites in the organism. As the silver ion is transferred into the cells of the target organism metabolic, the respiratory functions of the cell are altered and eventually cease, causing the cell to die.

Suitable sources of silver for use as the bioactive material include silver salts such a silver nitrate and silver chloride, wherein silver nitrate ($AgNO_3$) is preferred. Silver nitrate is extremely soluble (122 grams per 100 milliliters of water at 0°C) and this solubility presents a special challenge for controlled delivery of the bioactive material from a formulated product, such as an antimicrobial coating or composite. Silver nitrate is useful as a bioactive material as long as the delivery of silver ion from the formulated coating or composite to the surface is controlled at a rate and in a concentration balanced to supply the minimum control level for the target service life. Too rapid of a delivery will result in excessive concentration of silver ion on the surface to be protected, causing a discoloration of the surface and/or a rapid depletion the available reserves of silver nitrate in the bulk matrix, thereby reducing effective service life.

As discussed above, the AlP is made having an engineered porosity to provide a controlled diffusion rate and release/delivery of the bioactive constituent, e.g., silver ion, through the bulk matrix of the coating or composite. The incorporation of silver nitrate directly into a coating as a free component will not allow for controlled release. It is necessary to incorporate the silver nitrate (or silver ion source) in the AlP as engineered to moderate and control the solubility of the silver salt, control the diffusion of the dissolved silver ion through the film or composite matrix, and to control the resulting delivery of the silver ion to the surface.

As noted above, the porosity properties of AlP are engineered to provide a mechanism to control such reactions as hydrolysis and dissolution. Additionally, the AlP can be made hydroscopic so that it attracts water to itself specifically in a bulk matrix, thereby providing a medium for dissolution interactions. The feature of engineered porosity is the basis for controlled dissolution and ion release. In the case of silver ion, the diffusion rate of silver ion is dependent on the surface area and the porosity of the AlP. This also moderates the overall transport rate of the silver ion through the bulk matrix. Specifically, when water contacts the bulk matrix it is absorbed, and when the water in the bulk matrix contacts the highly soluble silver disposed within the bioactive-AlP complex (either as silver nitrate physically encapsulated within the AlP or as a silver ion chemically bonded to the AlP) the silver species is dissolved and the silver ion undergoes diffusion through the bulk matrix to the surface.

A feature of antimicrobial compositions as disclosed herein is that such compositions comprise the use of the AlP complex disposed within the bulk matrix of the binder polymer, wherein the AlP complex has a rate of bioactive constituent delivery that can be the same or different than the rate of bioactive constituent (released from the complex) migration or diffusion through the binder polymer. Thus, a formulator can engineer the porosity of the AlP complex to provide a desired release rate of the bioactive constituent therefrom, and can further engineer the formulation (by use of different binding polymers, fillers and the like) to influence the migration or diffusion rate of the bioactive constituent through the composition to meet certain end-use application demands. The combination of these features, i.e., the release rate of the bioactive constituent from the AlP complex, and the migration or diffusion rate of such released bioactive constituent through the binder polymer bulk matrix, provide for an enhanced level of antimicrobial composition customization not otherwise available. Such customization of release rates and migration/diffusion rates operate to provide a vast range of antimicrobial compositions that can be specifically tailored to address a variety of end-use applications.

The amount or concentration of the bioactive material that is incorporated into the AlP can and will vary depending on such factors as the type of bioactive material used,

the nature of the binding polymer used to form the coating or composite matrix, the type of AlP (amorphous, crystalline, or a combination thereof), and the engineered porosity of the AlP. Thus, the properties of the bioactive-AlP complex, such as the bioactive material concentration and the AlP engineered porosity can be controlled to address various exposure conditions such as temperature, relative humidity, ultra-violet exposure and the like.

In an example embodiment, it is desired that a sufficient amount of the bioactive material be present, and that the AlP have an engineered porosity that will result in the composition, when provided in the form of a dried film or composite, to provide a controlled delivery of the bioactive constituent (derived from contacting the bioactive material with moisture) of from about 5 to 1,000 ppm, preferably of from about 10 to 900 ppm, and more preferably in the range of from about 15 to 800 ppm. In a particular embodiment, where the bioactive constituent is silver ion, a desired optimum controlled delivery of the silver ion is greater than about 100 ppm, and most preferably about 120 ppm. In a preferred embodiment, an effective leaching rate, that is, amount of bioactive constituent, e.g., Ag, released on the surface of a cured coating or cured composite comprising the bioactive-AlP complex is at least about 30 $\mu g/m^2$, and is preferably about 36.9$\mu g/m^2$ or >2$\mu g/L$ in a rinse for bioactivity.

In order to provide the desired controlled delivery of the bioactive constituent, it is desired that certain amount of the bioactive material be used when forming the bioactive-AlP complex. In an example embodiment, the AlP complex comprises from about 1 to 10 percent by weight of the bioactive material, preferably from about 2 to 8 percent by weight of the bioactive material, and more preferably from about 3 to 6 percent by weight of the bioactive material based on the total weight of the bioactive-AlP complex.

Additionally, it has been discovered that mixed anti-microbial complexes based on silver and other bio-active materials can be synthesized which have synergistic effects. For example, in addition to silver-AlP complexes, other bio-active metals as copper and/or zinc can be introduced into the complex by their inclusion in the synthesis process as better described below. Further, certain organic bio-active molecules can be introduced into the complex through physical adsorption/encapsulation or by actual

reaction/condensation with the phosphate group of the complex. This provides a controlled release mechanism through subsequent hydrolysis in the bulk film by the diffusion of water.

AlPs can be made through the selective combination the materials noted above. The following selected methods of preparation are provided below as examples, and it is to be understood that other methods of preparation other than those specifically disclosed may be used. While the methods disclosed herein for making AlPs may reference and disclose the formation of amorphous aluminum phosphate (AAlP), it is to be understood that such methods may also produce or be adapted to produce other forms of AlP, such as the various crystalline aluminum phosphate forms and/or mixtures of amorphous and crystalline aluminum phosphates, depending on the end-use antimicrobial application performance properties. Example crystalline forms of AlPs formed as disclosed herein include and are not limited to orthorhombic and triclinic aluminum orthophosphates. Accordingly, the methods disclosed herein are understood to be useful for making different forms of AP, depending on the particular end-use applications and performance properties.

Binary Condensation Methods of Making

Generally, the AlP is an aluminum phosphate complex that is prepared by combining a suitable aluminum salt, such as aluminum hydroxide, aluminum sulfate and the like with phosphoric acid or other phosphorus-containing compound or material, depending on the particular type of aluminum salt selected for forming the aluminum phosphate. In an example embodiment, a preferred aluminum salt is aluminum hydroxide (ATH or $Al(OH)_3$), and a preferred source of the phosphorus-containing ingredient is phosphoric acid (H_3PO_4). Example methods as disclosed herein comprise forming AlP by a condensation process, wherein the AlP is formed by the condensation reaction of the aluminum salt ingredient with the phosphorous-containing ingredient to produce AlP particles in slurry form. The composition of the condensed solid resulting from such process of making depends on the ratio of the aluminum metal to phosphate anion. The properties of the resulting complex, i.e., the AlP, depends on the processing parameters employed during the condensation reaction, including choice of aluminum salt, temperature, the physical state of the reactants, order of addition of reactants, rate

of addition of reactants, the degree and duration of agitation, pretreatment of one or more of the reactants, and post treatment of the resulting condensation product.

Generally speaking, the condensed solid that results from this method of making, even after milling, has a very low oil absorption property and low surface area (as measured by BET method) when compared to aluminum phosphate prepared by other known methods. Oil absorption is defined as the amount (grams or pounds) of linseed oil required to wet out and fill the voids spaces around a pigment, ASTM – D-281-84, which is a measure of the binder demand or the amount of binder resin that a pigment may absorb in a given formulation. High binder demand adds to formulation cost and can affect certain barrier properties of the dry film. This is further surprising because the aluminum phosphate made by the binary condensation process disclosed herein also displays the controlled release property and water adsorption property usually associated with high surface area particles.

In an example embodiment, the condensed aluminum phosphate prepared herein has an oil absorption of less than about 50, preferably in the range of between about 10 to 40, and more preferably in the range of between about 20 to 30. In contrast, AlP that is made by other methods has an oil absorption of greater than about 50, and typically in the range of about 50 to 110.

In an example embodiment, the AlP prepared herein has a surface area of less than about 20 m^2/g, and preferably less than about 10 m^2/g. In an example embodiment, the surface area is in the range of between about 2 to 8 m^2/g, and more preferably in the range of between about 3 to5 m^2/g. In contrast, AlP made by other methods has a surface area greater than 20 m^2/g, e.g., from about 30 to 135 m^2/g.

AlPs made as a binary condensation product can be produced according to least five different methods, wherein two of which involve adding a base reactant to an acid reactant, one of which involves adding an acid reactant to a base reactant, one of which involves base-to-acid in-situ aggregation, and one of which involves acid-to-base in-situ aggregation. In such methods, selected starting materials including an aluminum source and a phosphorous source are combined under specific conditions of controlled material delivery, temperature, and agitation. The judicious selection of starting materials and

processing conditions produces AlPs having a material content and chemical structure intentionally created with the purpose of producing the above-noted engineered characteristics to provide the desired controlled delivery/release of the bioactive constituent when formulated into a coating composition or composite.

As noted above, aluminum sources useful for forming AlP by binary condensation method include aluminum salts, such as aluminum hydroxide, aluminum chloride, aluminum nitrate, aluminum sulfate, and the like. Preferred aluminum sources include aluminum hydroxide and aluminum sulfate. Phosphorous sources useful for forming AlP by condensation include phosphoric acid, and salts of phosphorus as orthophosphates or as polyphosphates. A suitable source of phosphorus is fertilizer grade phosphoric acid, from any origin, that has been clarified and discolored. For example, a commercial phosphoric acid containing approximately 54% of P_2O_5 may be chemically treated and/or diluted with treated water resulting in a concentration of approximately 20% of P_2.

AlPs useful for forming antimicrobial chemical compositions described herein can be made according to a number of different methods, which includes at least five variations of the binary condensation process. The following selected methods of preparation are provided below as examples, and it is to be understood that other methods of preparation other than those specifically disclosed may be used.

Example No. 1 – Binary Condensation Formation of the AlP (base-to-acid route)

In an example embodiment, AlP is prepared by adding aluminum hydroxide ($Al(OH)_3$) to phosphoric acid (H_3PO_4). The H_3PO_4 was diluted with water before being combined with the $Al(OH)_3$ and, prior to addition, the $Al(OH)_3$ was not wetted with water, although wetted $Al(OH)_3$ can be used. The reactants were quickly combined at room temperature without heating to produce a white slurry. However, if desired, the reaction can be heated. The H_3PO_4 was 85wt% in water provided by Sigma-Aldrich, and the $Al(OH)_3$ was reagent grade provided by Sigma-Aldrich. Specifically, approximately 57.3 g (0.5 mole) H_3PO_4 was diluted with 50 g of water before being combined with $Al(OH)_3$. Approximately 39 g (0.5 mole) of $Al(OH)_3$ was added to the solution quickly and the mixture was stirred slowly at room temperature to wet the powder. An AlP condensed solid was formed and existed as a dispersion of solid AlP

particles in water. In this particular embodiment, the AlP particles existed primarily in the form of amorphous aluminum phosphate (AAlP). Diluting the H_3PO_4 prior to addition of the $Al(OH)_3$ thereto is believed to contribute to forming exclusively AAlP, e.g., wherein there is little to no crystalline form produced. The suspension was filtered to isolate the AlP particles. The particles were washed and dried to an appropriate temperature, which may be less than about 300°C, and preferably from about 100°C to 200°C. A feature of the AlP so formed is that it may be combined with a binding polymer, e.g., used for formulating an antimicrobial coating composition, without the need for further heat treatment, tempering, or calcining. While heating the AlP at the extreme temperatures noted above may be useful for driving off water, such may also initiate conversion of the AlP from an amorphous form to a crystalline form. It may be desired to subject the AlP to elevated temperatures above 200°C, e.g., of between 300°C to 800°C, to either remove unwanted constituents therefrom and/or to influence physical characteristics of the AlP that may influence its end-use performance properties or characteristics in the antimicrobial composition. If a crystalline form of AlP is desired, the AlP so formed can be further heat treated or calcined to produce the desired crystalline AlP.

Alternatively, the AlP was prepared by adding the $Al(OH)_3$ to the H_3PO_4. However, unlike the example embodiment disclosed above, the H_3PO_4 was not diluted before combining with the $Al(OH)_3$. However, before combining, the H_3PO_4 was heated. Additionally, prior to combining with the H_3PO_4, the $Al(OH)_3$ was wetted with water. A feature of this method of preparing is that it does not include the addition of free water after combination of the reactants, although it is to be understood that the AlP can be made according to this method by including the addition of free water. In an example embodiment, the H_3PO_4 was 85wt% in water provided by Sigma-Aldrich, and the $Al(OH)_3$ was reagent grade provided by Sigma-Aldrich. Specifically, approximately 57.6 g H_3PO_4 was heated to a temperature of about 80°C. Approximately 39 g of $Al(OH)_3$ was wetted with about 2 g water and the wetted $Al(OH)_3$ was quickly added to the H_3PO_4 under fast mechanical stirring. An AALP solid was formed and existed as a dough-like ball that was removed and stored at room temperature. A feature of the AlP so formed is that further treatment in the form of filtering and washing was not necessary to isolate and obtain the desired AlP. Like the example embodiment

disclosed above, such AlP was dried and formed into the desired particle size useful for forming the antimicrobial chemical composition.

Example No. 2 – Binary Condensation Formation of the AlP (base-to-acid route)

In an example embodiment, AlP having the above-noted engineered physical properties or characteristics, e.g., porosity, is prepared by adding aluminum hydroxide ($Al(OH)_3$) to phosphoric acid (H_3PO_4) at an elevated temperature, e.g., at about 60°C, to form the desired AlP. The H_3PO_4 was diluted with water before being combined with the $Al(OH)_3$ and, prior to addition, the $Al(OH)_3$ was combined with water to form a slurry comprising between about 10 to 25 percent by weight, and in some cases up to about 40 percent by weight $Al(OH)_3$, depending on the grade of the $Al(OH)_3$. In preparing the $Al(OH)_3$ slurry, the water may be heated to facilitate dispersion of the aluminum hydroxide powder, e.g., to overcome certain properties of a specific grade of aluminum hydroxide. The heated slurry may be maintained at an elevated temperature and added to the acid. With very high-grade aluminum hydroxide, having a high degree of purity and small particle size and distribution, the $Al(OH)_3$ slurry can be made by adding to room temperature water.

The $Al(OH)_3$ slurry was added slowly to the diluted H_3PO_4 for the purpose of controlling the kinetics of the condensation reaction. In an example embodiment, the $Al(OH)_3$ slurry was added in a controlled manner, e.g., in a drop-wise fashion or the like, to the H_3PO_4 over a period of approximately 10 minutes to about one hour. The combined reactants were heated to a temperature of approximately 95°C, and the reactants were mixed together for a sufficient period of time, typically about 3 hours. In an example embodiment, the reaction takes place in a constant volume system that is essentially closed, e.g., a reflux condenser may be attached to maintain constant solvent volume (water) in the reaction system. In an example embodiment, the H_3PO_4 was 85wt% in water provided by Sigma-Aldrich, and the $Al(OH)_3$ was reagent grade, provided by Sigma-Aldrich. Specifically, approximately 864 g of 85% dilute H_3PO_4 was used, and the slurry was formed by combining 585 g of $Al(OH)_3$ with 1,650 g of deionized water. The combined reactants were contained in a mixing vessel and mixed at 1,300 to 1,500 rpms. Further water was added to the reactants and the combination was mixed for approximately 30 minutes to about 3 hours, e.g., more typically the latter.

If desired, a suitable chemical agent can be added to the reactants for the purpose of reducing the solubility of the components of the mother liquor, thereby providing still further increased control over the outcome of the reaction. In an example embodiment, such chemical agent can be calcium hydroxide ($Ca(OH)_2$), soluble amines such as diethylenetriamine (DETA), or the like.

An AlP condensed solid was formed and existed as a dispersion of solid acidic AlP particles in water. The suspension was filtered to isolate the acidic AlP particles. The particles were washed with water one or more times, and then filtered again. In an example embodiment, after the initial filtering, the particles were washed with a volume of water approximately six times the volume of the precipitate before being refiltered. Successive washings operate to remove unreacted starting material and any soluble byproducts from production. After being refiltered, the acidic AlP particles were reslurried by the addition of water, and were further treated in accordance with one of the following three different techniques.

In a first technique, the slurry is filtered to isolate the acidic AlP particles and the particles are heated. In an example embodiment, the AlP particles are heated to a temperature of about 110°C for about 24 hours to drive off the water, and produce acidic AlP particles. Alternatively, the AlP particles are heated to a temperature of about 250°C for about 12 to 48 hours, and produce acidic AlP particles that are both free of water and any by-products that decompose below 250°C. In addition, heat treatment at either temperature, but especially at the elevated temperature, provides the driving force to complete the conversion of any intermediates that may remain in the complex.

In a second technique, the slurry containing the acidic AlP is neutralized by adding a suitable neutralizing agent thereto. In an example embodiment, the neutralizing agent is ammonium hydroxide (NH_4OH) that is added to the slurry in a sufficient amount to increase the pH and to neutralize the AP to a desired pH, typically 5.5 to 7.0. The resulting slurry is filtered and the isolated AP particles are heated. In one example embodiment, the AlP particles are heated to a temperature of about 110°C for about 24 hours to drive off the water, and produce AlP particles. Alternatively, the AlP particles are heated to a temperature of about 250°C for about 24 hours to both drive off water

and other unwanted chemical constituents, to produce AlP particles and to effect any final conversion or neutralization of surface adsorbed or bulk absorbed reactive species such as phosphate anion or hydrogen phosphate anion. Any reactive amine may be used for this conversion or neutralization step, including but not limited to diethylenetriamine, triethylenetetramine, 2-amino-2-methyl-1-propanol.

In a third technique, the slurry containing the acidic AlP is neutralized by adding a suitable neutralizing agent thereto. In an example embodiment, the neutralizing agent is calcium hydroxide ($Ca(OH)_2$) that is added to the slurry in a sufficient amount to increase the pH and neutralize the acidic AlP. The resulting slurry is filtered and the isolated AlP particles are heated. In one example embodiment, the AlP particles are heated to a temperature of about 110°C for about 24 hours to drive off the water, and produce AlP particles. Alternatively, the AlP particles are heated to a temperature of about 250°C for about 24 hours to both drive off water and other unwanted chemical constituents, and produce AlP particles. Other hydroxide compounds of such divalent cations as barium, and magnesium may be used in place of calcium to effect the neutralization or pH adjustment.

As described above in Example 1, the AlP produced according to the methods disclosed in Example 2 comprised AAlP. However, it is to be understood that crystalline AlP and/or combinations of AAlP and crystalline AlP can be produced according to the methods disclosed, e.g., by running the condensation reaction at temperatures for periods of time of less than 3 hours above 90°C. Maintaining the reaction temperature between about 45 and 90°C, and preferably between about 60 and 70°C will produce AlP that is a combination of crystalline and amorphous forms. Running the reaction at a temperature below about 45°C will produce primarily AlP in the amorphous form.

Example No. 3 – Binary Condensation Formation of the AlP (acid-to-base route)

It has been discovered that changing the order of addition changes the nature of the catalysis of the condensation reaction, i.e., adding the acid to the basic slurry results in slower localized pH change and the reaction is primarily base catalyzed. The AlP particles form slower and are smaller in localized areas in solution. The particles that

form tend to have higher surface areas than particles formed by acid catalysis, and are less aggregated and agglomerated. In an example embodiment, the order of addition in Example 2 is reversed, that is, the required amount of phosphoric acid is added slowly to the aluminum hydroxide slurry. The slurry is prepared as described in Example 2. Phosphoric acid is added slowly to the slurry over a period of approximately 30 minutes to one hour, and the resulting mixture is mechanically stirred and heated to about 95°C for at least 3 hours. The AlP particles are isolated and purified, and dried as described in Example 2.

In addition to the acid-to-base route disclosed immediately above, it has been discovered that such acid-to-base route can be further enhanced by first dissolving a certain amount of the aluminum hydroxide in the phosphoric acid before adding the acid solution to the slurry. In an example embodiment, an amount of aluminum hydroxide, e.g., up to the solubility limit of aluminum hydroxide, is dissolved separately in the phosphoric acid. In an example embodiment, AlP is prepared according to a two-step process. In a first step, a portion of the aluminum hydroxide, typically one third of the stoichiometric amount, is first dissolved in phosphoric acid to form an acidic AlP solution. This acidic AlP solution contains all the phosphoric acid and phosphate needed to satisfy the stoichiometry of the reaction for a product having the desired 1:1 P to Al ratio. In a second step, the acidic AlP solution is then added to a slurry containing the remaining amount of aluminum hydroxide required for stoichiometry. The combination undergoes reaction at ambient temperature to form an AlP condensed solid comprising a dispersion of solid acidic AlP particles in water. Alternatively, the reaction can occur at elevated temperature conditions, e.g., of about 95°C, which is preferred for reaction efficiency and kinetic control of product forms. An advantage of this two-step approach is that part of the aluminum hydroxide required for the reaction is dissolved and pre-reacted before the acid solution is added to the slurry, thereby providing a subsequent heterogeneous reaction that is less viscous and requires less agitation, to thereby ensure more complete condensation.

Like the method disclosed in Example 2 above, such acid-to-base reaction routes are ones that are preferably conducted under constant volume conditions. The suspension was filtered to isolate the acidic AlP particles. The particles were washed with water one or more times, and then filtered again. In an example embodiment, after the initial

filtering, the particles were washed with a volume of water approximately six times the volume of the precipitate before being refiltered. In a preferred embodiment, the sequence is to filter and wash, which can be repeated any number of times to achieve the desired degree of purity. The resulting rewashed AlP particles can then be filtered and dried at a temperature of approximately 110ºC for about 24 hours to provide acidic AlP particles.

Alternatively, after rewashing, the AlP particles can be reslurried and then neutralized by adding a suitable neutralizing agent, e.g., such as those described above, thereto. In an example embodiment, a sufficient quantity of ammonium hydroxide (NH_4OH) was added to the reslurried AP, and the resulting mixture was filtered to isolate the AlP particles, and the particles are heated. In an example embodiment, the AlP particles are heated to a temperature of about 110°C for about 24 hours to drive off the water, and produce solid AAlP particles. Additionally, as described above, it is to be understood that the method disclosed herein can also be used to produce crystalline AlP or combinations of AAlP and crystalline AlP, e.g., by running the reaction at temperatures in excess of about 90°C.

Example 4 – Binary Condensation Formation of the AlP (base-to-acid in-situ aggregation)

In an example embodiment, AlP is prepared by adding aluminum hydroxide ($Al(OH)_3$) to phosphoric acid (H_3PO_4) to form the desired AlP, e.g., in the manner disclosed above in Examples 1 and 2. However, unlike Examples 1 and 2, the reaction is allowed to occur in an open system, wherein the reaction system is left open so as to allow solvent water to continuously evaporate, thereby causing the concentration of the reaction system to increase and its pH to decrease over time. At periodic intervals during the condensation reaction process, the water level is replenished to the initial volume. The reaction slurry is then diluted with an additional 50 g of water and stirred for 30 minutes to further facilitate dispersion of the AlP particles in the reaction slurry. The slurry is then filtered, washed with a volume of water approximately six times the volume of the precipitate, and filtered again. This filter-wash-filter cycle can be repeated until the desired purity level is achieved. Usually one to three cycles is sufficient to remove unreacted starting material and unwanted reaction by-products.

It has been discovered that by allowing the volume to vary as described, the resulting change in system concentration and pH causes sequential precipitation of AlP "oligomers" in solution onto AlP particles already formed and agglomerated. This sequential precipitation of AlP oligomers onto already-formed and agglomerated AlP particles operates to seal the surface porosity of the pre-existing AlP aggregates and particles, e.g., causing in-situ particle layering, which thereby reduces the surface porosity of such AlP aggregate and reduces such related properties as oil absorption. In an example embodiment, the AlP oligomers are AAlP and the AlP particles already formed are AAlP.

As noted above, allowing water levels to cycle during the condensation causes a change in the pH proportional to the concentration of the $Al(OH)_3$. When the volume decreases, the pH increases due to the higher concentration of the $Al(OH)_3$, and the solubility decreases allowing AlP oligomers to agglomerate. Adding $Ca(OH)_2$ to the condensation medium may also effect a similar change in pH, causing the precipitation of AlP and subsequent coating of pre-existing AlP particles. This process would also incorporate the alkaline earth metal cations as counter-ions for residual acid phosphate groups either adsorbed on the AlP particle surface or bonded as a pendant component.

A condensed solid was formed and existed as a dispersion of solid acidic-coated AAlP particles in water. The suspension was filtered to isolate the acidic coated AlP particles. The particles were washed with water one or more times, and then filtered again. In an example embodiment, after the initial filtering the particles were washed with a volume of water approximately six times the volume of the precipitate before being refiltered. Successive washings remove unreacted starting material and any byproducts from production. After being refiltered, the acidic-coated AlP particles were reslurried by the addition of water, and were further heat treated. In an example embodiment, the slurry is filtered to isolate the acidic coated AlP particles and the particles are heated to a temperature of about 110°C for about 24 hours to drive off the water, and produce acidic coated AlP particles. Alternatively, the coated AlP particles are heated to a temperature of about 250°C for about 12 to 48 hours, to produce dry acidic coated AP particles that are both free of water and any by-products that decompose below 250°C. Additionally, as described above, it is to be understood that

the method disclosed herein can be used to produce crystalline AlP, or a combination of AAlP and crystalline AlP.

Example 5 - Binary Condensation Formation of AlP (acid-to-base in-situ aggregation)

In an example embodiment, AlP is prepared by adding phosphoric acid (H_3PO_4) to aluminum hydroxide ($Al(OH)_3$) to form the desired AlP, e.g., in the manner disclosed above in Example 3. However, unlike Example 3, the reaction is allowed to occur in an open system, wherein the reaction system is left open so as to allow solvent water to continuously evaporate, thereby causing the concentration of the reaction system to increase and its pH to decrease over time. At periodic intervals during the condensation reaction process, the water level is replenished to the initial volume. The reaction slurry is then diluted with an additional 50 g of water and stirred for 30 minutes to further facilitate dispersion of the AlP particles in the reaction slurry. The slurry is then filtered, washed with a volume of water approximately six times the volume of the precipitate, and filtered again. This filter-wash-filter cycle can be repeated until the desired purity level is achieved. Usually one to three cycles is sufficient to remove unreacted starting material and unwanted reaction by-products.

As noted above in Example 4, it has been discovered that by allowing the volume to vary as described during the reaction, the resulting change in system concentration and pH causes sequential precipitation of AlP "oligomers" in solution onto AlP particles already formed and agglomerated. This sequential precipitation of AlP oligomers onto already-formed and agglomerated AlP particles operates to seal the surface porosity of the pre-existing AlP aggregates and particles, e.g., causing in-situ particle layering, which thereby reduces the surface porosity of such AP aggregate and reduces such related properties as oil absorption. In an example embodiment, the AP oligomers are AAlP and the AlP particles already formed are AAlP. Additionally, as described above, it is to be understood that the method disclosed herein can be used to produce crystalline AlP, or combinations of AAlP and crystalline AlP.

Example No. 6 – Formation of the Bioactive-AlP Complex (physical incorporation)

The AlP made as a binary condensation product, e.g., as set forth in Example Nos. 1 to 5, was constituted as a 34 percent by weight slurry, and was mixed with appropriate concentration silver nitrate solution. The later solution was made so that a 1.0% percent

and a 10% percent silver-to-AlP slurry solution was prepared. The combined slurry was mixed for approximately 5 minutes and then atomized in a spray drier under nitrogen, and dried at temperatures ranging from about 180°C inlet to about 79°C outlet. The solid powder was collected and analyzed. The resulting powder was a bioactive-AlP complex where the bioactive material was physically incorporated, enmeshed, encapsulated, or intertwined in the AlP polymer.

Alternatively, the AlP made as a binary condensation product, e.g., as set forth in Example Nos. 1 to 5, was constituted as a 34 percent by weight slurry, and was mixed with appropriate concentration silver nitrate solution. After stirring the combined slurry was filtered and washed once with hot water at a temperature of 40 to 60°C. The filtrate was dried at approximately 110°C for approximately 12 hours, divided into portions, and each heat treated for approximately 24 hours at approximately 250°C. Yields were the same regardless of heat treatment temperature, and the resulting powder was a bioactive-AlP complex where the bioactive material was physically incorporated, enmeshed, encapsulated, or intertwined in the AlP polymer.

Example No. 7 – Formation of the Bioactive-AlP Complex (chemical bonding)

AlPs were prepared by the binary condensation routes described above in Example Nos. 1 to 5, except that a silver nitrate solution of appropriate concentration was combined at the same time as the phosphoric acid and aluminum hydroxide where brought together. The resulting suspension comprised the bioactive-AlP complex condensate in solution, wherein the bioactive material, in the form of silver ion, was chemically bonded with the AlP polymer, e.g., incorporated into the AlP polymer backbone. The suspension was filtered in the manner described above, to isolate the bioactive-AlP complex particles. The particles were washed and dried at the temperatures described in the above-noted Examples to provide the desired engineered physical properties or characteristics, e.g., porosity.

In these example processes, a chemical reaction results in the formation of amorphous aluminum orthophosphate or of aluminum orthophosphates ($Al_2(HPO_4)_3$ or $Al(H_2PO_4)_3$. The reaction, is carried out through the mixture of the two ingredients (when forming the AlP separately), or through the mixture of the three ingredients

(when directly forming the bioactive-AlP complex). The reagents are dosed in a reactor equipped with a stirring device, and allowed to react for a short period of time, e.g., less than about 10 minutes.

Variables for forming AlP by the binary synthesis process that affect product outcome may include: (a) the type of ATH used; (b) the method of dispersing the ATH in the reaction slurry and the temperature at which it is done; (c) the concentration of the ATH in the reaction slurry; (d) the order and rate of combination (addition) of the ATH slurry to the phosphoric acid; that is acid to base (A to B) or base to acid (B to A); (e) the concentration of the reaction slurry; (f) the temperature at which the condensation reaction is run (e.g., room temperature or an elevated temperature such as 95°C); (f) the duration (time) of the reaction at temperature (e.g., 30 minutes or up to 4 hours); (g) the type of agitation (e.g., simple mixing or dispersion); and (h) post reaction treatment such as: filtration, followed by washing and drying of the condensate to a dry powder; or concentration of the condensate slurry to a gel or paste by partial evaporation of solvent (with or without pH adjustment).

With respect to the type of ATH used, it was discovered that the physical form of the AlP produced by the binary synthesis process depends on both the nature of the ATH used as starting material, and reaction conditions that control kinetics. Broadly two types of ATH are available; amorphous and crystalline. Crystalline ATH may exist in a variety of specific crystalline forms and mineral compositions. It has been discovered that certain of these types require considerable energy input in the form of heat and agitation to undergo the phosphate condensation reaction. The resulting AlP product produced using crystalline ATH is typically crystalline also (one of many are possible structures).

The use of amorphous ATH allows rapid room temperature reaction kinetics, and the resulting AlP formed therefrom is virtually always amorphous also. It has been discovered that to preserve desired silver functionality (when using silver as the antimicrobial agent) it is useful to run reactions at the lowest temperatures possible. It has been discovered that amorphous ATH is suitable for such use. It has also been discovered that moderately reactive crystalline ATH (characterized by DSC as having

an endothermic transition at around 310°C as opposed to lesser reactive ATH materials which have the endothermic transition at around 340°C), when condensed with phosphoric acid at room temperature, yields AlP made up of around 50% amorphous content (which contains the silver-aluminum-phosphate component) and around 50% unreacted ATH. This is actually a higher level of amorphous conversion than detected when using typical crystalline ATH and combining with phosphoric acid at room temperature and allowing for condensation where typically less than 10% conversion occurs. The so-formed AlP is amorphous and it is theorized that its composition is primarily ATH with a surface coating of phosphate. The higher levels of amorphous AlP conversion in the chemistry described herein are attributed to the presence of the other ingredients that facilitate surface reaction and/or inhibit the crystallization process (so that any AlP formed remains amorphous). It has been discovered in testing that this composition provides effective levels of antimicrobial activity as well as light stability.

An additional variable relating to the formation of the bioactive-AlP complex, e.g., Ag-AlP, may include the point of introduction of the bioactive agent (e.g., silver source such as silver nitrate) being: (a) to the ATH slurry before condensation (ATH + AgX + water); (b) to the phosphoric acid before condensation; (c) to the mixed condensate at the beginning of mixing as a solution; and (d) to the condensate at the end of mixing as a solution. While the variable of bioactive agent point of introduction is discussed above in the context of the binary condensation process, it is to be understood that this variable applies equally to the remaining methods of making the bioactive-AlP complex as disclosed herein.

