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Wendelin STARK, et al.
DrinkPure Water Purification

http://www.scidev.net/sub-saharan-africa/water/news/novel-water-purifying-filter.html

Researchers create novel water purifying filter

[CAPE TOWN] A team of researchers have developed a membrane-based water filter that can provide up to 300 litres of clean drinking water.

The WHO says about 780 million people worldwide, especially those in Sub-Saharan Africa, lack access to improved water source.

The researchers from the Swiss Federal Institute of Technology in Zurich (ETHZ) in Switzerland announced last month (22 July) that DrinkPure filter, which they have developed, is based on a simple screw-top design that fits onto any plastic bottle.

Wendelin Stark, a professor of functional materials engineering at ETHZ, who helped create the innovation, says: “It requires no manual, no electricity, and no additional tools or training needs. You simply screw it on, and you drink [the water].”

“One DrinkPure water filter provides enough drinking water for one person for one year, after which the membrane and activated carbon can be replaced over and over again.”

Jeremy Nussbaumer, Swiss Federal Institute of Technology, Zurich (ETHZ)

The researchers say they used a novel porous polymer membrane developed though nanotechnology, thus making DrinkPure allow the filtration of particles as small as 90 nanometres, including bacteria and protozoa, at rate of up to one litre a minute.

They add that the innovation which weighs less than 100 grams, with a target cost of less than US$20 a filter, has two pre-filtration components — a capture filter that separates large particles and an activated charcoal layer that removes odour and chemical contaminants.

In order to fund the tools to manufacture the filters, the researchers launched a crowdfunding campaign last month (17 July) with a goal of raising US$40,000 by this week (26 August), but have as of today raised more than US$71,000.

Nussbaumer says they plan to have the first filters completed and sent to project supporters for distribution by January 2015 in Sub-Saharan Africa.

Nussbaumer adds that Water & pH soluces, a Swiss NGO that works to provide sustainable, affordable access to safe water and sanitation to communities in Sub-Saharan Africa, plans to distribute DrinkPure for testing in five villages in Mali.

Stark tells SciDev.Net: “The aim is to develop partnerships with partners and local companies

who can develop the membranes themselves".

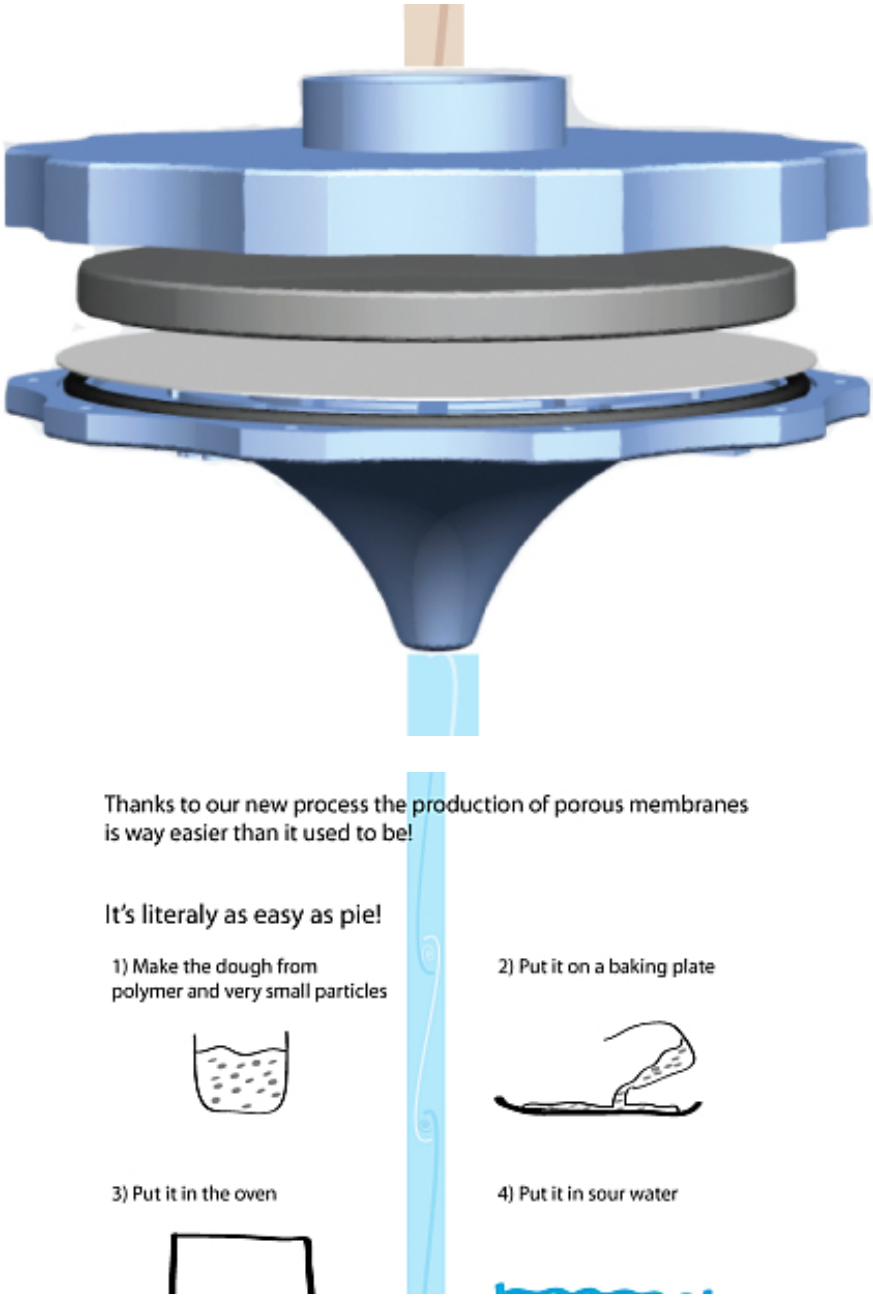
The researchers say DrinkPure water filter could be used as part of relief efforts following natural disasters, such as tsunamis. "We would like to see these membranes and filters used …in places experiencing environmental issues," says Christop Kellenberger, a member of the DrinkPure research team.

Nonhlanhla Kalebaila, a research manager of drinking water treatment and quality at the South Africa-based Water Research Commission, says the use of small-scale water purification systems in Africa is increasing rapidly. "Water quality and supply in Africa as a whole is a very touchy subject and has been the topic of strikes and protests in South Africa in the last few years," she says.

But Kalebaila adds that independent research is needed to ensure the accuracy of water filtration devices and the safety of water that flows from such tools.

Link to video of DrinkPure :

https://www.indiegogo.com/projects/drinkpure-a-novel-water-filtration-device



US2013299417
POROUS POLYMER MEMBRANES

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Manufacturing processes are provided for nano-porous polymer membranes. Also provided are intermediates suitable to obtain such membranes; polymer membranes as defined herein; shaped articles containing such membranes; and the use of such membranes, shaped articles and intermediates.

antee that they are complete, up-to-date or fit for specific purposes.

[0001] This application is a continuation in part of International Application No. PCT/EP2012/000142, filed Jan. 13, 2012, and published in the English language which claims priority to EP 11000311.8 filed Jan. 17, 2011.

TECHNICAL FIELD

[0002] The invention relates to manufacturing processes for porous polymer membranes; to intermediates suitable to obtain such membranes; to polymer membranes as defined herein; to shaped articles containing such membranes; to the use of such membranes, shaped articles and intermediates.

BACKGROUND

[0003] Nano-porous polymer membranes and corresponding manufacturing methods are already known. Typically, such membranes are obtained by a phase separation process, by stretching specific polymer foils or by a template based process. The known processes show certain disadvantages. While the first process is difficult to control, the second process is only applicable to specific starting materials. The third process is not yet in industrial application.

[0004] Johnson et al (Science 1999, vol. 283, p. 963 ff) disclose a template-based process; in this process, a pressed and sintered silica template is used to obtain a shaped polymeric article with pores in the range of 15-35 nm. This process is suited to obtain pellets, but not membranes.

[0005] Mikos et al (U.S. Pat. No. 5,514,378) disclose a template based process to obtain biocompatible membranes. The disclosed process requires long production times, making it unsuitable for industrial applications and/or continuous processes. Further, the pore size of the membranes obtained by this process may be varied only in a limited range, between 450 nm and 930 nm.

[0006] Eisen et al (WO 2009/024973) disclose a number of phase separation processes for manufacturing specific polysulfone membranes. In one embodiment, a multi-step process is disclosed in which-in a first step-in a solution containing solvent and polysulfone, a low amount of Fe_2O_3 nanoparticles is introduced into the polymer matrix by the use of a magnetic field. Phase separation is then induced by immersion precipitation to create a porous membrane. In a last step Fe_2O_3- nanoparticles are removed out of the porous structure to increase flux and pore accessibility of the membrane. This process requires specific equipment and is applicable to

specific combinations of starting materials only.

[0007] Consequently, there is a need for providing additional/improved manufacturing processes for nano-porous polymer membranes; there is also a need for new polymer membranes having beneficial properties.

SUMMARY

[0008] Thus, it is an object of the present invention to mitigate at least some of these drawbacks of the prior art. In particular, it is an aim of the present invention to provide improved manufacturing processes for porous polymer membranes. It is a further aim to provide nano-porous polymer membranes which are suitable for advanced applications, such as in breathable textile materials and filters.

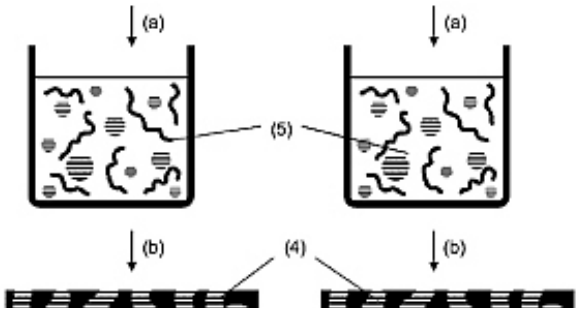
[0009] The present invention will be described in more detail below. It is understood that the various embodiments, preferences and ranges as provided/disclosed in this specification may be combined at will. Further, depending of the specific embodiment, selected definitions, embodiments or ranges may not apply. It is further understood that all references identified herein are incorporated by reference in its entirety.

[0010] The above objectives are achieved by providing a manufacturing process as defined in claim 1. Further aspects of the invention are disclosed in the specification and independent claims, preferred embodiments are disclosed in the specification and the dependent claims. The manufacturing process for nano-porous polymer membranes, as described herein, proves to be very versatile, reliable, simple to control. The process is particularly suitable for fast and low-cost production of large area membranes. Polymer membranes as described herein prove to be useful in applications as defined below and further enable the manufacture of improved articles and/or facilitate manufacture of articles as defined below.

[0011] As it will become apparent when reading this specification, the invention relates in a first aspect to a method for manufacturing polymer membranes; in a second aspect to intermediates suitable for manufacturing such polymer membranes; in a third aspect to novel polymer membranes; in a forth aspect to shaped articles comprising (i.e. containing or consisting of) such polymer membranes; and in a fifth aspect to uses of such membranes, shaped articles and intermediates.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] Further, the present invention will be better understood by reference to FIG. 1, which shows a schematic view of the inventive process, wherein process steps are as defined herein; wherein (1) represents the inventive porous membrane (unsupported; free-standing); (2) represents the inventive porous material, supported on a substrate (6); (4) represents a bi-continuous nano-structured network of a polymer and a salt, either unsupported ("free-standing") or supported on a substrate (6); (5) represents a dispersion comprising a dissolved polymer, diluent and metal salt nanoparticles.



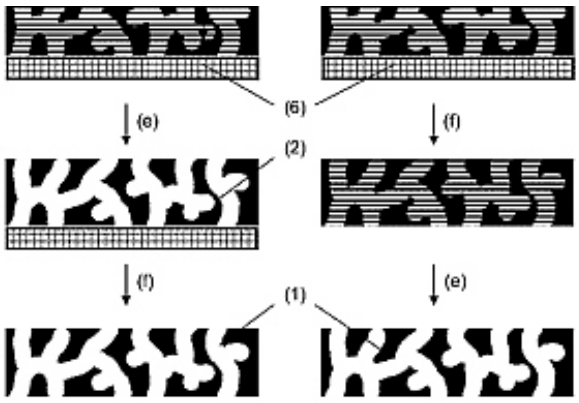


Fig. 1

DETAILED DESCRIPTION

[0013] Unless otherwise stated, the following definitions shall apply in this specification:

[0014] The term "nanoparticle" is known in the field and includes crystalline, semicrystalline or amorphous materials. Nanoparticles are particles having a diameter in the submicron size range. Primary particle sizes are preferably between 5-400 nm. Suitable methods for the determination of primary particle size can be found by Limbach et al. (Environmental Science & Technology, 2005. 39(23): p. 9370-9376). Nanoparticles may be obtained from a range of preparation methods, including high temperature-gas phase processes (such as flame synthesis, laser processes and plasma processes), and liquid phase chemical methods (such as precipitation and sol-gel processes). Nanoparticles particularly suitable in the context of the present invention may be obtained by a flame spray synthesis (FSP) process.

[0015] The term "salt" is known in the field. A salt is defined as the product formed from the neutralisation reaction of acids and bases. Salts are ionic compounds composed of cations and anions so that the product is electrically neutral. Examples of salt classes are halogenides (chlorides, fluorides, bromides, iodides), sulfates, phosphates, carbonates, nitrates, particularly phosphates, carbonates and halogenides. In inorganic salts, the cation is a metal ion and the anion is a non-metal ion; specific examples of inorganic salts include calcium phosphate, calcium carbonate, magnesium sulfate, sodium chloride. In the context of the present invention, metal oxides are not considered salts. Further, salts are preferably manufactured by a dry process, such as FSP.

[0016] The term "polymer" is known in the field. The term refers to a material of repeating structural units ("monomers"), particularly to synthetic polymers (comprising synthetic monomers). The term thus includes homo-polymers, co-polymers and blends thereof. The term further includes oligomers. Polymers may be cross-linked. Typically, amorphous polymers are soluble, while crystalline polymers are not.

[0017] The "specific surface area" of a material as described herein is the total airpolymer interface area per amount of polymer mass. This may be determined by nitrogen adsorption using the BET method (according to: Janssen et al, Journal of Applied Polymer Science 52, 1913, 1994). The BET method is widely used in surface science for the calculation of surface areas of solids by physical adsorption of gas molecules (e.g. Nitrogen molecules). The basic principle of the measurement is that a material with a high surface area can adsorb more molecular nitrogen on its surface (assuming a molecular monolayer).

[0018] The "porosity" of a material as described herein is the volumetric percentage of pores of the total material. Porosity can be determined by porosimetry, by measuring the apparent

material density, BET analysis or by microscope images.

[0019] The "permeability" of a material as described herein is defined as the flux of a fluid (i.e. a liquid medium or a gaseous medium) through interconnected pores of the material. Permeability can be determined by measuring the liquid or gas volume which passes a defined membrane area in a defined time at an applied pressure. A typical measure of this flux is millilitre per square centimetre, per bar and minute ([ml/(cm<2>*bar*min)]).

[0020] In general terms, the present invention relates in a first aspect to a method of manufacturing a porous polymer membrane (1) comprising the steps of (a) providing a dispersion (5) containing (i) one or more diluents, (ii) one or more polymers dissolved therein, (iii) one or more metal salt nanoparticles dispersed therein; (iv) optionally one or more additives dissolved therein; (b) coating a substrate (6) with said dispersion; (c) optionally subjecting the obtained material (4) to a drying step; (d) optionally subjecting the thus obtained material to a polymerisation or cross-linking step; (e) removing said one or more metal salt particles by a dissolution step; (f) optionally removing the obtained polymer membrane from said supporting material (6). This process is illustrated in FIG. 1, left hand side.

[0021] It is believed that the dissolution step (e) is a key element of the manufacturing process and also a key element to obtain the inventive polymer membranes. While the prior art uses as a starting material a combination of a polymer, a solvent and a non-solvent, the present invention uses as a starting material polymer(s), a solvent(s) and metal salt nanoparticles and selectively removes the metal salt to obtain the porous polymer membrane. This is considered advantageous, as chemical properties of metal salts and polymer significantly differ enabling a wide choice of combinations and process steps.

[0022] The manufacturing processes as described herein are considered advantageous, as the individual steps a) to f) are known in industry and already in commercial use. Further, the process described is very fast and may be implemented in a continuous process.

[0023] It was surprisingly found, that the use of nanoparticulate metal salts provides an improved process which, on the one hand, provides suitable pores in the membrane and on the other hand, provides an improved manufacturing rate. This is unexpected, as the skilled person (i) would not expect the dissolution of nanoparticulate material from a polymer film because nanoparticles are expected to be individually coated by polymer and thus protected from dissolution.

[0024] This aspect of the invention shall be explained in further detail below, whereby the process steps are described first and suitable materials are described afterwards:

[0025] Step a: A dispersion (5) containing a mixture of metal salt(s) nanoparticles, diluent(s), polymer(s) and optionally additives is provided first. Typically, the amount of diluent is at least 50 wt. %, preferably at least 80 wt. %, most preferably at least 90 wt. % of the dispersion. Such comparatively high amount of solvent ensures low viscosity and thereby thin film formation during the coating step. Typically, the ratio of polymer:nanoparticles (wt. %) is in the range of 2:1 to 0.2:1, preferably 1.25:1 to 0.25:1, most preferably 1.1:1 to 0.7:1. Such comparatively high amount of nanoparticles ensures proper pore formation within the manufactured membranes. Without being bound to theory, it is believed that a lower amount will not provide interconnecting necks, while a higher amount will cause the coating to collapse.

[0026] It was surprisingly found that the inventive process provides very good results without the addition of additives (particularly without the addition of surfactants) to the dispersion (5). Thus, in an advantageous embodiment, no additives (particularly no surfactants) are added to dispersion 5. In one embodiment, dispersion (5) consists of metal salt(s) nanoparticles,

diluent(s) and polymer(s).

[0027] Step b: The dispersion of step a) is applied to a substrate, e.g. by using conventional printing or coating methods. This results in a metal salt/polymer nanocomposite film (4) on said substrate (6). Suitable methods are known in the field and include spraying, roll-to-roll processes, dip-coating.

[0028] Step c: Afterwards, e.g. for faster solvent evaporation, the nanocomposite films may be subjected to a heat treatment (e.g. drying) to obtain a polymer film containing nanoparticles. The temperatures and treatment times may vary, depending on the starting materials (particularly the diluent) and are typically below 200[deg.] C. and preferably below the melting point of the polymer.

[0029] Step d: The coated material of step b) may be subjected to a polymerisation and/or cross-linking step. This step is optional and may be applied when appropriate starting materials are used. Particularly in case the polymer comprises oligomers and/or monomers that may be polymerised, optionally in the presences of an initiator (polymerisation); or in case the polymer comprises groups that may be crosslinked, optionally in the presence of a cross-linking agent (cross-linking step). Step d) and step c) may take place simultaneously or in subsequent steps.

[0030] Step e: The continuous salt phase in such nanocomposite membranes is dissolved which results in a nano-porous polymer film (the porous polymer membrane) on a substrate. Suitable are particularly aqueous solvents, such as water or acidic aqueous solutions. The choice of solvent particularly depends on the type of metal salt used. The solvent in step e) is selected to ensure dissolution of the metal salt nanoparticles without dissolving the polymer.

[0031] Step f: The substrate may be easily removed from the porous material, e.g. by pealing off (to obtain (1)) or by transfer to another substrate (to obtain (1)). This removal step may take place after to the washing step (e) (as outlined above) or prior to the washing step (e) (as outlined below). Step (f) may be performed using processes known per se. The removal step f), aims to remove substrate (6) to obtain an unsupported porous material (1) or to transfer the porous material to another supporting material to obtain a coated article.

[0032] In an alternative embodiment the invention provides a method as described herein, wherein said step (f) is performed prior to step (e), as illustrated in FIG. 1, right hand side. Consequently, the invention also relates to a method of manufacturing a polymer membrane (1) comprising the steps of (a) providing a dispersion (5) as described herein; (b) coating a substrate (6) with said dispersion; (c) optionally subjecting the obtained material (4) to a drying step; (d) optionally subjecting the thus obtained material to a polymerisation or cross-linking step; (f) removing the obtained material (4) from said supporting material (6) (e) removing said one or more metal salt particles by a dissolution step thereby obtaining the polymer membrane (1).

[0033] Suitable solvents may be selected from a broad range of known solvents and combinations thereof. Examples include organic solvents selected from the group consisting of alcohols, ethers, ketones, esters, halogenalkanes, alkanes, cycloalkanes, sulfoxides, amides, pyrrolidones, and lactams.

[0034] Suitable polymers may be selected from a broad range of known polymers and combinations thereof. In an advantageous embodiment, the polymers are selected from the group of amorphous polymers and semicrystalline polymers. Suitable polymers thus include polysulfones, polyethersulfones, polycarbonates, polystyrenes, polyacrylates, polysiloxanes, polyarylates, polyurethanes, halogenated polyolefins, such as polyvinylidene fluoride (PVDF), polyethylenes, polyimides, polyamides, liquid crystal polymers, cellulose acetates and polyether

ketones, such as polyetherether ketone (PEEK). The invention also includes the use of co-polymers and mixtures of polymers ("blends"). The invention further includes chemically modified polymers thereof, such as polymers, co-polymers or blends modified by sulfonation, amination and hydroxylation.

[0035] Suitable metal salt nanoparticles may be selected from a broad range of known metal salts and combinations thereof. Preferably, the metal salt particles are selected from the group consisting of carbonates (including hydrogencarbonates), sulphates, halogenides, nitrates and phosphates, preferably carbonates. Examples include $CaCO_3$, $BaCO_3$, $SrCO_3$, Na_2CO_3, K_2CO_3, NaCl. In one embodiment, the metal salt particles have a particle size in the range of 1-4000 nm, or in the range of greater than 400 to 4000 nm. Preferably, the metal salt particles have a particle size of 5-400 nm, preferably 15-200 nm.

[0036] Preferably, the metal salt particles are made by a dry process, particularly by an FSP process.

[0037] Preferably, the metal salts are prepared prior to step a) in a separate process. The invention thus also relates to a method as described herein, wherein the nanoparticles are not prepared in situ.

[0038] Preferably, the metal salt particles are selected from the group consisting of Carbonates (including Hydrogencarbonates) and the process is a continuous process (as described below). It was surprisingly found that a continuous manufacturing process of porous membranes may be realized when using such Carbonates as the starting material. This may be attributed to the particularly fast dissolution and complete removal of carbonates in aqueous (or acidic) solutions

[0039] Suitable additives may be selected from a broad range of known additives and mixtures thereof and are known in the field.

[0040] Suitable substrates may be selected from a broad range of known substrates. The substrate may be any support compatible with the manufacturing process; particularly, it needs to be inert towards the solvents used. It is further beneficial, if the coating adheres to the substrate during manufacturing and can be removed after manufacturing. Suitable materials for a substrate include polymer materials (preferably semi-crystalline or crystalline), glasses, metals and ceramics (in each case coated or uncoated).

[0041] Suitable dispersions may be prepared from the above starting materials using known techniques. Preferred dispersions contain from 50 to 99 wt.-% diluents and/or from 1 to 20 wt.-% polymers and/or from 0.5 to 40 wt.-% metal salt particles and/or from 0 to 5 wt.-% additives as defined herein. It was found suitable to combine the starting materials by vigorously stirring the components and/or subjecting the components to ultrasonic treatment.

[0042] In a further embodiment, inventive method provides a process for manufacturing polymer membranes without using a phase separation process/phase separation step. Such phase separation is limited to specific polymers and the corresponding pore formation is highly sensitive to various process parameters (e.g. temperature, humidity, time) which need to be carefully controlled simultaneously. It is apparent that such process is disadvantageous for fast and large-scale commercial manufacturing. Thus, the invention also provides a method as described herein, which does not involve a phase separation step. In the context of this invention, a phase separation step is considered a separate step in a manufacturing process that requires specific equipment. It is also noted that phase inversion is only observed for a limited number of polymers/combination of polymers. The present invention is not limited to such specific polymers or combinations thereof and thus considered much more versatile.

[0043] In a further embodiment, inventive method provides a process for manufacturing polymer membranes without using a stretching process/stretching step. Such stretching is limited to specific polymers and typically applied to a foil to obtain a membrane. Such additional step is difficult to control and thus disadvantageous for commercial manufacturing. Thus, the invention also provides a method as described herein, which does not involve a stretching step.

[0044] In a further embodiment, the invention provides a method of manufacturing a polymer membrane (1) as described herein comprising the step of subjecting a shaped article (containing substrate (6) and coating) to a dissolution step (e) and optionally removing from the thus obtained shaped article said support (step f). The dissolution step (e), as outlined above, aims to remove all or essentially all salt material from said article. The removal step (f), as outlined above, aims to remove substrate (6) to obtain an unsupported porous material (1) or to transfer the porous material to another supporting material to obtain a coated article.

[0045] In a further embodiment, the invention provides a method of manufacturing a polymer membrane (1) as described herein, consisting of the steps (a) providing a dispersion (5) as described herein; (b) coating a substrate (6) with said dispersion; (c) subjecting the obtained material (4) to a drying step (to remove the diluent); (e) subjecting the obtained material to a dissolution step (to remove the one or more metal salt particles); (f) removing the obtained polymer membrane from said supporting material (6) (to obtain the porous polymer membrane (1)).

[0046] In a further embodiment, the invention provides a process as described herein, wherein one or more, preferably all steps a) to f) are adapted to a continuous process, such as a Roll-To-Roll-process (R2R process).

[0047] In a further embodiment the process step e), may be repeated. This measure ensures a complete removal of metal salt nanoparticles. Thus, step e) also includes multiple washings and dryings. When using a multi-step protocol, either the same or different solvents may be used, for example a diluted aqueous acid first, followed by water.

[0048] The manufacturing process described provides porous materials in virtually unlimited size. As the manufacturing steps a) to e) do not provide a limitation regarding the size of the material (except for the equipment used) large sheet materials, in terms of length and width, are obtainable. Thus, the invention also provides a process as disclosed herein, wherein the polymer membrane has an area of more than 100 cm<2>, preferably more than 400 cm<2>.

[0049] By suitable selection of metal salt particles (size and amount) and by the selection of process parameters (such as coating thickness, drying time) porosity and pore size distribution may be varied over a broad range. Thus, the invention also provides a process as disclosed herein, wherein the polymer membrane has a porosity of 10-90%, preferably above 25% such as 28%. Thus, the invention also provides a process as disclosed herein, wherein the polymer membrane has a pore size of 1-4000 nm, preferably 1-1000 nm, more preferably 1-400 nm. In one embodiment, the invention provides a process as disclosed herein, wherein the polymer membrane has a pore size of greater than 400 nm to 4000 nm. In another embodiment, the invention provides a process as disclosed herein, wherein the polymer membrane has a pore size of 5-400 nm, preferably 15-200 nm.

[0050] The present invention relates in a second aspect to intermediates or starting materials which are useful in a manufacturing process as described herein. This aspect of the invention shall be explained in further detail below:

[0051] In one embodiment, the invention relates to a dispersion (5) comprising (i.e. containing

or consisting of) 40-99 wt % diluent; 1-20 wt % polymer; 0.5-40 wt % metal salt nanoparticles; and 0-5 wt % of additives. Such dispersions are suitable starting materials for the inventive process as described below. The individual components of the inventive dispersions are known per se, suitable components are identified above, in the context of the "first aspect". Particularly suitable components are identified below:

[0052] Diluent: Any liquid carrier suitable for dispersing the nanoparticles and dissolving the polymer may be used; preferred are the diluents identified above. The amount of diluent may vary over a broad range, depending on the intended following manufacturing step (such as spraying, coating or printing).

[0053] Polymers: Suitable polymers include polymers that are soluble in the diluent identified above, such as amorphous polymers as described herein, semicrystalline polymers, polymers that may be cross-linked, oligomers that may be polymerized.

[0054] Metal salt nanoparticles: In a broad sense, any metal salt nanoparticles may be used in the inventive dispersion. It was found advantageous to use premanufactured nanoparticles, while in situ formation of nanoparticles is less preferred. The manufacture of suitable nanoparticles is known in the field. It was found that nanoparticles made by a dry process, such as an FSP process, are particularly suitable.

[0055] Additives: Additives may be selected from the group consisting of surfactants, polymerisation initiators, stabilizers, cross-linking agents, wetting agents.

[0056] In certain embodiments, it was found the dispersion (5) has a shelf life of less than one day; particularly, as the nanoparticles separate from the diluent. The dispersions are nevertheless suitable for the inventive process but may be pretreated prior to use (e.g. by sonication). The invention thus relates to both, a dispersion as defined herein and a kit of parts, wherein a first part comprises (i.e. contains or consists of) metal salt nanoparticles as described herein and said second part comprises (i.e. contains or consists of) diluent, polymer and additives as described herein.

[0057] In a further embodiment, the invention relates to a material (4) comprising a substrate (6) and a coating, wherein said coating (i) contains metal salt nanoparticles, polymer(s), diluent(s) and optionally additive(s), each as defined herein; (ii) said nanoparticles are randomly distributed within said coating; (iii) and said coating has a thickness (d) between 0.05-50 [mu]m. The material (4) may be obtained by coating/printing a suspension (5) on a substrate (6), optionally followed by removing the above mentioned dispersing medium.

[0058] The present invention relates in a third aspect to novel polymer membranes and to shaped articles comprising such polymer membranes; this aspect of the invention shall be explained in further detail below.

[0059] In one embodiment, the invention relates to a polymer membrane, said polymer (i) is selected from the group consisting of polymers soluble in organic solvents and cross-linked polymers thereof; (ii) has pores with a diameter between 5-400 nm; (iii) has a thickness of 0.05-50 [mu]m. Due to the unique manufacturing process, as outlined herein, the present invention provides nanoporous membranes combining specific porosity and thickness for organic polymers.

[0060] Advantageous polymers and characteristics of the inventive membranes are outlined below.

[0061] Polymers: As outlined above, a wide variety of polymers may be used for the inventive

membranes. This is considered advantageous, as the presently known polymer membranes are limited in view of the materials suitable and/or the characteristics of its pores. Suitable polymers may be selected from the group of polymers soluble in organic solvents and include polyesters; polyethers, such as polyetherether ketone (PEEK); polysulfones (PSU); polyethersulfones; polyphenylene sulfone (PPSU); polycarbonates (PC); polyacrylates, such as polymethylmethacrylate (PMMA); polystyrenes (PS); polysiloxanes, such as polydimethyl siloxane (PDMS); polyimides; polyamides; polyethylenes (PE); halogenated polyolefins, such as polyvinylidene fluoride (PVDF); cellulose acetate (CA) and liquid crystal polymers.