Precipitation Methods of Making

The AlP is a phosphate complex prepared by dissolving a suitable salt, such as aluminum hydroxide, magnesium hydroxide, calcium hydroxide, aluminum sulfate and the like in phosphoric acid in molar amounts to achieve complete dissolution of the salt. The phosphate complex is precipitated from the acid solution by neutralizing with an alkaline solution or base such as sodium hydroxide, potassium hydroxide, ammonium hydroxide, sodium aluminate, potassium aluminate and the like. The composition of the resulting precipitated solid depends on the ratio of the metal to the phosphate anion. The properties of the precipitated complex, i.e., AlP, depend on the processing parameters employed during the dissolution of the salt in the acid and on the conditions

of the precipitation/neutralization, including choice of neutralizing agent, temperature, order of addition of reactants, rate of addition of reactants, and the degree and duration of agitation.

AlPs are made as a precipitation product by combining selected starting materials including an aluminum source and a phosphorous source under specific conditions of controlled material delivery, temperature, agitation, and pH. The judicious selection of starting materials and process conditions produces AlPs having a material content and chemical structure intentionally created with the purpose of producing the above-noted engineered physical property or characteristic, e.g., porosity, the provides the desired controlled delivery/release of the bioactive constituent.

Aluminum sources useful for forming AlP by-precipitation include aluminum salts, such as aluminum chloride, aluminum nitrate, aluminum sulfate and the like. Aluminum sources useful for forming AlP also include aluminate compounds, such as sodium aluminate and the like, aluminum hydroxide, or aluminum in metallic form. Phosphorous sources useful for forming AlP by precipitation include phosphoric acid, and salts of phosphorus as orthophosphates or as polyphosphates. An alkaline solution is used to control the pH or neutralize the reaction of the main ingredients. In an example embodiment, the alkaline solution can include ammonium hydroxide, sodium hydroxide, sodium carbonate, and combinations thereof. In an example embodiment, sodium hydroxide is used as the alkaline solution. Useful aluminum sources, phosphate sources, and alkaline sources include those disclosed in Published US Patent Applications 2006/0045831 and 2008/0038556, which are each incorporated herein by reference in their entirety.

AlPs can be made through the selective combination of the materials noted above. The following selected methods of preparation are provided below as examples, and it is to be understood that other methods of preparation other than those specifically disclosed may be used. While AlPs produced according to the precipitation route as better disclosed below comprise amorphous AlPs, it is to be understood that the precipitation methods of making AlP as disclosed herein can also be used or adapted to produce crystalline AlP or combinations of amorphous and crystalline AlP depending on the particular desired antimicrobial chemical composition properties.

Example No. 8 - Aluminum Sulfate Method of Making AlP

In an example embodiment, AlP having the above-noted engineered properties is prepared by combining aluminum sulfate, phosphoric acid and sodium hydroxide as disclosed in US Patent No. 7,951,309, which is incorporated herein by reference. The process steps used in this example process generally include: preparing the main reagents, such as a diluted solution of phosphoric acid, a diluted solution of aluminum sulfate, and a diluted solution of sodium hydroxide or ammonium hydroxide; simultaneous and controlled adding of the reagents in a reactor equipped with a sloshing system to keep the homogeneity of the mixture during the process; and controlling, during the addition of the reagents in the reactor, of the temperature and pH (acidity) of the mixture and the reaction time.

The main reagents in this example process can be prepared as follows. A source of phosphorus is fertilizer grade phosphoric acid, from any origin, that has been clarified and discolored. For example, a commercial phosphoric acid containing approximately 54% of P_2O_5 may be chemically treated and/or diluted with treated water resulting in a concentration of approximately 20% P_2O_5. Another reagent useful for this example process is commercial aluminum sulfate, which may be obtained by reaction between alumina (hydrate aluminum oxide) and concentrated sulfuric acid (98% H_2SO_4), that is clarified and stored at an approximate 28% concentration of Al_2O_3. For the reaction to have favorable kinetics, the aluminum sulfate is diluted with water treated at approximately 5% of Al_2O_3.

Neutralization of the reaction is carried out with a sodium hydroxide solution, which may be commercially purchased in different concentrations. A concentration of approximately 50% of NaOH may be purchased and diluted. For example, in a first phase of the reaction, when the initial reagents are being mixed, the sodium hydroxide may be used in the concentration of approximately 20% of NaOH. In a second phase of the reaction, to fine tune the product acidity, a sodium hydroxide solution with approximately 5% of NaOH may be used. As an alternative neutralizer, ammonium hydroxide or sodium carbonate (soda ash) may be used.

In this example process, a chemical reaction results in the formation of amorphous aluminum orthophosphate or of aluminum orthophosphates ($Al_2(HPO_4)_3$ or $Al(H_2PO_4)_3$. The reaction is carried out through the mixture of the three reagents, i.e., phosphoric acid solution, aluminum sulfate solution, and sodium hydroxide solution. The reagents are dosed in a reactor, typically containing a sloshing system, during about a 30 minute period. During the addition of the reagents in the reactor, the pH of the mixture is controlled within a 4 to 4.5 range and a reaction temperature, between 35ºC and 40ºC. The reaction is completed after about 15 minutes of the reagent mixture. In this period, the pH of the mixture may be adjusted to 5, with the addition of more diluted sodium hydroxide. In this example process, the temperature is preferably maintained below approximately 40ºC. At the end of the reaction, the suspension formed should contain a P:Al molar ratio of between about 0.8:1 to 1.2:1.

After the formation of the AlP, the suspension containing around 6.0% to 10.0% of solids, with a maximum approximate temperature of about 45°C, and density of about 1.15 to 1.25 g/cm^3, is processed for separation. In an example embodiment, the suspension is pumped to a conventional filter press. In the filter press, the liquid phase (sometimes referred to as the "liquor") is separated from the solid phase (sometimes referred to as the "cake"). The wet cake, containing approximately 35% to 45% of solids is kept in the filter for washing cycle. The filtered concentrate, which is basically a concentrated solution of sodium sulfate, is extracted from the filter and stored for future usage. While the use of a filter press has been disclosed as a separating technique, it is to be understood that other types of separating techniques can be used.

In an example embodiment, washing of the wet cake is performed in the filter itself and in multiple process steps. In a first washing ("displacement washing") the largest part of the filtered substance contaminating the cake is removed. The washing step is performed using treated water over the cake flowing at a preselected flow rate. A second washing step, also with treated water, may be carried out to further reduce, if not eliminate, the contaminants. A third washing step using a slightly alkaline solution may be used to neutralize the cake and to keep its pH in the 7.0 range. The cake may be blown with compressed air for a period of time. Preferably, the solids content of the wet product is between about 35% to 45%. While the use of a particular washing

technique and sequence has been disclosed, it is to be understood that other types of washing techniques can be used.

The cake dispersion may be processed in such a way that the filter cake, wet and washed, and containing approximately 35% of solids, is extracted from the press filter by a conveyor belt and transferred to a reactor/disperser. The dispersion of the cake is aided by the addition of a dilute solution of sodium tetrapyrophosphate.

After the dispersion step, the product is then dried, when the AAlP "mud," with a percentage of solids of between about 30% to 50%, is pumped to the drying unit. In an example embodiment, water removal from the material can be carried out with drying equipment, such as a "turbo dryer" type through an injection of a hot air stream, at a temperature of less than about 300°C, preferably temperatures of from about 100°C to 200°C as noted above to obtain the desired engineered porosity. While the use of a particular drying technique has been disclosed, it is to be understood that other types of drying techniques can be used.

Example No. 9 - Sodium Aluminate Method of Making AlP

In another example process, the AlP is prepared by using sodium aluminate as an aluminum source as disclosed in US Patent No. 7,951,309. In one such embodiment, the AAlP is prepared by a reaction between phosphoric acid and aluminum hydroxide. The process may further comprise a step of neutralizing that can be carried out by using sodium aluminate. In certain embodiments, the process for making an AlP comprises reacting phosphoric acid, aluminum hydroxide and sodium aluminate. In one embodiment, the process for making an amorphous sodium aluminum phosphate comprises reacting aluminum phosphate and sodium aluminate.

In one embodiment, the reaction comprises two steps. In a first step, phosphoric acid reacts with aluminum hydroxide to produce aluminum phosphate at an acidic pH. In one embodiment, AlP is produced as a water soluble aluminum phosphate. In certain embodiments, the pH of water soluble AlP is less than about 3.5. In certain embodiments, the pH is about 3, 2.5, 2, 1.5 or 1. In certain embodiments, AAlP is produced as a fine solid-liquid dispersion at a higher pH. In one embodiment, the pH is about 3, 4, 5 or 6.

In a second step, the acidic aqueous aluminum phosphate solution or dispersion from the first chemical step is reacted with sodium aluminate. In certain embodiments, the sodium aluminate is used as an aqueous solution at a pH greater than about 10. In one embodiment, the pH of the aqueous sodium aluminate solution is about 11, 12 or 13. In one embodiment, the pH of the aqueous sodium aluminate solution is greater than about 12. The AAlP is generated as a solid precipitate. In one embodiment, the solid aluminum-sodium phosphate has a molar ratio of P:Al of about 0.85, and a molar ratio of Na:Al of about 0.50. In one embodiment, the solid AAlP has a molar ratio of P:Al of about 1, and a molar ratio of Na:Al of about 0.76. In certain embodiments, the molecules with other formulation ratios can be obtained by the same procedure.

In one embodiment, the solid hydrated aluminum hydroxide is added to the phosphoric acid in the first chemical step. In another embodiment, the solid hydrated aluminum hydroxide is added to the purified liquid sodium aluminate solution to form a colloidal solution. In another embodiment, the solid hydrated aluminum hydroxide is added directly as solid or solid-liquid suspension in water in the second reaction step. In certain embodiments, the reaction is carried out in a single step.

Sodium aluminates useful for this example process include those that can be obtained by methods known to those skilled in the art. For example, the sodium aluminate can be provided in solution form as a standard chemical product resulting from the first step in the Bayer process in the alumina (Al_2O_3) extraction from Bauxite ore, often called "purified sodium pregnant solution". This liquid aqueous sodium aluminate solution is saturated at ambient temperature and stabilized with sodium hydroxide, NaOH. It's typical compositions are: sodium aluminate, 58 to 65% mass (25 to 28% mass of Al_2O_3) and sodium hydroxide, 3.5 to 5.5% mass (2.5 to 4% mass of free Na_2O). In certain embodiments, it has a molar ratio of Na:Al of from about 1.10 to 2.20 and low impurities (depending on the Bauxite origin: Fe=40 ppm, Heavy metals=20 ppm, and small amount of anions, Cl^- and SO_4^{2-}). In certain embodiments, the sodium aluminate water solution has a molar ratio of Na:Al of about 1.1 0, 1.15, 1.20, 1.25, 1.30, 1.35, 1.40, 1.45, 1.50, 1.55, 1.60, 1.65, 1.70, 1.75, 1.80, 1.85, 1.90, 1.95, 2.0, 2.05, 2.10, 2.15 or 2.2. The solution color, in certain embodiments, is amber. In certain embodiments, the viscosity of the solution is approximately 100 cP. In certain aspects,

the sodium aluminate solution is purified by polishing filtration. In certain embodiments, the sodium aluminate solution is regenerated from solid aluminum hydroxide and sodium hydroxide.

The solid hydrated aluminum hydroxide can be obtained by methods known to one of skill in the art. In one embodiment, aluminum hydroxide is an industrial chemical produced by the Bayer process. The solid hydrated aluminum hydroxide can be obtained from the "purified sodium aluminate pregnant solution" by precipitation which is accomplished via cooling the solution. In one embodiment, the sodium aluminate thus produced has a low level of impurities and a variable amount of humidity (cations about 70 ppm, chlorates about 0.85% mass and sulfates about 0.60% mass (these impurities are determined by the purification level of the "Purified Sodium Aluminate pregnant solution) and the total water, hydration and humidity, about 22.0 to 23.5% mass. In one aspect, both raw materials are standard primary industrial products, just first and second step from the bauxite processing, (commodities) produced in huge amounts by the ~~B~~ bauxite processors.

In one embodiment, the chemical reaction results in the formation of aluminum sodium phosphate ($Al(OH)_7Na_7(PO_4).1.7H_2O$). After the formation of aluminum sodium phosphate, the suspension containing around 6% to 10% of solids, with a maximum approximate temperature of 45°C, and density in a 1.15 to 1.25 g/cm^3 range, is pumped to a conventional filter press.

In a preferred embodiment, AlP prepared by the precipitation process is prepared by using sodium aluminate. It has been discovered that the sodium aluminate process provides for an improved degree of control over the desired characteristics of the AlP that does not otherwise exist in the aluminum sulfate process.

Example No. 10 - Formation of the Bioactive-AlP Complex (physical incorporation)

The AlP made by the precipitation methods described above in Example Nos. 8 and 9, was constituted as a 34 percent by weight slurry, and was mixed with appropriate concentration silver nitrate solution. The later solution was made so that a 1.0 percent and a 10 percent by weight silver-to-AlP complex was made and a slurry solution was prepared. The combined slurry was mixed for approximately 5 minutes and then

atomized in a spray drier under nitrogen, and dried at temperatures ranging from about 180°C inlet to about 79°C outlet. The solid powder was collected and analyzed. The resulting powder was a bioactive-AlP complex where the bioactive material was physically incorporated, enmeshed, encapsulated, or intertwined in the AlP polymer.

Alternatively, the AlP made by the precipitation processes disclosed above was constituted as a 34 percent by weight slurry, and was mixed with appropriate concentration silver nitrate solution. After stirring the combined slurry was filtered and washed once with hot water at a temperature of 40 to 60°C. The filtrate was dried at approximately 110°C for approximately 12 hours, divided into portions, and each heat treated for approximately 24 hours at approximately 250°C. Yields were the same regardless of heat treatment temperature, and the resulting powder was a bioactive-AlP complex where the bioactive material was physically incorporated, enmeshed, encapsulated, or intertwined in the AlP polymer.

Example No. 11 – Formation of the Bioactive-ALP Complex (chemical bonding)

An AlP was prepared similar to the precipitation process described above in Example Nos. 8 and 9, except that a silver nitrate solution of appropriate concentration was combined with the acidic aluminum phosphate solution (P:Al ratio of 3:1) and then neutralized with an appropriate amount of sodium aluminate. The resulting dispersion comprised the bioactive-AlP complex, wherein the bioactive material, in the form of silver ion, was chemically bonded with, e.g., incorporated into the polymer backbone of, the AlP polymer. The dispersion was filtered to isolate the bioactive-AALP complex particles. The particles were washed and dried at the temperatures described above to provide the desired engineered porosity.

Sol Gel Method of Making

AlP prepared by a sol-gel process involves the creation of inorganic molecular networks from molecular or ionic precursors through the formation of a colloidal suspension (sol) and the gelation of such sol to form a solid network in a continuous liquid phase (gel). The precursors for synthesizing these colloids typically comprise a metal or metalloid element surrounded by various reactive groups. Stated another way, in the sol gel process, simple molecular or ionic precursors are converted into nano-sized particles to form a colloidal suspension (sol). The colloidal nano-particles are

then linked with one another in a three-dimensional liquid filled solid network (gel). This transformation to a gel can be initiated in a number of ways, but the most convenient approach is to change the pH of the reaction solution.

The method used to remove the liquid from the solid will affect the sol gel's properties. For example, supercritical drying will maintain the three-dimensional structure in the dried solid, whereas slow drying in a fluid evaporation process collapses the network structure creating a high density material.

Advantages to preparing the AlP via a sol gel synthesis process include process versatility and simplicity resulting in the possibility to obtain highly pure and/or tailored materials, uniform particle size distribution, substantially spherical-shaped aggregate particles, nano-sized particles, and custom engineered compositions. While AlP as disclosed herein comprises substantially spherical aggregate particles, it is understood that some small amount of nonspherical particles may unintentionally be produced and may be present in the resulting antimicrobial chemical compositions.

As used herein, the term "gel" is understood to be a three-dimensional cage structure formed of linked large molecular mass polymers or aggregates in which liquid is trapped. The network of the structure typically consists of weak and/or reversible bonds between the core particles. The term "sol" as used herein is understood to be a colloidal dispersion of solids in a liquid. The solids comprise aluminum phosphate having nanometer scale average particle sizes. The gel comprises an aluminum phosphate sol as a dispersed phase in a semi-rigid mass enclosing all of the liquid. Post treatment of product produced by the sol gel process by filtration, washing, drying, and combinations thereof leads to aggregation of the colloidal solids in a controlled fashion to form a larger solid complex.

Generally, the sol gel process includes the following process steps: (1) nucleation or polymerization or condensation of the molecular precursors to form primary particles, e.g., nanometer in scale, to form the sol (colloidal dispersion or suspension); (2) growth of the particles or gelation; (3) linkage of the particles to form chains and the extension of such chains throughout the liquid medium to form a thickened gel; and (4) treating the sol gel material to remove the liquid to give a desired solid end-product.

In an example embodiment, the precursor solution is prepared by combining a suitable aluminum source, with a phosphorous source. Suitable aluminum sources can be selected from the group of aluminum salts such as aluminum chloride, aluminum nitrate, aluminum sulfate and the like. A preferred aluminum source is aluminum nitrate. Phosphorous sources useful for forming AAlP by sol gel process include phosphoric acid, and salts of phosphorus as orthophosphates or as polyphosphates. A source of phosphorus is fertilizer grade phosphoric acid, from any origin, that has been clarified and discolored.

The primary ingredients of the precursor solution are combined together in an aqueous environment with a gelling agent to produce a colloidal dispersion of solid aluminum phosphate particles in solution. In an example embodiment, the precursor solution is formed by combining aluminum nitrate with phosphoric acid (85% by weight) in the presence of water. Water can be present in one or more of the aluminum nitrate, the phosphoric acid, or as added water independent of either ingredient.

After the precursor ingredients are combined, the resulting system is stirred and a suitable alkaline ingredient is added to the stirred solution. Alkaline ingredients useful for this purpose include those conventionally used to change the pH of the system, e.g., increase the pH of the acidic system, and in an example embodiment is ammonium hydroxide. The presence of the ammonium hydroxide increases the pH and drives the process of nucleation and condensation forming a colloidal dispersion or sol. Depending on the concentration of nucleating agent, this step can be intermediate or final. Further addition of nucleating agent causes the primary aluminum phosphate particles to link together forming a gel, e.g., results in gelation, and further results in the colloidal particles being linked into the gel structure to form a sol gel.

In an example embodiment, it may be desired to control the sol gel process to isolate the colloidal dispersion before gelation. This can be done by controlling the reaction conditions so that only colloidal dispersion occurs (i.e., formation of a sol) and not full gelation. Controlling the process in this manner may provide certain manufacturing advantages and/or provide certain advantages relating to handling of the end-product.

The colloidal dispersion from this process can be filtered to recover the solids, and then thermally treated and/or washed as described below.

In an example embodiment, the phosphoric acid, aluminum nitrate, and/or ammonium hydroxide can be heated prior to being combined with one another, or can be heated after combination, e.g., during stirring. Additionally, the amount of water present and/or the rate of addition of the ammonium hydroxide, can be adjusted to produce a desired reaction product having a desired yield of AAlP.

In an example embodiment that amount of ammonium hydroxide, NH_4OH, that is added to the acid solution is sufficient to neutralize the acid system to initiate formation of colloidal aluminum phosphate particles, and for gelation exceeds the stoichiometric amount to form ammonium nitrate, NH_4NO_3,. The range can be from the stoichiometric amount of NH_4OH needed to form the NH_4NO_3 (1.0 stoichiometry) to about 3.0 stoichiometry, preferably between about 1.1 and 2.0, and more preferably between about 1.2 and 1.5.

The order of addition (i.e., base solution to acid precursor solution or vice versa) has been found to control the rate and extent of gelation. When base is added to stirred precursor solution in stoichiometric concentration ranges stated above (1.0 to 3.0) virtually instantaneous gelation occurs. It has been discovered that reversing the order of addition, i.e., adding the precursor solution to the base solution, provides control over the extent of growth from colloidal dispersion to full gelation. As discussed below, it has also been discovered that particle morphology can be controlled by the method of addition.

It has been found that concentrations of ammonia in excess of the 1.1 stoichiometric ratio are useful to minimize unreacted aluminum in the resulting complex. For the end-use application as an inhibitive pigment, it is desirable that the phosphate release rate from the complex when contacted with water be in the 200 to 400 ppm range. Testing has determined that phosphate anion elution is in the target range when the ammonia level in the reaction is around 1.2 to 3 stoichiometric ratio and after the solid has been thoroughly washed and/or thermally treated to remove the soluble by-products as described below.

In an example process, the sol gel is next subjected to post gelation treatment which may comprise heating, washing, and/or sizing. In an example embodiment, the sol gel powder formed is isolated by collapsing the dispersion or gel by driving off the liquid constituent. Various types of gels can be formed from the sol gel such as; xerogels that are solids formed by unhindered drying of the sol gel so as to yield high porosity and surface area (150 – 1,000 m^2/g) in solid form, aerogels that are solids formed by supercritical drying (e.g., freeze drying), hydrogels that are water insoluble colloidal polymer particles dispersed in water, and organogels that are amorphous, non-glassy solids comprising a liquid organic phase trapped in the solid matrix.

The sol gel consists of solid $AlPO_4$ connected through various pH dependent (amino, water, phosphate) linkages to form a solid dispersed phase as a mass enveloping all the liquid, the latter consisting of water and dissolved salts. Heating the gel, to a temperature above about 100°C, evaporates the water and any ammonia and collapses the mass to a solid consisting of aluminum phosphate, $AlPO_4$, and ammonium nitrate, NH_4NO_3. Heating the gel or the collapsed gel solid, to a temperature above about 215°C, thermally decomposes the ammonium nitrate, NH_4NO_3, thereby eliminating it from the powder product. Heating to temperatures above about 215°C leads to a decrease in pH, indicating that residual amino groups remaining after thermal decomposition of the ammonium nitrate, NH_4NO_3, most likely as substituent's on the PO group, are also thermally decomposed and replaced by hydrogen atoms thereby making the complex acidic. The solid product resulting from this treatment has been shown by analysis to be pure AAlP having a phosphate release rate of around 240 ppm and surface area greater than 125 m^2/gram.

Accordingly, the post gelation heat treatment can comprise a single step of heating the sol gel to a relatively high temperature above about 250°C for a period of time sufficient to achieve water evaporation, collapsing of the mass, and thermally decomposing the ammonium nitrate, NH_4NO_3. In an example embodiment, this can be done at about 250°C for approximately 12 to 72 hours. The resulting product from this heat treatment is substantially aluminum phosphate, i.e., there is very little if any ammonium phosphate or ammonium nitrate.

Alternatively, the post gelation heat treatment can comprise a single step of heating the sol gel at a lower temperature of about above about 100 to 150°C for a period of time sufficient to achieve water evaporation. In an example embodiment, this can be done at about 110°C for approximately 1 to 24 hours. The resulting product from this heating or drying treatment is AAlP and ammonium phosphate and ammonium nitrate.

This drying step can be followed by a heat treatment step at a temperature of between about 215 to 300°C. In a preferred embodiment, the drying step is at about 110°C for about 24 hours, and the heat treatment is about 250°C for up to 1 to 3 days (16 to 72 hours). The resulting AAlP has a moisture content of from about 5 to 20 percent by weight and the desired engineered porosity. The pH of the heat treated material can be adjusted by re-dispersing the complex and adjusting the pH with ammonium hydroxide solution. The resulting complex is then dried at 100 to 110°C to remove water and ammonia.

If desired, before drying or heat treatment, the sol gel material can be filtered to separate the solid particles from solution, and the separated solid, e.g., in the form of a cake, can be subjected to one or more wash cycles. The wash cycles use water and operate to rid the solid aluminum phosphate particles of any unwanted solubles, e.g., ammonium compounds such as ammonium nitrate, and ammonium phosphate that have been formed as a reaction by- product. The washed sample can then be dried and/or heat treated in the manner disclosed above to further evaporate water and/or thermally decompose any residual ammonium nitrate and ammonium phosphate in the washed aluminum phosphate, and densify the aluminum phosphate particles.

If desired, the sol material can be dried at about 100°C to evaporate water and collapse the mass, and the collapsed powder can be washed with water to remove ammonium nitrate , NH_4NO_3, to thereby recover instead of thermally decompose the by-product. The washed and dried mass can be heat treated above about 215°C to thermally decompose any residual ammonium nitrate, NH_4NO_3 , thereby providing substantially pure AAlP.

The basic chemistry of the sol gel process for forming only the AAlP is presented below as follows:

1. Precursor solution - Combination of all ingredients

$Al(NO_3)_3 \cdot 9H_2O + H_3PO_4 + H_2O$

2. Gelling Agent

$3NH_4OH + H_2O$

3. Sol-gel reaction

$AlPO_4 + (NH_4)_3PO_4 + H_2O \longrightarrow AlPO_4 + NH_4OH$

Reaction to form AAlP sol gel: as NH_4OH (28% NH_3 in water) is added, it neutralizes the acid system and drives formation of insoluble $AlPO_4$, that takes Al^{+3} out of the reaction and allows more NH_4^{+1} to combine with NO_3^{-1} to form soluble NH_4NO_3. Depending on the concentration and rate of addition of the NH_4OH colloidal particles of $AlPO_4$ will form. Adding more NH_3 to the reaction allows the $AlPO_4$ colloidal particles to aggregate and to eventually form bonds between the particles to form the gel structure.

The amount of NH_3 added must exceed the stoichiometric amount required to form NH_4NO_3 in order to have sufficient NH_3 to control pH and facilitate gel bridging. Depending on the amount of NH_3 added, the rate of addition, and the concentration, the gel will consist of a mass of $AlPO_4$ solid particles linked forming a cage, three-dimensional structure encapsulating ammonium nitrate, NH_4NO_3, dissolved in water. Ammonium phosphate may also be present as an intermediate, and extending reaction conditions (i.e., by further heating) will lead to full reaction with the aluminum in the system to condense to aluminum phosphate.

4. Filtration and washing - Optional to supplement or replace thermal purification to remove soluble ammonium salts.

5. Dehydration and drying - Drying at above at least 100°C to evaporate water and collapse the sol gel structure to form a densified solid.

$AlPO_4 + NH_4NO_3$

6. Thermal purification - Thermal treatment at 215 to 250°C to thermally decompose ammonium nitrate.

$AlPO_4$ (amorphous aluminum phosphate)

If desired, the order of ingredient addition can be changed from that disclosed above. For example, the acid solution may be added to a solution of the ammonium hydroxide in order to control the viscosity of the reaction system and/or impact the surface area of the colloidal solids. Such flexibility in the order of ingredient addition may be advantageous, e.g., for the scale-up of manufacturing where it may be desirable to avoid gelation in favor of the formation of a suspension of colloidal primary particles. The resulting composition after washing, drying and/or thermal treatment is essentially chemically the same regardless of the order of addition. However product morphology is affected by these processing parameters. Adding acid to base results in higher surface area and greater porosity. The sol gel process disclosed herein produces an aluminum phosphate composition consisting essentially of AAlP.

Base-to-acid sequencing causes rapid pH change and the rapid formation of sol particles followed by rapid gelation to form interlinked particles in the gel matrix. This reduces molecular mobility and prevents any further particle growth or morphological change. When acid is added to base, the pH change is slower and localized colloidal aluminum phosphate particles form. No gelation occurs so the system mobility allows for continued competing side reactions (increased solublization of ammonium nitrate and ammonium phosphate) allowing intermediate species to survive. When dehydration and thermal decomposition occur, small particles of aluminum phosphate exist in the presence of departing water and decomposition products (of ammonium nitrate), leading to more porosity in small aggregated aluminum phosphate particles.

The basic chemistry of the sol gel process for forming only the bioactive-AAlP complex (which involves adding the bioactive material, e.g., in the form of silver nitrate, to the aluminum nitrate and aqueous phosphoric acid) is presented below as follows:

1. Precursor solution - Combination of all ingredients

   $Al(NO_3)_3 \cdot 9H_2O + H_3PO_4 + H_2O + AgNO_3$

2. Gelling Agent

   $3NH_4OH + H_2O$

3. Sol-gel reaction

$AgAlPO_4 + (NH_4)_3NO_3 + H_2O + NH_3$

4. Filtration and washing - Optional to supplement or replace thermal purification to remove soluble ammonium salts.

5. Dehydration and drying - Drying at above at least 100°C to evaporate water and collapse the sol gel structure to form a densified solid.

$AgAlPO_4 + NH_4NO_3$

6. Thermal purification - Thermal treatment at 215 to 250°C to thermally decompose ammonium nitrate.

$AgAlPO_4$ (amorphous silver aluminum phosphate)

Example No. 12 - Formation of the Bioactive-AlP Complex (physical incorporation)

The AAlP made by the sol gel process as described above, was constituted as a 34 percent by weight slurry, and was mixed with appropriate concentration silver nitrate solution. The later solution was made so that a 1.0 percent and a 10 percent silver-to-AgAlP complex were prepared. The combined slurry was mixed for approximately 5 minutes and then atomized in a spray drier under nitrogen, and dried at temperatures ranging from about 180°C inlet to about 79°C outlet. The solid powder was collected and analyzed. The resulting powder was a bioactive-AlP complex where the bioactive material was physically incorporated, enmeshed, encapsulated, or intertwined in the AlP polymer.

Alternatively, the AAlP made by the sol gel process was constituted as a 34 percent by weight slurry, and was mixed with appropriate concentration silver nitrate solution. After stirring the combined slurry was filtered and washed once with hot water at a temperature of 40 to 60°C. The filtrate was dried at approximately 110°C for approximately 12 hours, divided into portions, and each heat treated for approximately 24 hours at approximately 250°C. Yields were the same regardless of heat treatment temperature, and the resulting powder was a bioactive-AlP complex where the bioactive material was physically incorporated, enmeshed, encapsulated, or intertwined in the AlP polymer.

Example No. 13 – Formation of the Bioactive-AAlP Complex (chemical bonding)

An AAlP was prepared similar to the sol gel process described above, except that a silver nitrate solution of appropriate concentration was combined at the same time as the aluminum nitrate and aqueous phosphoric acid. The resulting gel comprised the bioactive-AlP complex, wherein the bioactive material, in the form of silver ion, was chemically bonded with the AlP polymer. The dispersion was filtered, washed, and dried at the temperatures described above to provide the desired engineered porosity.

AlPs/bioactive-AlP complexes formed by the above-noted methods have a P:Al ratio of from about 0.5:1 to 1.5:1. It is desired that the AlPs/bioactive-AlP complexes have a P:Al ratio in this range because this provides a suitable range of particle morphology and properties that are compatible with desired formulation chemistries.

If desired, the bioactive-AlP complex as described herein can be initially made in the form of a concentrate, wherein an amount of the bioactive material is initially combined with a first amount of the AlP (in the case where the bioactive material is physically incorporated with the AlP polymer) or a first amount of the precursor materials used to form the AlP (in the case where the bioactive material is chemically bonded with the AlP polymer). This initially stage results in the formation of a bioactive-AlP complex condensate, i.e., having a high concentration of the bioactive material present. This complex condensate can then be used as feedstock to formulate a number of different formulations to meet different end-use applications. In an example embodiment, the complex condensate may be combined with further AlP to provide a bioactive-AlP complex having a relatively lower bioactive material content that is well suited for a certain end-use application. The ability to make such a complex condensation thereby adds a desired degree of flexibility to the process of obtaining different antimicrobial formulations for meeting different antimicrobial end-use applications.

AlP and bioactive-AlP complexes made in the manner described herein are provided in solid form as a white powder having a desired particle size or size distribution. The particle size will depend on such factors such as the binding polymer, and the particular end-use application. In an example embodiment, the AlP may have a particle size

distribution of D50 from about 0.5 to 8 microns. In an example embodiment, it is desired that the AlP have a P:Al ratio of from about 0.9 to 1, and have a particle size distribution of D50 of about 1 micron and D90 less than about 4 microns. For use in an antimicrobial chemical composition it is desired that the AlP have a particle size of less than about 20 microns, and preferably in the range of from about 0.5 to 10 microns, and more preferably in the range of from about 1.0 to 8.0 microns. Particle sizes of less than about 0.5 microns may interfere with the processing of certain chemical formulations and adversely affect film properties by increasing binder resin absorption.

AlP and bioactive-AlP complexes prepared in the manner described above may not be subjected to high-temperature drying or other thermal treatment for the purpose of retaining an amorphous structure and avoiding conversion to a crystalline structure. It has been discovered that AlPs formed in this manner retain the desired amorphous structure, even after low temperature drying. AlPs formed as disclosed herein have a structure comprising an engineered porosity that enables it to serve as a carrier for the bioactive material to provide the desired controlled delivery/release of the bioactive constituent for use in an antimicrobial chemical composition.

AAlPs as produced herein display a markedly increased water adsorption potential or degree of rehydration, when compared to crystalline AlP, that permits such AAlPs, once dehydrated by drying, to be rehydrated to contain up to about 25 percent by weight water. This feature is especially useful when the AlP is used in end-use applications calling for some degree of protection against corrosion, and wherein the AlP is present in a nonwater-borne binding polymer. In such application, the AlP acts, in addition to being a carrier for the bioactive material and being an corrosion inhibiting pigment, as a moisture scavenger to both slow water intrusion into the cured film and restrict water diffusion through the cured film.