[0062] Pores: As outlined above, the inventive material is porous. The inventive material is characterized by the size, type and amount of pores present. The size and type and amount of pores may be influenced by the starting materials, the ratio metal salt nanoparticles:polymer, the manufacturing process.

[0063] Size: The size of the pores of the inventive membranes (defined by the diameter of the salt nanoparticles) is in the nanoscale or microscale range, typically between 1-4000 nm, preferably 1-1000 nm, more preferably 1-400 nm. In one embodiment, the size of the pores of the inventive membrane is greater than 400 nm to 4000 nm. In another embodiment, the size of the pores of the inventive membranes is in the nanoscale range, typically between 5-400 nm, preferably 15-200 nm. The size of the pores may be determined by microscopy. Further, the pore size distribution may be precisely adjusted, due to the starting materials used.

[0064] Amount: The porosity, i.e. the volume of pores in relation to the volume of the membrane in total, may be varied in a broad range. Inventive materials show porosity in the range of 10-90 vol. %, preferably 20-90 vol. %, much preferred above 25 vol. %, such as 28 vol. %. The porosity may be determined by BET.

[0065] Type: The pores of the material may be arranged in a way that the material is permeable, partly permeable or impermeable. If essentially all pores of the material have dead ends, the material is impermeable. In the contrary, if essentially all pores of the material have open ends, the material is considered permeable. Consequently, if a fraction of the pores has dead ends, the material is considered partly permeable. In an advantageous embodiment, the present invention provides polymer membranes, wherein at least 90% of said pores are interconnected.

[0066] Thickness: The thickness of the inventive membranes may be varied over a broad range. Inventive membranes show a thickness between 50 nm-50,000 nm, preferably 300 nm-10,000 nm, such as 1000 nm. Such membranes may also be termed "sheet material" or "porous foils"; these terms indicate that the material has a length and width which is at least one magnitude larger (preferably two magnitudes larger) than the thickness of the material.

[0067] In a further embodiment, the invention relates to a polymer membrane as described herein which is impermeable to biologic material, including bacteria, viruses, cells, and/or impermeable to inorganic material, including nanoparticles. In a further embodiment, the invention relates to a polymer membrane as described herein which permeable to liquids, (including water), gases (including air), and dissolved material (including metal ions and proteins). Typically, the cut-off of the inventive membranes is in the range of 5-400 nm, such as 20 nm. Typically, the flow of the inventive polymer membranes is in the range of 0.01-100 ml/min/cm<2 >at 1 bar, such as 0.2 ml/min/cm<2 >at 1 bar.

[0068] In a further embodiment, the invention relates to a polymer membrane, particularly as described herein, obtainable by a process as described herein.

[0069] In a further embodiment, the invention relates to a polymer membrane, particularly as described herein, obtained by a process as described herein.

[0070] The present invention relates in a forth aspect to a shaped article comprising a polymer membrane as described herein. A wide variety of articles may be equipped with the inventive porous material. This aspect of the invention shall be explained in further detail below:

[0071] In one embodiment, the invention relates to a shaped article as described herein selected from the group consisting of (i) filters (preferably wherein said membrane is supported or unsupported); (ii) woven or non-woven textiles (wherein said membrane is laminated on said textile).

[0072] In a further embodiment, the shaped article comprises a support and a coating, preferably a top coating, wherein said coating consists of a porous material as defined herein.

[0073] In a further embodiment the invention relates to an article obtainable by or obtained by a method as described herein.

[0074] The present invention relates in a fifth aspect to uses/methods of use of the membranes, shaped articles and intermediates as described herein.

Membranes:

[0075] In one embodiment, the present invention relates to the use of a membrane as described herein in a filter device or as part of a woven or non-woven textile. The inventive membranes prove to be useful in a number of applications, including filter materials and textile materials. This aspect of the invention shall be explained in further detail below. The inventive membranes are self-supporting ("free standing"). Therefore, they distinguish from known membranes of similar thickness and porosity on a support. However, the inventive material is suitable for coating an appropriate support. The possibility of manufacturing such membrane independent from a specific support makes it very versatile.

[0076] The inventive membranes may be used in micro-filtration, ultrafiltration and/or nanofiltration, e.g. by using known methods. Microfiltration is used to separate particles of 100-1000 nm, such as bacteria; ultrafiltration is used to separate particles of 10-100 nm, such as viruses, proteins and colloids; nanofiltration is used to separate particles of 1-10 nm, such as salts, pesticides, sugars.

Shaped Articles:

[0077] In general, the inventive shaped articles retain the beneficial properties of the polymer membranes as defined herein and are thus suitable for all uses that are applicable to such membranes; this particularly includes the uses as disclosed herein, such as microfiltration, ultrafiltration, nanofiltration (e.g., sterile filtration or viral filtration or concentration of biological molecules (e.g. proteins)).

[0000] In a further embodiment, the present invention relates to the use of an article, as defined herein (i) in a filter; (ii) in a textile material.

Intermediates/Starting Materials:

[0078] The inventive intermediates may be used in a process for manufacturing a membrane as described herein.

[0079] To further illustrate the invention, the following examples are provided. These examples are provided with no intent to limit the scope of the invention.

I. Preparation of Starting Materials

[0080] The preparation of the salt nanoparticles is described in WO2005/087660. The synthesis of calcium carbonate (denoted as CaCO3), barium carbonate (denoted as BaCO3), strontium carbonate (denoted as SrCO3), potassium carbonate (denoted as K2CO3) and sodium carbonate (denoted as Na2CO3) nanoparticles is shortly described below; an FSP apparatus as described in WO2005/087660 is used.

[0081] a) Preparation of CaCO3 nanoparticles: Ca-2-Ethylhexanoate in 2-ethylhexanoic acid (Molekula) was diluted with tetrahydrofurane (THF) to a final Ca content of 3.9 wt %. This precursor is fed (9 ml/min, HNP Mikrosysteme, micro annular gear pump mzr-2900) to a spray nozzle, dispersed by oxygen (9 l/min, PanGas Tech.) and ignited by a premixed methane-oxygen flame (CH4, 1.2 l/min; O2, 2.2 l/min). The off-gas is filtered through a glass fiber filter (Whatman Ltd., USA) by a vacuum pump (Busch S.A., Switzerland). The resulting powder is collected on the glass fiber filter and removed by a spatula.

[0082] b) Preparation of BaCO3 nanoparticles: Ba-2-Ethylhexanoate in 2-ethylhexanoic acid (AlfaAesar) was diluted with tetrahydrofurane (THF) to a final Ba content of 4.6 wt %. The precursor is fed (5 ml/min, HNP Mikrosysteme, micro annular gear pump mzr-2900) to a spray nozzle, dispersed by oxygen (5 l/min, PanGas Tech.) and ignited by a premixed methane-oxygen flame (CH4, 1.2 l/min; O2, 2.2 l/min). The off-gas is filtered through a glass fiber filter (Whatman Ltd., USA) by a vacuum pump (Busch S.A., Switzerland). The resulting powder is collected on the glass fiber filter and removed by a spatula.

[0083] c) Preparation of SrCO3 nanoparticles: Sr-2-Ethylhexanoate in 2-ethylhexanoic acid (Strem Chemicals) was diluted with tetrahydrofurane (THF) to a final Sr content of 4.7 wt %. The precursor is fed (5 ml/min, HNP Mikrosysteme, micro annular gear pump mzr-2900) to a spray nozzle, dispersed by oxygen (5 l/min, PanGas Tech.) and ignited by a premixed methane-oxygen flame (CH4, 1.2 l/min; O2, 2.2 l/min). The off-gas is filtered through a glass fiber filter (Whatman Ltd., USA) by a vacuum pump (Busch S.A., Switzerland). The resulting powder is collected on the glass fiber filter and removed by a spatula.

[0084] d) Preparation of K2CO3 nanoparticles: 20 wt % of K-2-Ethylhexanoate (AlfaAesar) was dissolved in 2-ethylhexanoic acid and further diluted with tetrahydrofurane (THF) to a final K content of 3.5 wt %. The precursor is fed (5 ml/min, HNP Mikrosysteme, micro annular gear pump mzr-2900) to a spray nozzle, dispersed by oxygen (5 l/min, PanGas Tech.) and ignited by a premixed methane-oxygen flame (CH4, 1.2 l/min; O2, 2.2 l/min). The off-gas is filtered through a glass fiber filter (Whatman Ltd., USA) by a vacuum pump (Busch S.A., Switzerland). The resulting powder is collected on the glass fiber filter and removed by a spatula.

[0085] e) Preparation of Na2CO3 nanoparticles: 20 wt % of Na-2-Ethylhexanoate (Aldrich Fine Chemicals) was dissolved in 2-ethylhexanoic acid and further diluted with tetrahydrofurane (THF) to a final Na content of 2.4 wt %. The precursor is fed (5 ml/min, HNP Mikrosysteme, micro annular gear pump mzr-2900) to a spray nozzle, dispersed by oxygen (5 l/min, PanGas Tech.) and ignited by a premixed methane-oxygen flame (CH4, 1.2 l/min; O2, 2.2 l/min). The off-gas is filtered through a glass fiber filter (Whatman Ltd., USA) by a vacuum pump (Busch S.A., Switzerland). The resulting powder is collected on the glass fiber filter and removed by a spatula.

II. Preparation of Polymer Membranes.

[0086] Polymer membranes are generally produced in a multiple step process (see FIG. 1):

[0087] Step a) A dispersion is prepared consisting of a soluble polymer (pre-dissolved in an

appropriate solvent) and metal salt nanoparticles. This dispersion is achieved by manual mixing of the components and further ultra-sonication in order to obtain well dispersed salt nanoparticles.

[0088] Step b) The dispersion is applied on a substrate (e.g. glass) using spin coating or roll coating and dried afterwards. Optionally, a heating step can be applied for faster drying of the applied films (evaporation of the solvent; step c)).

[0089] Step e) The template salt nanoparticles are removed (dissolved) from the polymer matrix using a suitable acid to reveal the porous structure. The film is then washed in de-ionized water and ethanol and dried on air.

[0090] Specific preparation procedures for polymer membranes using different polymers, salts and solvents are given below and summarized in table 1.

[0091] a) Porous polysulfone membranes (porous PSU membranes)

a1) PSU dissolved in dichloromethane (denoted as DM)
PSU (Dolder AG, Udel P-1700) dissolved in DM (J. T. Baker, N L) is mixed with either CaCO3, K2CO3 or Na2CO3 nanoparticles. The weight ratio of polymer to salt is 52.5% to 47.5%. The weight ratio of polymer/salt to solvent is 6% to 94%. This mixture is sonicated (Hielscher ultrasonics, UP400s) for 1 minute at 400 W to disperse the nanoparticles. The dispersion is then applied on a glass substrate using spin-coating (Laurell Technologies Corp., WS-650SZ) or roll-coating (Zehntner GmbH, ZAA 2300) to achieve films of uniform thickness. For spin-coating, a drop of approximately 500 [mu]l is pipetted on the substrate and then spinned for 10 seconds at 1000 rpm and acceleration of 1000 rpm/s. For roll-coating, the coating knife has 50 [mu]m slots, forward speed is set to 18 mm/s. 1 ml of dispersion was used to create a film of approximately 10*10 cm<2 >area. Finally, the salt nanoparticles are dissolved in 1M hydrochloric acid (denoted as HCl) for 3 minutes to reveal the porous structure. The film is then washed in de-ionized water (Millipore, electrical resistivity >18M[Omega]cm) and ethanol and dried on air for 2 hours.
a2) PSU dissolved in dimethylacetamide (denoted as DMAC)

PSU (Dolder AG, Udel P-1700) dissolved in DMAC (Fluka, CH) is mixed with SrCO3 nanoparticles. The weight ratio of polymer to salt is 40.0% to 60.0%. The weight ratio of polymer/salt to solvent is 20.0% to 80.0%. This mixture is sonicated (Hielscher ultrasonics, UP400s) for 1 minute at 400 W to disperse the nanoparticles. The dispersion is then applied on a glass substrate using spin-coating (Laurell Technologies Corp., WS-650SZ) or roll-coating (Zehntner GmbH, ZAA 2300) to achieve films of uniform thickness. For spin-coating, a drop of approximately 500 [mu]l is pipetted on the substrate and then spinned for 30 seconds at 1000 rpm and acceleration of 1000 rpm/s. For roll-coating, the coating knife has 50 [mu]m slots, forward speed is set to 18 mm/s. 1 ml of dispersion was used to create a film of approximately 10*10 cm<2 >area. Subsequent heating for 1 minute at 120[deg.] C. in an ordinary lab oven (Memmert GmbH) is necessary for the quick evaporation of remaining solvent. Finally, the salt nanoparticles are dissolved in 1M hydrochloric acid (denoted as HCl) for 3 minutes to reveal the porous structure. The film is then washed thoroughly in de-ionized water (Millipore, electrical resistivity >18M[Omega]cm) and ethanol and dried on air for 2 hours.

[0094] b) Porous polyethersulfone membranes (porous PES membranes)

b1) PES dissolved in DMAC

PES (Dolder AG, Veradel A-201) dissolved in DMAC (Fluka, CH) is mixed with either BaCO3 or SrCO3 nanoparticles. The weight ratio of polymer to BaCO3 is 20.0% to 80.0%. The weight

ratio of polymer/BaCO3 to solvent is 40% to 60%. The weight ratio of polymer to SrCO3 is 40.0% to 60.0%. The weight ratio of polymer/SrCO3 to solvent is 20% to 80%. These mixtures are sonicated (Hielscher ultrasonics, UP400s) for 1 minute at 400 W to disperse the nanoparticles. The dispersions are then applied on glass substrates using spin-coating (Laurell Technologies Corp., WS-650SZ) or roll-coating (Zehntner GmbH, ZAA 2300) to achieve films of uniform thickness. For spin-coating, a drop of approximately 500 [mu]l is pipetted on the substrate and then spinned for 30 seconds at 1000 rpm and acceleration of 1000 rpm/s. For roll-coating, the coating knife has 50 [mu]m slots, forward speed is set to 18 mm/s. 1 ml of dispersion was used to create a film of approximately 10*10 cm<2 >area. Subsequent heating for 1 minute at 120[deg.] C. in an ordinary lab oven (Memmert GmbH) is necessary for the quick evaporation of remaining solvent. Finally, the salt nanoparticles are dissolved in 1M hydrochloric acid (denoted as HCl) for 3 minutes to reveal the porous structure. The film is then washed thoroughly in de-ionized water (Millipore, electrical resistivity >18M[Omega]cm) and ethanol and dried on air for 2 hours.

b2) PES dissolved in dimethylsulfoxide (denoted as DMSO)

PES (Dolder AG, Veradel A-201) dissolved in DMSO (Fluka, CH) is mixed with CaCO3 nanoparticles. The weight ratio of polymer to salt is 52.5% to 47.5%. The weight ratio of polymer/salt to solvent is 6.0% to 94.0%. This mixture is sonicated (Hielscher ultrasonics, UP400s) for 1 minute at 400 W to disperse the nanoparticles. The dispersion is then applied on a glass substrate using spin-coating (Laurell Technologies Corp., WS-650SZ) or roll-coating (Zehntner GmbH, ZAA 2300) to achieve films of uniform thickness. For spin-coating, a drop of approximately 500 [mu]l is pipetted on the substrate and then spinned for 1 minute at 1000 rpm and acceleration of 1000 rpm/s. For roll-coating, the coating knife has 50 [mu]m slots, forward speed is set to 18 mm/s. 1 ml of dispersion was used to create a film of approximately 10*10 cm<2 >area. Subsequent heating for 1 minute at 120[deg.] C. in an ordinary lab oven (Memmert GmbH) is necessary for the quick evaporation of remaining solvent. Finally, the salt nanoparticles are dissolved in 1M hydrochloric acid (denoted as HCl) for 3 minutes to reveal the porous structure. The film is then washed thoroughly in de-ionized water (Millipore, electrical resistivity >18M[Omega]cm) and ethanol and dried on air for 2 hours.

[0097] c) Porous polycarbonate membrane (porous PC membranes)

[0000] PC (Bayer Material Science, Makrolon OD2015) dissolved in DM (J. T. Baker, N L) is mixed with CaCO3 nanoparticles. The weight ratio of polymer to salt is 52.5% to 47.5%. The weight ratio of polymer/salt to solvent is 6% to 94%. This mixture is sonicated (Hielscher ultrasonics, UP400s) for 1 minute at 400 W to disperse the nanoparticles. The dispersion is then applied on a glass substrate using spin-coating (Laurell Technologies Corp., WS-650SZ) or roll-coating (Zehntner GmbH, ZAA 2300) to achieve films of uniform thickness. For spin-coating, a drop of approximately 500 [mu]l is pipetted on the substrate and then spinned for 10 seconds at 1000 rpm and acceleration of 1000 rpm/s. For roll-coating, the coating knife has 50 [mu]m slots, forward speed is set to 18 mm/s. 1 ml of dispersion was used to create a film of approximately 10*10 cm<2 >area. Finally, the salt nanoparticles are dissolved in 1M hydrochloric acid (denoted as HCl) for 3 minutes to reveal the porous structure. The film is then washed in de-ionized water (Millipore, electrical resistivity >18M[Omega]cm) and ethanol and dried on air for 2 hours.

[0098] d) Porous urea-polydimethylsiloxane membrane (porous urea-PDMS membrane)

[0000] Urea-PDMS (Wacker Chemie AG, Geniomer 200) dissolved in 2-Propanol (Fluka, CH) is mixed with CaCO3 nanoparticles. The weight ratio of polymer to salt is 52.5% to 47.5%. The weight ratio of polymer/salt to solvent is 6% to 94%. This mixture is sonicated (Hielscher ultrasonics, UP400s) for 1 minute at 400 W to disperse the nanoparticles. The dispersion is then

applied on a glass substrate using spin-coating (Laurell Technologies Corp., WS-650SZ) or roll-coating (Zehntner GmbH, ZAA 2300) to achieve films of uniform thickness. For spin-coating, drops of approximately 500 [mu]l are pipetted on the substrate and then spinned for 10 seconds at 1000 rpm and acceleration of 1000 rpm/s. For roll-coating, the coating knife has 50 [mu]m slots, forward speed is set to 18 mm/s. 1 ml of dispersion was used to create a film of approximately 10*10 cm<2 >area. Finally, the salt nanoparticles are dissolved in 1M hydrochloric acid (denoted as HCl) for 3 minutes to reveal the porous structure. The film is then washed in de-ionized water (Millipore, electrical resistivity >18M[Omega]cm) and ethanol and dried on air for 2 hours.

[0000]

TABLE 1
Summary of membrane preparation specifications:

Polymer/NP size* Polymer:salt salt:solv.
ex. Polymer Salt-NP solvent [nm] [wt %] [wt %]
a1) PSU CaCO3 DM 40 52.5:47.5 6.0:94.0
a1) PSU K2CO3 DM 30 52.5:47.5 6.0:94.0
a1) PSU Na2CO3 DM 30 52.5:47.5 6.0:94.0
a2) PSU SrCO3 DMAC 15 40.0:60.0 20.0:80.0
b1) PES BaCO3 DMAC 15 20.0:80.0 40.0:60.0
b1) PES SrCO3 DMAC 15 40.0:60.0 20.0:80.0
b2) PES CaCO3 DMSO 40 52.5:47.5 6.0:94.0
c) PC CaCO3 DM 40 52.5:47.5 6.0:94.0
d) Urea- CaCO3 <i>PrOH 40 52.5:47.5 6.0:94.0

PDMS

*NP size: Mean nanoparticles crystallite size, determined by X-ray diffraction

III. Dextran Rejection Profile Test.

[0099] The practicability of the hereby described membranes for filtration purposes has been tested on the PSU membrane (example a 1, CaCO3 as template nanoparticles). For this purpose, a dextran rejection test has been implemented to determine the molecular weight cut-off (denoted as MWCO, for details see: G. Tkacik, S. Michaels, Nature Biotechnology. 9:941-946, 1991). For example, a membrane capable of rejecting at least 90% of a macromolecule of 1000 kDa can be classified to have a MWCO of 1000 kDA. A 0.1 wt % mixture of different dextran standards (5 kDa, 25 kDa, 80 kDa, 150 kDa, 270 kDa, 410 kDa, 670 kDa, 1400 kDa) (Fluka, CH) was prepared in 0.1M sodium nitrate (denoted as NaNO3) buffer solution. The individual standards were mixed in equal amounts. The mixture was filtered (direct flow) through the membrane using a high vacuum pump (Edwards Vacuum Ltd). The permeate and the mixture were compared using gel permeation chromatography.

[0100] The PSU membrane of ex a1 (table 1) based on CaCO3 showed a minimal rejection of 95% for the 1400 kDa dextran standard molecules. The MWCO for the tested membrane can therefore be classified as 1400 kDa. This MWCO was proven several times which indicates that the membrane fabrication process is stable and reproducible.

POROUS MATERIALS
WO2011047805 (A1)

ANTIMICROBIAL MATERIAL
US2010150980

US8753601
FLAME SYNTHESIS OF METAL SALT NANOPARTICLES, IN PARTICULAR CALCIUM AND PHOSPHATE COMPRISING NANOPARTICLES

Described is a method for the production of metal salts, wherein the cationic metal is preferably selected from Group I to IV metals and mixtures thereof and the anionic group is selected from phosphates, silicates, sulfates, carbonates, hydroxides, fluorides and mixtures thereof, and wherein said method comprises forming a mixture of at least one metal source that is a metal carboxylate with a mean carbon value per carboxylate group of at least 3 and at least one anion source into droplets and oxiding said droplets in a high temperature environment, preferably a flame. This method is especially suited for the production of calcium phosphate biomaterials such as hydroxyapatite (HAp, Ca10(PO4)6(OH)2) and tricalcium phosphate (TCP, Ca3(PO4)2) that exhibit excellent biocompatibility and osteoconductivity and therefore are widely used for reparation of bony or periodontal defects, coating of metallic implants and bone space fillers.

TECHNICAL FIELD

This application relates to fine metal salt particles and a method for producing same by means of flame spray pyrolysis, in particular calcium and phosphate containing particles.

BACKGROUND ART

Flame spray pyrolysis <13 >currently established itself as a suitable method for the preparation of nano-particles, most notably, oxides containing main group and transition metals <41>. It has rapidly evolved into a scalable process to oxide nanoparticles for catalyst preparation <14,15 >and industrial-scale flame-aerosol synthesis today produces megaton quantities of carbon, silica and titania. Experimentally, the flame spray reactors consist of a capillary surrounded by a narrow adjustable orifice (see FIG. 1). The precursor liquid is dispersed at the tip resulting in a well-defined spray. The surrounding methane/oxygen supporting flame ignites the spray and the flame converts the precursor to the corresponding materials.

For many applications nanoparticulate materials are desired. Such materials comprise calcium phosphates such as tricalciumphosphates but also apatites. Calcium phosphate biomaterials have attracted a tremendous interest in clinical medicine. Both hydroxyapatite (HAp or OHAp, Ca 10(PO 4) 6(OH) 2) and tricalcium phosphate (TCP, Ca 3(PO 4) 2) exhibit excellent biocompatibility and osteoconductivity <1,2>. They are widely used for reparation of bony or periodontal defects, coating of metallic implants and bone space fillers. However, traditional methods (precipitation, sol-gel synthesis, hydrothermal method or solid-state reactions) <1,3-5 >suffer from a limited range of accessible materials and morphology. Wet-phase preparation generally requires time and cost intensive post treatments such as washing and drying. Solid-state reaction involves prolonged sintering and therefore results in low specific surface area powder. The rather dense materials display a lack of microporosity, reduce contact to the body fluid and hinder resorption in vivo.

Recently reported preparation methods comprise, plasma spraying6 and pulsed laser deposition <7,8>. They have resulted in advantageous coatings on implant surfaces. Moreover, amorphous calcium phosphates have shown to result in improved resorption properties <9-11 >and are promising materials for self-setting cements <12 >making them a most valuable target.

All these methods, however, have several drawbacks. They either lead to mixtures that can not be separated or only with considerable effort, and/or they lead to a too dense material, and/or they cannot be applied for bulk synthesis, and/or they are not usable in large scale production. Thus there is still a need for an improved production method allowing the production of pure materials, preferably also in large scale production, and an improved material obtainable by such method.

DISCLOSURE OF THE INVENTION

Hence, it is a general object of the invention to provide a method for the production of metal salts, wherein the anionic group is selected from phosphates, borates, silicates, sulfates, carbonates, hydroxides, fluorides and mixtures thereof, in particular nanoparticulate metal salts, preferably metal salts wherein the metal is selected from groups I, II, III, IV metals, the 3d transition metals, the lanthanoids (rare earth group) predominantly occurring in oxidation states II and III, but optionally also in oxidation state I or IV, and mixtures of the mentioned metals. Since all the above mentioned metals usually have oxidation states I to IV, they are further on considered to be encompassed by the term "group I to IV metals". Other metals can be present depending on the type of salt and area of application. In some cases, doped salts or mixtures or different salts are preferred.

Another object of the present invention was to provide nanoparticulate, optionally percolating metal salts.

Yet another object of the present invention was to provide uses for such metal salts.

Now, in order to implement these and still further objects of the invention, which will become more readily apparent as the description proceeds, the method is manifested by the features that a mixture of at least one metal source that is a metal carboxylate with a mean carbon value per carboxylate group of at least 3 and at least one anion source is formed into droplets and that said droplets are oxidized in a high temperature environment.

In preferred metal salts the metal comprises calcium. Much preferred are metal salts with a high calcium content of at least 80 atom-% calcium (sum of all cations is 100 atom-%), preferably at least 90%, most preferably at least 95%.

The sum of cationic metals may comprise further Group I-IV metals, preferably metals selected from the group consisting of sodium, potassium, magnesium, zinc, strontium and barium, rare earth metals, in particular gadolinium, and mixtures of two or more of said metals.

Preferably the sum of anionic groups comprises anionic groups selected from phosphates, sulfates, borates, hydroxides, carbonates, fluorides and mixtures thereof in amounts of at least 80 mole-% of the theoretically calculated necessary amount of anions if electron neutrality in the salt is assumed, preferably at least 90%, more preferred at least 95%. Most preferred are pure materials wherein more than 98% or even 99% of all negative charges in the salt are covered by one of the above anions. In much preferred compounds at least part of the anionic groups are phosphates, whereby compounds with a metal:phosphate molar ratio of 3:1 (e.g. Na 3PO 4) to 1:1 (e.g. AlPO 4, enamel) are preferred.

The method of the present invention is especially suited to produce a metal salt selected from the group consisting of amorphous tricalciumphosphate, alpha-tricalciumphosphate, beta-tricalciumphosphate, apatites and mixtures thereof.

Preferred apatites that are producible by the above method in high purity have the formula Ca 10(PO 4) 6(OH) 2xF 2y(CO 3) z whereby x, y and z each range from 0 to 1 and the sum of

x+y+Z is 1. Although z can vary from 0 to 1, dependent on the application specific ranges may be preferred. For e.g. medical applications, carbonate can be advantageous. The carbonate content in apatites can e.g. be 3-8 wt % carbonate measured by thermographimetric analysis. The CO 2 detection can be done by a differential scanning calorimeter coupled to a mass spectrometer.

The method of the present invention has been found suitable for the production of very pure products, such as phase pure amorphous tricalciumphosphate, alpha-tricalciumphosphate or beta-tricalciumphosphate, or tricalciumposphate poor or even tricalciumposphate free apatites. The purity of the compound formed that can be achieved is in the range of at least 96% by weight, preferably at least 98% by weight, most preferred at least 99% by weight. Preferred products that can be obtained in high purity comprise amorphous tricalciumphosphate, alpha-tricalciumphosphate or beta-tricalciumphosphate or hydroxyapatite or fluorapatite or hydroxyfluorapatite.

As mentioned above, the metal source is a metal carboxylate with a mean carbon value per carboxylate group of at least 3, preferably at least 4, much preferably at least 5, and most preferred between 5 and 8. Preferably, the metal carboxylate is selected from the group consisting of C1 to C18 carboxylates and mixtures thereof, more preferably C4 to C12 carboxylates and mixtures thereof, much preferably C5 to C8 carboxylates and mixtures thereof, in particular octoates such as 2-ethylhexanoic acid salts.

The metal carboxylate(s) and the one or more anion source(s), i.e. the phosphate and/or one or more other anion(s) or anions precursor(s) comprising droplets are preferably oxidized in a flame.

Prior to being formed into droplets, the metal carboxylate usually has a viscosity of at most 100 mPas, preferably at most 40 mPas, more preferably at most 20 mPas. If the metal carboxylate does not have such viscosity, such viscosity may be obtained by heating and/or by providing a mix of the at least one metal carboxylate and at least one viscosity reducing solvent.

Suitable viscosity reducing solvents may comprise one or more acids. While viscosity reducing solvents may consist of one or more acids, often 50% w/w total acid(s) or less may be used and in some cases acids are neither needed nor desired. Preferred acids are C1 to C10 carboxylic acids.

The solvent may comprise at least one low molecular weight and/or low viscosity apolar solvent, in particular an aromatic or aliphatic, unsubstituted, linear or branched hydrocarbon, preferably a solvent selected from the group consisting of toluene, xylene, lower aliphatic hydrocarbons and mixtures thereof.

The anion source is selected in view of sufficient solubility in the above defined solvent. Suitable anion sources comprise
a phosphate source selected from inorganic phosphorous compounds and/or organophosphorous compounds soluble in solvents or solvent mixtures having a combustion enthalpy of at least 13 kJ/g, preferably at least 22.5 kJ/g, most preferred at least 25.5 kJ/g, in particular phosphoric acid and/or organic esters of phosphoric acid and/or phosphines, in particular phosphorous compounds constituting solvents or leading to solvent mixtures with the above-mentioned properties, and/or
a fluoride source being a fluoride derivative of an organic compound, said fluoride derivative being soluble in the above defined solvent or solvent mixture, in particular trifluoroacetic acid, and/or
a silicate source selected from organic silicates and/or organosilicon compounds soluble in the above defined solvent or solvent mixture, in particular tetraethyl silicate, and/or

a sulfate source selected from organic sulfur containing compounds and/or sulfuric acid said sulfate source being soluble in the above defined solvent or solvent mixture, in particular dimethyl sulfoxide (DMSO)
a carbonate source selected from any organic carbon source, such as hydrocarbons, carboxylic acids, alcohols, metal carboxylates and mixtures thereof.

If metal carbonates shall be produced, the metal carboxylate used as metal source can simultaneously act as anion source, whereby the cool-down process (residence time of the particle containing off-gas at specific temperatures) is relevant for the purity.

Suitable apparatus for performing the flame oxidation are spray burners <42,43>, or in particular oil burners.