Additionally, the rehydration feature of AlPs disclosed herein can be beneficial when placed in low humidity end-use applications. In such applications, AlPs can be used having a high or saturated moisture content that can operate to drive the bioactive constituent, e.g., have a built-in transport mechanism, to a surface of the cured antimicrobial chemical composition or composite to promote the presence of such bioactive constituent at the surface in the absence of surrounding moisture. Engineered

in this manner, antimicrobial chemical compositions comprising such AlP can function to provide a desired level of bioactive constituent at the surface in low humidity/moisture applications.

Antimicrobial chemical compositions described herein are prepared by combining a selected binding polymer with the AlP and the bioactive material in the manner and in the amounts described above. The resulting bioactive-AlP complex can be provided for composition formulation in the form of a dried powder or can be provided in the form of a slurry or liquid suspension depending on the formulation conditions or preferences.

Antimicrobial chemical compositions described herein, comprising the bioactive-AlP complex, comprise from about 5 to 1000 ppm, preferably 10 to 900 ppm, and 15 to 800 ppm of the bioactive material based on the total weight of the chemical composition. Such antimicrobial chemical compositions may comprise other materials, agents, and/or additives (in addition to the bioactive-AlP complex and the binding polymer), such as pigments, fillers, rheological agents, flow stabilizers, light-control stabilizers, and the like. For example, antimicrobial chemical compositions comprising a silver bioactive material may comprise an additive designed to inhibit the photo reduction of the silver, to thereby preserve the active state of the silver, contained within the composition, dried film and/or composite formed therefrom, to help ensure its effective service life.

Complexing the Bioactive Agent

It has been discovered that complexing the bioactive agent (when such is silver salt) with any of a number of organic complexing agents has an unexpected benefit on both the stabilization of the silver ion in the Ag-AlP complex and in enhancing its antimicrobial properties. Ag^+ will complex with a variety of ligands such as ammonia, imidazole (IMI), substituted IMI, and combinations thereof. The most common coordination number (the number of groups with which a metal may bond) for Ag^+ is 2, indicating that, in the simplest case, the structure for silver complexed with ammonia will be: $[Ag(NH_3)_2]^{+2}$. The reduction potential of Ag^+ is +0.799V and this provides a strong thermodynamic driving force for the reduction of Ag^+ ion to silver metal. However, complexing the silver ion with ammonia changes the reduction potential to 0.37V, making reduction harder. Hence stabilizing the silver ion by complexation

operates to increase its resistance to reduction and resulting discoloration and deactivation.

Further, chelated Ag^+ was found to be more effective by several orders of magnitude than free silver ion in antimicrobial activity. It is believed that Ag^+ ions are actively transported in the organism intracellularly by the chelating ligand in a protected complex and not by the free ion. Hence, successful complexation of the silver ion in Ag-AlP not only protects the silver ion (in the formulated product) from reduction and discoloration, but may also render it a more effective antimicrobial agent. This gives the product formulator more flexibility concerning loading levels, service scope and life, and price points.

The silver-ammonium complex is a simple linear structure: $[NH_3---Ag---NH_3]^{+2}$. In an example embodiment, IMI was selected as a complexing ligand for silver. Studies were conducted using IMI to determine whether benefits in stabilization and increased efficacy would accrue to the AlP system incorporating this complexed silver compound. IMI is a cyclic, planar, five membered ring exhibiting aromaticity. The non-protonated nitrogen atom has a lone pair of electrons that are not part of the aromatic pi (π) cloud that describes the electronic bonding structure of the molecule. These electrons provide a point of attack for protons or electrophilic groups (e.g., silver ion). It is believed that the silver ion will bond with two IMI molecules through their non-protonated nitrogen groups. However, there may also be weak bonding between silver atoms, in effect, aggregating more than one Ag-IMI complex together. Therefore, the different ratios of IMI to silver content were evaluated.

With respect to the nature of any interaction between the phosphate groups present in the various AlP compositions with silver ion or silver ion complexes, by analogy to the behavior of chlorates (which have four electronegative oxygen groups similar to phosphate), it is theorized that electrostatic attraction occurs between the oxygen in phosphate and the hydrogen in IMI as well as directly with the silver ion (where IMI is not present or where kinetic factors allow first interaction between the $P\text{-}O^-$ and the Ag^+).

In an example embodiment, the following factors relating to forming the silver complex and an Ag-AlP complex comprising the same were evaluated: (a) the ratio between silver ion and IMI in the system (two levels were picked at 1:2 and 1:4, Ag:IMI molar ratio); (b) preparing the complex in advance of the AlP condensation reaction (referred hereafter as "pre-mix") vs. in situ formation during AlP condensation; (c) order and point of addition of the silver-IMI complex (before or after AlP condensation); (d) temperature of the condensation reaction (room temperature or an elevated temperature such as 95°C); (e) effect of post-condensation neutralization (with ammonia) on the product; (f) overall order of addition for the condensation reaction (B to A, or A to B); and (g) presentation of the silver-IMI-phosphate product as a powder or a gel/slurry.

The testing showed that, changes to the binary condensation process as disclosed above for making Ag-AlP may provide certain desired improvements, wherein such changes may include: (a) reducing the addition time for all steps, which operated to provide improved properties of color stability and/or silver content retention after processing; (b) hot conditions in any step typically led to lower silver retention (because side reactions were enhanced that lead to such undesirable by-products as silver phosphate or silver oxide); (c) preparing each component separately (e.g., silver-IMI complex; aluminum hydroxide (ATH) slurry) and then combining them together and finally combining that combination with phosphoric acid gave the best possible result. It is believed that preparing the components separately rather than in situ allows each to form completely and in its purest form. Hence, when the aluminum phosphate condensation reaction occurs, the silver ion or the silver ion complex is already formed and it will be trapped within the forming AlP complex for maximum interaction with the AlP.

It was discovered that the addition of either Ag-IMI (1:2) or Ag-IMI (1:4) solution to 85% phosphoric acid gave a white slurry. Subsequent neutralization with ammonium hydroxide gave a white precipitate that could be dried to a white powder at about 110°C for 24 hours. This result is theorized to indicate that there is a fundamental chemical interaction between the silver complex and phosphate that leads to a discrete product (other than silver phosphate which is a yellow solid).

It was also discovered that the addition of slurry consisting of ATH and silver nitrate in the appropriate proportions to 85% phosphoric acid gave a stable white gel-like composition. The stability of this product is based on the uniform entrapment of the silver ion within the AlP matrix. Such stabilization is believed to be due to the formation of an ionic complex between the silver ion and the phosphate groups of the AlP in the slurry.

In view of the above test results, an example synthesis route for forming an Ag-AlP complex comprising the above-described Ag complex is as follows: (a) Pre-make a silver-IMI-nitrate complex [Ag-IMI] by the simple combination of silver nitrate with IMI in water at room temperature with stirring; (b) Pre-make an ATH slurry (20% solids be weight) by dispersing ATH in water at room temperature; (c) combine the ATH slurry with the Ag-IMI complex at room temperature by stirring to form a mixture; (d) add the ATH/Ag-IMI mixture (base) to 85% phosphoric acid at room temperature with stirring for a period of time, e.g., about one hour (in this order of addition, the acid pH operates to stabilize the silver ion in the complex); (e) allow the mixture to react at room temperature for an additional amount of time, e.g., one hour, after combining; and (f) the reaction mixture becomes a viscous gel-like composition, wherein the gel can either be isolated for use in water-based application, or can be dried to a white powder by heating, e.g., at about 110°C for a period of time, e.g., about 24 hours.

While the feature of forming an Ag-AlP complex comprising a complexed silver salt has been disclosed in the context of using the binary condensation process of making the Ag-AlP complex, it is to be understood that complexed bioactive material, e.g., silver salts, as disclosed herein can be used to form Ag-AlP complexes according to the other remaining methods or process of making Ag-AlP complexes as disclosed herein, wherein in such other methods the bioactive material, e.g., silver salt is replaced with the complexed bioactive material, e.g., complexed silver salt.

Also, while an example of combining the complexed bioactive material with the aluminum source prior to forming the AlP complex has been disclosed, it is to be understood that the complexed bioactive material can be added separately while the aluminum source and phosphate source are combined together, or can be precombined with the phosphate source as an alternative to precombining with the aluminum source.

Addition of Oxides of Metal

Various oxides of metals such as zinc and/or copper and the like may be incorporated into bioactive-AlP complexes as disclosed herein. In an example, it is theorized that the presence of zinc oxide in the bioactive-AlP complex may be useful for the purpose of absorbing ultraviolet light and providing inherent antimicrobial properties. In an example, zinc oxide was added to the ATH slurry pre-make (from step (b) above) and the chemical composition and performance properties were determined. XRD analysis of product from this reaction showed no crystal structures due to any zinc oxide or zinc phosphate crystalline component, indicating that the zinc was included in the amorphous component as part of the Ag-AlP complex. As noted above, the presence of the zinc component operates to both enhance the light stability and expand the antimicrobial activity of the composition.

While zinc oxide has been noted as an example metal oxide for incorporating into bioactive-AlP complexes as disclosed herein, it is to be understood that other oxides of metal including and not limited to copper, magnesium, barium, calcium, and combinations thereof, are intended to be within the scope of antimicrobial compositions as disclosed herein. Additionally, it is to be understood that the addition of one or more metal oxides to form bioactive-AlP complexes as disclosed herein can be performed by any one of the different methods or processes of making the bioactive-AlP complex as disclosed herein.

The metal oxide can be introduced during the process of making the bioactive-AlP complex prior to the step of forming the AlP, during the step of forming the AlP, or after the step of forming the AlP. In an example, the metal oxide is present at the time of forming the AlP, which means it may be precombined with the bioactive material or may be combined separately from the bioactive material at the time that the AlP is being formed. The metal oxide may be presented separately, may be presented in combination with the bioactive material, e.g., silver salt, and/or may be precombined with one or both of the aluminum source and phosphate source. In an example where the bioactive material is complexed, the metal oxide may be added to the bioactive material before or after complexing. In an example embodiment, the metal oxide is added after the bioactive material has been complexed.

Further Examples of Bioactive-AlP Complexes

Further examples of bioactive-AlP complexes as disclosed herein are provided for reference. These examples were prepared as described and tested for antimicrobial efficacy by determining the minimum inhibitory concentration (MIC) against the micro-organisms noted below, and were tested for light stability as described below.

Further Example 1: [CL20] Ag-AlP Complex

Preparation of ATH slurry – approximately 98.3 grams of ATH was dispersed in 560 grams of distilled water. In a separate vessel, approximately 11 grams of $AgNO_3$ was dissolved in 60 grams of distilled water. The $AgNO_3$ solution was added drop wise to the ATH slurry with stirring.

Condensation reaction – approximately 144 grams of 85% phosphoric acid was added to a reaction flask. The ATH/$AgNO_3$ slurry was added drop wise to the acid with stirring. The reaction mixture was stirred for two hours at room temperature in the dark. When the reaction was complete it formed an Ag-AlP complex, and the mixture was a wet cake without a distinct liquid layer. The percent solids of the cake was measured, and the Ag-AlP complex was suitable for use directly as an antimicrobial additive in water based formulations.

Further Example 2: [CL21] AgIMI(1:2)-AlP Complex

Preparation of pre-mixed components – approximately 14.1 grams of IMI was combined with 50 grams of distilled water. In a separate container, approximately 17.7 grams of $AgNO_3$ was dissolved in 50 grams of distilled water (run and store reaction in dark). The IMI solution was added drop wise to the $AgNO_3$ solution, and the solution was stirred for 30 minutes at room temperature in the dark forming an Ag-IMI complex. In a separate container, approximately 157.3 grams of ATH was dispersed in 560 grams of distilled water. The Ag-IMI complex solution was added drop wise with stirring to the ATH slurry, and the resulting mixture was mixed at room temperature in the dark for 30 minutes.

Condensation reaction – approximately 230 grams of 85% phosphoric acid was added to a reaction flask. The ATH and Ag-IMI complex mixture was added to the acid

drop wise with stirring at room temperature. The reaction mixture was stirred for two hours at room temperature in the dark. When the reaction was complete, the mixture was a wet cake made of AgIMI-AlP complex without a distinct liquid layer. The percent solids of the cake was measured, and the AgIMI-AlP complex was suitable for use directly as an antimicrobial additive in water based formulations.

Further Example 3: [CL22] AgIMI(1:4)-AlP Complex

The procedure of Further Example 2 was followed except that approximately 28.3 grams of IMI was used.

Further Example 4: [CL47] AgIMI(1:4)-ZnO-AlP Complex

Preparation of pre-mixed components – approximately 27.2 grams of IMI was combined with 50 grams of distilled water. In a separate vessel, approximately 17.7 grams of $AgNO_3$ was dissolved in 50 grams of distilled water. The IMI solution was added drop wise to the $AgNO_3$ solution and the mixture was stirred for 30 minutes at room temperature in the dark forming an AgIMI complex. In a separate vessel, approximately 157.3 grams of ATH and 53.1 grams of ZnO were combined with 550 grams of distilled water and dispersed for 30 minutes at room temperature. The AgIMI solution was added drop wise to the ATH-ZnO slurry and mixed for 30 minutes at room temperature.

Condensation reaction - the ATH-ZnO and AgIMI slurry was added drop wise to approximately 227.8 grams of 85% phosphoric acid. The glassware was washed with 50 grams of distilled water and the wash was added to the reaction mixture. The reaction mixture is stirred for two hours at room temperature in the dark forming an AgIMI-ZnO-AlP Complex.

Neutralization option to adjust pH - the resulting reaction slurry was titrated with approximately 28% NH_4OH to the target pH. Typically the pH of the slurry at the end of the reaction is between about 2.5 and 3.0. In the example, approximately 174.7 grams of 28% NH_4OH was used to bring the pH of the slurry to 7.03.

Post processing option - the slurry mixture resulting from the reaction and comprising the AgIMI-ZnO-AlP complex may be used directly as the gel (some

concentration by water evaporation may helpful to reach a specified solids content). Or the reaction slurry may be filtered, and the filter cake dried to a white powder at an elevated temperature, e.g., of about 110°C for 24 hours, or as low as about 60°C under vacuum for 24 hours.

Further Example 5: [CL50] Ag-ZnO-AlP Complex

Preparation of pre-mixed components – approximately 1 gram of $AgNO_3$ was dissolved in 50 grams of distilled water. Separately, approximately 84.5 grams of ATH and approximately 20.8 grams of ZnO were combined with 560 grams of distilled water and dispersed at room temperature for 30 minutes. The $AgNO_3$ solution was added drop wise to the ATH-ZnO slurry and mixed for 30 minutes at room temperature in the dark.

Condensation reaction - the ATH-ZnO-$AgNO_3$ slurry was added drop wise to approximately 122.5 grams of 85% phosphoric acid. Glassware was washed with 50 grams of distilled water and added to the reaction mixture. The mixture is stirred for two hours at room temperature in the dark forming an Ag-ZnO-AlP complex.

Post processing option – same as disclosed above in Further Example 4.

Further Example 6: [CL49] AgIMI(1:2)-ZnO-AlP Complex

Preparation of pre-mixed components – approximately 13.6 grams of IMI was dissolved in 50 grams of distilled water. Separately, approximately 17.7 grams of $AgNO_3$ was dissolved in 50 grams of distilled water. The IMI solution was added drop wise to the $AgNO_3$ solution and was stirred for 30 minutes in the dark at room temperature forming an AgIMI complex. Separately, approximately 123.9 grams of ATH and 33.5 grams of ZnO were combined with 560 grams of distilled water and dispersed at room temperature for 30 minutes. The AgIMI solution was added drop wise to the ATH-ZnO slurry and stirred for 30 minutes at room temperature in the dark.

Condensation reaction - the ATH-AgIMI-ZnO slurry was added drop wise at room temperature to approximately 179.4 grams of 85% phosphoric acid. Glassware was washed with 50 grams of distilled water and added to the reaction mixture. The

reaction slurry is stirred for two hours at room temperature in the dark producing an AgIMI-ZnO-AlP Complex.

Post processing option – same as disclosed above in Further Example 4.

Further Example 7: [CL48] AgIMI(1:4)-ZnO-AlP Complex

The procedure of Further Example 6 was followed except that approximately 27.2 grams of IMI was used.

Further Example 8: [CL51/52] AgIMI(1:4)-Cu_2O(Ag:Cu=1:1)-AlP Complex

Preparation of pre-mixed components – approximately 27.2 grams of IMI was dissolved in 50 grams of distilled water. Separately, approximately 17.7 grams of $AgNO_3$ was dissolved in 50 grams of distilled water. The IMI solution was added drop wise to the $AgNO_3$ solution and was stirred for 30 minutes in the dark at room temperature to form an AgIMI complex. Separately, approximately 153.3 grams of ATH and approximately 12.7 grams of Cu_2O were mixed with 560 grams of water and dispersed for 30 minutes. The AgIMI solution was added drop wise to the ATH-Cu_2O slurry and mixed for 30 minutes in the dark at room temperature.

Condensation reaction - the ATH-AgIMI-Cu_2O slurry was added drop wise at room temperature to approximately 222.1 grams of 85% phosphoric acid. Glassware was washed with 50 grams of distilled water and added to the reaction mixture. The reaction slurry was stirred for two hours at room temperature in the dark producing a AgIMI-Cu_2O-AlP complex.

The reaction mixture was filtered and dried at an elevated temperature, e.g., of about 110°C for 24 hours, to form a white powder. [CL51].

Neutralization option to adjust pH - procedure of Further Example 4. [CL52] – treated with ammonia.

Further Example 9: [CL53/54] Ag-ZnO-Cu_2O(Ag:Cu 1:0.5; Ag:Zn 1:3)-AlP Complex

Preparation of pre-mixed components – approximately 17.7 grams of $AgNO_3$ was dissolved in 50 grams of distilled water. Separately, approximately 153.3 grams of ATH and approximately 41.8 grams of ZnO and approximately 6.3 grams of Cu_2O were combined with 560 grams of distilled water and dispersed at room temperature for 30 minutes. The $AgNO_3$ solution was added drop wise to the ATH-ZnO-Cu_2O slurry and mixed for 30 minutes at room temperature in the dark.

Condensation reaction - the ATH-$AgNO_3$-ZnO-Cu_2O slurry was added drop wise at room temperature to approximately 222.1 grams of 85% phosphoric acid. Glassware was washed with 50 grams of distilled water and added to the reaction mixture. The reaction slurry was stirred for two hours at room temperature in the dark producing an Ag-ZnO-Cu_2O-AlP complex.

Cl53 is not filtered - the condensation reaction mixture is dried to a white powder at an elevated temperature, e.g., of about 110°C for 24 hours.

CL54 is filtered – the condensation reaction mixture is filtered and dried at an elevated temperature, e.g., of about 110°C for 24 hours, to form a white powder.

Further Example 10: [CL55/56/57] AgIMI(1:4)-ZnO-Cu_2O(Ag:Cu 1:0.5; Ag:Zn 1:3)-AlP Complex

Preparation of pre-mixed components – approximately 27.2 grams of IMI was dissolved in 50 grams of distilled water. Separately, approximately 6.3 grams of Cu_2O was dissolved in 50 grams of distilled water. The IMI solution was added drop wise to the Cu_2O solution and was stirred for 30 minutes in the dark at room temperature. Separately, approximately 17.7 grams of $AgNO_3$ was dissolved in 50 grams of distilled water. The $AgNO_3$ solution was added drop wise to the Cu_2O-IMI solution and stirred for 30 minutes at room temperature in the dark producing an AgIMI-Cu complex.

Separately, approximately 137.6 grams of ATH and approximately 41.8 grams of ZnO were mixed with 560 grams of distilled water and dispersed for 30 minutes.

The AgIMI-Cu_2O solution was added drop wise to the ATH-ZnO slurry and mixed for 30 minutes in the dark at room temperature forming an ATH-AgIMI-Cu_2OZnO solution.

Condensation reaction - the ATH-AgIMI-Cu_2O-ZnO slurry was added drop wise at room temperature to approximately 199.4 grams of 85% phosphoric acid. Glassware was washed with 50 grams of distilled water and added to the reaction mixture. The reaction slurry was stirred for two hours at room temperature in the dark producing an AgIMI-Cu_2OZnO-AlP complex.

CL55 - half of the final reaction mixture was filtered and dried at an elevated temperature, e.g., of about 110°C for 24 hours, to form a white powder.

The remaining half of the reaction was neutralized as described above.

CL56 – the final reaction mixture was neutralized and dried at an elevated temperature, e.g., of about 110°C for 24 hours, but not filtered.

CL57- the final reaction mixture was neutralized, filtered, and dried at an elevated temperature, e.g., of about 110°C for 24 hours.

Compositional Effects on Antimicrobial Activity (MIC)

The antimicrobial efficacy of the further examples was determined by measuring the MIC for each against the following: (a) Pseudomonas aeruginosa (bacteria); (b) Escherichia coli (bacteria); (c) Staphylococcus aureus; (d) Candida albicans (yeast); and (d) Aspergillus niger (fungi). MIC is the lowest concentration (ppm) of active ingredient at which organism growth is inhibited. The standard dilution method was used.

As illustrated in Table 1 below, series examples CL20 through CL50 demonstrated the effect of AgAlP, AgIMI complexation, and ZnO inclusion on MIC performance, which is summarized as follows:

1. All examples of AgAlP are effective in inhibiting bacterial growth at less than about 4 ppm, and in several cases, below about 1 ppm;

2. The addition of ZnO to the composition significantly decreases the MIC required to control yeast and fungi;
3. The combination of AgIMI complex and ZnO further minimize fungal growth.

Series CL51 through CL57 were a test of the effect of copper (as Cu_2O) on the properties of the system. At the concentration levels tested, copper had no significant effect on the antimicrobial performance of the Ag-IMI-AlP-Zn system [CL47=CL57=CL54]. However, the inclusion of these levels of copper in the composition had a surprising and beneficial effect on the color stability of formulations containing the composition, as discussed below.

Table 1.

Summary of MIC Testing

						MIC - ppm				
		AP Complex Type	Comment	pH	report	p. aerug	e. coli	s. aureus	yeast	fungi
CL20	gel	$AgNO_3$	Ag-AP control	2.5	#1		2	<1	63	16
			acidic							
CL21	gel	AgIMI (1:2)	Ag-IMI complex in AP	2.6	#1		<1	<1	125	63
			acidic							
CL22	gel	AgIMI (1:4)	Ag-IMI complex in AP	2.6	#1		<1	<1	125	63
CL47	pwdr	AgIMI (1:4) NH_3 ZnO	Ag-IMI complex and ZnO in AP	7.6	#1		2	2	7.8	125
			neutralized with NH_4		#2	0.78	3	0.78	12.5	100
CL48	slurry	AgIMI (1:4) ZnO	Ag-IMI complex and ZnO in AP	3.1	#1		3.8	2	7.8	16
			higher IMI level							
CL49	slurry	AgIMI (1:2) ZnO	Ag-IMI complex and ZnO in AP	2.9	#1		<1	<1	<1	7.8
					#2	0.39	1.5	0.39	12.5	50
CL50	slurry	$AgNO_3$ ZnO	Ag with ZnO in AP	2.6	#1		<1	<1	<1	16
					#2	0.78	3	0.78	12.5	25
CL51	pwd	AgIMI(1:4)-Ag:Cu (1:1)	Ag-IMI complex with Cu_2O in AP	6.7						
CL52	pwd	AgIMI(1:4)-Ag:Cu (1:1)	Ag-IMI complex with Cu_2O in AP	6.8	#2	12.5	12.5	12.5	100	100
			neutralized with NH_4							
CL53	pwd	$AgNO_3$ -AgCu(1:0.5)-AgZn(1:3)	AgAP complex with ZnO and Cu_2O	5.4	#2	50	100	100	50	100
			no IMI complex; not filtered							
CL54	pwd	$AgNO_3$ -AgCu(1:0.5)-AgZn(1:3)	AgAP complex with ZnO and Cu_2O	4.7	#2	25	50	25	25	100
			no IMI complex; filtered							
CL55	pwd	AgIMI(1:4)-AgCu(1:0.5)-AgZn(1:3)	AgIMI complex with ZnO and Cu_2O	6.3	#2					
			in AP;not filtered;not neutralized							
CL56	pwd	AgIMI(1:4)-AgCu(1:0.5)-AgZn(1:3)	AgIMI complex with ZnO and Cu_2O	6.6	#2	0.78	3.1	1.56	12.5	100
			in AP;not filtered;neutralized							
CL57	pwd	AgIMI(1:4)-AgCu(1:0.5)-AgZn(1:3)	AgIMI complex with ZnO and Cu_2O	6.7	#2	0.78	3.1	0.78	12.5	100
			in AP;filtered;not neutralized							

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Compositional Effects on Light Stability/Color Change – UV Stability Testing

Sample chemical compositions in the form of paints were prepared using latex as the binding polymer in an amount within the ranges presented above. The property of the Ag-AlP complexes incorporated in such paint formulation was tested at two levels, 100 ppm and 500 ppm of silver in the dry film.

Color Stability data are summarized in Table 2 presented below.

TABLE 2

COLOR STABILITY ΔE - QUV (B bulb) - 28 days exposure			
Sample	Composition	ΔE	ΔE
		100 ppm	500 ppm
CL42	AgIMI (no ZnO)	12.41	
CL47	AgIMI + ZnO	3.5	
CL50	AgAP + ZnO (no IMI)	5.4	
CL52	CL47 + Cu_2O (high)	1.91	5.43
CL53	CL50 + Cu_2O(low)	4.02	10.77
CL56	CL47 + Cu_2O (low) NF	2.26	10.11
CL57	CL47 + Cu_2O(low)F	2.52	
NF - not filtered; F - filtered			

The data presented in Table 2 shows color change (measured as ΔE using BYK Spectro-Guide Sphere Gloss Spectrophotometer) after exposure to UV light in a QUV chamber (UV B bulb) for 28 days. Color changes of less than about 2.0 are barely visible to the eye, while color changes of about 5.0 or less show very slight shading difference compared to the initial condition of the sample and would be considered acceptable in most applications.

Comparing CL42 and CL47, the positive effect of ZnO on color stability is clearly demonstrated. The color change is reduced from 12.41 to barely a perceptible 3.5.

The addition of cuprous oxide adds to this benefit, and is seen as a function of its concentration (i.e., the higher the level of cuprous oxide the better the effect). This trend is further illustrated for the results of CL51 (1.91), CL56 (2.26), and CL57 (2.52).

Generally, the presence of ZnO in the Ag-AlP complex is shown to provide further enhanced light stabilization. IMI-Ag complexation contributes a secondary/complementary light stabilization effect. While the inclusion of cuprous oxide contributes still further to light stabilization.

Antimicrobial chemical compositions disclosed herein may be provided in the form of a coating composition for applying to a desired substrate surface to provide a desired level of antimicrobial resistance. Such antimicrobial coating compositions can be formulated for use as a primer, a mid coat, or a top coat. Additionally such antimicrobial coating compositions may be used with or without a primer, as a mid or a top coat. Further, antimicrobial chemical compositions as disclosed herein may be formulated as a clear coating for placement over an existing substrate surface or underlying coating that may or may not be colored, thereby facilitating use of such clear coating over a variety of substrates or underlying coating surface to provide antimicrobial resistance without the need for special pigmenting to match existing substrate colors or the like.

Bioactive-AlP complexes as described herein provide bioactive components in a manner that ensures surface antimicrobial efficacy while permitting ease of formulation to meet a variety of end-use applications. The bioactive-AlP complex provides for uniform distribution of the bioactive ingredient, e.g., silver ion, throughout the chemical composition, dried film, composite, or formulated article. The bioactive-AlP complex provides the formulated bulk matrix with properties engineered to accommodate moisture induced transport: absorption, adsorption, desorption, diffusion of water and dissolved species in bulk. The bioactive-AlP complex is specifically engineered to release one or more bioactive constituent, e.g., silver ion, based on the concentration of the bioactive material incorporated and by the hydrophilicity and morphology of the complex (surface area and porosity). The bioactive-AlP complex as described herein can be introduced into formulated products such as pigments, or as an additive through bonding the phosphate functionality to certain functional groups of the binder matrix of

the bulk composite or film. Additionally, the bioactive-AlP complexes in thermally stable form can be incorporated into powder coating formulations to render such surfaces antimicrobial.

In one example embodiment, antimicrobial chemical compositions as described herein can be formulated into a film in which the bulk of the article serves as a reservoir or depot for the bioactive material or its constituent, e.g., silver ion. Such formulation can be engineered to optimize the following aspects of the antimicrobial mechanism: water diffusion into the film, water absorption and adsorption into the bioactive-AlP complex, salt dissolution within the complex, ion transport out of the complex, and bioactive material or its constituent transport through the matrix to the surface to be protected.

Alternatively, antimicrobial chemical compositions as described herein can be formulated into an enriched thin film (e.g., having a film thickness of less than about 25μ, and preferably less than about 10μ) engineered for physical durability balanced with water diffusion/bioactive material or its constituent transport properties to impart antimicrobial properties to a surface without incorporating the antimicrobial into the bulk of the article, e.g., where such incorporation may not be practical from a cost standpoint, or where the operative control mechanism may not be possible, e.g., a water impermeable plastic.

As described above, the combined AlP and bioactive material is provided in the form of a bioactive-AlP complex, where the bioactive material is either chemically bonded with, e.g., provided in the backbone of the AlP polymer, or is physically incorporated, enmeshed, encapsulated, or intertwined with the AlP polymer, depending on the particular method used to make the complex. Additionally, the bioactive material or its constituent may be present in the AlP polymer both chemically and physically. For example, when the bioactive-AlP complex is formed by combining the desired bioactive material at the time of forming the AlP, thereby facilitating chemical bonding between the bioactive material or its constituent with the AlP, a stoichiometric excess of the additional bioactive material may result in it being physically incorporated into the AlP molecule, in which case the resulting bioactive-AlP complex would include the

bioactive material or its constituent present in both chemically-bonded and physically-incorporated form.

As demonstrated above, embodiments of the invention provide a novel antimicrobial chemical compositions, novel bioactive-AlP complexes, and novel methods for making the same. While each has been described with respect to a limited number of embodiments, the specific features of one embodiment should not be attributed to other embodiments of the invention. No single embodiment is representative of all aspects of the invention. In some embodiments, the compositions or methods may include numerous compounds or steps not mentioned herein.

For example, if desired, antimicrobial chemical compositions can be prepared to additionally include one or more bioactive materials separately or in combination other than those specifically described that are known to have bioactive value. Any such additional bioactive material may or may not be incorporated with the bioactive-AlP complex, e.g., can exist as a separate dispersion with the binding polymer, and can operate to increase or complement or provide a synergistic antimicrobial effect of the chemical composition.

Additionally, while antimicrobial chemical compositions as presented in the examples provided herein have been described as comprising AlP in amorphous form, it is to be understood that antimicrobial chemical compositions as described herein can additionally comprise AlP in its known crystalline forms, and can comprise AlP in a combination of amorphous and crystalline forms.

In other embodiments, the compositions or methods do not include, or are substantially free of, any compounds or steps not enumerated herein. Variations and modifications from the described embodiments exist. The method of making the chemical compositions and/or AlP is described as comprising a number of acts or steps. These steps or acts may be practiced in any sequence or order unless otherwise indicated. Finally, any number disclosed herein should be construed to mean approximate, regardless of whether the word "about" or "approximately" is used in describing the number. The appended claims intend to cover all those modifications and variations as falling within the scope of the invention.

What is Claimed:

1. An antimicrobial chemical composition comprising;

a complex comprising a bioactive constituent, wherein the complex releases the bioactive constituent at a rate upon contact of the complex with moisture; and

a binder polymer forming a bulk matrix of the composition, wherein the complex is disposed within bulk matrix, and wherein the bulk matrix enables the bioactive constituent that is released from the complex to diffuse therethrough at a rate;

wherein the rate of release of the bioactive constituent from the complex is the same or different from the rate of diffusion of the bioactive constituent through the bulk matrix.

2. The chemical composition as recited in claim 1 wherein the complex comprises aluminum phosphate.

3. The chemical composition as recited in claim 2 wherein the aluminum phosphate is amorphous aluminum phosphate.

4. The chemical composition as recited in claim 2 wherein the aluminum phosphate is crystalline aluminum phosphate.

5. The chemical composition as recited in claim 2 wherein the aluminum phosphate is a combination of amorphous and crystalline aluminum phosphate.

6. The chemical composition as recited in claim 1 wherein the rate of release of the bioactive constituent is different from the rate of diffusion of the bioactive constituent.

7. The chemical composition as recited in claim 6 wherein the rate of release of the bioactive constituent is greater than the rate of diffusion of the bioactive constituent.

8. The chemical composition as recited in claim 6 wherein the rate of release of the bioactive constituent is less than the rate of diffusion of the bioactive constituent.

9. The chemical composition as recited in claim 1 wherein the complex comprises amorphous aluminum phosphate, wherein the complex has a porosity, and wherein the rate of release of the bioactive constituent is a function of the porosity.

10. The chemical composition as recited in claim 1 wherein the bioactive constituent is present in a bioactive material comprising a complexed silver material.

11. The chemical composition as recited in claim 10 wherein the complexed silver material comprises a complexing agent selected from the group consisting of ligands.