Usually the oxidation is performed at a temperature of at least 600[deg.] C., preferably at least 800[deg.] C., more preferably at least 1000[deg.] C. and most preferably in a range of 1200 to 2600[deg.] C., in particular at about 1600[deg.] C.

A suitable method for preparing the metal carboxylate starts from a metal oxide, a metal hydroxide, a metal carbonate, a metal halide, such as a chloride or bromide, or a metal lower alkyl oxide, in particular a C1 to C4 alkyl oxide. For good results the enthalpy of the metal carboxylate or the metal carboxylate comprising solution should be at least 13 kJ/g, preferably at least 18 kJ/g, more preferred at least 22.5 kJ/g and most preferred at least 25.5 kJ/g.

It is possible to get a high production rate if the solution comprises metal carboxylate(s) in an amount corresponding to at least 0.15 moles metal per liter, and anion source(s) in an amount corresponding to at least 0.05 moles anionic groups per liter. It is, however, also possible to make the solution up to 10 times more concentrated, whereby concentrations of about 0.8 to 2 moles metal and corresponding amounts of anionic groups/anion precursors are presently preferred. Since the conversion of the metal source to the metal salt is almost free of any loss, a high production rate, only dependent on the solubility of the starting materials, the viscosity of the solution to be sprayed and the nozzle/burner capacity is obtained. By adding at least 1 anionic group per 3 metal atoms/ions, the conversion to a metal salt of the present invention and not a metal oxide is achieved.

In order to bring the nanoparticle manufacture from the pilot-scale production to an industrial scale synthesis (kg to ton quantities), some additional problems are to be faced. The most prominent is the choice of readily accessible metal precursors that allow sufficiently high production rates. The present invention links the manufacture of nanoparticles to specific metal containing products and anion sources, as well as optionally specific solvents. Besides of the specific selection of starting materials, production rate is also influenced by the burner. Using multiple arrays as described in WO 02/061163 entails problems with maintenance, nozzle clogging, space, reproducibility and others. Thus it is much preferred to use few burners to make the same quantity of powder, preferably common oil burners. Oil burners with well above 100 kg oil/h are available and thus they are well suited for high production rates. As it will become apparent within this invention, such a burner can (without any scale-up) achieve amounts of 8 kg Ca 3(PO 4) 2 or 9 kg hydroxyapatite particles per hour (for 100 kg feed/hour). with scale-up amounts of about 12 or 13 kg, respectively, are expected. Commercially available oil-burners suitable to convert the here described liquid into corresponding metal salts are-to only mention a few-available from Vescal AG, Heizsysteme, Industries-trasse 461, CH-4703 Kestenholz under the designation of OEN-151LEV, or OEN-143LEV, or OEN-331LZ to OEN-334LZ.

The method of the present invention can also be applied for the production of substoichiometric metal salts. In such production the flame comprises insufficient oxygen for full combustion or

conversion of the reactants. Thus, substoichiometric means that e.g. a metal is present in different oxidation states.

The metal salt as-prepared (as-prepared designates a product directly after high temperature production, in particular directly after the burner/flame) may comprise some carbonate. In case that less or no carbonate is desired, a heat treatment, optionally in the presence of humidity may be performed. In the case of apatite such treatment allows to reduce the CO 2 content to close to zero. Suitably such treatment is performed at temperatures of from 500[deg.] C. to 900[deg.] C. and a water partial pressure of 0.1 to 100 mbar.

Dependent on the CO 2 removal conditions, this step may simultaneously act as tempering/sintering procedure, or a separate tempering/sintering procedure may be provided. By such temperature treatment, the crystal structure may be influenced and/or a percolating product with specific features may be obtained. Suitable sintering methods can be found by applying the analytical methods described below in connection with calcium phosphate (Ca/P) samples. Such methods comprise mercury porosimetry and nitrogen adsorption (BET) such as outlined in Rigby et al. (2004) <40 >for determining the specific surface area and pore size and pore structure analysis. Further methods are transmission electron microscopy (TEM) and scanning electron microscopy (SEM) for morphological studies, Fourier transform infrared (FTIR) spectroscopy and X-ray diffraction for product characterization, as well as differential thermal analysis (DTA) for monitoring temperature dependent changes.

A further aspect of the present invention is a metal salt, in particular a metal salt obtainable by the above described method.

Metal salts of the present invention comprise the following features:

They have a BET equivalent diameter as-prepared in the range of 5 to 200 nm, preferably of about 20 nm. In specific cases, larger than 20 nm diameters such as 50 nm or 100 nm are obtained, especially if the melting point of the corresponding salt is below 1000[deg.] C.

Furthermore, the salts of the present invention are characterized in that they usually do not release more than 7.5 wt % water upon heating to 900[deg.] C. at a heating rate of 10[deg.] C. per minute. Preferably, they have less than 5 wt % water release, most preferred less than 4.5 wt % water release.

The salts of the present invention usually release more than 90 wt % of all water upon heating to 500[deg.] C. at a heating rate of 10[deg.] C. per minute. Preferably, upon heating to 400[deg.] C., most preferably upon heating to 350[deg.] C. The water release curve (see e.g. FIG. 5) supports the assumption that water is only present adsorbed on the surface.

The water release criteria markedly distinguish the material of the present invention from wet phase material. Such material slowly releases water in a large temperature range of several hundreds [deg.] C. The release curve of wet phase product supports the assumption that water is incorporated within the crystal lattice such that it is kept much stronger.

Dependent on the preparation method final, sintered products with different morphology and bulk density (measured according to DIN ISO 697 (1984-01)) are obtained. The bulk density of e.g. wet-phase prepared amorphous tricalciumphosphate is often higher than 500 kg/m <3>, whereas the product produced by the method of the present invention is in the range of 100 to 300 kg/m <3>. The bulk density of alpha-tricalciumphosphate or beta-tricalciumphosphate produced by state of the art high temperature solid state reaction is in the range of 1000 to 2000 kg/m <3 >whereas respective products produced by the method of the present invention have bulk densities of below 800 kg/m <3 >for beta-tricalciumphosphate and below 500 kg/m <3

>for alpha-tricalciumphosphate.

The specific surface area (measured by nitrogen adsorption at -196[deg.] C. according to the BET-method) of state of the art alpha-tricalciumphosphate is below 2 m <2>/g, whereas alpha-tricalciumphosphate produced according to the present invention has more than 3 m <2>/g, often and preferably more than 5 m <2>/g and more preferably more than 8 m <2>/g. The specific surface area of state of the art beta-tricalciumphosphate is below 0.8 m <2>/g, whereas beta-tricalciumphosphate of the present invention has more than 1 m <2>/g, often and preferably more than 1.5 m <2>/g and more preferably more than 2 m <2>/g.

Preferred metal salts of the present invention are biomaterials.

Such metal salts may be used in medical applications, e.g. as bone cement and/or resorbable material for implants, as additive to tooth pastes, e.g. as fluoride source and/or abrasive aid, as fluoride source in foodstuffs, e.g. chewing gums, sweets and table salt, as catalyst support, as molecular sieve, as filler for polymers, as UV stabilizer and/or degradation activator in biodegradable or bioresorbable materials.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be better understood and objects other than those set forth above will become apparent when consideration is given to the following detailed description thereof. Such description makes reference to the annexed drawings, wherein:

FIG. 1A shows the flame of a 2-phase nozzle burner where a spray of metal containing liquid is dispersed and ignited. The burning spray is the reactor itself. Particles form from this hot gas and can be collected on top of the burner.

FIG. 1B is a schematic presentation of the flame indicating the material streams. FIG. 2A is the picture of tricalcium phosphate as-prepared, i.e. before sintering.

FIG. 2B shows the reduction in specific surface area due to thermal treatment of as-prepared material as shown in FIG. 2A.

FIG. 3 shows transmission electron microscopy pictures (left two pictures) and scanning electron microscopy images (right two pictures) of calcium phosphate (Ca/P=1.5) after sintering at 700[deg.] C. (top two pictures) and after sintering at 900[deg.] C. (bottom two pictures).

FIG. 4 shows the differential thermo analysis (DTA) data of Ca/P=1.5 samples with different excesses In P and Ca in a temperature range from RT to 1320[deg.] C. and at a heating rate of 10[deg.] C./min (left side) and the X-ray diffraction pattern of some Ca/P samples after thermal treatment at specific temperatures (right side).

FIG. 5 shows the theromographimetric analysis (TG, top graph) of a Ca/P=1.67 sample and the corresponding differential scanning calorimetric trace (DTA, top graph) with a single exothermic peak showing the crystallization of the sample. The bottom graph depicts carbon dioxide (CO 2) and water (H 2O) evolution as measured simultaneously by a mass spectrometer that was coupled to the TG/DTA analysis. This setup allows simultaneous detection of crystallization, gas release and mass loss.

FIG. 6 shows Fourier transform infrared (FTIR) spectra of samples with different Ca/P ratio as-prepared and after treatment at 700[deg.] C.

FIG. 7 shows FTIR spectra of samples with different Ca/P ratio after calcination at 900[deg.] C. for 30 minutes.

FIG. 8 compares the XRD pattern of several apatites as-prepared and after temperature treatment at 700[deg.] C.

FIG. 9 compares the FTIR spectra of hydroxyapatite, hydroxyfluorapatite and fluorapatite after calcination at 700[deg.] C.

FIG. 10 shows the formation of different calcium phosphates dependent on the Ca/P ratio after calcinations at 700[deg.] C. for 30 minutes.

FIG. 11 shows the formation of different calcium phosphates dependent on the Ca/P ratio after calcinations at 900[deg.] C. for 30 minutes.

FIG. 12 shows that in magnesium doped tricalcium phosphate containing 1 atom-% Mg with respect to calcium no separate phase is visible and the XRD pattern corresponds to alpha-TCP (after 700[deg.] C. sintering) or beta-TCP (after 900[deg.] C. sintering). This corroborates the good dispersion and incorporation of Mg in the lattice.

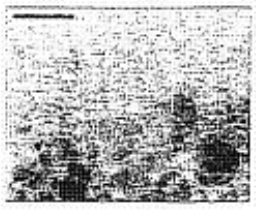
FIG. 13 shows that in magnesium doped apatite containing 1 atom-% Mg with respect to calcium no separate phase is visible and the XRD pattern corresponds to hydroxyl apatite (after 700[deg.] C. sintering) and remains stable (after 900[deg.] C. sintering). This corroborates the good dispersion and incorporation of Mg in the lattice.

FIG. 14 shows that in zinc doped tricalcium phosphate containing 1 atom-% Zn with respect to calcium no separate phase is visible and the XRD pattern corresponds to alpha-TCP (after 700[deg.] C. sintering) or beta-TCP (after 900[deg.] C. sintering). This corroborates the good dispersion and incorporation of Zn in the lattice.

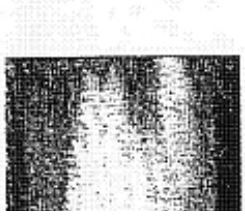
FIG. 15 shows that in zinc doped apatite containing 1 atom-% Zn with respect to calcium no separate phase is visible and the XRD pattern corresponds to hydroxyl apatite (after 700[deg.] C. sintering) and remains stable (after 900[deg.] C. sintering). This corroborates the good dispersion and incorporation of Zn in the lattice.

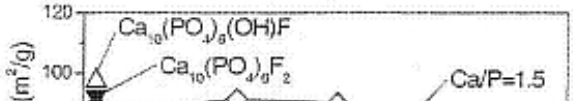
FIG. 16 shows that the XRD pattern for calcium carbonate nanoparticles prepared by flame spray synthesis corresponds to calcium carbonate with some impurity of calcium oxide. These particles of the invention are made in a single step from calcium octoate in a flame spray burner.

FIG. 17 shows the XRD of anhydrite (calcium sulfate) nanoparticles, obtained by feeding calcium octoate and dimethylsulfoxide (DMSO) into a flame spray burner. Small amounts of calcium oxide are present.



Figur 2A





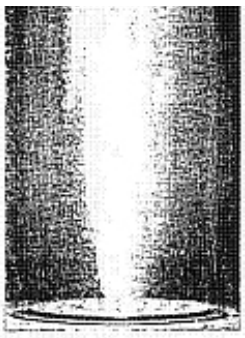


Figure 1A

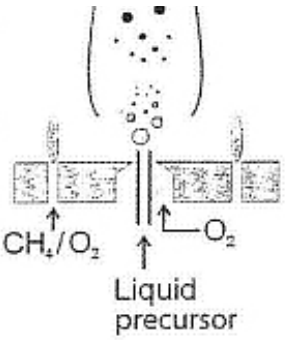


Figure 1B

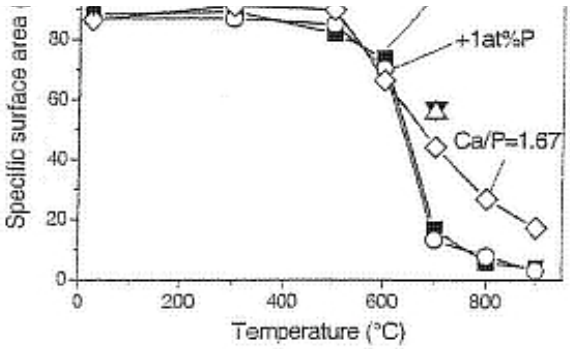


Figure 2B

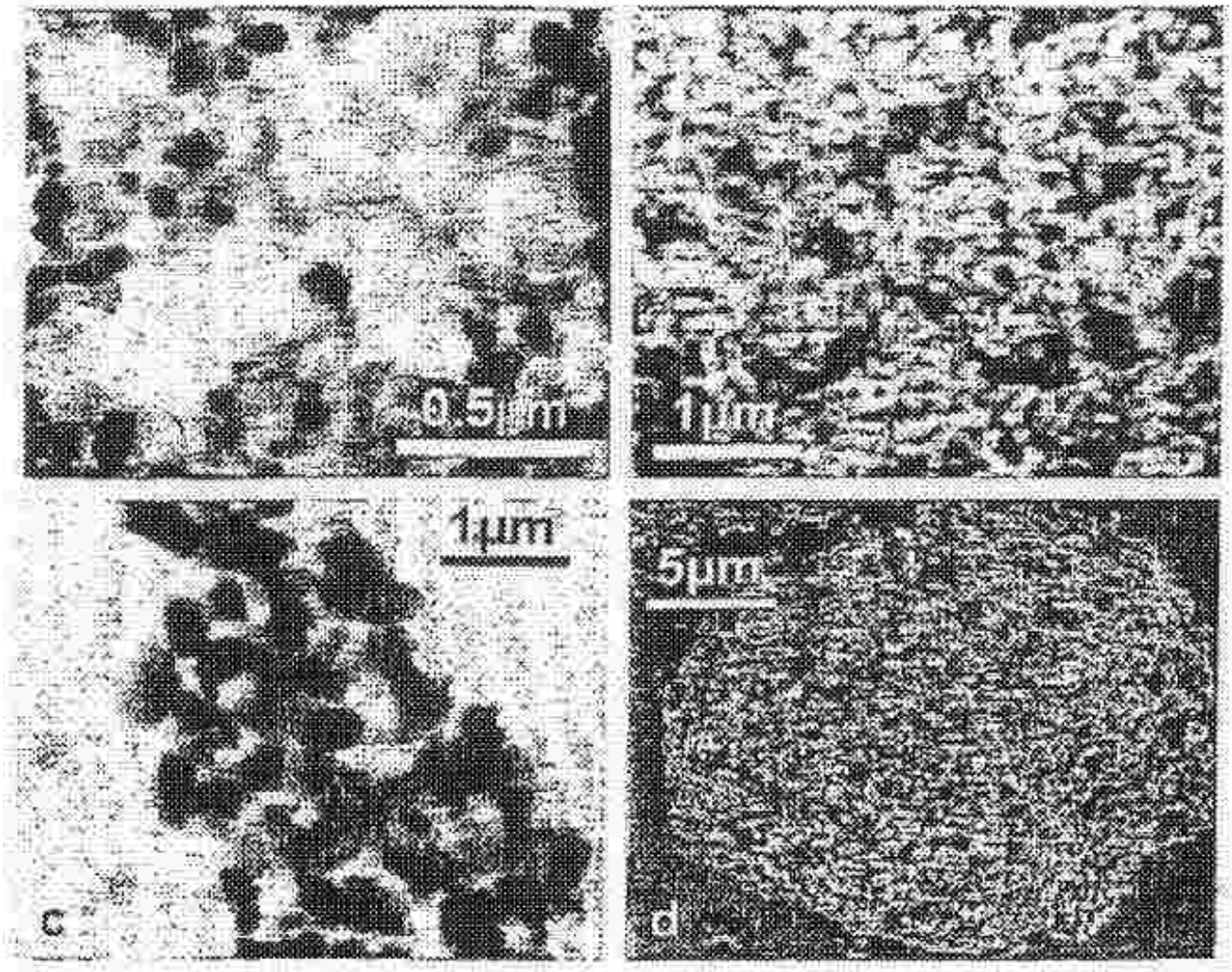
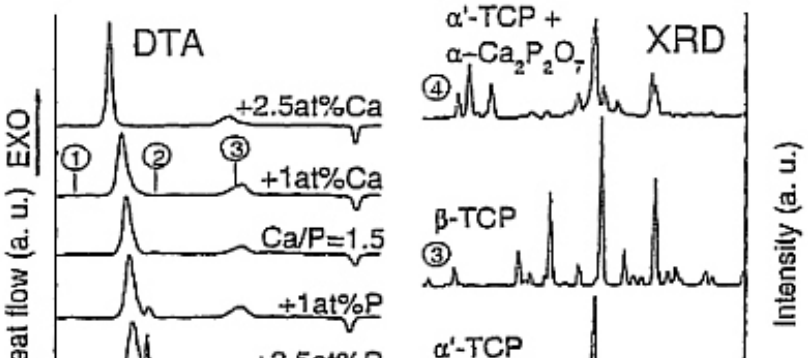


Figure 3



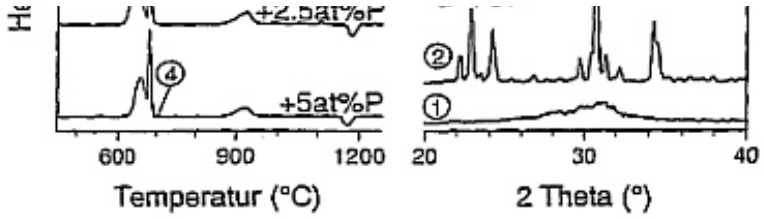
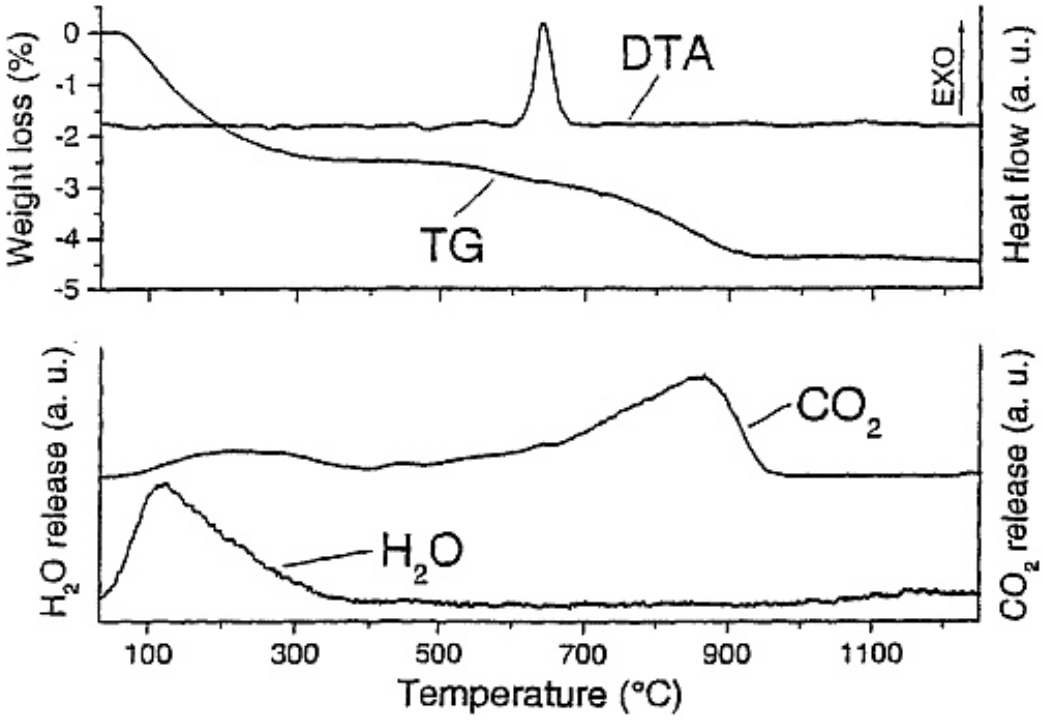
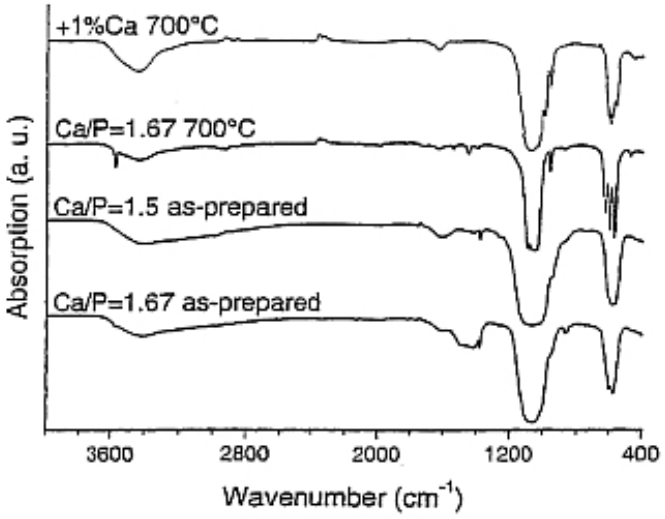
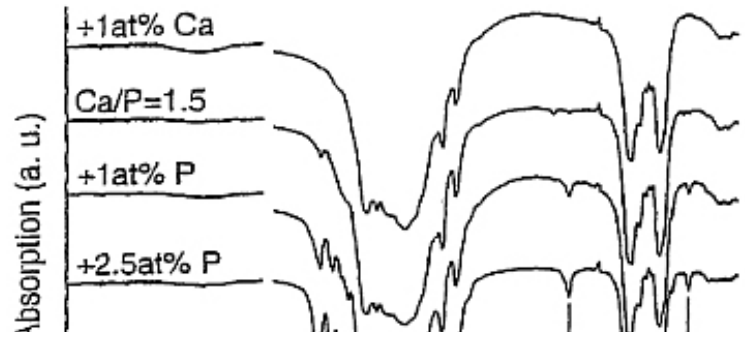
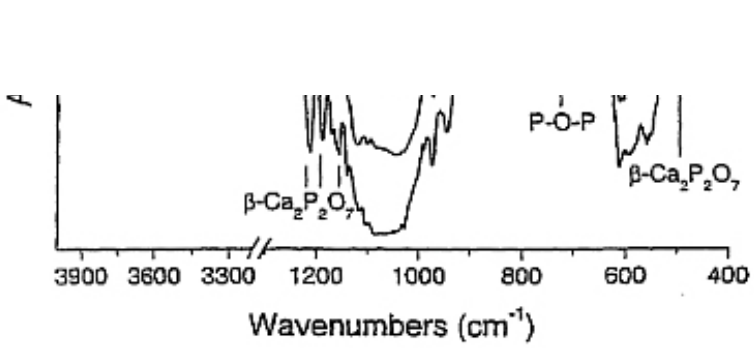

+2.5at%P
④
+5at%P
600
900
1200
Temperatur (°C)
②
①
20
30
40
2 Theta (°)

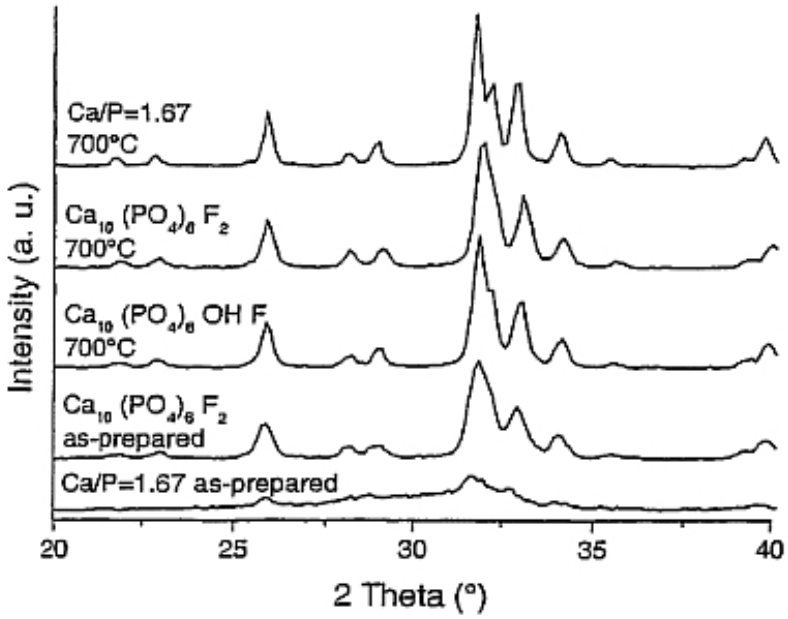
Figure 4

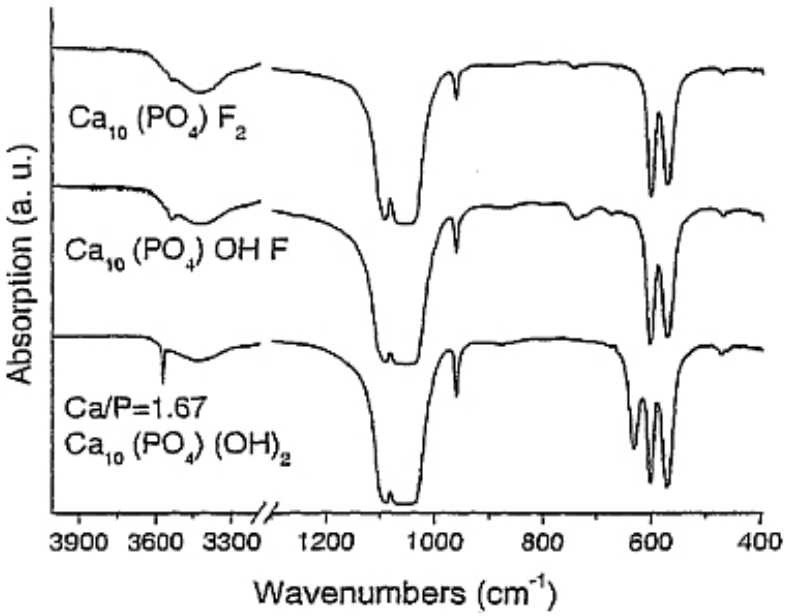

Weight loss (%)
0
-1
-2
-3
-4
-5
DTA
EXO
TG
Heat flow (a. u.)
H2O release (a. u.)
CO2
H2O
CO2 release (a. u.)
100
300
500
700
900
1100
Temperature (°C)

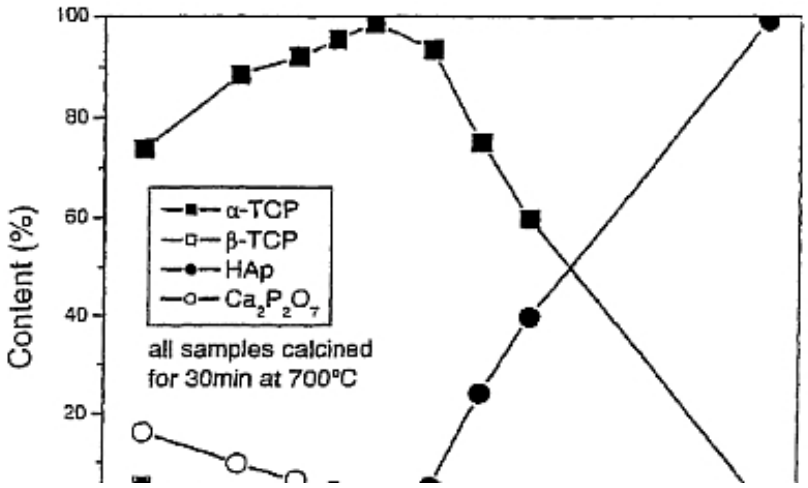

+1%Ca 700°C
Ca/P=1.67 700°C
Ca/P=1.5 as-prepared
Ca/P=1.67 as-prepared
Absorption (a. u.)
3600
2800
2000
1200
400
Wavenumber (cm-1)

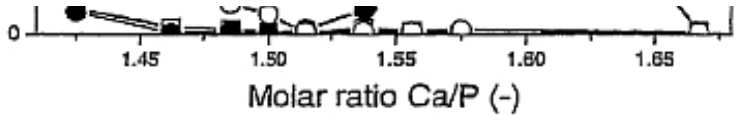

+1at% Ca
Ca/P=1.5
+1at% P
+2.5at% P
Absorption (a. u.)