12. The chemical composition as recited in claim 11 wherein the ligands are selected from the group consisting of imidazole, substituted imidazole, ammonia, and combinations thereof.

13. The chemical composition as recited in claim 12 wherein the silver material comprises a silver salt and the ligand is imidazole.

14. The chemical composition as recited in claim 10 wherein the bioactive material further comprises a metal oxide.

15. The chemical composition as recited in claim 14 wherein the metal oxide is selected from the group of oxides that include metals consisting of copper, zinc, and combinations thereof.

16. An antimicrobial chemical composition comprising:

a binding polymer; and

a bioactive-aluminum phosphate complex dispersed within the binding polymer, the complex comprising an aluminum phosphate polymer and a bioactive material;

wherein the aluminum phosphate complex has an engineered porosity that, when the composition is cured, provides a controlled delivery of a bioactive constituent derived from the bioactive material when exposed to moisture.

17. The chemical composition as recited in claim 16 wherein the aluminum phosphate polymer is amorphous aluminum phosphate.

18. The chemical composition as recited in claim 16 wherein the aluminum phosphate polymer is crystalline aluminum phosphate.

19. The chemical composition as recited in claim 16 wherein the aluminum phosphate polymer is a combination of amorphous and crystalline aluminum phosphate

20. The chemical composition as recited in claim 16 wherein the controlled delivery of the bioactive constituent is in the range of from about 15 to 800 ppm.

21. The chemical composition as recited in claim 16 wherein the controlled delivery of the bioactive constituent is at least about 30 $\mu g/m^2$.

22. The chemical composition as recited in claim 16 wherein the amount of the bioactive material present in the complex is in the range of from 1 to 10 percent of the total weight of the complex.

23. The chemical composition as recited in claim 16 wherein the ratio of phosphate to aluminum is in the range of from about 0.5:1 to 1.5:1.

24. The chemical composition as recited in claim 16 wherein the bioactive material is physically interspersed in the aluminum phosphate polymer.

25. The chemical composition as recited in claim 16 wherein the bioactive material is a metal salt selected from the group consisting of metal ions of silver, calcium, copper, zinc, silver salts, copper salts, zinc salts, calcium salts, and combinations thereof.

26. The chemical composition as recited in claim 16 wherein the bioactive material is selected from the group consisting of silver ion, silver salts, and silver compounds capable of releasing silver ion when contacted by water, and combinations thereof.

27. The chemical composition as recited in claim 16 wherein the bioactive material is chemically bonded with the aluminum phosphate polymer.

28. The chemical composition as recited in claim 27 wherein the bioactive material is incorporated into the backbone of the aluminum phosphate polymer.

29. The chemical composition as recited in claim 16 wherein the bioactive material is a metal salt physically combined with the aluminum phosphate polymer.

30. The chemical composition as recited in claim 16 wherein the complex has a surface area greater than about 100 m^2/g.

31. The chemical composition as recited in claim 16 wherein the complex has a surface area of less than about 100 m^2/g.

32. The chemical composition as recited in claim 16 wherein the complex has a surface area of less than about 20 m^2/g

33. The chemical composition as recited in claim 16 wherein the controlled delivery of the bioactive constituent is different than a diffusion rate of the bioactive constituent through the binder polymer.

34. The chemical composition as recited in claim 16 comprising in the range of from about 0.01 to 1 weight percent of the bioactive material based on the total weight of the chemical composition.

35. The chemical composition as recited in claim 16 comprising in the range of from about 0.05 to 5 weight percent of the complex based on the total weight of the chemical composition.

36. The chemical composition as recited in claim 16 comprising in the range of from about 0.1 to 2 weight percent of the complex based on the total weight of the chemical composition.

37. The chemical composition as recited in claim 16 wherein the binding polymer is selected from the group consisting of polyurethanes, polyesters, solvent-based epoxies, solventless epoxies, water-borne epoxies, epoxy copolymers, acrylics, acrylic

copolymers, silicones, silicone copolymers, polysiloxanes, polysiloxane copolymers, alkyds and combinations thereof.

38. The chemical composition as recited in claim 16 wherein the bioactive-aluminum phosphate complex has a water adsorption potential of up to about 25 percent by weight water.

39. The chemical composition as recited in claim 16 wherein the bioactive-aluminum phosphate complex is has a controlled delivery of phosphate anion of less than about 1,500 ppm upon exposure to moisture.

40. The chemical composition as recited in claim 39 wherein the controlled delivery of phosphate anion is between about 100 to 500 ppm.

41. The chemical composition as recited in claim 16 wherein the bioactive material comprises a metal salt, and wherein the metal salt is combined with a material selected from the group consisting of ligands, metal oxides, and combinations thereof.

42. The chemical composition as recited in claim 41 wherein the metal salt is silver nitrate and the ligand is selected from the group consisting of ammonia, imidazole, substituted imidazole, and combinations thereof.

43. The chemical composition as recited in claim 12 wherein the metal salt is combined with a metal oxide.

44. A primer coating formed from the chemical composition recited in claim 16.

45. A mid-coat or top-coat of a coating system formed from the chemical composition recited in claim 16.

46. A system for providing antimicrobial protection comprising a coating composition applied to substrate and cured to form a film, the coating composition comprising a binding polymer with a bioactive-aluminum phosphate complex dispersed therein, wherein the complex comprises an aluminum phosphate combined with a

bioactive material, and wherein the complex is engineered to provide a controlled delivery of a bioactive constituent when exposed to moisture.

47. The system as recited in claim 46 wherein the bioactive material is combined with a further material selected from the group consisting of ligands, metal oxides, and combinations thereof.

48. The system as recited in claim 47 wherein the bioactive material is silver nitrate and is complexed with a ligand selected from the group consisting of ammonia, imidazole, substituted imidazole, and combinations thereof.

49. The system as recited in claim 48 wherein the bioactive material is combined with a metal oxide.

50. The system as recited in claim 49 wherein the metal oxide is selected from the group including oxides of metals consisting of copper, zinc, and combinations thereof.

51. The system as recited in claim 46 wherein the controlled delivery from the complex occurs at a release rate, and wherein the binding polymer has a diffusion rate for the bioactive constituent released from the complex, and wherein the release rate is different from the diffusion rate.

52. The system as recited in claim 46 wherein complex has a surface area greater than about 100 m^2/g.

53. The system as recited in claim 46 wherein the complex has a surface area less than about 20 m^2/g.

54. The system as recited in claim 46 wherein the controlled delivery of the bioactive constituent is in the range of from about 5 to 1,000 ppm.

55. The system as recited in claim 54 wherein the controlled delivery of the bioactive constituent is in the range of from about 10 to 900 ppm.

56. The system as recited in claim 54 wherein the controlled delivery of the bioactive constituent is in the range of from about 15 to 800 ppm.

57. The system as recited in claim 46 wherein the controlled delivery of the bioactive constituent is at least about 30 $\mu g/m^2$.

58. The system as recited in claim 46 wherein the bioactive material is a metal ion selected from the group consisting of silver, copper, zinc, and combinations thereof, and wherein the metal ion is incorporated in the backbone of the aluminum phosphate.

59. The system as recited in claim 58 wherein the metal ion is chemically bonded in the aluminum phosphate complex.

60. The system as recited in claim 46 wherein the bioactive material is a metal salt selected from the group consisting of silver, copper, zinc, calcium, and combinations thereof, which is physically incorporated with the aluminum phosphate.

61. The system as recited in claim 60 wherein the bioactive material is a metal ion selected from the group consisting of silver, copper, zinc, calcium, and combinations thereof, which is incorporated in the backbone of the aluminum phosphate .

62. The system as recited in claim 46 comprising a controlled release rate of phosphate anion of between about 100 and 1,500 ppm upon exposure to moisture.

63. The system as recited in claim 46 wherein the binding polymer is selected from the group consisting of polyurethanes, polyesters, solvent-based epoxies, solventless epoxies, water-borne epoxies, epoxy copolymers, acrylics, acrylic copolymers, silicones, silicone copolymers, polysiloxanes, polysiloxane copolymers, alkyds and combinations thereof.

64. A method for making a bioactive-aluminum phosphate complex comprising the steps of:

forming an amorphous aluminum phosphate by combining an aluminum source, with a phosphate source in an aqueous solution at suitable pH to form a dispersion of aluminum phosphate; and

adding a bioactive material during or after the step of forming so that the bioactive material is combined with the aluminum phosphate to form the bioactive-aluminum phosphate complex.

65. The method as recited in claim 64 wherein during the step of forming, the dispersion is amorphous aluminum phosphate.

66. The method as recited in claim 64 wherein during the step of forming, the dispersion is crystalline aluminum phosphate.

67. The method as recited in claim 64 wherein the step of forming, the dispersion is a combination of amorphous and crystalline aluminum phosphate

68. The method as recited in claim 64 comprising the further step of adding further aluminum phosphate to the bioactive-aluminum phosphate complex.

69. A method for making an antimicrobial chemical composition comprising adding a polymer binding material to the bioactive-aluminum phosphate complex prepared according to claim 64, wherein the composition when cured provides a controlled delivery of a bioactive constituent derived from the bioactive material upon exposure to moisture.

70. The method as recited in claim 64 wherein the controlled delivery of the bioactive constituent is in the range of from about 10 to 900 ppm.

71. The method as recited in claim 64 wherein the controlled delivery of the bioactive constituent is about 100 ppm or greater.

72. The method as recited in claim 64 wherein the controlled delivery of the bioactive constituent is at least about 30 $\mu g/m^2$.

73. The method as recited in claim 64 wherein the amount of the bioactive material in the complex is in the range of from about 1 to 10 percent by weight of the total complex.

74. The method as recited in claim 64 wherein the ratio of phosphate to aluminum is in the range of from about 0.5:1 to 1.5:1.

75. The method as recited in claim 64 wherein the bioactive material comprises a metal salt, and wherein the metal salt is complexed with a ligand before the step of adding.

76. The method as recited in claim 75 wherein the metal salt is silver nitrate and the ligand is selected from the group consisting of imidazole, substituted imidazole, ammonia, and combinations thereof.

77. The method as recited in claim 75 wherein the complex further comprises a metal oxide.

78. The method as recited in claim 64 wherein the bioactive material comprises a metal salt, and wherein the complex further comprises a metal oxide.

79. The method as recited in claim 75 wherein the aluminum source is aluminum hydroxide and the phosphate source is phosphoric acid, wherein the aluminum source is in aqueous form and is premixed with the complexed metal salt to form a complexed metal salt-aluminum hydroxide mixture, and during the step of adding the complexed metal salt-aluminum hydroxide mixture is added to the phosphoric acid.

80. A method for making an antimicrobial chemical composition comprising a bioactive material dispersed within an aluminum phosphate, the method comprising the steps of:

forming an aluminum phosphate by combining an aluminum source, with a phosphate source in an aqueous solution at suitable pH to form a dispersion of aluminum phosphate;

adding a bioactive material during or after the step of forming so that the bioactive material is disposed in the aluminum phosphate forming a bioactive-aluminum phosphate complex; and

combining a polymer binding material with the bioactive-aluminum phosphate complex to form the antimicrobial chemical composition;

wherein the composition when cured provides a controlled delivery of a bioactive constituent derived from the bioactive material upon exposure to moisture of from about 10 to 900 ppm.

81. The method as recited in claim 80 wherein the step of adding is performed after the step of forming, and the bioactive material is physically combined with the aluminum phosphate.

82. The method as recited in claim 81 wherein the bioactive material is a metal salt selected from the group consisting of silver salts, copper salts, zinc salts, calcium salts, and combinations thereof.

83. The method as recited in claim 80 wherein the step of adding is performed during the step of forming, and the bioactive material is chemically bonded with the aluminum phosphate.

84. The method as recited in claim 83 wherein the bioactive material is a metal ion selected from the group consisting of silver, copper, zinc, calcium, and combinations thereof.

85. The method as recited in claim 80 wherein during the step of forming, the dispersion is amorphous aluminum phosphate.

86. The method as recited in claim 80 wherein during the step of forming, the dispersion is crystalline aluminum phosphate.

87. The method as recited in claim 80 wherein during the step of forming, the dispersion is a combination of amorphous and crystalline aluminum phosphate

88. The method as recited in claim 80 wherein the step of forming comprises:

combining an aluminum salt with phosphoric acid in an aqueous solution; and

adding a sufficient amount of base material to increase the pH of the solution to form a gel structure, wherein the gel comprises a three-dimensional structure of linked-together amorphous aluminum phosphate particles.

89. The method as recited in claim 88 wherein the aluminum salt is aluminum nitrate, and the base material is ammonium hydroxide.

90. The method as recited in claim 88 further comprising, before the step of combining the polymer binder material, drying the gel to an elevated temperature sufficient to remove unwanted materials therefrom.

91. The method as recited in claim 90 wherein the step of drying takes place at greater than about 200°C to remove ammonium nitrate, ammonia, and water from the gel.

92. The method as recited in claim 88 further comprising, before the step of combining the polymer binder material, drying the gel at an elevated temperature to provide a desired porosity that promotes the controlled delivery of the bioactive material.

93. The method as recited in claim 88 wherein the amorphous aluminum phosphate has a surface area greater than about 100 m^2/g.

94. The method as recited in claim 80 wherein the step of forming comprises combining aluminum hydroxide and phosphoric acid to form a solution comprising an acidic aluminum phosphate.

95. The method as recited in claim 94 wherein the step of adding comprises:
adding the bioactive material in the form of a metal salt to the acidic aluminum phosphate; and
neutralizing the mixture of bioactive material and acidic aluminum phosphate to form the aluminum phosphate.

96. The method as recited in claim 95 wherein the metal salt is silver nitrate and the mixture is neutralized with sodium aluminate.

97. The method as recited in claim 80 wherein before the step of combining, drying the mixture to a temperature of less than about 200°C.

98. The method as recited in the claim 80 wherein the complex has a surface area of less than about 20 m^2/g

99. The method as recited in the claim 98 wherein the surface area is between about 100 and 250 m^2/g.

100. The method as recited in claim 80 wherein the controlled delivery is about 100 ppm or greater.

101. The method as recited in claim 80 wherein the bioactive aluminum phosphate complex comprises in the range of from about 1 to 10 weight percent of the bioactive material.

102. The method as recited in claim 80 comprising in the range of from about 0.1 to 2 weight percent of the bioactive material based on the total weight of the chemical composition.

103. The method as recited in claim 80 wherein the chemical composition is engineered to provide a controlled delivery of phosphate anion of less than about 1,500 ppm upon exposure to moisture.

104. The method as recited in claim 103 wherein the controlled delivery of phosphate anion is between about 100 to 500 ppm.

105. A method for making an antimicrobial chemical composition comprising a bioactive material combined with an aluminum phosphate, the method comprising the steps of:

forming an aluminum phosphate by combining an aluminum source, with a phosphate source in an aqueous solution at suitable pH to form a dispersion of aluminum phosphate;

adding a bioactive material to the amorphous aluminum phosphate after the step of forming to provide a complex wherein the bioactive material is physically incorporated in the aluminum phosphate to form a bioactive-aluminum phosphate complex; and

combining a polymer binding material with the complex to form the antimicrobial chemical composition;

wherein the composition when cured provides a controlled delivery of a bioactive constituent derived from the bioactive material of 100 ppm or greater upon exposure to moisture.

106. The method as recited in claim 105 wherein during the step of forming, the dispersion is amorphous aluminum phosphate.

107. The method as recited in claim 105 wherein during the step of forming, the dispersion is crystalline aluminum phosphate.

108. The method as recited in claim 105 wherein during the step of forming, the dispersion is combination of amorphous and crystalline aluminum phosphate

109. The method as recited in claim 105 wherein the aluminum phosphate has a surface area of less than about 100 m^2/g.

110. The method as recited in claim 105 wherein during the step of adding, an amount of the bioactive material in the form of a metal ion is chemically bonded to the aluminum phosphate.

111. The method as recited in claim 105 wherein the step of forming comprises:

combining an aluminum salt with phosphoric acid in an aqueous solution; and

adding a sufficient amount of base material to increase the pH of the solution to form a gel structure, wherein the gel comprises a three-dimensional structure of linked-together amorphous aluminum phosphate particles.

112. The method as recited in claim 105 wherein the step of combining comprises:

combining aluminum hydroxide and phosphoric acid to form a solution comprising an acidic aluminum phosphate condensate; and

neutralizing the condensate to form amorphous aluminum phosphate.

113. A method for making an antimicrobial chemical composition comprising a bioactive material combined with aluminum phosphate, the method comprising the steps of:

combining aluminum hydroxide and phosphoric acid to form a solution comprising an acidic aluminum phosphate condensate;

combining a bioactive material during or after the step of forming the acidic aluminum phosphate condensate to form mixture comprising a bioactive-aluminum phosphate complex comprising the bioactive material; and

combining a polymer binding material with the complex to form the chemical composition.

114. The method as recited in claim 113 wherein the complex comprises amorphous aluminum phosphate.

115. The method as recited in claim 113 wherein the complex comprises crystalline aluminum phosphate.

116. The method as recited in claim 113 further comprising the step of adding a neutralizing agent to the acidic aluminum phosphate complex to increase its pH.

117. The method as recited in claim 113 wherein the complex comprises the bioactive material chemically bonded with the aluminum phosphate.

118. The method as recited in claim 113 wherein after the step of combining the bioactive material, adding further aluminum hydroxide to the mixture.

119. The method as recited in claim 113 wherein during the step of combining the aluminum hydroxide and phosphoric acid, the aluminum hydroxide is provided in slurry form and is added slowly to the phosphoric acid.

120. The method as recited in claim 113 wherein during the step of combining the aluminum hydroxide and phosphoric acid, the phosphoric acid is slowly added to the aluminum hydroxide.

121. The method as recited in claim 113 wherein the step of combining the aluminum hydroxide and phosphoric acid comprises the steps of:

adding the phosphoric acid to a first amount of the aluminum hydroxide to form an acidic aluminum phosphate solution; and

adding the acidic aluminum phosphate solution to a second amount of the aluminum hydroxide to form the condensate.

122. The method as recited in claim 113 wherein the bioactive-aluminum phosphate complex has surface area of less than about 20 m^2/g, and wherein when the composition is cured it provides a controlled delivery of the bioactive constituent of from about 10 to 900 ppm upon exposure to moisture.

123. The method as recited in claim 116 wherein the neutralizing agent is selected from the group consisting of aluminum hydroxide, calcium hydroxide, and combinations thereof, and wherein the bioactive material constituent is a metal ion selected from the group consisting of silver, copper, zinc, calcium, and combinations thereof.

124. The method as recited in claim 113 wherein, before the step of combining the polymer binding material, drying the aluminum phosphate to a temperature of less than about 200°C.

125. The method as recited in claim 113 wherein the bioactive material is selected from the group of metal salts consisting of silver salts, copper salts, zinc salts, calcium salts, and combinations thereof.

126. A method for making an antimicrobial chemical composition comprising a bioactive material combined with an amorphous aluminum phosphate, the method comprising the steps of:

combining a bioactive material with aluminum nitrate and phosphoric acid to form a solution, and neutralizing the solution to form a gel comprising amorphous aluminum phosphate, wherein the gel comprises a bioactive constituent of the bioactive material incorporated into a backbone of the amorphous aluminum phosphate, thereby forming a bioactive-aluminum phosphate complex; and

combining a polymer binding material with the complex to form the chemical composition.

127. The method as recited in claim 126 wherein the complex has a surface area of greater than about $100m^2/g$, and wherein when the composition provides a controlled delivery of the bioactive constituent of from about 10 to 900 ppm upon exposure to moisture.

128. The method as recited in claim 126 wherein the solution is neutralized by adding ammonium hydroxide, and the bioactive material constituent is a metal ion selected from the group consisting of silver, copper, zinc, calcium, and combinations thereof.

129. The method as recited in claim 126 wherein, before the step of combining the polymer binding material, drying the amorphous aluminum phosphate to a temperature of greater than about 200°C.

130. The method as recited in claim 126 wherein the bioactive material is selected from the group of metal salts consisting of silver salts, copper salts, zinc salts, calcium salts, and combinations thereof.

131. A method for making an antimicrobial chemical composition comprising a bioactive material combined with aluminum phosphate, the method comprising the steps of:

combining a bioactive material with aluminum hydroxide to form a mixture;

adding the mixture to phosphoric acid to form a bioactive-aluminum phosphate complex comprising the bioactive material; and

combining a polymer binding material with the complex to form the chemical composition.

132. The method as recited in claim 131 wherein the bioactive material comprises a metal salt.

133. The method as recited in claim 132 wherein before the step of combining, a complex is formed by combing the metal salt with a ligand.

134. The method as recited in claim 133 wherein the metal salt is silver nitrate and the ligand is selected from the group consisting of ammonia, imidazole, substituted imidazole, and combinations thereof.

135. The method as recited in claim 133 wherein the bioactive-aluminum phosphate complex further comprises a metal oxide.

136. The method as recited in claim 131 wherein the bioactive-aluminum phosphate complex further comprises a metal oxide.

137. The method as recited in claim 131 wherein the steps of adding and combining are performed at room temperature.

138. The method as recited in claim 131 wherein the aluminum hydroxide comprises amorphous aluminum hydroxide.

139. The method as recited in claim 131 wherein the complex comprises amorphous aluminum phosphate.

140. The method as recited in claim 131 wherein the complex comprises crystalline aluminum phosphate.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/036672

A. CLASSIFICATION OF SUBJECT MATTER
INV. A01N59/16 A01N25/08 A01N25/10 A01N25/22 A01P1/00
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ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A01N A01P C09D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 116 865 A1 (KANEBO LTD [JP]; KANTO KAGAKU [JP]) 29 August 1984 (1984-08-29) page 1, lines 1-5 page 3, line 8 - page 4, line 15 examples 1-5	1,6,10, 14,15
X	EP 0 253 663 A2 (HAGIWARA ZENJI [JP]; KANEBO LTD [JP]) 20 January 1988 (1988-01-20) page 1, lines 4-7, 39-56 pages 20-33; examples 1-12	1,6,10, 14,15

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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C09D 5/14(2006.01)

权利要求书9页 说明书30页

(54)发明名称

抗菌化学组合物

(57)摘要

抗菌化学组合物，包括分散在粘结剂聚合物中的磷酸铝(AlP)固体，其中一种或多种生物活性材料包含在AlP中，形成生物活性-AlP配合物。该配合物所包含的生物活性材料可以化学性地连接该AlP，物理性地与该AlP组合，或两者皆有。该配合物可以用沉淀、缩合或溶胶-凝胶的方法来形成。该配合物经过改造，以在接触水分时，向由所述组合物形成的膜或复合材料以所需抗菌水平受控递送生物活性材料或其成分，至少为约30μg/m^2，且还可以通过释放钝化磷酸盐离子，来提供期望的防腐水平。与已知的抗菌化学组合物相比，所述抗菌化学组合物提高了针对大范围微生物的有效、持久抗性水平。

CN 104640450 A

1. 一种抗菌化学组合物，包括：

包含生物活性成分的配合物，其中所述配合物在与水分接触时以一定速率释放所述生物活性成分；以及

形成所述组合物的主体基质的粘结剂聚合物，其中所述配合物位于主体基质中，且所述主体基质使得从所述配合物释放的所述生物活性成分能够以一定速率在该主体基质中扩散；其中，所述生物活性成分从所述配合物释放的速率与所述生物活性成分在所述主体基质中的扩散速率相同或不同。

2. 根据权利要求 1 所述的化学组合物，其特征在于，所述配合物包括磷酸铝。

3. 根据权利要求 2 所述的化学组合物，其特征在于，所述磷酸铝为非结晶磷酸铝。

4. 根据权利要求 2 所述的化学组合物，其特征在于，所述磷酸铝为结晶磷酸铝。

5. 根据权利要求 2 所述的化学组合物，其特征在于，所述磷酸铝是非结晶磷酸铝和结晶磷酸铝的组合。

6. 根据权利要求 1 所述的化学组合物，其特征在于，所述生物活性成分的释放速率不同于所述生物活性成分的扩散速率。

7. 根据权利要求 6 所述的化学组合物，其特征在于，所述生物活性成分的释放速率高于所述生物活性成分的扩散速率。

8. 根据权利要求 6 所述的化学组合物，其特征在于，所述生物活性成分的释放速率低于所述生物活性成分的扩散速率。

9. 根据权利要求 1 所述的化学组合物，其特征在于，所述配合物包含非结晶磷酸铝，所述配合物具有孔隙度，且所述生物活性成分的释放速率是所述孔隙度的函数。

10. 根据权利要求 1 所述的化学组合物，其特征在于，所述生物活性成分存在于包含复合银材料的生物活性材料中。

11. 根据权利要求 10 所述的化学组合物，其特征在于，所述复合银材料包含选自配体的配合剂。

12. 根据权利要求 11 所述的化学组合物，其特征在于，所述配体选自：咪唑、取代咪唑、氨及其组合。

13. 根据权利要求 12 所述的化学组合物，其特征在于，所述银材料包括银盐，且所述配体为咪唑。

14. 根据权利要求 10 所述的化学组合物，其特征在于，所述生物活性材料还包括金属氧化物。

15. 根据权利要求 14 所述的化学组合物，其特征在于，所述金属氧化物选自含有铜、锌及其组合的氧化物。

16. 一种抗菌化学组合物，包括：

粘结剂聚合物；以及

散布在所述粘结剂聚合物中的生物活性 - 磷酸铝配合物，所述配合物包含磷酸铝聚合物和生物活性材料；其中所述磷酸铝配合物具有改造的孔隙度，由此当所述组合物固化时，能够在当所述生物活性材料接触水分时，提供来自所述生物活性材料的生物活性成分的受控递送。

17. 根据权利要求 16 所述的化学组合物，其特征在于，所述磷酸铝聚合物为非结晶磷

酸铝。

18. 根据权利要求 16 所述的化学组合物，其特征在于，所述磷酸铝聚合物为结晶磷酸铝。

19. 根据权利要求 16 所述的化学组合物，其特征在于，所述磷酸铝聚合物是非结晶磷酸铝和结晶磷酸铝的组合。

20. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性成分的受控递送在约 15-800ppm 的范围内。

21. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性成分的受控递送为至少约 30 μg/m^2。

22. 根据权利要求 16 所述的化学组合物，其特征在于，所述配合物中的生物活性材料含量在配合物总重量的 1-10% 范围内。

23. 根据权利要求 16 所述的化学组合物，其特征在于，所述磷酸与铝的比率范围为约 0.5: 1 至 1.5: 1。

24. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性材料是物理性地散布在磷酸铝聚合物中的。

25. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性材料为金属盐，该金属盐选自：银、钙、铜、锌金属离子，银盐，铜盐，锌盐，钙盐，及其组合。

26. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性材料选自能够在接触水时释放银离子的银离子、银盐和银化合物及其组合。

27. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性材料与磷酸铝聚合物化学性结合。

28. 根据权利要求 27 所述的化学组合物，其特征在于，所述生物活性材料被结合进磷酸铝聚合物的骨架中。

29. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性材料是与磷酸铝聚合物物理性结合的金属盐。

30. 根据权利要求 16 所述的化学组合物，其特征在于，所述配合物的表面积大于约 100 m^2/g。

31. 根据权利要求 16 所述的化学组合物，其特征在于，所述配合物的表面积小于约 100 m^2/g。

32. 根据权利要求 16 所述的化学组合物，其特征在于，所述配合物的表面积小于约 20 m^2/g。

33. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性成分的受控递送与所述生物活性成分在所述粘结剂聚合物中的扩散速率不同。

34. 根据权利要求 16 所述的化学组合物，其特征在于，其中包括了占所述化学组合物总重量约 0.01-1% 重量百分比的生物活性材料。

35. 根据权利要求 16 所述的化学组合物，其特征在于，其中包括了占所述化学组合物总重量约 0.05-5% 重量百分比的所述配合物。

36. 根据权利要求 16 所述的化学组合物，其特征在于，其中包括了占所述化学组合物总重量约 0.1-2% 重量百分比的所述配合物。

37. 根据权利要求 16 所述的化学组合物，其特征在于，所述粘结剂聚合物选自聚氨酯、聚酯、溶剂型环氧树脂、不溶性环氧树脂、水性环氧树脂、环氧树脂共聚物、亚克力、亚克力共聚物、硅胶、硅胶共聚物、聚硅氧烷、聚硅氧烷共聚物、醇酸树脂及其组合。

38. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性－磷酸铝配合物的水吸附势为多至约 25% 水重。

39. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性－磷酸铝配合物在接触水分时受控递送约 1500ppm 以下的磷阴离子。

40. 根据权利要求 39 所述的化学组合物，其特征在于，所述受控递送磷阴离子在约 100-500ppm 之间。

41. 根据权利要求 16 所述的化学组合物，其特征在于，所述生物活性材料包括金属盐，且所述金属盐与选自配体、金属氧化物及其组合的材料相结合。

42. 根据权利要求 41 所述的化学组合物，其特征在于，所述金属盐为硝酸银，所述配体选自氨、咪唑、取代咪唑及其组合。

43. 根据权利要求 12 所述的化学组合物，其特征在于，所述金属盐与金属氧化物相结合。

44. 用根据权利要求 16 所述的化学组合物制成的底漆涂层。

45. 用根据权利要求 16 所述的化学组合物制成的涂层系统的中间涂层或面漆涂层。

46. 一种用于提供抗菌保护的系统，包括施加在底物上并固化以形成膜的涂层组合物，所述涂层组合物包括内部分散有生物活性－磷酸铝配合物的粘结剂聚合物，其中所述配合物包括与生物活性材料结合的磷酸铝，且所述配合物经过改造以在接触水分时提供生物活性成分的受控递送。

47. 根据权利要求 46 所述的系统，其特征在于，所述生物活性材料与另一种选自配体、金属氧化物及其组合的材料相组合。

48. 根据权利要求 47 所述的系统，其特征在于，所述生物活性材料是硝酸银，且与选自氨、咪唑、取代咪唑及其组合的配体相复合。

49. 根据权利要求 48 所述的系统，其特征在于，所述生物活性材料与金属氧化物相结合。

50. 根据权利要 49 所述的系统，其特征在于，所述金属氧化物选自铜、锌及其组合的金属的氧化物。

51. 根据权利要求 46 所述的系统，其特征在于，从配合物的受控递送以一定的释放速率发生，且从所述配合物释放的生物活性成分在所述粘结剂聚合物中具有一扩散速率，且所述释放速率不同于所述扩散速率。

52. 根据权利要求 46 所述的系统，其特征在于，所述配合物的表面积大于约 100 m^2/g。

53. 根据权利要求 46 所述的系统，其特征在于，所述配合物的表面积低于约 20 m^2/g。

54. 根据权利要求 46 所述的系统，其特征在于，所述生物活性成分的受控递送在约 5-1000ppm 范围内。

55. 根据权利要求 54 所述的系统，其特征在于，所述生物活性成分的受控递送在约 10-900ppm 范围内。

56. 根据权利要求 54 所述的系统，其特征在于，所述生物活性成分的受控递送在约

15-800ppm 的范围内。

57. 根据权利要求 46 所述的系统，其特征在于，所述生物活性成分的受控递送至少为约 30μg/m^2。

58. 根据权利要求 46 所述的系统，其特征在于，所述生物活性材料是选自银、铜、锌及其组合的金属离子，且所述金属离子被结合进所述磷酸铝的骨架中。

59. 根据权利要求 58 所述的系统，其特征在于，所述金属离子化学键合在所述磷酸铝配合物中。

60. 根据权利要求 46 所述的系统，其特征在于，所述生物活性材料是选自银、铜、锌、钙及其组合的金属盐，且物理性地结合在所述磷酸铝中。

61. 根据权利要求 60 所述的系统，其特征在于，所述生物活性材料是选自选自银、铜、锌、钙及其组合的金属离子，且结合在所述磷酸铝的骨架中。

62. 根据权利要求 46 所述的系统，其特征在于，所述磷阴离子在接触水分时的受控释放速率在约 100-1500ppm 之间。

63. 根据权利要求 46 所述的系统，其特征在于，所述粘结剂聚合物选自聚氨酯、聚酯、溶剂型环氧树脂、不溶性环氧树脂、水性环氧树脂、环氧树脂共聚物、亚克力、亚克力共聚物、硅胶、硅胶共聚物、聚硅氧烷、聚硅氧烷共聚物、醇酸树脂及其组合。

64. 一种用于制备生物活性 - 磷酸铝配合物的方法，包括以下步骤：

通过在适当 pH 的水溶液中，令铝源与磷酸源结合形成磷酸铝分散系，以形成非结晶磷酸铝；

在上述形成步骤期间或之后添加生物活性材料，从而令该生物活性材料与所述磷酸铝结合，以形成所述生物活性 - 磷酸铝配合物。

65. 根据权利要求 64 所述的方法，其特征在于，在所述形成步骤中，所得分散系是非结晶磷酸铝。

66. 根据权利要求 64 所述的方法，其特征在于，在所述形成步骤中，所述分散系为结晶磷酸铝。

67. 根据权利要求 64 所述的方法，其特征在于，在所述形成步骤中，所述分散系为非结晶磷酸铝和结晶磷酸铝的组合。

68. 根据权利要求 64 所述的方法，其特征在于，包括又一个向所述生物活性 - 磷酸铝配合物添加更多磷酸铝的步骤。

69. 一种用于制备抗菌化学组合物的方法，包括向根据权利要求 64 所述方法制备而成的生物活性 - 磷酸铝配合物中添加聚合物，其中所述组合物在固化后，在接触水分时提供来自所述生物活性材料的生物活性成分的受控递送。