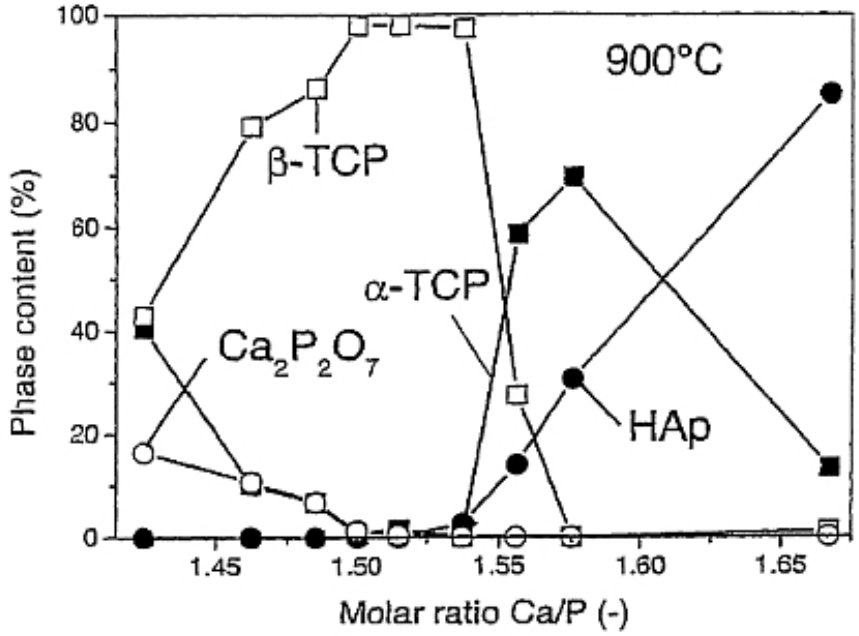

P-O-P
β-Ca2P2O7
β-Ca2P2O7
3900 3600 3300 1200 1000 800 600 400
Wavenumbers (cm-1)

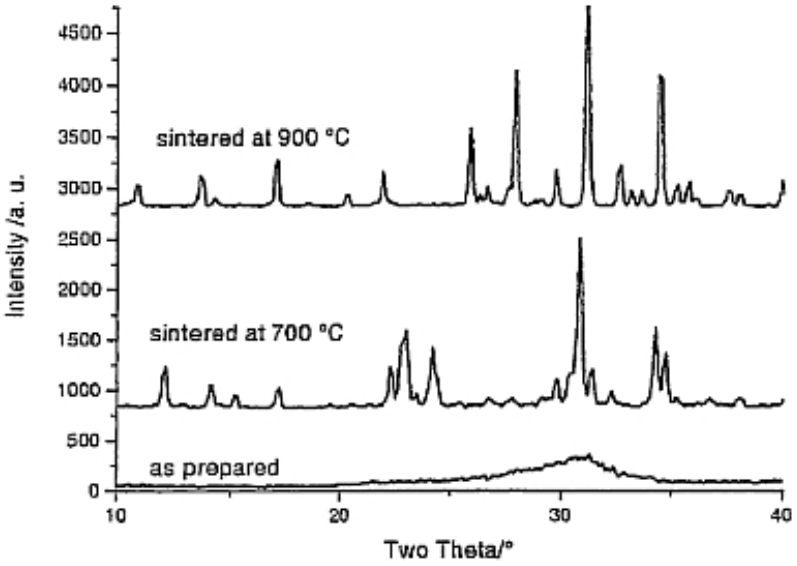

Ca/P=1.67
700°C
Ca10 (PO4)6 F2
700°C
Ca10 (PO4)6 OH F
700°C
Ca10 (PO4)6 F2
as-prepared
Ca/P=1.67 as-prepared
Intensity (a. u.)
20 25 30 35 40
2 Theta (°)

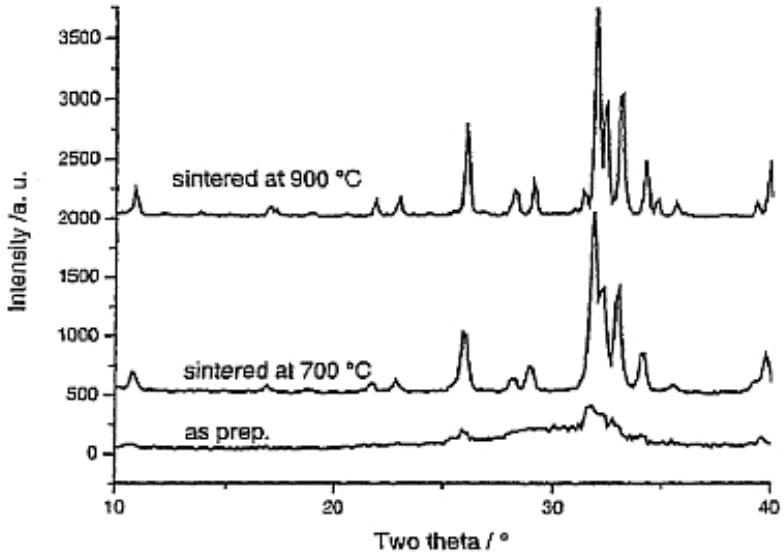

Ca10 (PO4) F2
Ca10 (PO4) OH F
Ca/P=1.67
Ca10 (PO4) (OH)2
Absorption (a. u.)
3900 3600 3300 1200 1000 800 600 400
Wavenumbers (cm-1)


α-TCP
β-TCP
HAp
Ca2P2O7
all samples calcined
for 30min at 700°C
Content (%)
100
80
60
40
20

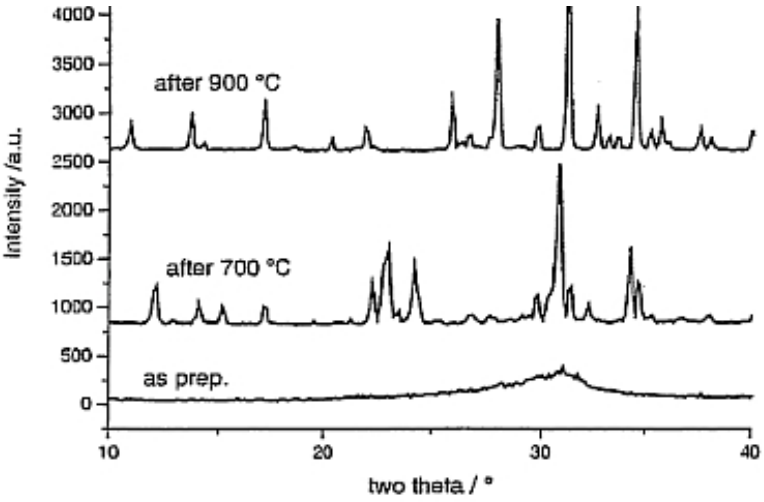

0
1.45
1.50
1.55
1.60
1.65
Molar ratio Ca/P (-)

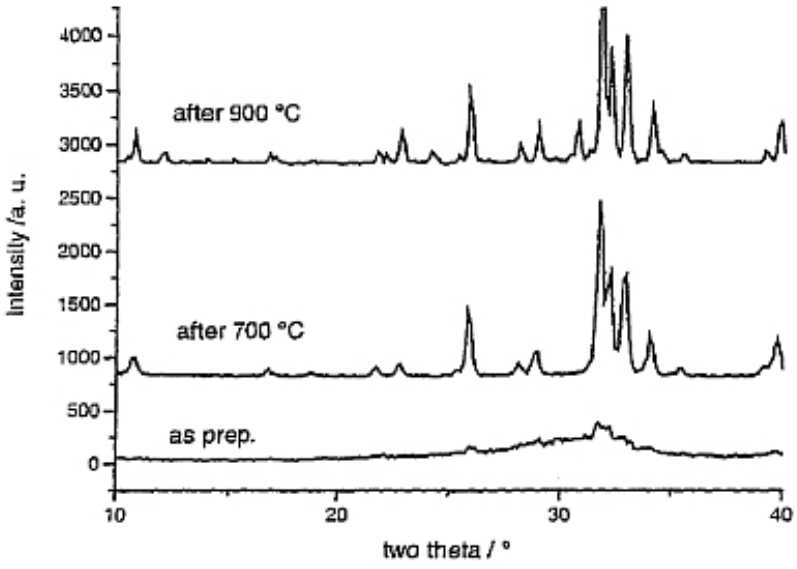

100
80
60
40
20
0
Phase content (%)
900°C
β-TCP
α-TCP
$Ca_2P_2O_7$
HAp
1.45
1.50
1.55
1.60
1.65
Molar ratio Ca/P (-)

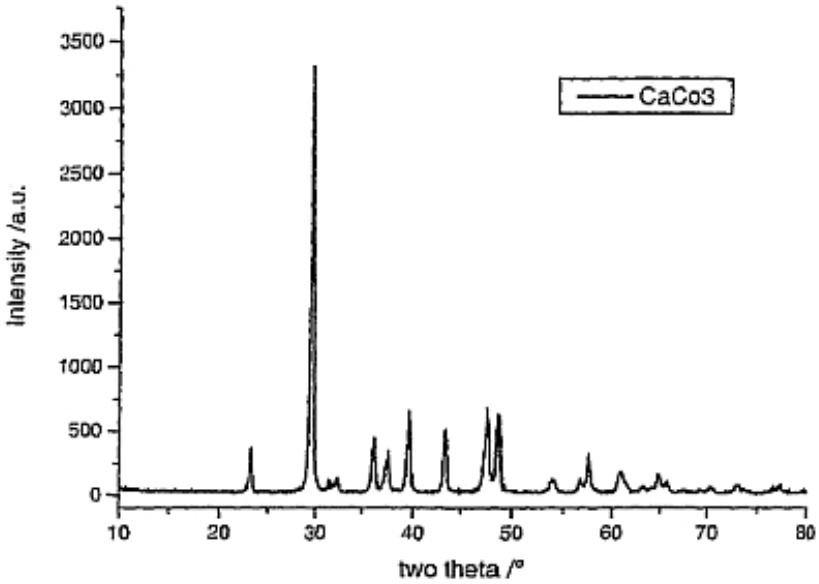

4500
4000
3500
3000
2500
2000
1500
1000
500
0
Intensity /a. u.
sintered at 900 °C
sintered at 700 °C
as prepared
10
20
30
40
Two Theta/°


3500
3000
2500
2000
1500
1000
500
0
Intensity /a. u.
sintered at 900 °C
sintered at 700 °C
as prep.
10
20
30
40
Two theta / °

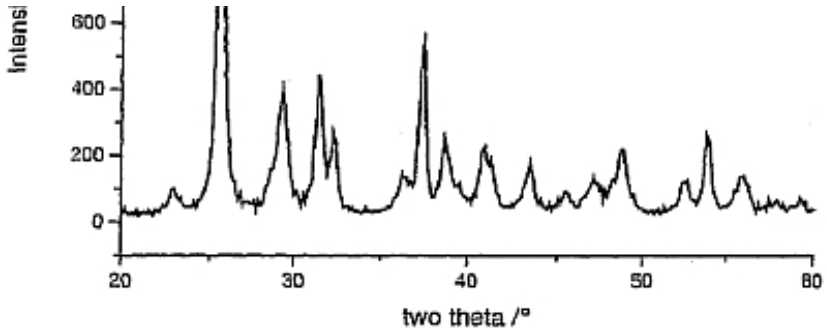
4500


after 900 °C
after 700 °C
as prep.
Intensity /a.u.
two theta / °


after 900 °C
after 700 °C
as prep.
Intensity /a. u.
two theta / °


CaCo3
Intensity /a.u.
two theta /°

CaSO4 as prepared



MODES FOR CARRYING OUT THE INVENTION

The invention is now further described for calcium phosphates, in particular calcium phosphates that are suitable as biomaterials.

In the scope of the present invention it has been found that flame synthesis offers a most versatile tool to materials that due to the resulting morphology, the high purity and the obtainable high crystal phase content are applicable as biomaterials. Furthermore, the direct gas-phase process allows facile substitution of both cations and anions.

Reproducible preparation of tricalcium phosphate (Ca/P=1.5) and different apatites (Ca/P=1.67) offers a challenge to conventional methods. By the inventive method materials with an accurately defined calcium to phosphorous molar ratio Ca/P ranging from 1.425 to 1.67 are obtainable. Such materials optionally may be doped with other anions or cations such as magnesium, zinc, barium, gadolinium, silicate, sulfate or fluoride. Tricalcium phosphate samples with an excess of either calcium or phosphorous are designated with their additional atomic fraction in respect of the stoichiometric sample (stoichiometric sample Ca/P=1.5). Tricalcium phosphate with an excess of calcium (Ca/P>1.5) is marked e.g. "+2.5at % Ca", and tricalcium phosphate with an excess phosphorous (Ca/P<1.5) is marked e.g. "+2.5at % p". A comparison of the Ca/P ratio and the respective at % is shown in Table 1.

TABLE 1
Theoretical Ca/ expressed as additional P molar ratio at % over stoichiometric

1.425 +5at % P
1.4624 +2.5at % P
1.485 +1at % P
1.5 Ca 3 (PO 4) 2 stoichiometric
1.515 +1at % Ca
1.5375 +2.5at % Ca
1.575 +5at % Ca
1.67 (hydroxyapatite) +11.1at % Ca

The desired composition, i.e. fluorapatite (FAp), hydroxyfluoapatite (OHFAp/HFAp) and/or any doping can be obtained by admixing the respective anions or cations to the initial solution. By e.g. admixing magnesium octoate, zinc naphthenate, trifluoracetic acid or mixtures thereof to the calcium and phosphate precursor solution, magnesium and/or zinc doped materials and/or fluorapatite Ca 10(PO 4) 6F 2) or hydroxyfluorapatite (Ca 10(PO 4) 6(OH)F)can be manufactured in a single step. Beyond doped calcium phosphate, also pure metal salts of other metals than calcium can be obtained by the same method. Similarly, metal salts with an anion other can phosphate can be made. Examples of other materials are calcium carbonate (limestone) nanoparticles or anhydrite nanoparticles (CaSO 4) which are described in the experimental section.

Spherical, highly agglomerated particles of 10-30 nm diameters (FIG. 2A) can be collected after synthesis. Thermal stability and evolution of different crystal phases can be monitored by nitrogen adsorption (BET) and X-ray diffraction (XRD). Samples typically start with 90 m <2>g <-1 >(BET equivalent diameter 20 nm) and calcination results in a steep decrease of specific surface area around 600[deg.] C. showing the onset of strong sintering and crystallization. While a slight excess of phosphorous (+1 at % P) has no significant influence on the thermal stability of tricalcium phosphate (Ca/P=1.5), hydroxyapatite (Ca/P=1.67) is considerably more stable and maintains above 15 m <2>g <-1 >at 900[deg.] C. Half (Ca 10(PO 4) 6(OH)F) and fully (Ca 10(PO 4) 6F 2) substituted fluorapatite were more resistant to sintering than unsubstituted hydroxyapatite.

In vivo histological behavior of biomaterials can be determined by morphology and phase composition. Macropores (diameter >100 [mu]m) have been found to provide a scaffold for bone cell colonization <16 >and therefore favour bone ingrowth <17,18>. The content of micropores (diameter <10 [mu]m) is given by the preparation method and the temperature and duration of sintering. Interconnective microporosity guarantees body fluid circulation and is even believed to be responsible for the observed osteoinductive properties of certain bioceramics <19-24>. Electron microscopy images of Ca/P=1.5 prepared by the inventive method after calcination at 700[deg.] C. (FIG. 3, pictures a and b) revealed that the material had fused together building clearly visible sinter necks. This sintered product preserves a high porosity with a primary particle size of about 100 nm. Sintering at 900[deg.] C. (FIG. 3, pictures c and d) results in much larger primary particles of approximately 0.5 [mu]m in diameter. The highly regular structure with interconnecting micropores provides both sintered products with excellent resorption properties and furthers the induction of bone formation in vivo. Such structures are also described as percolating phases.

As-prepared calcium phosphate consists of amorphous nanoparticles indicating that the fast cooling after the formation in the flame did not allow the material to crystallize. In the scope of the present invention, it has now also been found that such amorphous calcium phosphate can be heat treated at different temperatures to crystallize in a selected crystallinic phase in high selectivity/purity. The presence of a glassy structure of the product as-prepared has been confirmed by differential thermal analysis. A coupled mass spectroscopy (DTA-MS) apparatus allowed simultaneous detection of desorbing water and carbon dioxide. The combination of DTA and XRD patterns (FIG. 4) allows to confirm crystallization and phase transformations. The exothermic peak around 600[deg.] C. correlates to the crystallization of the amorphous material. The sample +1% at Ca, amorphous at 500[deg.] C. (FIG. 4, label 1), crystallizes to meta-stable [alpha]-TCP <25>, often referred to as [alpha]'-TCP (FIG. 4, label 2). At 915[deg.] C. [alpha]'-TCP transforms into the thermodynamically favoured [beta]-TCP (FIG. 4, label 3). At 1190[deg.] C., [beta]-TCP transforms back into the high-temperature polymorph [alpha]-TCP. Adding excess phosphorous to the Ca 3(PO 4) 2 stoichiometry (Ca/P=1.5) provokes the formation of pyrophosphate Ca 2P 2O 7. Crystallization of [alpha]-dicalcium pyrophosphate results in a second peak at 690[deg.] C. slightly above the crystallization of tricalcium phosphate (FIG. 4 label 4). The ratio of pyrophosphate to TCP follows the stoichiometry. Minute amounts of pyrophosphate are present in the stoichiometric sample (Ca/P=1.5), they fully vanish with a slight calcium excess (+1at % Ca). For all samples a change in weight due to absorbed water on the high-surface materials was detected by thermo-gravimetry (TG) below 520[deg.] C. Unlike calcium phosphates prepared by wet-phase chemistry, the weight loss of flame-made Ca/P ceramics does not exceed 4%. The Ca/P=1.67 sample crystallizes above 600[deg.] C. (FIG. 5 top) to hydroxyapatite (XRD pattern, FIG. 8). No further phase transformation or decomposition was detected up to 1250[deg.] C. A second weight loss (2%) occurred between 500[deg.] C. and 950[deg.] C. (FIG. 5 top). This weight loss correlates to the release of CO2 (FIG. 5 bottom) and was already previously attributed to the decomposition of carbonate in apatite <26,27>. The presence of carbonate results in absorption peaks between 1490 cm <-1 >and 1420 cm <-1 >and around 870 cm <-1 >in the Fourier transform infrared

(FTIR) spectra <28,29 >(FIG. 6). The as-prepared Ca/P=1.5 sample does not show any of these carbonate absorptions. Broad unresolved absorption bands of phosphate around 1060 cm <-1 >and 580 cm <-1 >verify the amorphous structure of the materials after preparation (FIG. 6). Clear absorption peaks are obtained after crystallization and correspond to hydroxyapatite <30 >for Ca/P=1.67 and to [alpha]'-TCP <31 >for +1 at % Ca. Weak water absorption bands are found around 3400 cm <-1 >and 1660 cm <-1 >with varying intensity. The crystallized hydroxyapatite still shows minor absorption bands between 1550 cm <-1 >and 1400 cm <-1 >due to residual carbonate <28,29>. From the TG curves the carbonate content can be calculated and was found to be 6.6 wt % CaCO 3 which is similar to the carbonate content (3-8 wt %) in human bone <32,33>. Carbonate increases the solubility of hydroxyapatite and results in enhanced biodegradation <9,34,35>.

The evidence of calcium pyrophosphate in biomaterials is routinely done by FTIR spectroscopy. Spectra of the samples calcined at 900[deg.] C. (FIG. 7) indicating the presence of Ca 2P 2O 7 from DTA/XRD measurements show very sharp peaks underlining the high crystallinity of the material. The peak group in the range of 1215 cm <-1 >to 1140 cm <-1 >and two clear peaks at 727 cm <-1 >and 496 cm <-1>, to be best seen in the sample +2.5at % P, correspond to [beta]-calcium pyrophosphate ([beta]-Ca 2P 2O 7) absorption bands and are consistent with literature <36-38>. A continuous decrease of absorption for these bands is seen by decreasing the phosphorous content. In agreement with DTA measurements the pyrophosphate present in the sample is determined by an excess of phosphorous in the precursor. Consequently, the suppression or promotion of the formation of calcium pyrophosphate can be accessed by varying the Ca/P ratio in the precursor. No Calcium pyrophosphate was detected in the sample +1 at % Ca by DTA and FTIR, where the infrared spectrum matches well with the one of [beta]-TCP <31,39>.

The formation of a specific product is dependent on the Ca/P ratio as well as of the calcinations temperature (see FIGS. 10 and 11). Almost pure alphatricalcium phosphate is obtained at a Ca/P ratio slightly above 1.5 but below 1.55 and 30 minutes calcination at 700[deg.] C. (FIG. 10). Almost pure hydroxyapatite is obtained at a Ca/P ratio of about 1.67 and 30 minutes calcinations at 700[deg.] C. (FIG. 10). For the production of almost pure beta-tricalcium phosphate the same Ca/P ratio can be chosen as for the production of alpha-tricalcium phosphate, but the calcination temperature has to be enhanced to 900[deg.] C. (FIG. 11).

TABLE 2

Theoretical	**Measured**	**Sample name**	**Ca/P ratio**	**Ca/P ratio error**
Ca/P = 1.5	1.500	1.50	0.01	
+1at % Ca	1.515	1.51	0.01	
Ca/P = 1.67	1.667	1.64	0.01	
Commercial ref. (see below)	1.500	-		

Commercial reference examples are e.g.:

CalciResorb (manufactured by Céraver Ostéal), characterized by FTIR and XRD: TCP content >96 wt %, less than 4 wt % Hydroxyapatite. Composition: 1.48<Ca/P<1.51.

Biosorb (SBM S.A.)r more than 95 wt % TCP, Composition: 1.49<Ca/P<1.51.

Bioresorb (Oraltronics), phase pure (>95 wt % TCP).

The application of calcium phosphate biomaterials is not restricted to hydroxyapatite and tricalcium phosphate. Recent studies about alternative calcium phosphate materials have

focused on fluoride substituted hydroxyapatite. As shown above r fluoride substituted apatites can easily be obtained by the method of the present invention. Differentiation of fluorapatite and hydroxyfluorapatite from hydroxyapatite can be done by FTIR spectroscopy. Spectra of the three apatites after calcination at 700[deg.] C. are shown in FIG. 9. Fluoride comprising apatites, due to them being neutral with regard to calcium content in the animal body can not only be used as substitutes for fluorapatite but also as a non-toxic fluoride source.

By adding a magnesium source such as magnesium octoate in desired amounts (e.g. 1 at-%) to the precursor mixture for the preparation of tricalciumphosphate the corresponding doped calcium phosphate polymorph phases can be prepared without phase segregation such as the segregation of MgO rich phases. Thus, by the method of the present invention phase pure magnesium doped metal salts, such as amorphous tricalciumpholphate, alpha-tricalciumpholphate, beta-tricalciumpholphate, or apatites, can be produced (see FIG. 12 and FIG. 13). Similar results are obtained using a zinc source such as zinc naphthenates or zinc octoates (see FIG. 14 and FIG. 15).

Other metal salts can be obtained as described above for calcium and phosphate comprising salts. By e.g. using a calcium source such as calcium octoate and a carbonate source such as a hydrocarbon or the calcium octoate itself, calciumcarbonate is obtained (see FIG. 16) and by using the above described calcium source together with a sulfate source, e.g. dimethylsulfoxide (DMSO), calcium sulfate is obtained (see FIG. 17).

EXAMPLES
Powder Preparation

Calcium phosphate biomaterials were prepared by flame spray pyrolysis using calcium oxide (99.9%, Aldrich) dissolved in 2-ethylhexanoic acid (purum., >=98%, Fluka) and tributyl phosphate (puriss., >=99%, Fluka) as precursors. The calcium content of the Ca precursor was determined by complexometry with ethylenediaminetetraacetic acid disodium salt dihydrate (ref.) (>=99%, Fluka) to be 0.768 mol kg <-1>. Starting from a parent solution (38 ml per run) with a calcium to phosphorous molar ratio (Ca/P) of 1.5, the various mixtures ranging from 1.425<=Ca/P<=1.667 have been obtained by adding corresponding amounts of either calcium 2-ethylhexanoate or tributyl phosphate. For the half (Ca 10(PO 4) 6OH F) and fully (Ca 10(PO 4) 6F 2) fluorine substituted hydroxyapatites, tri-fluoroacetic acid (>99%, Riedel deHaen) has been correspondingly mixed with precursors having a molar ratio of Ca/P=1.67. Throughout all the experiments the concentration of the precursor solutions was kept constant (0.667 mol L <-1>) by adding xylene (96%, Riedel deHaen). The liquid mixtures were fed through a capillary (diameter 0.4 mm) into a methane/oxygen flame at a rate of 5 ml min <-1>. Oxygen (5 L min <-1>, 99.8%, Pan Gas) was used to disperse the liquid leaving the capillary. The pressure drop at the capillary tip (1.5 bar) was kept constant by adjusting the orifice gap area at the nozzle. A stable combustion was achieved by applying a sheath gas (oxygen, 230 L h <-1>, 99.8%, Pan Gas) through a concentric sinter metal ring (see FIG. 1A, 1B). Calibrated mass flow controllers (Bronkhorst) were used to monitor all gas flows. The as formed particles were collected on a glass fibre filter (Whatmann GF/A, 15 cm in diameter) which was placed on a cylinder mounted above the flame by the aid of a vacuum pump (Vaccubrand). Thermal treatment (30 min at specified temperature) was conducted in a preheated laboratory furnace (Thermolyne Type 48000) followed by quenching in air at ambient conditions.

Powder Characterization

The specific surface area of the powders was analyzed on a Tristar (Micromeritics Instruments) by nitrogen adsorption at 77 K using Brunauer-Emmett-Teller (BET) method. All samples were outgassed at 150[deg.] C. for 1 hour. The X-ray diffraction spectroscopy (XRD) data were collected on a Burker D 8 Advance diffractometer from 20[deg.] to 40[deg.] at a step size of

0.12[deg.] and a scan speed of 2.4[deg.] min <-1 >at ambient condition. For Fourier transform infrared (FTIR) spectroscopy, pellets of 200 mg KBr (>=99.5%, Fluka) and 0.5-0.7 mg sample were prepared and dehydrated in a drying furnace (VT 6025, Gerber Instruments) at 80[deg.] C./<10 mbar for at least 8h before examination (400 cm <-1><[lambda]<4000 cm <-1>) on a Perkin Elmer Spectrum BX (4 scans) with 4 cm <-1 >resolution. Elemental analysis was performed by laser ablation ion-coupled plasma mass spectroscopy (LA-ICP-MS). Samples were pressed into plates and irradiated with an excimer laser (Lambda Phisyk Compex 110 I; ArF, 193 nm, pulse energy 150 mJ, frequency 10 Hz). The vaporized material was carried by a helium stream to an ICP mass spectrometer (Perkin Elmer Elan 6100) and analyzed for calcium and phosphorous. As an internal standard a fluorapatite (Durango) was used. The transmission electron microscopy (TEM) pictures were recorded on a CM30 ST (Philips, LaB6 cathode, operated at 300 kV, point resolution ~2 {acute over (Å)}). Particles were deposited onto a carbon foil supported on a copper grid. Scanning electron microscopy (SEM) investigations were performed with a Leo 1530 Gemini (Zeiss).

Detailed Preparation Example

111 g calcium oxide (Aldrich, >99%) are dissolved in 1980 g 2-Ethylhexanoic acid (Fluka, 99%) and 20 ml of acetic anhydride (Fluka, >99%) by heating the mixture to 140[deg.] C. under reflux. After cooling some remaining calcium acetate is removed by decanting the clear solution. After adding toluene, a 0.768 M solution is obtained as determined by titration using Ethylendiamine-tetraacetate-disodium salt (Fluka, 99%) and Eriochromschwarz-T as an indicator (Fluka, >95%).

0.685 kg of the above solution (stable at room temperature for at least 3 month) are mixed with 93.44 g Tributyl-phosphate (Fluka, puriss, >99%) and toluene added to a total volume of 1 liter at room temperature (298 K). For a single run, 38 ml of this solution are mixed with 2 ml toluene and flame sprayed. Combustion enthalpy of such a precursor liquid is above 25 kJ/g and the viscosity below 10 mPas.
All materials described herein have been prepared at a liquid flow rate of 5 ml/min using a dispersion gas (oxygen, Pan Gas, >99.8%) flow of 5 liters/min.

While all products obtainable by the method of the present invention have a lot of applications, e.g. as catalyst support, as molecular sieve, as filler for polymers and/or as UV stabilizers, due to their natural occurrence in human and non human animals, in particular mammals, the calcium phosphates described above, are much preferred for some applications, e.g.

in dental and medical applications, alone or together with other substances such as preferably biopolymers, such applications comprising the application as bone cement and/or resorbable material for implants, as implant coatings, in the repair of bony defects or peridontal defects, as bone space filler etc.,
as additive to tooth pastes, e.g. as fluoride source and/or abrasive aid,
as fluoride source in foodstuffs, e.g. chewing gums, sweets and table salt,
as degradation activator in biodegradable or bioresorbable materials.

In medical applications such as implants and bone cement, the product produced according to the present invention is favorable since it can easily be obtained in high purity, and since it can be sintered to form a product with desired percolating phases (interconnected pores), probably due to the extremely light and open structure of the aerogel that is used as a starting material. Combined with low amounts of water, few sintering and a reduced volume loss compared to conventionally prepared powder assure a maximum degree of interconnected porosity. Another great advantage of the materials produced by the method of the present invention is that they can be doped with e.g. barium and/or gadolinium such that the degradation of a bioresorbable material can be controlled by non-invasive methods such as X-ray imaging or nuclear magnetic

resonance imaging.

As ingredient to tooth pastes in particular fluorapatite is preferred. It is known that hydroxidefluoride-exchange in apatite is very fast such that fluorapatite can replace the hitherto used fluoride source in tooth pastes. Since, however, fluorapatite is "calcium neutral", i.e. does not affect the calcium content of the body, in particular the teeth and the bones, the amount of it is uncritical such that it can be added in much higher amounts than other fluoride sources and simultaneously act as e.g. abrasion aid to improve the plaque removal.

The above addressed benefit of fluorapatite also applies with regard to foodstuffs. With hitherto available fluoride sources only very specific foodstuffs such as table salt and water, the maximal intake of which by a person can be estimated, could be fluoride enriched. By using fluorapatite, in view of its being non toxic even in large amounts and its fluoride release properties exclusively making up for a fluoride deficiency in body apatite, a lot of foodstuffs can be supplemented such as e.g. chewing gums, candies, sweets but also the already hitherto fluoride enriched table salt and drinking water. The supplementation of such foodstuffs as chewing gums, candies, sweets (including snacks, cakes, chocolate etc.) and salted snacks, yogurts, and other foodstuffs that are largely consumed during the day when tooth cleaning may be impossible, is much desirable in view of tooth health.

Microorganisms necessary for biodegradation of e.g. biodegradable polymeric materials often need a large amount of specific ions such as calcium and phosphate. Due to the inventive production method not only large amounts of nanoparticulate calcium and phosphates comprising compounds can be obtained, but also doped materials that can be adapted with regard to solubility (e.g. by some CO 2 in an apatite) and content of further desirable metals other than calcium.

The products of the present invention in general do not segregate and they improve the flowability/pourability. Thus, they have similar fields of applications as the product AEROSIL(R) of Degussa.

The products of the present invention can e.g. be used to improve the pourability of e.g. table salt, but also to improve the flowability of tooth pastes or of a solid component in a manufacturing process e.g. an additive in the polymer manufacturing or a spice mixture in the snack production etc. Other applications are as rheology or thixotropy improving agents, as mechanical stability, UV resistance or other features improving additives, as admixtures or fillers not only in biodegradable but also in common plastics.

If suitably doped (for example by adding silver ions into the material), the products of the present invention can also be provided with antibacterial features making them suitable for antibacterially equipped polymers or polymers comprising products such as coatings paints adhesives etc.

While there are shown and described presently preferred embodiments of the invention, it is to be distinctly understood that the invention is not limited thereto but may be otherwise variously embodied and practiced within the scope of the following claims.

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