70. 根据权利要求 64 所述的方法，其特征在于，所述生物活性成分的受控递送的范围在约 10-900ppm 之间。

71. 根据权利要求 64 所述的方法，其特征在于，所述生物活性成分的受控递送的范围在约 100ppm 或以上。

72. 根据权利要求 64 所述的方法，其特征在于，所述生物活性成分的受控递送至少为约 30 μg/m^2。

73. 根据权利要求 64 所述的方法，其特征在于，所述配合物中的生物活性材料的量为

占配合物总重量的约 1-10%。

74. 根据权利要求 64 所述的方法，其特征在于，所述磷 :铝的比率在约 0.5:1 至 1.5:1 的范围内。

75. 根据权利要求 64 所述的方法，其特征在于，所述生物活性材料包括金属盐，所述金属盐在添加步骤前与配体复合。

76. 根据权利要求 75 所述的方法，其特征在于，所述金属盐为硝酸银，所述配体选自氨、咪唑、取代咪唑及其组合。

77. 根据权利要求 75 所述的方法，其特征在于，所述配合物还包含金属氧化物。

78. 根据权利要求 64 所述的方法，其特征在于，所述生物活性材料包括金属盐，且所述配合物进一步包含金属氧化物。

79. 根据权利要求 75 所述的方法，其特征在于，所述铝源为氢氧化铝，且所述磷源是磷酸，所述磷源存在于水性形式且与复合金属盐预先混合以形成复合金属盐 - 氢氧化铝混合物，且在添加步骤中，将所述复合金属盐 - 氢氧化铝混合物添加至所述磷酸。

80. 一种用于制备抗菌化学组合物的方法，所述抗菌化学组合物含有分散在磷酸铝中的生物活性材料，所述方法包括以下步骤 :

通过使铝源和磷酸盐源在适当 pH 的水溶液中相结合来形成磷酸铝分散系，以形成磷酸铝 ;

在上述形成步骤期间或之后，添加生物活性材料，使得该生物活性材料分散在磷酸铝中，形成生物活性 - 磷酸铝配合物 ;以及

使聚合物粘结材料与所述生物活性 - 磷酸铝配合物相结合，以形成所述抗菌化学组合物 ;

其中，所述组合物固化后，在接触水分时提供从所述生物活性材料受控递送的生物活性成分为约 10-900ppm。

81. 根据权利要求 80 所述的方法，其特征在于，所述添加步骤在形成步骤之后执行，且所述生物活性材料与所述磷酸铝物理性地组合。

82. 根据权利要求 81 所述的方法，其特征在于，所述生物活性材料是选自银盐、铜盐、锌盐、钙盐及其组合的金属盐。

83. 根据权利要求 80 所述的方法，其特征在于，所述添加步骤在形成步骤期间进行，且所述生物活性材料与所述磷酸铝化学性地结合。

84. 根据权利要求 83 所述的方法，其特征在于，所述生物活性材料是选自银、铜、锌、钙及其组合的金属离子。

85. 根据权利要求 80 所述的方法，其特征在于，所述形成步骤中，所述分散系是非结晶磷酸铝。

86. 根据权利要求 80 所述的方法，其特征在于，所述形成步骤中，所述分散系是结晶磷酸铝。

87. 根据权利要求 80 所述的方法，其特征在于，所述形成步骤中，所述分散系是非结晶和结晶磷酸铝的组合。

88. 根据权利要求 80 所述的方法，其特征在于，所述形成步骤包括 :

使铝盐与磷酸水溶液相结合 ;并添加足量的碱性材料以提高该溶液的 pH，以形成凝胶

结构，其中所述凝胶包括相互连接的非结晶磷酸铝颗粒三维结构。

89. 根据权利要求 88 所述的方法，其特征在于，所述铝盐是硝酸铝，且所述碱性材料是氢氧化铵。

90. 根据权利要求 88 所述的方法，其特征在于，进一步包括，在结合聚合物粘结材料的步骤之前，在足够高的温度下干燥所述凝胶，以去除其中的不需要的材料。

91. 根据权利要求 90 所述的方法，其特征在于，所述干燥步骤在大于约 200° C 的温度下进行，以除去凝胶中的硝酸铵、氨和水。

92. 根据权利要求 88 所述的方法，其特征在于，在结合聚合物粘结材料步骤之前，在高温下干燥所述凝胶，以提供能够促进所述生物活性材料的受控递送所需的孔隙度。

93. 根据权利要求 88 所述的方法，其特征在于，所述非结晶磷酸铝的表面积大于约 100 m^2/g。

94. 根据权利要求 80 所述的方法，其特征在于，所述形成步骤包括使氢氧化铝与磷酸相结合以形成含有酸性磷酸铝的溶液的步骤。

95. 根据权利要求 94 所述的方法，其特征在于，所述添加步骤包括 ：

向所述酸性磷酸铝中添加金属盐形式的生物活性材料 ；以及

中和所述生物活性材料与酸性磷酸铝的混合物，以形成所述磷酸铝。

96. 根据权利要求 95 所述的方法，其特征在于，所述金属盐是硝酸银，且所述混合物用铝酸钠进行中和。

97. 根据权利要求 80 所述的方法，其特征在于，所述混合步骤之前，在低于约 200° C 的温度下干燥所述混合物。

98. 根据权利要求 80 所述的方法，其特征在于，所述配合物的表面积低于约 20 m^2/g。

99. 根据权利要求 98 所述的方法，其特征在于，所述表面积在约 100-250 m^2/g 之间。

100. 根据权利要求 80 所述的方法，其特征在于，所述受控递送是约 100ppm 或以上。

101. 根据权利要求 80 所述的方法，其特征在于，所述生物活性磷酸铝配合物中包含约 1-10% 重量百分比的生物活性材料。

102. 根据权利要求 80 所述的方法，其特征在于，所述生物活性材料的含量为占所述化学组合物总重量的约 0.1-2%。

103. 根据权利要求 80 所述的方法，其特征在于，所述化学组合物被改造为，在接触水分时提供低于约 1500ppm 磷酸盐离子的受控递送。

104. 根据权利要求 103 所述的方法，其特征在于，所述磷酸盐离子的受控递送在约 100-500ppm 之间。

105. 一种用于制备抗菌化学组合物的方法，所述抗菌化学组合物中包含与磷酸铝相结合的生物活性材料，所述方法包括以下步骤 ：

通过使铝源和磷酸盐源在适当 pH 的水溶液中结合来形成磷酸铝分散系，以形成磷酸铝 ；

在上述形成步骤之后，向非结晶磷酸铝中添加生物活性材料，以形成配合物，其中所述生物活性材料物理性地结合在所述磷酸铝中，以形成生物活性 - 磷酸铝配合物 ；以及

使聚合物粘结材料与所述配合物相结合，以形成所述抗菌化学组合物 ；

其中，所述组合物固化后，在接触水分时提供从所述生物活性材料受控递送的生物活

性成分为 100ppm 或以上。

106. 根据权利要求 105 所述的方法，其特征在于，所述形成步骤中，所述分散系为非结晶磷酸铝。

107. 根据权利要求 105 所述的方法，其特征在于，所述形成步骤中，所述分散系是结晶磷酸铝。

108. 根据权利要求 105 所述的方法，其特征在于，所述形成步骤中，所述分散系是非结晶和结晶磷酸铝的组合。

109. 根据权利要求 105 所述的方法，其特征在于，所述磷酸铝的表面积小于约 100 m^2/g。

110. 根据权利要求 105 所述的方法，其特征在于，在所述添加步骤中，一定量的金属离子形式的所述生物活性材料化学性地与所述磷酸铝结合。

111. 根据权利要求 105 所述的方法，其特征在于，所述形成步骤包括 ：使铝盐与磷酸水溶液相结合 ；以及，添加足量碱性材料以提高溶液 pH，从而形成凝胶结构，其中所述凝胶包括相互连接的非结晶磷酸铝颗粒三维结构。

112. 根据权利要求 105 所述的方法，其特征在于，所述结合步骤包括 ：使氢氧化铝与磷酸相结合，以形成含有酸性磷酸铝缩合物的溶液 ；以及

中和所述缩合物以形成非结晶磷酸铝。

113. 一种用于制备抗菌化学组合物的方法，所述抗菌化学组合物包含与磷酸铝结合的生物活性材料，其特征在于，所述方法包括以下步骤 ：

使氢氧化铝和磷酸结合，以形成含有酸性磷酸铝缩合物的溶液 ；

在上述形成酸性磷酸铝缩合物的步骤期间或之后，加入生物活性材料，以形成含有生物活性－磷酸铝配合物的混合物，所述生物活性－磷酸铝配合物中含有生物活性材料 ；以及

使聚合物粘结材料与所述配合物结合，以形成所述化学组合物。

114. 根据权利要求 113 所述的方法，其特征在于，所述配合物包括非结晶磷酸铝。

115. 根据权利要求 113 所述的方法，其特征在于，所述配合物包括结晶磷酸铝。

116. 根据权利要求 113 所述的方法，其特征在于，还包括向所述酸性磷酸铝配合物添加中和剂的步骤，以增加其 pH。

117. 根据权利要求 113 所述的方法，其特征在于，所述配合物包含与所述磷酸铝化学性键合的所述生物活性材料。

118. 根据权利要求 113 所述的方法，其特征在于，在添加生物活性材料的步骤之后，进一步添加氢氧化铝。

119. 根据权利要求 113 所述的方法，其特征在于，在所述使氢氧化铝和磷酸结合的步骤中，所述氢氧化铝以浆体形式提供，并被缓慢地添加到磷酸中。

120. 根据权利要求 113 所述的方法，其特征在于，所述使氢氧化铝和磷酸结合的步骤中，将所述磷酸缓慢地添加到氢氧化铝中。

121. 根据权利要求 113 所述的方法，其特征在于，所述使氢氧化铝和磷酸结合的步骤包含以下步骤 ：

将所述磷酸添加到第一数量的氢氧化铝中，以形成酸性磷酸铝溶液 ；以及

将所述酸性磷酸铝溶液添加到第二数量的氢氧化铝中，以形成所述缩合物。

122. 根据权利要求 113 所述的方法，其特征在于，所述生物活性－磷酸铝配合物的表面积小于约 20 m^2/g，且当所述组合物固化时，其在接触水分时提供的受控递送的生物成分为约 10-900ppm。

123. 根据权利要求 116 所述的方法，其特征在于，所述中和剂选自氢氧化铝、氢氧化钙及其组合，且所述生物活性材料成分是选自银、铜、锌、钙及其组合的金属离子。

124. 根据权利要求 113 所述的方法，其特征在于，所述加入聚合物粘合材料的步骤之前，在低于约 200° C 的温度下，干燥所述磷酸铝。

125. 根据权利要求 113 所述的方法，其特征在于，所述生物活性材料为选自银盐、铜盐、锌盐、钙盐及其组合的金属盐。

126. 一种用于制备抗菌化学组合物的方法，所述抗菌化学组合物包含与非结晶磷酸铝结合的生物活性材料，所述方法包括以下步骤：

使生物活性材料与硝酸铝和磷酸结合，以形成溶液；中和该溶液以形成含有非结晶磷酸铝的凝胶，其中所述凝胶包括结合到所述非结晶磷酸铝骨架中的所述生物活性材料的生物活性成分，由此形成生物活性－磷酸铝配合物；和

使聚合物粘结材料与所述配合物结合，以形成所述化学组合物。

127. 根据权利要求 126 所述的方法，其特征在于，所述配合物的表面积大于约 100 m^2/g，且所述组合物接触水分时提供的从所述生物活性材料受控递送的生物活性成分为约 10-900ppm。

128. 根据权利要求 126 所述的方法，其特征在于，所述溶液通过添加氢氧化铵进行中和，且所述生物活性材料成分是选自银、铜、锌、钙及其组合的金属离子。

129. 根据权利要求 126 所述的方法，其特征在于，在添加聚合物粘结材料的步骤之前，在大于约 200° C 的温度下干燥所述非结晶磷酸铝。

130. 根据权利要求 126 所述的方法，其特征在于，所述生物活性材料是选自银盐、铜盐、锌盐、钙盐及其组合的金属盐。

131. 一种用于制备抗菌化学组合物的方法，所述抗菌化学组合物包含与磷酸铝结合的生物活性材料，所述方法包括以下步骤：

使生物活性材料与氢氧化铝结合，以形成混合物；将所述混合物添加到磷酸中，以形成含有所述生物活性材料的生物活性－磷酸铝配合物；以及

使聚合物粘结材料与所述配合物结合，以形成所述化学组合物。

132. 根据权利要求 131 所述的方法，其特征在于，所述生物活性材料包括金属盐。

133. 根据权利要求 132 所述的方法，其特征在于，在所述结合步骤之前，通过使所述金属盐和配体结合来形成配合物。

134. 根据权利要求 133 所述的方法，其特征在于，所述金属盐为硝酸银，所述配体选自氨、咪唑、取代咪唑及其组合。

135. 根据权利要求 133 所述的方法，其特征在于，所述生物活性－磷酸铝配合物进一步包含金属氧化物。

136. 根据权利要求 131 所述的方法，其特征在于，所述生物活性－磷酸铝配合物还包含金属氧化物。

137. 根据权利要求 131 所述的方法，其特征在于，所述添加和结合的步骤在室温下进

行。

138. 根据权利要求 131 所述的方法，其特征在于，所述氢氧化铝包括非结晶氢氧化铝。

139. 根据权利要求 131 所述的方法，其特征在于，所述配合物包含非结晶磷酸铝。

140. 根据权利要求 131 所述的方法，其特征在于，所述配合物包含结晶磷酸铝。

抗菌化学组合物

技术领域

[0001] 本发明涉及具有抗菌性质的化学组合物，更具体而言，涉及专门配方的包括含一种或多种抗菌剂的磷酸铝配合物的化学组合物，及其制备方法。

技术背景

[0002] 配方中包括一种或多种提供抗菌性质的抗菌组合物(例如用于在基础底物表面形成薄膜层的涂层组合物的形式等)，是本领域已知的。所述抗菌化学组合物采用了已知的抗菌试剂来针对有害微生物提供一定保护。

[0003] 本领域已知的常规抗菌化学组合物，例如水性涂料和涂层等制成产品，包括含在产品内以在贮藏期间保藏液体组合物不受微生物损坏的生物杀灭剂。所述常规涂料和涂层，通过包含能够防止所应用的干燥膜在使用中被霉菌和 / 或霉生长所损坏的试剂，从而提供抗菌保护。

[0004] 虽然已知常规抗菌化学组合物能够针对有害细菌提供一定的保护，但所提供的保护多少受限于其活性，以及受限于能够针对有害微生物提供期望抗性水平的时间长度。这很大程度上是因为配方的性质及其所含抗菌试剂的有限活性所决定的，因此导致无法提供活性高且持续久的有害微生物抗性。因此，虽然所述常规抗菌化学组合物能够提供一定程度的微生物抗性，却无法提供期望或需求水平的充分微生物控制来满足某些终端应用用途的要求。

[0005] 要满足需求，需要提供针对细菌、霉菌、霉及其他有害微生物的有效、持久的广谱抗性，以防止疾病和 / 或产品感染腐坏的共同影响。防止敏感环境中的表面接触导致感染和产品腐坏对一些目标终端应用至关重要，此类例子包括 :医院和医疗设施 ;厨房和食物处理及储藏区域 ;乳品厂 ;酿酒厂 ;浴室及卫生间设施 ;宾馆 ;学校、娱乐、消遣及运动设施。虽然已知抗菌添加剂能够提供一定量的抗菌作用，其在所述配方产品(如涂料和涂层)中的有效性受限于达到抗菌作用所需的材料量，该材料量超过了 :(1)配方产品的成本限制 ;(2)因非目标毒性造成的使用限制 ;(3)能够包含在配方产品中的实际极限 ;以及(4)受限于递送至需保护的物体表面的递送机制。

[0006] 因此，需要配制一种抗菌化学组合物，使其与已知抗菌化学组合物相比，能够针对包括细菌、霉菌及其他微生物种类提供所需的有效、持久抗性，以防止疾病和产品腐坏的协同影响，由此满足某些终端应用用途的要求。需要对所述抗菌化学组合物进行改造，以针对有效解决不同终端应用用途相关的特定抗菌需求的目的，促进有效定制、校正和 / 或调整所述配方的效能特征变化。进一步地，需要所述抗菌化学组合物用已知可用的材料和 / 或方法配制，从而无需外来设备即易于生产化学组合物，由此不仅节省过度劳力，还经济可行。

发明内容

[0007] 本文所述的抗菌化学组合物一般包括分散在粘结剂聚合物中的磷酸铝(AlP)固

体。该AlP中含有或组合有一种或多种生物活性材料，以形成生物活性-AlP配合物。该配合物的特点之一，在于其经过专门改造，由此当该组合物以干燥膜或复合材料的形式提供时，能够向该膜或复合材料表面受控递送生物活性成分(源于生物活性材料与水的接触)，以提供期望的抗菌水平。用于形成该配合物的AlP可以是非结晶形式，结晶形式，或其组合。在一个示例实施例中，该AlP包括非结晶AlP。

[0008] 用于制备该配合物的生物活性材料或源于该生物活性材料的生物活性成分，根据用于制备配合物的特定方法，可以与AlP聚合物化学性键合(例如包含在AlP聚合物骨架中)，或可以物理性包含、网络、包括或交缠在AlP聚合物中。该生物活性材料可以是有机材料和/或是金属盐或金属氧化物，例如包括银盐、铜盐、锌盐、钙盐及其组合，和/或可以是金属离子，例如包括银、铜、锌、钙及其组合。此外，该生物活性材料可以包括一种或多种金属氧化物，可以包括但不限于，氧化锌、氧化铜、氧化镁、氧化钡、氧化钙或其组合，这些材料可以提高生物活性材料的抗菌有效性和/或光稳定性。此外，生物活性材料可以在组合前进行复合，来形成生物活性-AlP配合物，这可以增加生物活性材料的颜色或光稳定性。在一个实施例中，所述生物活性材料包括金属盐，例如硝酸银，该金属盐可以在与用于形成生物活性-AlP配合物的其他成分组合之前，与配体复合，所述配体可以是氨、咪唑、取代咪唑及其组合。用于形成该组合物的粘结剂聚合物可以包括聚氨酯、聚酯、溶剂型环氧树脂、无溶剂环氧树脂、水性环氧树脂、环氧树脂共聚物、亚克力、亚克力共聚物、聚硅酮、聚硅酮共聚物、聚硅氧烷、聚硅氧烷共聚物、醇酸树脂及其组合。

[0009] 在一个示例实施例中，对AlP进行改造，以在该化学组合物处于固化形式(例如处于膜涂层或复合材料结构中)时，提供约5-1000ppm的有控制的生物活性成分递送，优选为约10-900ppm，最优选为约15-800ppm。在一个示例实施例中，需要提供至少100ppm或以上的生物活性成分的受控递送。该生物活性材料(例如Ag)的量可以在基于配合物总重量的约1-10%重量百分比的范围内，优选为约2-8%重量百分比，更优选为约3-6%重量百分比。配合物中，磷酸盐与铝的比率在约0.5:1至1.5:1的范围内。该化学组合物中的生物活性-AlP配合物包括约0.1-2%干燥膜重量，或20-1000ppm生物活性成分(例如涂料中的Ag)。在一个优选实施例中，生物活性材料(例如Ag)的有效浸出率，即释放至包含生物活性-AlP配合物的固化涂层或固化复合材料表面的量，为至少约30μg/m^2，且优选为约36.9μg/m^2或在生物活性淋洗中>2μg/L。

[0010] 在一个示例实施例中，该抗菌化学组合物还可以提供期望程度的防腐抗性，例如在用于金属基底涂层的配方中。在所述实施例中，AlP被配制为，除了提供生物活性成分的受控递送/释放之外，还在接触水分时，提供有控制的钝化阴离子(例如磷酸阴离子)递送。在一个示例实施例中，所述抗菌化学组合物可以提供大于约100ppm的磷酸阴离子受控递送。

[0011] 制备本文所述的抗菌化学组合物，首先形成生物活性-AlP配合物，包括在适合形成AlP的反应条件下(例如在适当pH和适当温度的水溶液中)通过混合期望铝源和期望磷酸盐源来形成AlP。在形成AlP的步骤期间和/或之后，添加生物活性材料，由此令该生物活性材料分散在AlP中或与其组合，从而形成生物活性-AlP配合物。根据需要，还可以向生物活性-AlP配合物添加更多的AlP，然后再将其与粘结剂聚合物相混合。

[0012] 根据一种示例性的制备方法，在形成AlP后，添加生物活性材料；在此情况下，制

得的生物活性 -AlP 配合物包括物理性地包含、网罗、包括或交缠在 AlP 聚合物中的生物活性材料。根据另一种示例性的制备方法，在形成 AlP 期间向 AlP 添加生物活性材料，在此情况下，AlP 原位形成所得生物活性 -AlP 配合物，并包括与 AlP 聚合物化学性键合（例如作为 AlP 聚合物骨架的一部分）的生物活性材料的生物活性成分。

[0013] 在一个实施例中，制备了一种生物活性 - 磷酸铝配合物 :将铝源（例如非结晶和 / 或结晶形式的氢氧化铝）与磷源（例如磷酸）在存在生物活性材料的情况下形成反应混合物。该生物活性材料可以作为单独的成分提供，或与铝源和磷源中的一种或两种以预混形式组合提供。铝源和磷源中的一种或两种可以以水溶液的形式提供。允许该反应混合物进行反应（例如，在室温下）以形成生物活性 - 磷酸铝配合物，其中所述生物活性材料与磷酸铝键合。在一个实施例中，生物活性材料可以是硝酸银，该硝酸银可以与咪唑或氨复合，和 / 或可以与氧化锌和 / 或氧化铜组合。由此形成的生物活性 - 磷酸铝配合物与期望的聚合物粘结剂相组合，从而形成本文公开的抗菌化学组合物。

[0014] 与已知抗菌化学组合物相比，本文所述的抗菌化学组合物经过特定改造，以对广谱微生物，包括细菌、霉菌、霉和其他微生物种类提供有效持久的抗性，以防止疾病和产品腐败的协同影响，由此满足某些终端应用用途配方的需要，其中所述应用包括 :涂料、涂层、粘合剂、复合材料、水泥、塑料等。所述抗菌化学组合物是从已知可用的材料和 / 或方法制备而成的，因此通过避免外来设备和劳动强度过大，从而促进生产，且经济可行。

[0015] 详细说明

本申请所述的抗菌化学组合物通常包括分散在粘结剂聚合物中的磷酸铝（AlP），所述粘结剂聚合物形成该组合物的主体基质。磷酸铝中分散有一种或多种生物活性物质，由此形成生物活性 -AlP 配合物，且磷酸铝经过专门改造，以在接触水分时受控递送或释放源自生物活性材料的生物活性成分。所述抗菌化学组合物由此述的多种方法制备而成，且能够配制用作油漆、涂料、粘合剂、复合材料、水泥、塑料等等。

[0016] 可用于此方面的磷酸铝包括非结晶磷酸铝、结晶磷酸铝及其组合。可用于此方面的磷酸铝的例子为非结晶磷酸铝 (AAlPs)，且优选的 AAlPs 为非结晶正磷酸铝。由于 AAlPs 据观察具有某些非常适合用作生物活性材料载体的特性，由此希望采用 AAlPs，但是，应当理解，结晶 AlPs 以及非结晶和结晶 AlPs 的组合物亦可用于此方面，且涵盖在本申请所述的抗菌化学组合物的范围之内。

[0017] 在一个示例实施例中，非结晶正磷酸铝是非结晶羟基磷酸铝。非结晶羟基磷酸铝使得化合物内的分散性质均匀，且该分散可在该制剂的贮存期内保持稳定。非结晶羟基磷酸铝的羟基成分通过提供与该配方的粘结剂聚合物的适当基团（例如羰基、氨基、羟基、酸根等等）之间的氢键，来提供基质稳定性。这是非结晶羟基磷酸铝的独有特性，且不存在于结晶磷酸铝或其他种类的非结晶磷酸盐中，因此有助于提供独特的分散性质。

[0018] 本公开中用于形成抗菌化学组合物的 AlPs 是专门设计的，对各种用于终端应用用途的不同粘结剂聚合物或粘结剂聚合物系统均具有高相容性水平，由此为配制所述组合物提供了高灵活度和选择度，以符合多种不同最终使用工业中的各种最终用途的要求和条件。

[0019] 该化学组合物的生物活性成分的受控递送和 / 或释放，主要依赖于该生物活性成分在该组合物（涂层形式或复合材料形式）的主体基质中的扩散速率。该生物活性成分的扩

散速率取决于该主体基质的结构特征对生物活性物质和水分传递的控制。这些特征包括但不限于：交联密度、颜料体积比(PVC)、生物活性材料载体性质、成分亲水性以及成分孔隙度。

[0020] 本申请所公开的抗菌化学组合物使用 AlP 作为生物活性载体材料，其中 AlP 设计为，向其内部所含的生物活性材料有控制地扩散水分，且向包含所述 AlP 的涂层或复合材料表面扩散或递送或释放所述生物活性成分，以达到提供所需抗菌度。相应地，该生物活性材料并入 AlP 内，且该 AlP 经过专门制备，以调节和控制该生物活性成分的可溶性，以及控制已溶解的生物活性成分通过组合物膜或复合材料主体基质的扩散。

[0021] 据发现，能影响 AlP 水分扩散和生物活性材料递送的一个特性 / 指标，是 AlP 分子的孔隙度。本申请中所公开的 AlP 配合物的一项特性，是能够通过选择合成方法，来改造所述配合物的形态和孔隙度。本文所称的术语“改造的孔隙度”定义为固体材料内由颗粒孔隙构成的空间体积、颗粒聚集体(aggregate)中的颗粒之间的孔隙空间，以及团聚体(agglomerate)中的聚集体之间的孔隙空间。使用水银孔隙度计来描述固体和颜料的孔隙度性质。重要的量度包括：

1. 总侵入体积 (ml/g)：测量样品中能吸入水银的总空间，将其作为压力的函数。

[0022] 2. 总孔隙面积 (m^2/g)：将体积转换为面积，并定义由总侵入体积占据的面积大小。

[0023] 3. 平均孔隙容积 (4ν / A = μ)：以面积表示体积分布，即平均有多少体积进入不同孔径的孔隙。

[0024] 4. BET (m^2/g)：测试条件下氮气可接触的总表面积的量度。BET 和孔隙度具有相关性。

[0025] 含有金属盐或金属离子(例如银)作为生物活性物质且由溶胶 - 凝胶方法(下文将更详细描述)形成的 AlP 配合物，得到含有纳米级初级粒子的极高表面积和孔隙度的聚集体。具有所述高表面积和孔隙度的一个优点在于，保证了与水的优化扩散接触以及随后银离子在粘结剂聚合物主体基质形成的膜中的释放，由此提高了该配合物在所述膜或复合材料中的均匀分布，且促进了所述生物活性材料在接触水时从所述配合物的相对迅速释放。

[0026] 由溶胶 - 凝胶法制备的含有金属盐或金属离子(如银)作为生物活性材料的 AlP 配合物，其 BET 表面积在约 100-250 m^2/g 范围内，优选地在约 125-200 m^2/g 范围内，最优选为在约 140-160 m^2/g 范围内。所述 AlP 配合物的总侵入体积在约 1-2 mL/g 之间，优选为在约 1.3-1.8 mL/g 之间。所述 AlP 配合物的平均孔隙容积在约 0.02-0.06μm 之间，优选为约 0.04-0.05μm 之间。

[0027] 与之相比，由沉淀或缩合法制备的含有金属盐或金属离子(如银)作为生物活性材料的 AlP 配合物(下文将更详细描述)，得到含有纳米级初级粒子的相对较低表面积和低孔隙度的聚集体。所述低表面积和孔隙度的一个优点在于，保证与水的扩散接触程度降低，以及降低了后续银离子在粘结剂聚合物主体基质形成的膜中的释放，由此提高了该配合物在所述膜或复合材料中的均匀分布，且促进了所述生物活性材料在接触水时从所述配合物的相对缓慢的释放。

[0028] 由沉淀或缩合法制备的含有金属盐或金属离子(如银)作为生物活性材料的 AlP 配合物，其 BET 表面积在约 2-10 m^2/g 之间范围，总侵入体积在约 0.5-0.9 mL/g 之间，且平均

孔隙容积在约 0.4-0.6μm之间。

[0029] 因此，可用于制备抗菌化学组合的AlP的特性之一，在于具有改造的孔隙度，改造后的孔隙度经过计算以提供所需水分扩散率，以及处于终端应用中时促进所需活性和抗菌度水平的生物活性成分的递送速率。

[0030] 因此，应理解，AlP的期望孔隙度随着每个不同终端应用的某些要求而变化。但是，通常要求AlP的孔隙度不要大到在一接触水时即迅速失去生物活性成分，即高度活泼但有效使用寿命大大降低。生物活性材料负荷和/或所用生物活性材料也会影响活性和有效使用寿命。相应地，AlP的孔隙度反映了指定生物活性材料在指定量或通常负荷水平范围下，所需抗菌活性水平与所需有效使用寿命之间的平衡或折衷。

[0031] AlP孔隙度的改造是在制备AlP过程中和/或成形后处理(例如干燥和/或其他加热处理)中进行的，下文将更详细描述。

[0032] 本文所公开的AlPs，除了用作生物活性材料载体以有控制地按需要递送/释放生物活性成分外，还在接触水分时通过递送磷酸阴离子提供防腐保护。相应地，对于同时需要抗菌和防腐性质的终端应用，例如当该组合物配方用作金属底物的涂层时，AlP还可以被改造来提供磷酸阴离子的受控递送，以通过钝化来向金属底物提供所需的抗腐蚀保护水平。

[0033] 在一个示范实施例中，还需要所述抗腐蚀性，AlP被改造为，当存在于终端应用用途中的固化膜或复合材料中时，释放约50-500ppm，优选为100-200ppm范围内的钝化性磷酸阴离子。需递送的钝化性阴离子量取决于若干不同因素，例如所用的AlP负荷或含量、所用粘接聚合物种类、所保护的金属底物种类、终端应用用途所处的环境类型。在优选实施例中，受保护的金属底物包括铁，腐蚀环境包括水、氧和其他腐蚀性盐类，所述AlP被改造为释放约160ppm的钝化性磷酸阴离子。

[0034] 粘结剂聚合物的例子包括目前用于制备已知抗菌化学组合物的粘结剂聚合物，且可以选自常见的选项，包括：水性聚合物、溶剂型聚合物及其混合物和组合物。可用于制备抗腐蚀涂层组合物的水性聚合物的例子包括丙烯酸和丙烯酸共聚物、醇酸树脂、环氧树脂、聚氨酯和硅树脂，以及聚硅氧烷聚合物。可用于制备抗腐蚀涂层组合物的溶剂型和/或非水性聚合物的例子包括丙烯酸和丙烯酸共聚物、环氧树脂、聚氨酯、硅树脂、聚硅氧烷、聚酯和醇酸树脂。优选的粘结剂聚合物包括丙烯酸共聚物乳胶、醇酸树脂、聚氨酯和环氧树脂共聚物。

[0035] 在一个示例实施例中，抗菌化学组合物包括范围在约15-75%重量百分比，优选为约20-60%重量百分比，更优选为20-35%重量百分比(基于该化学组合物在预固化或湿态下的总重量)的粘结剂聚合物。含有低于约15%重量百分比的粘结剂聚合物的抗菌化学组合物，所包括的生物活性材料(以生物活性-AlP配合物的形式存在)量可以高于提供期望抗菌保护水平的必要量。含有高于约75%重量百分比的粘结剂聚合物的抗菌化学组合物，所包括的生物活性材料(以生物活性-AlP配合物的形式存在)量可能不足以提供期望抗菌保护水平。当提供了某个粘结剂聚合物量时，应当理解，用于配制抗菌化学组合物的粘结剂聚合物的确切量将根据某些因素而变化，例如所用粘接聚合物种类、用于形成化学组合物的其他材料的种类和含量、所用的生物活性材料的种类和/或数量，和/或具体的终端抗菌应用用途。

[0036] 可用于形成本文所述的抗菌化学组合物的生物活性材料或试剂可以选自各种生

物活性材料和 / 或种类，包括但不限于 :(1) 抗菌添加剂，含有生物杀灭剂(杀死微生物)或生物静态剂(微生物失活)的有机分子 ;(2)生物农药，一般是对微生物具有生物静态或生物杀灭效果的多肽 ;(3)能够天然抑制或防止目标生物体生长的天然产品 ;(4)能够干涉目标微生物的生长和 / 或发育的“友好”细菌 ;(5) 在某些环境条件下释放或产生灭菌化学种类的矿物质和金属 ;以及 (6) 上述选项的组合。最常用于向配方产品赋予抗菌性质的是有机抗菌添加剂和基于金属的生物杀灭剂。

[0037] 基于金属并可用作生物活性材料或试剂的材料包括金属离子和金属盐。合适的金属离子包括选自银、铜、锌、钙及其组合的离子。合适的金属盐包括上述金属离子的盐。在一个示例实施例中，银是希望使用的生物活性材料，因为银具有数种优点，前提是它能够与将它包含其中的粘结剂聚合物配方相容，且能在该配方中保持活性状态，以在接触水分时能以稳定且高性价比的方式递送至表面。银优于有机材料的原因在于，银具有较高的热稳定性，对非目标有机体的毒性低于典型的有机生物杀灭剂，且 UV 稳定性较高。

[0038] 银离子 (Ag^+) 具有生物活性，且浓度足够时刻杀灭各种微生物。银被证实具有抗菌活性，且已知对某些抗药性细菌有效。它具有广谱抗菌活性且对哺乳类细胞毒性极小。银一般配制或包含在载体成分中 (浓度水平一般为 <5% 重量百分比)，例如玻璃、硅胶或沸石。基于银的材料在控制微生物方面的作用机理，涉及银离子响应环境水分而释放。银离子在接触水时形成，与生物体接触并与其体内多个结合位点相互作用。随着银离子进入目标生物体的细胞中，该细胞的新陈代谢和呼吸功能被改变并最终停止，导致细胞死亡。

[0039] 用作生物活性材料的适当银离子源包括银盐，例如硝酸银和氯化银，其中优选为硝酸银 ($AgNO_3$)。硝酸银溶解度极高 (0° C 下每 1000ml 水溶解 122g) 且该溶解度对于从配方产品 (例如抗菌涂层或复合材料) 有控制地释放生物活性材料提出了特别挑战。只要能将配方涂层或复合材料中的银离子向表面的释放控制在一个速率和浓度，使其能以最小控制水平供应，以平衡目标使用寿命，就可以将硝酸银用作生物活性材料。递送太快会使得受保护表面的银离子浓度过高，造成表面的褪色和 / 或主体基质中的硝酸银可用储备迅速耗尽，由此降低有效使用寿命。

[0040] 如上所述，所制备的 AlP 改造了孔隙度，以通过涂层或复合材料主体基质提供生物活性成分 (例如银离子) 的有控制的扩散速率和释放 / 递送。作为自由组分直接包含在涂层中的硝酸银不允许有控制的释放。必须将硝酸银 (或银离子源) 包含在改造后的 AlP 中，以调节和控制银盐的可溶性，控制溶解的阴离子通过膜或复合材料基质的扩散，及控制所产生的银离子向表面的递送。

[0041] 如上所述，AlP 的孔隙度性质经过改造，以提供控制所述水解和溶解反应等的机制。此外，AlP 可被制备为吸湿性的，由此能够自身吸引水分，尤其当其处于主体基质中时，由此提供溶解作用的介质。改造的孔隙度这一特征是有控制的溶解和离子释放的基础。对于银离子而言，银离子的扩散速率取决于 AlP 的表面积和孔隙度。这也调节了银离子在主体基质的总转移率。特别地，当水接触主体基质时即被吸收，当主体基质中的水接触到置于生物活性 -AlP 配合物中的高溶解性的银 (物理性地密封在 AlP 中的硝酸银，或化学性地接合在 AlP 上的银离子) 时，该银类溶解，银离子经过主体基质扩散到表面。

[0042] 本申请中公开的抗菌组合物的一个特征在于，该组合物包括将 AlP 配合物置于粘结剂聚合物的主体基质中，其中 AlP 配合物的生物活性成分递送率可以与生物活性成分

(从配合物中释放)在粘结剂聚合物中的转移或扩散速率相同或不同。因此,配方设计师可以改造 AlP 配合物的孔隙度,以提供所期望的生物活性物质从该配合物释放的速率,且可以进一步改造该配方(通过使用不同的粘结剂聚合物、填料等)以影响生物活性成分在该组合物中的迁移或扩散速率,以符合某些终端应用用途的要求。这些特征的组合,即生物活性物质从 AlP 配合物的释放速率以及所述释放的生物活性物质在所述粘结剂聚合物主体基质中的迁移或扩散速率,提供了一种以其他方式不可获得的提高的抗菌组合物定制化水平。所述对释放速率和迁移 / 扩散速率的定制操作,为解决各种终端应用用途提供了可专门定制的范围广泛的抗菌组合物。

[0043] 包含在 AlP 中的生物活性材料的含量或浓度可以且将会根据所用的生物活性材料种类、用来形成涂层或复合材料基质的粘结剂聚合物的性质、AlP 种类(非结晶、结晶或其组合)以及 AlP 的改造孔隙度等因素而变化。因此,生物活性 -AlP 配合物的性质,例如生物活性材料浓度以及 AlP 的改造孔隙度,可以有控制地适用于多种暴露条件,例如温度、相对湿度、紫外线暴露等等。

[0044] 在一个示例实施例中,需要存在充分的生物活性材料含量,且需要改造 AlP 的孔隙度,从而当以干燥膜或复合材料的形式提供时,该组合物能够提供生物活性成分(生物活性材料与水分接触所得)的受控释放,其浓度为约 5-1000ppm,优选为约 10-900ppm,更优选为约 15-800ppm。在一个特定实施例中,生物活性成分为银离子,期望的银离子优化受控递送为大于约 100ppm,且最优选为约 120ppm。在一个优选实施例中,有效浸出率(即释放到含生物活性 -AlP 配合物的固化涂层或固化复合材料表面的生物活性成分(如银)量)为至少约 30μg/m^2,优选为约 36 μg/m^2或在生物活性淋洗中 >2μg/L。

[0045] 为了提供符合期望的生物活性成分受控递送,需要在形成生物活性 -AlP 配合物时使用一定量的生物活性材料。在一个示例实施例中,AlP 配合物包括的生物活性材料为约 1-10% 重量百分比,优选为约 2-8% 重量百分比,且更优选为约 3-6% 重量百分比,所述重量百分比是相对于该生物活性 -AlP 配合物的总重量而言。

[0046] 此外,据发现,可以合成基于银与其他生物活性材料的混合抗菌配合物,其具有协同效果。例如,除了银 -AlP 配合物外,还可以在合成中将其他生物活性金属(例如铜和 / 或锌)以内含物的形式引入配合物中,下面将更详细地叙述。此外,还可以通过物理吸附 / 包括或通过与配合物磷酸基团的实际反应 / 缩合的形式,将某些有机生物活性分子引入复合体中。这通过水扩散在膜主体中引起的后续水解,提供了有控制的释放机制。

[0047] AlPs 可以通过上述材料的选择性组合来制备。下列选定的制备方法仅作为示例提供,可以理解,还可以使用除在此具体公开的方法之外的制备方法。虽然在此公开的 AlPs 制备方法可能引用和公开了非结晶磷酸铝(AAlP)的形成,应当理解,所述方法还可以生成或可适用于生辰其他 AlP 形式,例如各种结晶磷酸铝形式和 / 或非结晶和结晶磷酸铝混合物,取决于终端使用抗菌应用的性能性质。本公开中的 AlPs 的示例结晶形式包括但不限于正交晶和三斜晶正磷酸铝。相应地,再次公开的方法应理解为,可根据特定的终端应用用途和性能性质,用于制备不同形式的 AlP。

[0048] 二元缩合制备法

一般而言,AlP 是通过合适的铝盐(例如氢氧化铝、硫酸铝等等)与磷酸或其他含磷化合物或材料(根据选择来进行磷酸铝制备的特定铝盐种类而定)结合制成的磷酸铝配合物。

在一个示例实施例中，优选的铝盐是氢氧化铝（ATH 或 $Al(OH)_3$），且优选的含磷成分是磷酸（H_3PO_4）。在此公开的示例方法包括：通过缩合法来形成 AlP，其中 AlP 是由铝盐成分与含磷成分缩合反应，生成浆体形式的 AlP 微粒。根据该制备步骤生成的该缩合固体的构成，取决于铝金属与磷阴离子的比率。所得配合物（即 AlP）的性质取决于缩合反应中所用的工艺参数，包括对铝盐、温度、试剂物理状态、试剂添加顺序、试剂添加量、搅拌程度和时长、一种或多种试剂的预处理以及所得缩合产物后处理的选择。

[0049] 一般来说，该制备方法所得的缩合固体，即使在研磨后，吸油量性质和表面积也远低于已知方法制备的磷酸铝。吸油量指的是浸湿和填满颜料（ASTM - D-281-84）周围的孔隙空间所需的亚麻籽油量（克或磅），是指定配方中的颜料可以吸收的粘合剂要求或粘合树脂量。高粘合剂要求增加制剂成本，并影像干燥膜的某些屏障性质。亦令人吃惊地，以本公开中的二元缩合法所制备的磷酸铝，还显示出受控递送性质和吸水性，通常与高表面积颗粒相关。

[0050] 在一个示例实施例中，按此制备的缩合磷酸铝的吸油量低于约 50，优选为在约 10-40 范围内，更优选为在 20-30 范围内。与之相比，以其他方法制备的 AlP 的吸油量大于约 50，一般在约 50-110 的范围内。

[0051] 在一个示例实施例中，按此制备的 AlP 的表面积低于约 20 m^2/g，优选为低于约 10 m^2/g。在一个示例实施例中，表面积的范围在约 2-8 m^2/g 之间，更优选为约 3-5 m^2/g 之间。与之相比，以其他方法制备的表面积大于 20 m^2/g，例如，在约 30-135 m^2/g 之间。

[0052] 可以根据至少 5 种不同方法来制备二元缩合产物 AlPs，其中 2 种涉及向酸试剂添加碱试剂，1 种涉及向碱试剂添加酸试剂，1 种涉及碱到酸的原位聚集，1 种涉及酸到碱的原位聚集。在所述方法中，选定的初始材料包括铝源和磷源，将其在有控制材料递送、温度和搅拌的特定条件下结合。正确地选择初始材料和处理条件，其目的在于令生成的 AlP 的物质含量和化学结构产生上述的改造性质，从而当其存在于涂层组合物或复合材料配方中时，提供所述生物活性成分的符合期望的受控递送 / 释放。

[0053] 如上所述，可用于通过二元缩合形成 AlP 的铝源包括铝盐，例如氢氧化铝、氯化铝、硝酸铝、硫酸铝等。优选的铝源包括氢氧化铝和硫化铝。可用于在缩合反应中形成 AlP 的磷源包括磷酸以及磷酸盐（例如正磷酸盐或多磷酸盐）。适当的磷源可以是由任何原料制得并经过澄清和脱色的肥料品级磷酸。例如，含约 54% 的 P_2O_5 商用磷酸可以经过化学处理和 / 或用处理过的水稀释，得到浓度近似 20% 的 P_2。

[0054] 本文所述的可用于形成抗菌化学组合物的 AlPs，可以按照若干不同方法制得，其中包括所述二元缩合法的至少 5 种变形形式。下列以举例形式提供了一些选定的制备方法，应当理解，还可以采用其他未在此处具体公开的制备方法。

[0055] 实施例 1 - 二元缩合反应制备 AlP（碱到酸途径）

在一个示例实施例中，AlP 是通过向磷酸（H_3PO_4）添加氢氧化铝（$Al(OH)_3$）来制备的。在与 $Al(OH)_3$ 结合前，将 H_3PO_4 用水稀释，而 $Al(OH)_3$ 在添加前未用水润湿，虽然也可以采用润湿的 $Al(OH)_3$。这些试剂在室温下无需加热即迅速结合，生成白色浆体。但是，根据需要，也可以在加热下反应。H_3PO_4 是 Sigma-Aldrich 所供应的 85 wt% H_3PO_4 水溶液，且 $Al(OH)_3$ 是 Sigma-Aldrich 生产的试剂品级 $Al(OH)_3$。具体而言，以 50g 水稀释 57.3g（0.5mol）H_3PO_4，然后与 $Al(OH)_3$ 结合。迅速向该溶液中加入 39g（0.5mol）$Al(OH)_3$，并在室温下缓慢搅拌混

合物以润湿粉末，得到以水中的固体AlP粒子分散系形式存在的AlP缩合固体。在此特定实施例中，AlP粒子主要是以非结晶磷酸铝（AAlP）的形式存在。在添加$Al(OH)_3$之前将H_3PO_4稀释，相信可以有助于仅形成AlP，例如，不产生或仅产生少量结晶形式。过滤悬浊液以分离AlP颗粒，洗涤，并在适当温度下干燥（可以是低于约300℃），且优选地在约100-200℃之间。如此形成的AlP的特征之一在于，可以与粘结剂聚合物相结合，例如用于配制抗菌涂层组合物，而无需进一步加热处理、回火或煅烧。虽然在上述极端温度下加热AlP可能对去除水分有益，但也可能触发AlP从非结晶形式向结晶形式的转变。可能需要令AlP与高于200℃的高温接触，例如300° C至800° C，以从其中去除不需要的成分，和/或影响AlP的物理性质从而影响其在终端使用中的性能特性或在抗菌组合物中的特征。若想要AlP的结晶形式，则可以对由此获得的AlP进一步加热处理或煅烧，以产生所需的结晶AlP。

[0056] 可选地，AlP可以通过向H_3PO_4中加入$Al(OH)_3$来制备。但是，与上述示例实施例不同，H_3PO_4在加入$Al(OH)_3$之前并不进行稀释。该制备方法的特征之一在于，并不包括在试剂接触后加入自由水的步骤，但应当理解，根据该方法制备的AlP时，也可以包括加入自由水的步骤。在示例实施例中，H_3PO_4是Sigma-Aldrich所供应的85 wt%H3PO4水溶液，且$Al(OH)_3$是Sigma-Aldrich生产的试剂品级$Al(OH)_3$。具体而言，将约57.6g H_3PO_4，加热至约80℃。用约2g水润湿约39g $Al(OH)_3$，然后在快速机械搅拌下，迅速将润湿的$Al(OH)_3$向加入H_3PO_4中，得到形式为面团球状的AAlP固体，取出在室温下贮藏。由此形成的AlP的特诊之一在于，无需通过进一步的过滤和洗涤处理来分离和获取所制得的AlP。如上所述的示例实施例中，干燥所述AlP，令其形成可用于制备抗菌化学组合物的所需颗粒大小。

[0057] 实施例2 二元缩合反应制备AlP（碱到酸途径）

在一个示例实施例中，具有上述的改造后的物理性质或特征（例如孔隙度）的AlP，是在高温下（例如约60℃）将氢氧化铝（$Al(OH)_3$）添加至磷酸（H_3PO_4）中，以形成所需的AlP。在与$Al(OH)_3$结合前，将H_3PO_4用水稀释，而$Al(OH)_3$在添加前则与水混合形成占约10-25%重量百分比的浆体，在一些情况下，根据$Al(OH)_3$的品级，$Al(OH)_3$所占的重量百分比高达约40%。在制备$Al(OH)_3$浆体时，可以将水加热以帮助氢氧化铝粉末分散，例如，以克服特定品级氢氧化铝的某些性质。加热的浆体可以保持在高温下加入酸中。对于具有高纯度和小粒径的极高品级氢氧化铝而言，可以通过将其加入室温的水中来制备$Al(OH)_3$浆体。

[0058] 将$Al(OH)_3$浆体缓慢地加入稀释的H_3PO_4中，以控制缩合反应的动力学。在一个示例实施例中，在约10分钟至1小时的时间内有控制地添加$Al(OH)_3$浆体至H_3PO_4中，例如以逐滴等方式。试剂混合加热至约95° C，并共同搅拌足够长的时间，一般是约3小时。在一个示例实施例中，该反应发生在体积恒定的实质封闭系统中，例如可以连接回流冷凝器，以在反应系统中保持恒定的溶剂体积（水）。在示例实施例中，H_3PO_4是Sigma-Aldrich所供应的85 wt%H3PO4水溶液，且$Al(OH)_3$是Sigma-Aldrich生产的试剂品级$Al(OH)_3$。具体而言，使用了约864g的85 wt%H3PO4水溶液，并通过将585g的$Al(OH)_3$与1650g去离子水混合形成浆体。混合试剂装在搅拌器中，并以1300-1500rpms混合。再次向反应物加水，并将混合物搅拌混合约30分钟至约3小时，例如一般是3小时。

[0059] 根据需要，可以向反应物中加入适当的化学试剂，以降低母液成分的可溶性，由此进一步增强对整个反应结果的控制。在一个示例实施例中，所述化学试剂可以是氢氧化钙（$Ca(OH)_2$）、水溶性胺（例如二亚乙基三胺，即DETA）等。

[0060] 得到的 AlP 缩合固体以分散在水中的固体酸性 AlP 颗粒存在。过滤所述悬浊液以分离酸性 AlP 颗粒。用水洗涤这些颗粒一次或多次，然后再次过滤。在一个示例实施例中，初始过滤后，在再次过滤前以约 6 倍于沉淀物体积的水洗涤所述颗粒。连续洗涤操作，以从产物中移除未反应的初始原料和任何可溶性副产物。再次过滤后，加水以重新悬浮酸性 AlP 颗粒，并根据下列 3 种不同技术之一来进一步处理。

[0061] 在第一种技术中，过滤该浆体以分离酸性 AlP 颗粒，加热所述颗粒。在一个示例实施例中，将 AlP 颗粒加热至约 110℃约 24 小时以去除水分，生成酸性 AlP 颗粒。可选地，将 AlP 颗粒加热至约 250° C 约 12 至 48 小时，生成不含水分和任何在 250° C 以下可分解的副产物的酸性 AlP 颗粒。此外，在上述任一温度下加热处理，但尤其是在高温下，能够提供令配合物中可能残留的任何中间体完成转化的驱动力量。

[0062] 在第二种技术中，加入合适的中和剂，以中和含有酸性 AlP 的浆体。在一个示例实施例中，所述中和剂为氢氧化铵(NH_4OH)，将足量的 NH_4OH 加入浆体中，以提高 pH 并中和 AlP 至所需的 pH，一般为 5.5-7.0。所得浆体过滤，并加热分离得到 AlP 颗粒。在一个示例实施例中，将 AlP 颗粒加热至约 110℃约 24 小时以去除水分，生成 AlP 颗粒。可选地，将 AlP 颗粒加热至约 250° C 约 24 小时，去除水分和任何不需要的化学成分，得到 AlP 颗粒，并影响任何表面吸附或整体吸附的反应种类(例如磷酸阴离子或磷酸氢盐离子)的最终转化或中和。可以用于该转化或中和步骤的任意反应胺，包括但不限于，EDTA、三亚乙基四胺、2- 胺 -2- 甲基 -1- 丙醇。

[0063] 在第三种技术中，通过添加合适的中和剂，来中和含酸性 AlP 的浆体。在一个示例实施例中，该中和剂为氢氧化铵(NH_4OH)，将足量的 NH_4OH 加入浆体中，以提高 pH 并中和 AlP 至所需的 pH，一般为 5.5-7.0。所得浆体过滤，并加热分离得到的 AlP 颗粒。在一个示例实施例中，将 AlP 颗粒加热至约 110℃约 24 小时以去除水分，生成 AlP 颗粒。可选地，将 AlP 颗粒加热至约 250° C 约 24 小时，去除水分和任何不需要的化学成分，得到 AlP 颗粒。也可以使用所述二价阳离子(例如钡、镁)的氢氧化合物来代替钙，进行中和或 pH 调节。

[0064] 如实施例 1 所述，按照实施例 2 中公开的方法所制备的 AlP 含有 AAlP。但是，应当理解，可以根据上述方法(例如，通过在 90℃以上的温度下，进行低于 3 小时的缩合反应)，来制备结晶 AlP 和 / 或 AAlP 和结晶 AlP 的组合物。将反应温度保持在约 45-90℃，优选为 60-70℃，将生成结晶形式和非结晶形式 AlP 的组合物。在低于约 45℃的温度下进行该反应，将主要生成非结晶形式的 AlP。

[0065] 实施例 3 二元缩合反应制备 AlP (酸到碱途径)

据发现，改变添加顺序会改变缩合反应的催化性质，亦即 :向碱性浆体添加酸，会得到较慢的局部 pH 变化，且该反应主要是碱催化。溶液的局部化区域中，AlP 颗粒形成较慢，颗粒也较小。所形成的颗粒的表面积常常高于酸催化所得的颗粒，且较少聚集和团聚。在一个示例实施例中，颠倒实施例 2 中的添加顺序，也就是说，缓慢地向氢氧化铝浆体中加入磷酸要求量。所述浆体的制备如实施例 2 所述。缓慢地在约 30 分钟至 1 小时的时间内添加磷酸，且机械性地搅拌所得混合物，并加热至约 95° C，持续 3 小时。如实施例 2 所述地分离、纯化、干燥 AlP 颗粒。

[0066] 除上述公开的酸到碱途径外，还发现，在将酸溶液加入到浆体前，首先将一定量的氢氧化铝溶解在磷酸中 ， 可以进一步改进所述酸到碱途径。在一个示例实施例中，将一定

量氢氧化铝，例如达到氢氧化铝溶解度上限的量，单独溶解在磷酸中。在一个示例实施例中，根据两步法制备 AlP。第一步，首先将部分氢氧化铝（一般是化学计量的三分之一）溶解在磷酸中，以形成酸性 AlP 溶液。该酸性 AlP 溶液包括满足反应产物中 P :Al 比例为期待值 1 :1 的反应化学计量的所有磷酸和磷酸盐。第二步，将该酸性 AlP 溶液加入含有满足化学计量要求的剩余氢氧化铝量的浆体中。混合物在环境温度下进行反应，形成含有分散于水中的固体酸性 AlP 颗粒的 AlP 缩合固体。可选地，该反应可以发生在高温条件下，例如约 95℃，即反应效率和产物形式的动力学控制的优选温度。该两步法的优点之一，在于反应所需的部分氢氧化铝在将酸溶液加入浆体前就已溶解并预反应，由此所得的后续多相反应粘度较低，搅拌需求低，从而保证更完全的缩合。

[0067] 如上所述的实施例 2 中所述的方法，所述酸到碱反应途径优选为在恒定体积条件下进行。过滤悬浊液以分离酸性 AlP 颗粒。用水洗涤这些颗粒一次或多次，然后再次过滤。在一个示例实施例中，初始过滤后，以约 6 倍于沉淀物体积的水洗涤所述颗粒，然后再次过滤。在一个优选实施例中，顺序是过滤、洗涤，可以重复任意次数，来达到期望的纯化度。然后，可以过滤所得再洗后的 AlP 颗粒，并在约 110° C 温度下干燥约 24 小时，以提供酸性 AlP 颗粒。

[0068] 可选地，在再洗后，可以再悬浮 AlP 颗粒，然后通过加入合适的中和剂来进行中和，例如如上所述。在一个示例实施例中，向再悬浮的 AlP 中加入足量的氢氧化铵 (NH_4OH)，并过滤所得混合物，以分离 AlP 颗粒，并加热。在一个示例实施例中，AlP 颗粒加热至约 110° C 约 24 小时，以除去水分，并生成固体 AAlP 颗粒。此外，如上所述地，应当理解，在此所公开的方法还可以用于生成结晶 AlP，或 AAlP 和结晶 AlP 的组合物，例如，通过在超过约 90° C 的温度下进行反应。

[0069] 实施例 4 - 二元缩合反应制备 AlP（碱到酸原位聚集）

在一个示例实施例中，通过向磷酸（H_3PO_4）中添加氢氧化铝（$Al(OH)_3$）形成所需 AlP，例如以实施例 1 和 2 中所公开的方式，来制备 AlP。但是，与实施例 1 和 2 不同，该反应能够在开放系统中进行，其中所述反应系统敞开，由此允许溶剂水持续蒸发，从而使得反应系统的浓度随时间增加，而 pH 随时间降低。缩合反应法中的定周期时段中，重新补充水以使水位回到初始体积。该反应浆体随后以约 50g 水稀释，并搅拌 30 分钟，以进一步促进 AlP 颗粒在反应浆体中的分散。该浆体随后过滤、以约沉淀物体积六倍的水洗涤，并再次过滤。该过滤 - 洗涤 - 过滤的循环可以重复直至达到期望的纯度水平。通常，一次到三次循环就足以去除未反应初始材料及不需要的反应副产物了。

[0070] 据发现，通过允许上述的体积变化，系统浓度和 pH 中的所得变化使得溶液中的 AlP “寡聚物”向已经形成和聚团的 AlP 颗粒连续沉淀。AlP “寡聚物”向已经形成和聚团的 AlP 颗粒连续沉淀的操作，封闭了现有 AlP 聚团和颗粒的表面孔隙，例如，形成原位颗粒层，由此降低所述 AlP 聚集物的表面孔隙度，并降低其相关性质例如吸油度。在一个示例实施例中，所述 AlP 寡聚物为 AAlP，且已经形成的 AlP 颗粒为 AAlP。

[0071] 如上所述，允许水位在缩合反应中循环，使得 pH 与 $Al(OH)_3$ 浓度成比例地变化。当体积下降时，$Al(OH)_3$ 浓度升高，pH 因而上升，且溶解度下降，允许 AlP 寡聚物团集。向缩合物介质添加 $Ca(OH)_2$，也可以对 pH 变化有相似影响，引起 AlP 沉淀及随之而来的对现有 AlP 颗粒的涂覆。该过程还可以加入碱土金属阳离子，以作为残余酸性磷酸盐基团的反离子，吸

附在 AlP 颗粒表面或作为悬垂部分连接。

[0072] 形成的缩合固体的存在形式为酸包覆的固体 AAlP 颗粒在水中的分散系。过滤该悬浊液以分离该酸包覆的 AlP 颗粒，用水洗涤一次或多次，然后再次过滤。在一个示例实施例中，在最初过滤后，用约沉淀物六倍体积的水洗涤颗粒，然后再次过滤。连续洗涤来移除未反应初始材料和任何反应副产物。再次过滤后，加水重悬浮酸包覆 AlP 颗粒，并进一步加热处理。在一个示例实施例中，该浆体过滤以分离酸包覆 AlP 颗粒，且加热该颗粒至约 110° C 度约 24 小时，以除去水分并生成酸包覆 AlP 颗粒。可选地，将包覆 AlP 颗粒加热至约 250° C 温度约 12-48 小时，来生成不含水分和任何能在 250° C 以下分解的副产物的干燥的酸包覆 AlP 颗粒。此外，如上所述，应当理解，在此公开的方法可用于产生结晶 AlP 或 AAlP 和结晶 AlP 的组合物。

[0073] 实施例 5 :二元缩合反应形成 AlP（酸到碱原位聚集）

在一个示例实施例中，通过向氢氧化铝（$Al(OH)_3$）中添加磷酸（H_3PO_4）来形成所需 AlP，例如以实施例 3 中所公开的方式，来制备 AlP。但是，与实施例 3 不同，该反应能够在开放系统中进行，其中所述反应系统敞开，由此允许溶剂水持续蒸发，由此使得反应系统的浓度随时间增加，而 pH 随时间降低。缩合反应法中的定周期时段中，重新补充水以使水位回到初始体积。该反应浆体随后以约 50g 水稀释，并搅拌 30 分钟，以进一步促进 AlP 颗粒在反应浆体中的分散。该浆体随后过滤，以约沉淀物体积六倍的水洗涤，并再次过滤。该过滤 - 洗涤 - 过滤的循环可以重复直至达到期望的纯度水平。通常，一次到三次循环就足以去除未反应初始材料及不需要的反应副产物了。

[0074] 如实施例 4 所述，据发现，通过允许上述的反应过程中的体积变化，系统浓度和 pH 中的所得变化使得溶液中的 AlP“寡聚物”向已经形成和聚团的 AlP 颗粒连续沉淀。AlP“寡聚物”向已经形成和聚团的 AlP 颗粒连续沉淀，封闭了现有 AlP 聚团和颗粒的表面孔隙，例如，形成原位颗粒层，由此降低所述 AlP 聚集物的表面孔隙度，并降低其相关性质例如吸油度。在一个示例实施例中，所述 AlP 寡聚物为 AAlP，且已经形成的 AlP 颗粒为 AAlP。此外，如上所述，应当理解，在此公开的方法可用于产生结晶 AlP 或 AAlP 和结晶 AlP 的组合物。

[0075] 实施例 6 :形成生物活性 -AlP 配合物（物理性包含）

作为二元缩合产物所得的 AlP（如实施例 1-5 中所述）构成约占 34% 重量百分比的浆体，并与适当浓度的硝酸银溶液混合。后者溶液的制备，在于制备银和浆体各占 1.0% 和 10% 的银 -AlP 浆体溶液。混合所述浆体混合物约 5 分钟，然后在氮气中以喷雾干燥机雾化，并在入口处约 180° C 及出口处约 79° C 的温度下干燥。收集固体粉末并分析。所得粉末是生物活性 -AlP 配合物，其中生物活性材料物理性地包含、网罗、包裹或交缠在 AlP 聚合物中。

[0076] 可选地，二元缩合产物形式的 AlP（例如如实施例 1-5 中所列举）构成浆体中的 34% 重量百分比，并与适当浓度的硝酸银溶液混合。搅拌后，过滤所述混合浆体，并以 40-60° C 的热水洗涤一次。将过滤物在约 110° C 下干燥约 12 小时，分为几个部分，分别在约 250° C 下加热处理约 24 小时。不管加热处理温度为何，产量是相同的，且所得粉末是生物活性 -AlP 配合物，其中生物活性材料物理性地包含、网罗、包裹或交缠在 AlP 聚合物中。

[0077] 实施例 7 :形成生物活性 -AlP 配合物（化学性键合）

如实施例 1-5 所述地以二元缩合途径制备 AlPs，但在混合磷酸和氢氧化铝的同时，也

加入适当浓度的硝酸银溶液。所得悬浊液包括了溶液中的生物活性 -AlP 配合物的缩合物，其中所述生物活性材料为银离子形式，且与 AlP 聚合物化学性键合，例如，包含在 AlP 聚合物的骨架中。如上所述地过滤该悬浊液，以分离生物活性 -AlP 配合物颗粒。洗涤所述颗粒，并在上述实施例中所述温度下干燥，以提供所需的改造物理性质或特性，例如孔隙度。

[0078] 在这些示例过程中，通过化学反应形成非结晶正磷酸铝，或形成正磷酸铝（$Al_2(HPO_4)_3$或 Al（$H_2PO_4)_3$）。该反应通过混合两种成分（单独形成 AlP 时）或混合三种成分（直接形成生物活性 -AlP 配合物时）来进行。在配备有搅拌装置的反应器中加入一定量的试剂，并允许其反应一段短时间，例如，低于约 10 分钟。

[0079] 在二元合成形成 AlP 的过程中，影响产物结果的变量可以包括 :（a）使用的 ATH 种类 ;（b）将 ATH 分散在反应浆体中的方法及采用的温度 ;（c）反应浆体中的 ATH 浓度 ;（d）ATH 浆体到磷酸的混合（添加）顺序和用量 ;即酸到碱（A 到 B）或碱到酸（B 到 A）;（e）反应浆体的浓度 ;（f）缩合反应进行的温度（例如，室温或高温如 95° C）;（f）在所述温度下的反应时长（时间）（例如，30 分钟或直至 4 小时）;（g）搅拌类型（例如，简单混合或分散）;以及（h）反应后处理，例如过滤，随后洗涤并干燥所述缩合物至干燥粉末 ;或通过蒸发部分溶剂（调整或不调整 pH）将缩合物浆体浓缩为凝胶或糊状物。

[0080] 关于所用的 ATH 类型，据发现，二元合成法所制得的 AlP 的物理形式取决于用做初始材料的 ATH 性质，以及控制着动力学的反应条件。一般而言，可以用两种 ATH 类型 :非结晶和结晶。结晶 ATH 可以存在于各种具体结晶形式和矿物质组合物中。据发现，某些所述种类需要相当大的热能形式的能量输入和搅拌才能进行磷酸盐缩合反应。使用结晶 ATH 所得的 AlP 产物一般也是结晶（多种可能结构之一）。

[0081] 使用非结晶 ATH 允许室温下的快速反应动力学，且所得的 AlP 也几乎总是非结晶的。据发现，以尽可能低的温度进行反应，对保存银的所需功能性（当银用作抗菌剂时）是有用的。据发现，非结晶 ATH 适用于所述用途。据发现，当中度反应性的结晶 ATH（根据 DSC 在约 310° C 左右发生吸热转换，与之相比，反应性较低的 ATH 材料的吸热转换发生在约 340° C 左右）与磷酸在室温下缩合时，产生的 AlP 由约 50% 非结晶成分（包括银 - 铝 - 磷酸盐成分）和约 50% 未反应的 ATH。该非结晶转换水平实际上高于使用典型的结晶 ATH 与磷酸在室温下混合的缩合反应，后者一般产生低于 10% 的转换。所得到的 AlP 为非结晶，且据推理，其组成成分主要是表面覆盖磷酸盐的 ATH。此述化学反应中的较高水平的非结晶 AlP 转换，归因于其他促进表面反应和 / 或抑制结晶化过程（从而使得形成的 AlP 保留非结晶形式）的成分的存在。据测试发现，该组合物提供了有效的抗菌活性水平和光稳定性。

[0082] 与生物活性 -AlP 配合物（例如 Ag-AlP）的形成相关的另一个变量，可以包括 :生物活性剂（例如银源，例如硝酸银）的引入点为 :（a）在缩合反应前加入 ATH 浆体（ATH+AgX+ 水）;（b）在缩合反应前加入磷酸 ;（c）在混合开始时作为溶液加入到混合的缩合物中 ;以及（d）在混合结束时作为溶液加入缩合物中。在进行二元缩合反应的背景下，讨论了生物活性剂的引入点，但是应当理解，该变量也同样适用于制备本文所公开的生物活性 -AlP 配合物的其他方法。

[0083] 沉淀法制备

AlP 是将适当的盐（例如氢氧化铝、氢氧化镁、氢氧化钙、硫酸铝等）溶解于能够足以完全溶解所述盐的摩尔量的磷酸中，所制得的磷酸盐配合物。使用碱溶液或碱（例如氢氧化

钠、氢氧化钾、氢氧化铵、铝酸钠、铝酸钾等）中和，令该磷酸盐配合物从酸溶液中沉淀出来。所得的沉淀固体的组成成分取决于金属与磷酸盐银离子的比率。沉淀配合物（即 AlP）的性质，取决于将所述盐溶于酸时所用的工艺参数以及沉淀 / 中和条件，包括中和剂的选择、温度、反应物添加顺序、反应物添加量以及搅拌程度和时长。

[0084] 通过在有控制的材料递送、温度、搅拌和 pH 的特定条件下，混合选定的初始材料，包括铝源和磷源，以沉淀产物的形式制备 AlP。合理选择初始材料和工艺条件，获得的 AlPs 具有能够满足上述改造后物理性质或特性（例如孔隙度）的物质成分和化学结构，从而提供所期望的生物活性成分的受控递送 / 释放。

[0085] 可用于沉淀形成 AlP 的铝源包括铝盐，例如氯化铝、硝酸铝、硫酸铝等。可用于形成 AlP 的铝源还包括铝盐化合物，例如铝酸钠等、氢氧化铝或金属形式的铝。可用于沉淀形成 AlP 的磷源包括磷酸以及磷酸盐，例如正磷酸盐或多磷酸盐。使用碱溶液来控制主要成分的 pH 或中和其反应。在一个示例实施例中，该碱溶液可以包括氢氧化铝、氢氧化钠、碳酸钠及其组合。在一个示例实施例中，氢氧化钠用作碱溶液。可用的铝源、磷酸盐源和碱源包括已公开的美国专利申请 2006/0045831 和 2008/0038556 中所公开的内容，其均已引用方式全文并入本文。

[0086] 可以用上述材料的选择性组合来制备 AlPs。下文中将选择性地提供如下的制备方法作为示例，应当理解，除了在此具体公开的方法外，还可以使用其他制备方法。虽然沉淀法所制备的 AlP 在下文中公开为包括非结晶 AlPs，应当理解，在此公开的制备 AlP 的沉淀法还可以用于或适用于生产结晶 AlP 或非结晶和结晶 AlP 的组合，取决于特定的抗菌化学组合物性质需求。

[0087] 实施例 8 :硫酸铝方法制备 AlP

在一个示例实施例中，具有上述改造性质的 AlP 是通过如美国专利 7951309 所公开地混合硫酸铝、磷酸和氢氧化钠而制得的，该专利以引用方式并入本文。用于该实施例中的工艺步骤通常包括 :制备主要试剂，例如磷酸稀释溶液、硫酸铝稀释溶液以及氢氧化钠或氢氧化铵稀释溶液 ;向配备有晃动系统的反应器中同时且有控制地加入试剂，以在该过程中保持混合物的均匀 ;以及，在向反应器中添加试剂期间，控制混合物的温度和 pH （酸性）以及反应时间。

[0088] 该示例过程中的主要试剂可如下制备。一种磷源是肥料品级的磷酸，任何原料来源均可，并经过澄清和脱色。例如，可以将含有约 54% P_2O_5的磷酸进行化学处理和 / 或以处理过的水稀释，得到浓度约为 20% 的 P_2O_5。可用于此示例过程的另一试剂为商用硫酸铝，其可以通过氧化铝（水合氧化铝）和浓硫酸（98% H_2SO_4）的反应获得，并经过澄清，在约 28% AI_2O_3的浓度下贮藏。为了获得有利的反应动力学，硫酸铝可以用处理过的水稀释为约 5% AI_2O_3。

[0089] 用氢氧化钠溶液对该反应进行中和，氢氧化钠溶液可以是市购的不同浓度的氢氧化钠。可以购买浓度约为 50% 的 NaOH 并稀释。例如，在反应第一阶段中，当混合初始试剂时，可以使用浓度约为 20%NaOH 的氢氧化钠。在反应的第二阶段中，为了微调产物酸性，可以使用约含 5%NaOH 的氢氧化钠溶液。可使用氢氧化铵或碳酸钠（苏打粉）作为替代性的中和剂。

[0090] 在此示例过程中，化学反应形成的产物是非结晶正磷酸铝或正磷酸铝（Al_2（HPO_4）

$_3$或 Al（H_2PO_4）$_3$）。该反应通过混合三种试剂来进行，即磷酸溶液、硫酸铝溶液和氢氧化钠溶液。在反应器（一般配备有搅拌装置）中，在约 30 分钟内加入一定量的试剂。在向反应器中添加试剂的过程中，混合物的 pH 控制在 4-4.5 的范围内，且反应温度范围为 35° C 至 40° C 之间。该反应在试剂混合后约 15 分钟后完成。在此期间，混合物的 pH 可以通过添加更多的稀释氢氧化钠，调整至 5。在此示例过程中，温度优选为保持在约 40° C 以下。反应结束时，所形成的悬浊液所包含的 P :Al 摩尔比应当在约 0.8:1 至 1.2:1 之间。

[0091] AlP 形成后，悬浊液含有约 6.0% 至 10.0% 固体，最大近似温度为约 45° C，且密度为约 1.1.5-1.25 g/cm^3，对其进行分离处理。在一个示例实施例中，将悬浊液泵入常规压滤机。在该压滤机中，令液相（有时也称为“液”）和固相（有时也称为“饼”）分离。含有约 35-45% 固体的湿滤饼留在过滤机中进行洗涤循环。过滤后的浓缩物基本为硫酸钠的浓缩溶液，将其从过滤机中抽提出来，并贮藏以待将来使用。在此公开的分离技术是压滤机，但应当理解，也可以使用其他种类的分离技术。

[0092] 在一个示例实施例中，对湿滤饼的洗涤在过滤机自身中进行，并包括多个处理步骤。在第一洗涤（“置换洗涤”）中，移除了污染该湿滤饼的最大部分过滤物。该洗涤步骤是以预定流速流动的处理水来对滤饼执行的。可以执行第二洗涤步骤，仍然使用处理水，来进一步降低（如果未消除）污染物。可以使用第三洗涤步骤，采用轻度碱溶液来中和该滤饼并将其 pH 保持在 7.0 范围内。可以用压缩空气吹该滤饼一段时间。优选地，该湿产物的固体成分在约 35-45% 之间。虽然在此公开了对特定洗涤技术和顺序的使用，但是应当理解，还可以使用其他种类的洗涤技术。

[0093] 对该滤饼可以如此进行分散 :可以将该湿润并洗涤后含有约 35% 固体的滤饼，以传送带从压滤机中抽提出来，转移至反应器 / 分散器。添加四焦磷酸钠的稀释溶液，来辅助该滤饼的分散。

[0094] 在该分散步骤后，将含有约 30-50% 固体的该 AAlP “泥浆”泵入干燥装置中以干燥该产物。在一个示例实施例中，可以使用干燥设备移除材料中的水，例如使用“涡轮干燥器”，注入温度低于约 300° C 的热空气流，优选为约 100-200° C 的温度，如上所述，以获得期望的改造孔隙度。虽然在此公开了特定的干燥技术，但应当理解，也可以使用其他的干燥技术种类。

[0095] 实施例 9 :氯酸钠法制备 AlP

在又一个示例过程中，使用铝酸钠作为铝源来制备 AlP，如美国专利 7951309 所述。在一个所述实施例中，通过磷酸和氢氧化铝之间的反应制备 AAlP。该过程可以进一步包括中和步骤，该步骤可以使用铝酸钠来进行。在某些实施例中，制备 AlP 的过程包括令磷酸、氢氧化铝和铝酸钠反应。在一个实施例中，制备非结晶磷酸铝钠的过程包括令磷酸铝和铝酸钠反应。

[0096] 在一个实施例中，该反应包括 2 个步骤。在第一步骤中，磷酸与氢氧化铝反应，以生成酸性 pH 下的磷酸铝。在一个实施例中，制得的 AlP 为水溶性磷酸铝。在某些实施例中，制得的 AlP 为水溶性磷酸铝。在某些实施例中，水溶性 AlP 的 pH 为低于约 3.5。在某些实施例中，该 pH 为约 3、2.5、2、1.5 或 1。在某些实施例中，制得的 AAlP 为较高 pH 下的微细固体 - 液体分散系。在一个实施例中，该 pH 为约 3、4、5 或 6。

[0097] 在第二步骤中，来自第一化学步骤的该酸性水性磷酸铝溶液或分散系与铝酸钠反

应。在某些实施例中，使用的铝酸钠为 pH 大于约 10 的水溶液。在一个实施例中，该水性铝酸钠溶液的 pH 为约 11、12 或 13。在一个实施例中，该水性铝酸钠溶液的 pH 为大于约 12。所制得的 AAlP 为固体沉淀物。在一个实施例中，该固体铝 - 钠磷酸盐的 P :Al 摩尔比率为约 0.85，且 Na :Al 摩尔比率为约 0.50。在一个实施例中，固体 AAlP 的 P :Al 摩尔比率为约 1，且 Na :Al 摩尔比率为约 0.76。在某些实施例中，可以用同样的步骤获得其他配制比率的分子。

[0098] 在一个实施例中，在第一化学步骤中向磷酸中加入固体水合氢氧化铝。在又一个实施例中，向纯化的液体铝酸钠溶液中加入该固体水合氢氧化铝形成胶体溶液。在又一个实施例中，在第二反应步骤中，直接添加固体或固体 - 液体悬浊液形式的固体水合氢氧化铝。在某些实施例中，该反应在单一步骤中进行。

[0099] 可用于该示例过程的铝酸钠包括可通过本领域技术人员已知的方法得到的铝酸钠。例如，可以使用溶液形式的铝酸钠，其可以是来自拜耳法的第一步骤的标准化学产物，存在于来自铝土矿的氧化铝 (AI_2O_3) 提取液（常称为“纯化钠富液（purified sodium pregnant solution）”）中。该液态铝酸钠水溶液在常温下是饱和的，并以氢氧化钠（NaOH）稳定化。它的典型组成成分为 :58 至 65% 质量 (25 至 28% 质量的 AI_2O_3) 的铝酸钠 ;3.5 至 5.5% 质量 (2.5 至 4% 质量的自由 Na_2O) 的氢氧化钠。在某些实施例中，它的 Na :Al 摩尔比率为约 1.10 至 2.20，且杂质低（取决于铝土矿源，有 :Fe=40 ppm，重金属 =20 ppm，以及少量阴离子，CI^- 和 SO_4^{2-}）。在某些实施例中，铝酸钠水溶液的 Na :Al 摩尔比率为约 1.10、1.15、1.20、1.25、1.30、1.35、1.40、1.45、1.50、1.55、1.60、1.65、1.70、1.75、1.80、1.85、1.90、1.95、2.0、2.05、2.10、2.15 或 2.2。在某些实施例中，溶液颜色为琥珀色。在某些实施例中，溶液的年度为约 100cP。在某些方面中，通过抛光过滤来纯化该铝酸钠溶液。在某些实施例中，从氢氧化铝钠和氢氧化钠中再生得到该铝酸钠溶液。

[0100] 可以使用本领域技术人员已知方法来获得固体水合氢氧化铝。在一个实施例中，氢氧化铝是根据拜耳法所制得的工业化学品。可以冷却 “纯化铝酸钠富液”来进行沉淀，得到固体水合氢氧化铝。在一个实施例中，由此制得的铝酸钠具有低杂质水平和可变湿度（阳离子约 70ppm，氯酸盐约 0.85% 质量，硫酸盐约 0.60% 质量（这些杂质是由“纯化铝酸钠富液”的纯化水平决定的），且总水量（即水合作用和湿度）约 22.0-23.5% 质量）。在一个方面中，两种原材料均为标准初级工业产品，是由铝土矿处理器大量生产、从铝土矿处理的第一步骤和第二步骤中得来的商品。

[0101] 在一个实施例中，该化学反应得到磷酸铝钠 ($Al(OH)_7Na_7(PO_4).1.7H_2O$)。磷酸铝钠形成后，该悬浊液含有约 6-10% 固体，最大近似温度为 45° C，且密度在 1.15 至 1.25 g/cm^3 的范围。将其泵吸至常规压滤机中。

[0102] 在一个优选实施例中，用铝酸钠通过该沉淀法制备 AlP。据发现，该铝酸钠法提高了对 AlP 期望特性的控制水平，而这在硫酸钠法中是无法得到的。

[0103] 实施例 10 :生物活性 -AlP 配合物的形成（物理性包含）

根据实施例 8 和 9 所述的沉淀法制备的 AlP 构成浆体重量百分比的 34%，将其与适当浓度的硝酸银溶液混合。后者溶液使得制得的银 -AlP 配合物中的银和 AlP 重量比为 1.0% 和 10%，由此得到浆体溶液。将混合浆体混合约 5 分钟，然后以喷雾干燥器在氮气中将其雾化，并在入口约 180° C 到出口约 79° C 的温度范围下进行干燥。收集固体粉末并进行分

析。所得粉末即为生物活性 -AlP 配合物，所述 AlP 聚合物中物理性地包含、网罗、包裹或缠绕有生物活性材料。

[0104] 可选地，根据上述沉淀法制备的 AlP 构成浆体重量百分比为 34%，将其与适当浓度的硝酸银溶液混合。搅拌混合浆体后，将其过滤并以温度为 40-60 ° C 的热水洗涤一次。在约 110 ° C 下干燥滤液约 12 小时，分为若干部分，将各部分在约 250 ° C 下热处理约 24 小时。无论热处理温度为何，其产量相同，且所得粉末为生物活性 -AlP 配合物，所述 AlP 聚合物中物理性地包含、网罗、包裹或缠绕有生物活性材料。

[0105] 实施例 11 :生物活性 -AlP 配合物的形成(化学性键合)

使用类似于实施例 8 和 9 中所述的沉淀法的方法来制备 AlP，但适当浓度的硝酸银溶液与酸性磷酸铝溶液(P :Al 比率为 3 :1)混合之后，再以适量磷酸钠中和。所得分散系包括生物活性 -AlP 配合物，其中银离子形式的生物活性材料与 AlP 聚合物化学性键合，例如包含在聚合物骨架中。过滤该分散系从而分离该生物活性 -AAlP 配合物颗粒。洗涤所述颗粒并在上述温度下干燥，以提供所需的改造的孔隙度。

[0106] 溶胶 - 凝胶制备法

以溶胶 - 凝胶法制备的 AlP 涉及 :通过分子或离子前体形成胶体悬浮液(溶胶)以及所述溶胶的凝胶化，来在连续液相中形成固体网络(凝胶)，从而建立无机分子网络。用于合成所述交替的前体一般包括被各种活性基团所包围的金属或非金属元素。换言之，在该溶胶 - 凝胶法中，简单分子或离子前体被转换为纳米级颗粒，以形成胶体悬浮液(溶胶)。然后，该胶体纳米颗粒相互连接形成充满液体的三维固体网络(凝胶)。该凝胶化转变可以用多种方法启动，但最方便的方法是改变反应溶液的 pH。

[0107] 用于从所述固体中去除液体的方法，会影响溶胶 - 凝胶的性质。例如，超临界干燥可以保持干燥固体中的三维结构，而流体蒸发法的缓慢干燥会令网络结构收缩，形成高密度材料。

[0108] 使用溶胶 - 凝胶合成法制备 AlP 的好处包括 :过程的多功能性和简便性，由此可能得到高纯度和 / 或定制化的材料、均匀的粒径分布、基本球形的聚集颗粒、纳米级颗粒以及定制设计的组成成分。虽然在此公开的 AlP 包括基本球形的聚集颗粒，但应当理解，也会偶然生成少量的非球形颗粒，存在于所得的抗菌化学组合物中。

[0109] 本文所称的术语“凝胶”应当理解为由交联的大分子量聚合物或聚集物形成的三维笼状结构，其中嵌有液体。该结构网络一般由核心颗粒之间的弱键合和 / 或可逆键合组成。本文所称的术语“溶胶”应当理解为液体中的固体胶体分散系。所述固体包括具有纳米级平均粒径的磷酸铝。所述交替包括磷酸铝溶胶，其形式为包括所有液体的半刚性物质中的分散相。溶胶 - 凝胶法中的产品后处理，包括过滤、洗涤、干燥及其组合，使得交替固体以有控制的形式聚集，以形成较大的固体配合物。

[0110] 一般而言，溶胶 - 凝胶法包括如下处理步骤 :(1)分子前体经过成核或聚合或缩合反应，形成初级粒子，例如纳米级粒子，从而形成溶胶(胶体分散系或悬浊液);(2) 颗粒的生长或凝胶化 ;(3) 颗粒的交联以形成链或所述链在液体介质中延伸以形成增厚的凝胶 ;以及 (4) 处理该溶胶 - 凝胶材料，以移除液体，得到所需的固体终产物。

[0111] 在一个示例实施例中，该前体溶液是通过混合适当的铝源和磷源来制备的。适当的铝源可以选自以下铝盐 :例如氯化铝、硝酸铝、硫酸铝等。优选的铝源为硝酸铝。可用于

以溶胶－凝胶法制备 AAlP 的磷源包括磷酸以及磷酸盐(例如正磷酸盐或多磷酸盐)。其中一种磷源为任何原料来源的经过澄清和脱色的肥料品级磷酸。

[0112] 在水相环境中,将前体溶液的主要成分与胶凝剂混合,以生成固体磷酸铝颗粒的溶液胶体分散系。在一个示例实施例中,该前体溶液是通过在水的存在下,混合硝酸铝和磷酸(85% 重量百分比)来得到的。水可以存在于以下一种或多种中 :硝酸铝、磷酸或作为独立于各成分的添加水。

[0113] 混合前体成分之后,搅拌所得系统,并向搅拌后的溶液添加合适的碱性成分。可用于此目的的碱性成分包括用于改变系统 pH (例如提高酸性系统的 pH) 的常规碱性成分,在一个示例实施例中为氢氧化铝。氢氧化铝的存在,提高了 pH,并驱动了成核和缩合反应过程,形成了胶体分散系或溶胶。

[0114] 根据成核剂的浓度,该步骤可以是中间步骤或终步骤。添加更多的成核剂使得初级磷酸铝颗粒相互交联形成凝胶,例如产生凝胶化,并进一步使得胶体颗粒与凝胶结构交联,以形成溶胶－凝胶。

[0115] 在一个示例实施例中,可能需要控制该溶胶－凝胶过程,以在凝胶化之前分离该胶体分散系。这可以通过控制反应条件来达成,从而仅发生胶体分散(即形成溶胶)而非完全凝胶化。照此控制该过程,可以提供某些生产上的优势和 / 或某些终产品处理方面的优势。

[0116] 由此方法得到的胶体分散系,可过滤来回收固体,然后如下所述地进行热处理和 / 或洗涤。

[0117] 在一个示例实施例中,可以加热磷酸、硝酸铝和 / 或氢氧化铵,然后再进行混合,或在混合后进行加热,例如边搅拌边加热。此外,可以调整含水量和 / 或氢氧化铵添加速率,以产生具有 AAlP 期望产量的期望反应产物。

[0118] 在一个示例实施例中,添加到酸溶液中的氢氧化铵(NH_4OH)量,足以中和酸系统来触发胶体磷酸铝颗粒的形成,且能令超过化学计量的凝胶化形成硝酸铵(NH_4NO_3)。氢氧化铵(NH_4OH)量的范围可以是从形成 NH_4NO_3所需的 NH_4OH 化学计量(1.0 化学计量)到约 3.0 化学计量,优选为在约 1.1 到 2.0 之间,更优选为在约 1.2 和 1.5 之间。

[0119] 据发现,添加顺序(即碱溶液到酸性前体溶液,或反过来)可控制凝胶化的速率和程度。当以上述化学计量浓度范围(1.0 到 3.0)将碱加入搅拌后的前体溶液后,凝胶化几乎立刻发生。据发现,颠倒添加顺序,即将前体溶液加入碱溶液中,能够控制从胶体分散系到完全凝胶化的生长程度。如下文所述,据发现,还可以用添加方法来控制颗粒形态。

[0120] 据发现,超过 1.1 化学计量比率的氨浓度,可以令反应配合物中的未反应铝最小化。在终端应用用途为抑制性颜料时,需要配合物接触水时的磷酸盐释放速率在 200-400ppm 的范围内。据测试确定,当反应中的氨水平在约 1.2 到 3 化学计量比率,且如下地经过固体彻底洗涤和 / 或热处理以去除可溶副产物之后,磷酸阴离子洗脱液在目标范围内。

[0121] 在一个示例过程中,溶胶－凝胶接下来进行凝胶后处理,可包括加热、洗涤和 / 或筛分。在一个示例实施例中,通过去除液体成分令分散系收缩,来分离所得的溶胶－凝胶粉末。从该溶胶－凝胶可以形成各种类型的凝胶,例如 :干凝胶(溶胶－凝胶顺利干燥从而形成高孔隙度和表面积(150 － 1,000 m^2/g)的固体),气凝胶(超临界干燥(例如冷冻干燥)所

得的固体)，水凝胶(分散于水中的水溶性胶体聚合物颗粒)，以及有机凝胶(非结晶、非玻璃状的固体，含有嵌在固体基质中的液体有机相)。

[0122] 该溶胶－凝胶由固体 $AlPO_4$组成，所述 $AlPO_4$通过各种 pH 依赖性(氨、水、磷酸盐)连接来形成包裹所有液体的物质的固体分散相，所述液体由水和溶解盐类组成。加热该凝胶至大于约 100° C 的温度，蒸发水和所有氨，并令物质收缩为由磷酸铝($AlPO_4$)和硝酸铵(NH_4NO_3)组成的固体。加热该凝胶或收缩凝胶固体至高于约 215° C 的温度以热分解硝酸铵(NH_4NO_3)，从而将此从粉末产物中去除。加热到高于约 215° C 的温度，造成了 pH 下降，表明硝酸铵(NH_4NO_3)热分解后的残余氨基(很可能是作为 PO 基团上的取代基)也热分解了，并被氢原子取代，从而使得配合物呈酸性。由此热处理得到的固体产物，据分析显示，是磷酸盐释放率为约 240ppm 且表面积大于 125 约 m^2/g 的纯净 AAlP。

[0123] 相应地，凝胶化后的热处理可以包括在约 250° C 的较高温度下加热溶胶－凝胶的单一步骤，其中加热时间足以达到水蒸发、物质收缩和热分解硝酸铵(NH_4NO_3)。在一个示例实施例中，这可以在约 250° C 下处理约 12-72 小时。从该热处理所得的产物基本为磷酸铝，即非常少或几乎没有磷酸铝或硝酸铵。

[0124] 可选地，凝胶化后的热处理可以包括在约 100-150° C 的较低温度下加热溶胶－凝胶足以达到水蒸发的时间的单一步骤。在一个示例实施例中，这可以在约 110° C 下进行约 1-24 小时。从该加热或干燥处理所得的产物为 AAlP、磷酸铵和硝酸铵。

[0125] 该干燥步骤后，可以以约 215-300° C 之间的温度进行热处理步骤。在一个优选实施例中，该干燥步骤为约 110 下约 24 小时，且该热处理为约 250° C 下 1-3 天(16-72 小时)。所得的 AAlP 具有重量百分数为约 5-20% 的水分含量，且具有期望的改造孔隙度。热处理物质的 pH 可以通过再分散配合物来调整，并以氢氧化铵溶液调整 pH。然后，在 100-110° C 下干燥所得配合物，以移除水和氨。

[0126] 根据需要，在干燥或加热处理前，可以过滤所述溶胶－凝胶材料，以从溶液中分离固体颗粒，且分离所得固体(例如饼状形式)可进行一个或多个洗涤循环。所述洗涤循环使用水，并用于从固体磷酸铝颗粒中去除任何不需要的可溶物，例如氨化合物，例如作为反应副产物形成的硝酸铵和磷酸铵。洗涤后的样品可以随后以上述公开的干燥和／或热处理，以在洗涤后的磷酸铝中进一步蒸发水和／或热分解任何参与硝酸铵和磷酸铵，并使磷酸铝颗粒致密化。

[0127] 根据需要，可以在约 100° C 下干燥溶胶材料，令水蒸发并其物质塌缩，所得粉末可以用水洗涤来去除硝酸铵(NH_4NO_3)，由此回收副产物，而非令其热分解。洗涤和干燥后的物质可以在大于约 215° C 下进行热处理，从而得到基本纯净的 AAlP。

[0128] 用于形成仅 AAlP 的溶胶－凝胶法的基础化学如下所示：

1. 前体溶液：所有成分的组合：

$Al(NO_3)_3 \cdot 9H_2O + H_3PO_4 + H_2O$

2. 胶凝剂

$3NH_4OH + H_2O$

3. 溶胶－凝胶反应

$AlPO_4 + (NH_4)_3PO_4 + H_2O \rightarrow AlPO_4 + NH_4OH$

形成AAlP溶胶－凝胶的反应：随着NH_4OH (28% NH_3水溶液)的添加，它中和了酸系统并

驱动不可溶Al PO_4的形成，使得Al^{+3} 离开反应并允许NH_4^{+3}与$NO3^{-1}$ 结合以形成可溶NH_4NO_3。根据 NH_4OH 的浓度和添加速率，将会形成 $AlPO_4$的胶体颗粒。向反应添加更多的 NH_3 ，允许$AlPO_4$的胶体颗粒聚集并最终在该颗粒之间成键，以形成凝胶结构。

[0129] NH_3 添加量必须超过形成 NH_4NO_3的化学计量要求，以具有足够的 NH_3来控制 pH 并促进凝胶桥接。

[0130] 根据 NH_3 添加量、添加速率和浓度，该凝胶会由交联的 $AlPO_4$固体颗粒组成，所述固体颗粒形成笼状三维结构，包裹溶于水中的硝酸铵（NH_4NO_3）。磷酸铵也可能作为中间体存在，且延伸反应条件（即进一步加热）将在系统中引起与铝的完全反应，以缩合为磷酸铝。

[0131] 4. 过滤和洗涤：可选选项，以补充或替代热纯化，以去除可溶性铵盐。

[0132] 5. 脱水和干燥：在高于至少 100° C 的温度下干燥，以蒸发水并收缩溶胶－凝胶结构以形成致密化固体。

[0133] $AlPO_4$ + NH_4NO_3

6. 热纯化：在 215-250° C 下进行热处理，以热分解硝酸铵。

[0134] $AlPO_4$（非结晶磷酸铝）

根据需要，可以改变成分添加顺序，使其与上述不同。例如，可以向氢氧化铵溶液中加入酸溶液，以控制反应系统的粘度和／或影响胶状固体的表面积。所述成分添加顺序的灵活性可以是有利的，例如，对于扩大生产规模而言，可能需要避免凝胶化，以促进主要胶体颗粒的悬浮液的形成。不管添加顺序为何，所得组合物在洗涤、干燥和／或热处理后，化学上实质相同。但是，产物形态收到处理参数的影响。将酸加入碱中，得到较高的表面积和较大的孔隙度。本文所公开的溶胶－凝胶法产生了实质由 AAlP 组成的磷酸铝组合物。

[0135] 碱到酸的顺序造成快速的 pH 变化和迅速的溶胶颗粒形成，随后是快速的凝胶化，在凝胶基质中形成交联颗粒。这降低了分子流动性并防止了所有进一步的颗粒生长或形态变化。当将酸加到碱时，pH 变化较为缓慢，且形成局部胶体磷酸铝颗粒。无胶体化发生，因此系统流动性允许继续与副反应竞争（提高硝酸铵和磷酸铵的溶解性），允许中间产物种类存在。当发生脱水和热分解时，脱离的水和（硝酸铵的）分解产物中存在磷酸铝小颗粒，在聚集磷酸铝小颗粒中引入更高的孔隙度。

[0136] 下面列举了用于仅形成生物活性 -AAlP 配合物的溶胶－凝胶法（涉及将生物活性材料（例如硝酸银形式）加入到硝酸铝和磷酸水溶液）的基础化学：

1. 前体溶液：所有成分的组合：

$Al(NO_3)_3 \cdot 9H_2O$ + H_3PO_4 + H_2O + $AgNO_3$

2. 胶凝剂

$3NH_4OH$ + H_2O

3. 溶胶－凝胶反应

$AgAlPO_4$ + $(NH_4)_3NO_3$ + H_2O + NH_3

4. 过滤和洗涤：可选选项，以补充或替代热纯化，以去除可溶性铵盐。

[0137] 5. 脱水和干燥：在高于至少 100° C 的温度下干燥，以蒸发水并收缩溶胶－凝胶结构以形成致密化固体。

[0138] $AgAlPO_4$ + NH_4NO_3

6. 热纯化：在 215-250° C 下进行热处理，以热分解硝酸铵。

[0139] $AgAlPO_4$（非结晶磷酸铝钠）

实施例 12：生物活性 -AlP 配合物的形成(物理性包含)

按照如上溶胶 - 凝胶法制备的 AAlP 构成浆体重量百分比的 34%，将其与适当浓度的硝酸银溶液混合。后者溶液使得制得的银 -AlP 配合物中的银和 AlP 重量比为 1.0% 和 10%。将混合浆体混合约 5 分钟，然后以喷雾干燥器在氮气中将其雾化，并在入口约 180° C 到出口约 79° C 的温度范围下进行干燥。收集固体粉末并进行分析。所得粉末即为生物活性 -AlP 配合物，所述 AlP 聚合物中物理性地包含、网罗、包裹或缠绕有生物活性材料。

[0140] 可选地，根据上述溶胶 - 凝胶法制备的 AlP 构成浆体重量百分比为 34%，将其与适当浓度的硝酸银溶液混合。搅拌混合浆体后，将其过滤并以温度为 40-60 ° C 的热水洗涤一次。在约 110 ° C 下干燥滤液约 12 小时，分为若干部分，将各部分在约 250 ° C 下热处理约 24 小时。无论热处理温度为何，其产量相同，且所得粉末为生物活性 -AlP 配合物，所述 AlP 聚合物中物理性地包含、网罗、包裹或缠绕有生物活性材料。

[0141] 实施例 13：生物活性 -AlP 配合物的形成(化学性键合)

使用类似于上述溶胶 - 凝胶法来制备 AlP，但令适当浓度的硝酸银溶液同时与硝酸铝和水性磷酸混合。所得凝胶包括生物活性 -AlP 配合物，其中银离子形式的生物活性材料与 AlP 聚合物化学性键合。过滤、洗涤并在上述温度下干燥该分散系以提供所需的改造的孔隙度。

[0142] 以上述方法制备的 AlPs/ 生物活性 -AlP 配合物的 P：Al 比率为约 0.5:1 至 1.5:1。以此为 AlPs/ 生物活性 -AlP 配合物的 P：Al 比率期望范围，是因为由此提供了与所需的配方化学相容的适当的颗粒形态和性质。

[0143] 根据需要，此述的生物活性 -AlP 配合物可以首先制为浓缩物形式，其中一定量的生物活性材料中，首先加入第一数量的 AlP(在生物活性材料物理性包含于 AlP 聚合物的情况下)或第一数量的用于形成 AlP 的前体物质(在生物活性材料是化学键合于 AlP 聚合物的情况下)。该初始阶段得到生物活性 -AlP 复合缩合物，即具有高浓度的生物活性材料。该复合缩合物可用作原料，来配制各种不同配方，以满足不同终端应用用途。在一个示例实施例中，该复合缩合物可以与更多 AlP 混合，以提供具有相对低含量生物活性物质以适用于某些终端应用用途的生物活性 -AlP 配合物。由此，制备所述复合缩合物的能力，对获得不同抗菌配方以满足不同抗菌终端应用用途的工艺，增添了所需的灵活性。

[0144] 以此述方式制备的 AlP 和生物活性 -AlP 配合物，以具有期望粒径或粒径分布的白色粉末的固体形式存在。该粒径取决于例如粘结剂聚合物和特定终端应用用途等因素。在一个示例实施例中，AlP 的 D50 粒径分布可以是约 0.5-8 微米。在一个示例实施例中，需要 AlP 的 P：Al 比率为约 0.9-1，且 D50 粒径分布为约 1 微米且 D90 小于约 4 微米。为了用于抗菌化学组合物中，需要 AlP 的粒径小于约 20 微米，且优选为在约 0.5-10 微米范围内，更优选为在约 1.0-8.0 微米范围内。小于约 0.5 微米的粒径可能干扰某些化学配方的处理，并通过增加粘结剂数值吸收而对膜性质造成负面影响。

[0145] 以此述方式制备的 AlP 和生物活性 -AlP 配合物不可高温干燥或其他热处理，以保持非结晶结构并避免向晶体结构转化。据发现，照此制得的 AlP 甚至在低温干燥后都仍保持所需的非结晶结构。根据本公开制得的 AlP 的结构包含改造后的孔隙度，允许它用作生物活性材料的载体，从而提供所需的生物活性成分受控递送 / 释放，以用于抗菌化学组合

物中。

[0146] 与结晶 AlP 相比，由此制得的 AAlP 展现出显著提高的吸水势或复水度，这允许所述 AAlP 一旦被干燥失水后，能够复水以含有高达约 25% 重量百分比的水。在 AlP 用于要求一定的防腐保护且 AlP 存在于无水粘结剂聚合物中时，该特征尤为有用。在所述应用中，AlP 除了是生物活性材料的载体和防腐颜料外，还充当了去湿剂，以减缓水对固化膜的侵入并抑制固化膜中的水扩散。

[0147] 此外，当置于低湿度终端应用用途时，本文公开的 AlPs 复水特征可以是有利的。在所述应用中，适用的 AlPs 具有高含水量或饱和含水量，其水分可驱动生物活性成分至固化抗菌化学组合物或复合材料表面(例如具有内建运输机制)，以在缺乏环境水分的情况下，提高所述生物活性成分在表面的含量。经过如此改造，含有所述 AlP 的抗菌化学组合物能够在湿度 / 水分低的应用中向表面提供期望水平的生物活性成分。

[0148] 本文所述的抗菌化学组合物，是通过根据上述的方式和用量来混合选定的粘结剂聚合物和 AlP 和生物活性物质而制备的。所得的生物活性 -AlP 配合物的组合物制型可以是干燥粉末形式或浆体或液体悬浊液形式，取决于配置条件或偏好。

[0149] 本文所述的抗菌化学组合物含有生物活性 -AlP 配合物，且所含的生物活性材料占该化学组合物总重量的约为 5-1000ppm，优选为 10-900ppm，以及 15-800ppm。所述抗菌化学组合物可以包括其他物质、试剂和 / 或添加剂(除生物活性 -AlP 配合物和粘结剂聚合物之外)，例如颜料、填料、流变剂、流量稳定剂、光控制稳定剂等。例如，含银生物活性材料的抗菌化学组合物，可以含有用于抑制银光还原反应的添加剂，由此维持制得的组合物、干燥膜和 / 或复合材料所含的银的活性状态，以帮助保证有效使用寿命。

[0150] 生物活性剂的复合

据发现，将生物活性剂(当其为银盐时)与多种有机配合剂中的任一种复合时，对银离子在 Ag-AlP 配合物中的稳定性及提高抗菌性质上均有意想不到的益处。Ag^+可以与各种配体复合，例如氨、咪唑(IMI)、取代 IMI 及其组合。Ag^+最常见的配位数(金属可以键合的基团数)为 2，这表明在最简单的情况下，银与氨的复合结构将会是：$[Ag(NH_3)_2]^{+2}$。Ag^+的还原势为 +0.799V，这为将 Ag^+还原为银金属提供了强力的热力学驱动力。

[0151] 但是，银离子与氨的复合，将还原势改变为 0.37V，使还原更困难。因此，通过复合来稳定银离子，能够提高它对还原及还原所导致的脱色、失活的抗性。

[0152] 此外，据发现，Ag^+螯合物的抗菌活性比自由银离子高几个数量级。人们认为，Ag^+离子通过受保护的配合物中的螯合配体在有机体细胞间主动转运，而不是通过自由离子。因此，银离子在 Ag-AlP 中的成功复合，不仅保护了银离子(在配方产品中)不被还原和脱色，还可以使它成为更有效的抗菌剂。这在负荷水平、使用范围和使用寿命以及价格点方面，给予产品配置人员更多的灵活性。

[0153] 该银 - 氨配合物是简单线性结构：$[NH_3— Ag— H_3]^{+2}$。在一个示例实施例中，选用 IMI 作为银的复合配体。对 IMI 进行了研究，以确定稳定化和效力增加的益处是否应归因于含有该复合银化合物的 AlP 系统。IMI 是具有芳香族性质的环形平面五元环。非质子化氮原子具有一对未共用电子对，该电子对并不是用于描述分子的电子键合结构的芳香族 π 电子云的一部分。这些电子为质子或亲电子基团(例如银离子)提供了攻击点。银离子被认为是通过非质子化的氮基团与两个 IMI 分子键合。但是，银原子之间可能也存在弱键合作

用，将多个 Ag-IMI 配合物聚集在一起。因此，评估了不同的 IMI :银含量比率。

[0154] 对于存在于各种 AlP 组合物中的磷酸盐基团与银离子或银离子配合物之间的任何相互作用的性质而言，以氯酸盐(具有 4 个负电氧基团，类似于磷酸盐)进行类推，可推理，磷酸盐中的氧与 IMI 中的氢之间以及直接与银离子之间存在静电吸引(当无 IMI 或热力学因素允许 P-O 与 Ag^+之间存在第一相互作用时)。

[0155] 在一个示例实施例中，评估了下列与形成银配合物相关的因素 :(a) 系统中银离子和 IMI 之间的比率(选择了 Ag:IMI 摩尔比 =1:2 和 1:4 这两个水平);(b) 在 AlP 缩合反应前制备配合物(下文中称为“预混”) vs. AlP 缩合期间原位成形 ;(c) 添加银 -IMI 配合物的顺序和时间点(AlP 缩合反应之前或之后);(d) 缩合反应温度(室温或高温如 95° C);(e) 缩合后中和(以氨) 对产物的影响 ;(f) 缩合反应的整体添加顺序(B 到 A 或 A 到 B);以及(g) 银 -IMI- 磷酸盐产物以粉末或凝胶 / 浆体存在。

[0156] 测试显示，如上所述地改变制备 Ag-AlP 的二元缩合反应法，可以提供期望的某些进步，其中所述改变可以包括 :(a) 降低所有步骤的添加时间，用以提高加工后的颜色稳定性和 / 或银成分滞留 ;(b) 任何步骤中，热条件一般都导致银滞留量低(因为促进了导致例如磷酸银或氧化银等有害副产物的副反应);(c) 分别制备每种成分(例如，银 -IMI 配合物 ;氢氧化铝(ATH) 浆体)，然后将其混合在一起，最后向混合物加入磷酸，从而得到最好的可能结果。分开制备各成分，而不是原位制备，被认为能够允许每个成分完全成形并达到其最纯形式。因此，当发生磷酸铝缩合反应时，银离子或银离子配合物已经形成，并将会被缠绕在形成中的 AlP 配合物中，达到与 AlP 的最大相互作用。

[0157] 据发现，将 Ag-IMI (1 :2) 或 Ag-IMI (1 :4) 溶液添加至 85% 磷酸中，得到白色浆体。随后以氢氧化铵进行中和，得到白色沉淀，可以在约 110° C 下干燥 24 小时得到白色粉末。据推理，该结果表明银配合物和磷酸盐之间的基础化学相互作用，产生了分离性产物(除磷酸银黄色固体之外)。

[0158] 还发现，将含有适当比例 ATH 和硝酸银的浆体加入 85% 磷酸中，得到稳定白色凝胶状组合物。该产物的稳定性基于 AlP 基质中的银离子的均匀截留。所述稳定化被认为是源于浆体中银离子和 AlP 的磷酸集团之间的离子配合物。

[0159] 鉴于上述测试结果，一种用于形成含有上述 Ag 配合物的 Ag-AlP 配合物的示例性合成途径如下 :(a) 室温下，将硝酸银和 IMI 在水中搅拌而简单混合，以预制银 -IMI- 硝酸配合物 [Ag-IMI];(b) 室温下，将 ATH 分散在水中，以预制 ATH 浆体(20% 重量百分比的固体);(c) 室温下，搅拌混合 ATH 浆体和 Ag-IMI 配合物，以形成混合物 ;(d) 室温下，将 ATH/Ag-IMI 混合物(碱性) 加入到 85% 磷酸中，并搅拌一段时间，例如约 1 小时(在此添加顺序下，酸性 pH 用于稳定配合物中的银离子);(e) 混合后，允许混合物在室温下再反应一段时间，例如一小时 ;以及(f) 反应混合物变成粘胶状组合物，其中该凝胶可以分离以用于水性应用中，或可以加热干燥成白色粉末，例如在约 110° C 下加热一段时间，例如约 24 小时。

[0160] 虽然在使用二元缩合法制备 Ag-AlP 配合物的背景下，公开了形成含有复合银盐的 Ag-AlP 配合物这一特征，但可以理解，也可以根据本文所公开的其他 Ag-AlP 配合物制备方法或过程，来将本文公开的复合生物活性材料，例如银盐，制备成 Ag-AlP 配合物，其中所述其他方法中，生物活性材料，例如银盐，由复合生物活性材料代替，例如复合银盐。

[0161] 而且，虽然公开了在形成 AlP 配合物之前就混合复合生物活性材料和铝源的示

例，但是应当理解，还可以在铝源和磷源混合在一起时单独添加复合生物活性材料，或者可以将其与磷源预混合，以替代将其与铝源预混合的做法。

[0162] 添加金属氧化物

可以将各种金属(例如锌和/或铜等)的氧化物并入本文公开的生物活性-AlP配合物。在此实施例中，据推理，生物活性-AlP配合物中若含有氧化锌，可以有助于吸收紫外光并提供内在抗菌性质。在一个实施例中，向ATH预制浆体(来自上述步骤(b))和化学组合物添加氧化锌，并测定功能性质。对该反应产物的XRD分析显示，不存在由任何氧化锌或磷酸锌晶体成分导致的晶体结构，表明锌作为Ag-AlP配合物的一部分被包含在其非结晶成分中。如上所述，锌成分的存在，可以提高该组合物的光稳定性并扩展其抗菌活性。

[0163] 虽然上文中使用氧化锌作为并入本文公开的生物活性-AlP配合物的示例金属氧化物，但是应当理解，本文公开的抗菌组合物的范围内还应当包括其他金属的氧化物，包括但不限于：铜、镁、钡、钙及其组合。此外，应当理解，可以使用本文公开的生物活性-AlP配合物制备方法或过程中的任何一种，来添加一种或多种金属氧化物以形成本文公开的生物活性-AlP配合物。

[0164] 可以在形成AlP的步骤之前、期间或之后，将金属氧化物引入生物活性-AlP配合物的制备过程。在一个实施例中，金属氧化物存在于形成AlP的时候，意味着它可以与生物活性材料预先混合，或可以在形成AlP的时候独立于生物活性材料地添加。金属氧化物可以单独存在，可以与生物活性材料(例如银盐)组合存在，和/或与磷源、铝源或其组合预混。在一个实施例中，生物活性材料为配合物，金属氧化物可以在复合之前或之后添加到生物活性材料中。在一个示例实施例中，金属氧化物在金属活性材料已成为配合物之后添加。

[0165] 生物活性-AlP配合物的附加实施例

本文将公开生物活性-AlP配合物的附加实施例，以供参考。这些实施例如上所述地制备，并通过测定其针对下文所述的微生物的最低抑菌浓度(MIC)来测试其抗菌效力，并如下所述地测试其光稳定性。

[0166] 附加实施例1：[CL20]Ag-AlP配合物

制备ATH浆体：在560g蒸馏水中分散约98.3g ATH。另取一个容器，在60g蒸馏水中溶解约11g $AgNO_3$。边搅拌边向ATH浆体中逐滴加入$AgNO_3$溶液。

[0167] 缩合反应：向反应烧瓶中加入约144g 85%磷酸。向酸中边搅拌边逐滴加入ATH/$AgNO_3$浆体。室温下避光搅拌反应混合物2小时。当反应完成时，形成Ag-AlP配合物，且混合物是无明显液体层的湿饼。测量该饼的固体%，该Ag-AlP配合物适用于直接用作水性配方中的抗菌添加剂。

[0168] 附加实施例2：[CL21] AgIMI（1：2）-AlP配合物

制备预混成分：在50g蒸馏水中溶解约14.1g IMI。另取一个容器，在50g蒸馏水中溶解约17.7g $AgNO_3$(避光反应和贮藏)。边搅拌边向$AgNO_3$溶液逐滴加入该IMI溶液，室温下避光搅拌反应混合物30分钟，以形成Ag-IMI配合物。另取一个容器，在560g蒸馏水中分散约157.3g ATH。边搅拌边向ATH浆体逐滴加入Ag-IMI配合物溶液，室温下避光搅拌所得混合物30分钟。

[0169] 缩合反应：向反应烧瓶中加入约230g 85%磷酸。向酸中边搅拌边逐滴加入ATH和Ag-IMI配合物的混合物。室温下避光搅拌反应混合物2小时。当反应完成时，形成Ag-IMI

配合物无明显液体层的湿饼。测量该饼的固体%，该 Ag-AlP 配合物适用于直接用作水性配方中的抗菌添加剂。

[0170] 附加实施例 3：[CL22] AgIMI（1：4）-AlP 配合物

按照附加实施例 2 所述的流程，但不同的是，采用了约 28.3g IMI。

[0171] 附加实施例 4：[CL47] AgIMI（1：4）-AlP 配合物

制备预混成分：在 50g 蒸馏水中加入约 27.2g IMI。另取一个容器，在 50g 蒸馏水中溶解约 17.7g $AgNO_3$。边搅拌边向 $AgNO_3$溶液逐滴加入该 IMI 溶液，室温下避光搅拌反应混合物 30 分钟，以形成 Ag-IMI 配合物。另取一个容器，在 550g 蒸馏水中加入约 157.3g ATH 和 53.1g ZnO，室温下分散 30 分钟向 ATH-ZnO 浆体中逐滴加入 Ag-IMI 配合物溶液，室温下混合 30 分钟。

[0172] 缩合反应：向约 227.8g 85% 磷酸中逐滴加入 ATH-ZnO 和 Ag-IMI 浆体。以 50g 蒸馏水洗涤玻璃器皿，并将洗涤水加入反应混合物中。室温下避光搅拌反应混合物 2 小时，形成 AgIMI-ZnO-AlP 配合物。

[0173] 可选的中和调整 pH：用约 28% 的 NH_4OH 滴定所得反应浆体至目标 pH。一般来说，反应结束后的浆体的 pH 在约 2.5 至 3.0 之间。在此实施例中，使用了约 174.7g 的 28% 的 NH_4OH 来将浆体的 pH 提升至 7.03。

[0174] 后处理选项：反应所得的包含 AglMI-ZnO-AlP 配合物的浆体混合物，可直接用作凝胶（蒸发水以进行一定程度的浓缩，对达到特定固体含量可能是有用的）。或者，可以过滤反应浆体，且在高温（例如 110° C）下干燥滤饼 24 小时，或在低至 60° C 真空干燥 24 小时，至生成白色粉末。

[0175] 附加实施例 5：[CL50] Ag-ZnO-AlP 配合物

制备预混成分：在 50g 蒸馏水中溶解约 1g $AgNO_3$。另取一个容器，在 560g 蒸馏水中溶解约 84.5g ATH 和约 20.8g ZnO，并在室温下分散约 30 分钟。向 ATH-ZnO 浆体中逐滴加入 $AgNO_3$溶液，室温下避光搅拌反应混合物 30 分钟。

[0176] 缩合反应：向约 122.5g 85% 磷酸中逐滴加入 ATH-ZnO-Ag- $AgNO_3$浆体。以 50g 蒸馏水洗涤玻璃器皿，并将洗涤水加入反应混合物中。室温下避光搅拌反应混合物 2 小时，形成 Ag-ZnO-AlP 配合物。

[0177] 后处理选项：如上附加实施例 4 中所述。

[0178] 附加实施例 6：[CL49] AgIMI（1：2）- ZnO-AlP 配合物

制备预混成分：在 50g 蒸馏水中溶解约 13.6g IMI。另取一个容器，在 50g 蒸馏水中溶解约 17.7g $AgNO_3$。向 $AgNO_3$溶液逐滴加入该 IMI 溶液，室温下避光搅拌反应混合物 30 分钟，以形成 Ag-IMI 配合物。另取一个容器，在 560g 蒸馏水中加入约 123.9g ATH 和 33.5g ZnO，室温下分散 30 分钟。边搅拌边向 ATH-ZnO 浆体中逐滴加入 AgIMI 溶液，室温下避光混合 30 分钟。

[0179] 缩合反应：向约 179.4g 85% 磷酸中逐滴加入 ATH-AgIMI-ZnO 浆体。以 50g 蒸馏水洗涤玻璃器皿，并将洗涤水加入反应混合物中。室温下避光搅拌反应混合物 2 小时，形成 AgIMI-ZnO-AlP 配合物。

[0180] 后处理选项：如上附加实施例 4 中所述。

[0181] 附加实施例 7：

按照附加实施例 6 所述的方法，但不同的是，使用了约 27.2g IMI。

[0182] 附加实施例 8 :[CL51/52] AgIMI（1 :4）- Cu_2O（Ag :Cu=1:1）-AlP 配合物

制备预混成分 :在 50g 蒸馏水中溶解约 27.2g IMI。另取一个容器，在 50g 蒸馏水中溶解约 17.7g $AgNO_3$。向 $AgNO_3$溶液逐滴加入该 IMI 溶液，室温下避光搅拌反应混合物 30 分钟，以形成 Ag-IMI 配合物。另取一个容器，在 560g 蒸馏水中加入约 153.3g ATH 和 12.7g Cu_2O，室温下分散 30 分钟。边搅拌边向 ATH- Cu_2O 浆体中逐滴加入 AgIMI 溶液，室温下避光混合 30 分钟。

[0183] 缩合反应 :向约 222.1g 85% 磷酸中逐滴加入 ATH-AgIMI- Cu_2O 浆体。以 50g 蒸馏水洗涤玻璃器皿，并将洗涤水加入反应混合物中。室温下避光搅拌反应浆体 2 小时，形成 AgIMI- Cu_2O-AlP 配合物。

[0184] 过滤反应浆体，且在高温（例如 110° C）下干燥 24 小时，至生成白色粉末。[CL51]

可选的中和调整 pH :参见附加实施例 4 的方法。[CL52]- 以氨处理。

[0185] 附加实施例 9 :[CL53/54] Ag-ZnO-Cu_2O(Ag :Cu 1 :0.5 ;Ag :Zn 1 :3)-AlP 配合物

制备预混成分 :在 50g 蒸馏水中溶解约 17.7g $AgNO_3$。另取一个容器，在 560g 蒸馏水中加入约 153.3g ATH、41.8gZnO 和约 6.3g Cu_2O，室温下分散 30 分钟。边搅拌边向 ATH-ZnO-Cu_2O 浆体中逐滴加入 $AgNO_3$溶液，室温下避光混合 30 分钟。

[0186] 缩合反应 :向约 222.1g 85% 磷酸中逐滴加入 ATH-AgIMI- ZnO-Cu_2O 浆体。

[0187] 以 50g 蒸馏水洗涤玻璃器皿，并将洗涤水加入反应混合物中。室温下避光搅拌反应浆体 2 小时，形成 Ag-ZnO- Cu_2O-AlP 配合物。

[0188] CL53 无需过滤 :缩合反应混合物在高温（例如 110° C）下干燥 24 小时，至生成白色粉末。

[0189] CL54 需过滤 :缩合反应混合物过滤后，在高温（例如 110° C）下干燥 24 小时，至生成白色粉末。

[0190] 附加实施例 10 :[CL55/56/57] AgIMI（1:4）-ZnO-Cu_2O（Ag :Cu 1:0.5 ;Ag :Zn 1:3）-AlP 配合物

制备预混成分 :在 50g 蒸馏水中溶解约 27.2g IMI。另取一个容器，在 50g 蒸馏水中溶解约 6.3g Cu_2O。向 Cu_2O 溶液逐滴加入该 IMI 溶液，室温下避光搅拌反应混合物 30 分钟。另取一个容器，在 50g 蒸馏水中溶解约 17.7g $AgNO_3$。边搅拌边向 Cu_2O-IMI 溶液中逐滴加入 $AgNO_3$溶液，室温下避光混合 30 分钟，生成 AgIMI-Cu 配合物。

[0191] 另取一个容器，在 560g 蒸馏水中混合约 137.6g ATH 和约 41.8g ZnO，室温下分散 30 分钟。

[0192] 向 ATH-ZnO 浆体中逐滴加入 AgrMI-Cu_2O 溶液，室温下避光混合 30 分钟，以形成 ATH-AgIMI-Cu_2OZnO 溶液。

[0193] 缩合反应 :室温下，向约 199.4g 85% 磷酸中逐滴加入 ATH-AgIMI- Cu_2O-ZnO 浆体。以 50g 蒸馏水洗涤玻璃器皿，并将洗涤水加入反应混合物中。室温下避光搅拌反应浆体 2 小时，形成 AgIMI-Cu_2OZnO-AlP 配合物。

[0194] CL55 :取最终反应混合物的一半，过滤并在高温（例如 110° C）下干燥 24 小时，至生成白色粉末。

[0195] 对剩余的一半反应物如上所述地进行中和。

[0196] CL56：中和最终反应混合物，并在高温(例如 110° C)下干燥 24 小时，但不过滤。

[0197] CL57：中和最终反应混合物，过滤，并在高温(例如 110° C)下干燥 24 小时。

[0198] 组合物成分对抗菌活性的影响(MIC)

通过测量附加实施例对下列每项的 MIC，来测定附加实施例的抗菌效力：(a) 绿脓杆菌(Pseudomonas aeruginosa)(细菌)；(b) 大肠杆菌(Escherichia coli)(细菌)；(c) 金黄色葡萄球菌(Staphylococcus aureus)；(d) 白色念珠菌(Candida albicans)(酵母菌)；以及 (d) 黑曲霉(Aspergillus niger)(真菌)。

[0199] 如下表 1 所示，CL20 至 CL50 的系列实施例展示了 AgAlP、AgIMI 配合物和 ZnO 内含物对 MIC 效力的作用，总结如下：

1. 所有 AgAlP 实施例均能以小于约 4ppm 的浓度抑制细菌生长，在数个实施例中，低于约 1ppm。

[0200] 2. 将 ZnO 添加入组合物中，显著降低了控制酵母菌和真菌的 MIC 要求；

3. AgIMI 配合物和 ZnO 的组合进一步将真菌生长最小化。

[0201] CL51 至 CL57 系列是对铜(作为 Cu_2O)对系统性质的作用。在测试的浓度水平上，铜对 Ag-IMI-AlP-Zn 系统 [CL47=CL57=CL54] 的抗菌效力无显著作用。但是，所述组合物中含有所述水平的铜，对含有该组合物的配方的颜色稳定性具有出乎意料的有益效果，如下所述。

[0202] 表 1：

MIC 测试总结

						MIC-ppm				
		AP 配合物类型	备注	pH	报告号	绿脓杆菌	大肠杆菌	金黄葡萄球菌	酵母菌	真菌
CL20	凝胶	$AgNO_3$	Ag-AP 对照	2.5	#1		2	<1	63	16
			酸性							
CL21	凝胶	AgIMI(1:2)	AP 中的 Ag-IMI 配合物	2.6	#1		<1	<1	125	63
			酸性							
CL22	凝胶	AgIMI(1:4):	AP 中的 Ag-IMI 配合物	2.6	#1		<1	<1	125	63
CL47	粉末	AgIMI(1:4)NH_3ZnO	AP 中的 Ag-IMI 和 ZnO 配合物	7.6	#1		2	2	7.8	125
			以 NH_4 中和		#2	0.78	3	0.78	12.5	100
CL48	浆体	AgIMI(1:4):ZnO	AP 中的 Ag-IMI 和 ZnO 配合物	3.1	#1		3.8	2	7.8	16
			较高 IMI 浓度							
CL49	浆体	AgIMI(1:2)ZnO	AP 中的 Ag-IMI 和 ZnO 配合物	2.9	#1		<1	<1	<1	7.8
					#2	0.39	1.5	0.39	12.5	50
CL50	浆体	$AgNO_3$ZnO	AP 中的 Ag 和 ZnO	2.6	#1		<1	<1	<1	16
					#2	0.78	3	0.78	12.5	25
CL51	粉末	AgIMI(1:4)-Ag:Cu(1:1)	AP 中的 Ag-IMI 和 Cu_2O 配合物	6.7						
CL52	粉末	AgIMI(1:4)-Ag:Cu(1:1)	AP 中的 Ag-IMI 和 Cu_2O 配合物	608	#2	12.5	12.5	12.5	100	100
			以 NH_4 中和							

CL53	粉末	AgIMI(1:4)-Ag:Cu(1:1)	AgAP 与 ZnO 和 Cu_2O 的配合物	5.4	#2	50	100	100	50	100
			无 IMI 配合物：未过滤							
CL54	粉末	$AgNO_3$-AgCu(1:0.5)-AgZn(1:3)	AgAP 与 ZnO 和 Cu_2O 的配合物	4.7	#2	25	50	25	25	100
			无 IMI 配合物：过滤							
CL55	粉末	AgIMI(1:4)-AgCu(1:0.5)-AgZn(1:3)	AgIMI 与 ZnO 和 Cu_2O 的配合物	6.3	#2					
			在 AP 中：未过滤：未中和							
CL56	粉末	AgIMI(1:4)-AgCu(1:0.5)-AgZn(1:3)	AgIMI 与 ZnO 和 Cu_2O 的配合物	3.3	#2	0.78	3.1	1.56	12.5	100
			在 AP 中：未过滤：中和							
CL57	粉末	AgIMI(1:4)-AgCu(1:0.5)-AgZn(1:3)	AgIMI 与 ZnO 和 Cu_2O 的配合物	6.7	#2	0.78	3.1	0.78	12.5	100
			在 AP 中：过滤：未中和							

组合物成分对光稳定性 / 颜色变化的影响 :UV 稳定性测试

使用乳胶作为粘结剂聚合物(按照上述用量范围),制备涂料形式的化学组合物样品。以两种干燥膜含银水平,100ppm 和 500ppm,对包含在所述涂料配方中的 Ag-AlP 配合物的性质进行测试。

[0203] 颜色稳定性数据总结在如下的表 2 中。

[0204] 表 2

颜色稳定性 ΔE - *QUV (B* 灯泡) - 曝晒28天			
样品	组合物	ΔE	ΔE
		100 ppm	500 ppm
CL42	AgIMI (无ZnO)	12.41	
CL47	AgIMI + ZnO	3.5	
CL50	AgAP + ZnO (无 IMI)	5.4	
CL52	CL47 + Cu_2O (高)	1.91	5.43
CL53	CL50 + Cu_2O(低)	4.02	10.77
CL56	CL47 + Cu_2O (低) NF	2.26	10.11
CL57	CL47 + Cu_2O(低)F	2.52	
NF - 未过滤； *F* - 过滤			

表 2 中的数据显示了在 QUV 室中 UV 光曝晒 28 天后的颜色变化(以 ΔE 量度,使用了 BYK 光谱导向球面光泽分光光度计(BYK Spectro-Guide Sphere Gloss Spectrophotometer))。低于约 2.0 的颜色变化肉眼几乎不可见,而约 5.0 或以下的颜色变化与样品的初始状态相比,显示出的明暗差异非常轻微,在大多数应用中可以视为可接受。

[0205] 比较 CL42 和 CL47 可清楚地展示 ZnO 对颜色稳定性的正面影响。颜色变化从 12.41

降低到几乎不可见的 3.5。

[0206] 添加氧化亚铜提高了该有益效果，且可视为其浓度的函数(即，氧化亚铜浓度越高，有益效果越高)。CL51 (1.91)、CL56 (2.26) 和 CL57 (2.52) 的结果进一步说明了该趋势。

[0207] 一般来说，据发现，Ag-AlP 配合物中存在 ZnO 能进一步提高光稳定性。IMI-Ag 配合物提供了第二 / 补充光稳定性效果，同时，包含氧化亚铜也进一步提高光稳定性。

[0208] 本文公开的抗菌化学组合物可以用涂料组合物的形式提供，用于施加于所需底物表面上，以提供所需的抗菌抗性水平。所述抗菌涂料组合物可以配制用作面漆、中间涂层或底漆。此外，所述抗菌涂料组合物可在有或无面漆、中间涂层或底漆的情况下使用。此外，本文公开的抗菌化学组合物可以配制为置于既有底物表面的无色涂层，或有色或无色的底层涂料，从而便于将该无色涂料用于各种底物或底层涂层表面以提供抗菌抗性，而无需特定颜色来匹配当前底物颜色等。

[0209] 本文所述的生物活性 -AlP 配合物提供的生物活性成分形式，能够保证表面抗菌活性，同时允许便利配制以满足各种终端使用用途。该生物活性 -AlP 配合物允许生物活性成分(例如银离子)在该化学组合物、干燥膜、复合材料或配方产品中均匀分布。该生物活性 -AlP 配合物允许改造配方主体基质的性质，以提供水分引起的运输 :吸附、解吸附、水和溶质在主体中的扩散。该生物活性 -AlP 配合物可以特定改造，以基于所含的生物活性材料浓度以及配合物的亲水性和形态(表面积和孔隙度)，释放一种或多种生物活性成分，例如银离子。通过将磷酸功能与主体复合材料或膜的粘结剂基质的某个功能基团相连接，可以将本文所述的该生物活性 -AlP 配合物引入配方产品，例如颜料，或作为添加剂。此外，可以将热稳定形式的生物活性 -AlP 配合物并入粉末涂层配方中，以所得所述表面具有抗菌性。

[0210] 在一个示例实施例中，本文所述的抗菌化学组合物可以配制为膜，其中物品主体充当生物活性材料或其成分(例如银离子)的容器或仓储。所述配方可经过改造，以优化下列抗菌机制 :水进入膜的扩散性，水进入该生物活性 -AlP 配合物的吸收性和吸附性，配合物中的盐溶解性，离开该配合物的离子转运，以及生物活性材料或其成分在基质中转运至欲保护的表面。

[0211] 可选地，本文所述的抗菌化学组合物可配置为经过改造的富集薄膜(例如，膜厚度低于约 25μ，且优选为低于约 10μ)，该改造平衡了物理耐久度与水扩散 / 生物活性材料或其成分的转运性质，以给予表面抗菌性质，同时无需将抗菌物质包含在物品主体中，例如当所述包含从成本角度而言可能不实际，或操作控制机制不太可能(例如不透水塑料)的时候。

[0212] 如上所述，以生物活性 -AlP 配合物的形式提供 AlP 和生物活性材料的组合物，其中该生物活性材料可以是与 AlP 聚合物化学键合，例如含在 AlP 聚合物的骨架中，或物理性地包含、网罗、包裹或纠缠在 AlP 聚合物中，取决于制备该配合物的特定方法。此外，生物活性材料或其成分可以化学性和物理性地存在于 AlP 聚合物中。例如，当通过在形成 AlP 的时候混合所需生物活性材料来形成生物活性 -AlP 配合物，从而促进生物活性材料或其成分与 AlP 之间的化学键合时，化学计量过量的额外生物活性材料，可能使得过量材料物理性地包含在 AlP 分子中，在此情况下，所得生物活性 -AlP 配合物可以包括同时以化学键合和物理性包含形式存在的生物活性材料或其成分。

[0213] 如上所示，本发明的实施例提供了新型抗菌化学组合物，新型生物活性 -AlP 配合物，及新型的制备方法。虽然对每个方面的描述均是参考有限数量的实施例进行描述的，一个实施例的特定特征不应当被归因于本发明的其他实施例。没有一个单一实施例能够代表本发明的所有方面。在一些实施例中，所述组合物或方法可以包括本文未提及的多种化合物或步骤。

[0214] 例如，除了具体描述的那些已知具有生物活性价值的生物活性材料外，根据需要，抗菌化学组合物还可以制备为额外包括一种或多种单独或组合的生物活性材料。所述生物活性 -AlP 配合物中可以包含或不包含所述任意所述额外生物活性材料，即，所述额外生物活性材料可以是粘结剂聚合物中的单独分散系，且可用于增加或补充或提供该化学组合物的协同抗菌作用。

[0215] 此外，虽然如本文实施例所述的抗菌化学组合物被描述为包含非结晶形式的 AlP，应当理解，本文所述的抗菌化学组合物也可以额外包括已知结晶形式的 AlP，且可以包括非结晶和结晶形式的 AlP 的组合物。

[0216] 在其他实施例中，所述组合物或方法不包括或实质上不含有本文所列举的任何化合物或步骤。存在已描述实施例的变形形式和改进形式。制备该化学组合物和 / 或 AlP 的方法被描述为包括一定数量的动作或步骤。这些步骤或动作可以按照任何顺序或次序执行，除非另有说明。最后，本文公开的任何数字应当被理解为指代近似值，无论描述该数字的词语是“约”或“近似”。附属的权利要求的目的在于涵盖所有这些包含在本发明范围中的改进形式和变形形式。

Abstract

Antimicrobial chemical compositions comprise an aluminum phosphate (AlP) solid dispersed within a binding polymer, wherein one or more bioactive materials are disposed within AlP forming a bioactive-AlP complex. The complex may comprise the bioactive material chemically bonded with the AlP, physically combined with the AlP, or a combination of both. The complex may be formed according to precipitation, condensation and sol-gel methods of forming. The complex is engineered to provide a controlled delivery of the bioactive material or a constituent thereof upon exposure to moisture to give a desired level of antimicrobial resistance to a film or composite formed from the composition of at least about 30 mug/m2, and may also provide a desired degree of corrosion resistance through the release of passivating phosphate anion. Such antimicrobial chemical compositions provide an improved degree of active, long-term resistance to a broad range of micro-organisms when compared to known antimicrobial chemical compositions.