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(54) Title: AIR ABRASION TREATMENT POWDER

(57) Abstract: The invention relates to the air abrasion powder that consists of substances with bioactive, osteogenic and antibacterial activity such as calcium phosphate compounds, nano-titanium and boron compounds in nanoparticle structure, and particles that increase antibacterial activity such as nanosilver, for air abrasion devices that can be used in the subgingival and submucosal (the groove below the gingival line, surrounding the tooth and dental implant) region.

DESCRIPTION
AIR ABRASION TREATMENT POWDER

TECHNICAL FIELD

The invention relates to the air abrasion powder that consists of substances with bioactive, osteogenic and antibacterial activity such as calcium phosphate compounds, nano-titanium and boron compounds in nanoparticle structure, and particles that increase antibacterial activity such as nanosilver, for air abrasion devices that can be used in the subgingival and submucosal (the groove below the gingival line, surrounding the tooth and dental implant) region.

PRIOR ART

Air abrasion devices were first introduced to dentistry in 1945 and have been used for mechanical tooth cleaning since the 1980s. Intraoral air abrasion is a technique in which abrasive particles are used. The underlying principle of this method is to create a stream in which compressed air and water are mixed and contain small particles. This method usually does not require anesthesia and reduces the risk of tooth fragmentation/microfracture. Air abrasion is classically used in dental cavity preparation in dentistry to remove metal, porcelain and composite debris from tooth surfaces and to roughen the tooth surface before applying the adhesive resin. Apart from these, they are also widely used in the fields of periodontology and implantology. It is used to remove dental plaque biofilm from the surfaces of natural teeth and dental implants. In this technique, powders in different properties suitable for clinical use are used. The application areas have expanded from supragingival (the area formed above the gingival level) to subgingival (the groove-shaped area surrounding the tooth, below the gingival line) using highly abrasive sodium bicarbonate powders. Later, less abrasive and degradable (degradable/soluble) erythrole and glycine powders were developed especially for use in subgingival areas. Amino acids such as glycine and erythrole powders are used on implant surfaces, which have a similar effect with sodium bicarbonate powders in terms of bacterial biofilm removal, but do not cause significant changes on the surface. Since these powders are not biocompatible for the body, residual powder particles can cause allergy/foreign body reactions and adversely affect the treatment results.

BRIEF DESCRIPTION OF THE INVENTION

It will be a useful solution if the particles remaining on the surface after air abrasion are biocompatible and have features that will support bone formation. Today, there is no powder that can contribute to the periodontal regeneration around the teeth and rebuild the bone tissue lost as a result of peri-implantitis around the implant, and that can also show anti-bacterial activity.

The invention relates to a new air abrasion powder created by gaining technical properties such as osteogenic potential, antibacterial properties, increasing clot adhesion and increasing osteogenic potential by using Sodium, Hydroxy Apatite and Boron, which are not found in air abrasion powders in known techniques.

The invention is an air abrasion powder consisting of nanoparticle calcium phosphate compounds and substances with bioactive, osteogenic and antibacterial activities such as nano-titanium and boron compounds in air abrasion devices, and particles that increase antibacterial activity such as nano-silver. In addition, the invention makes the treated blood products such as Platelet Rich Fibrin (PRF), autogenous bone, autogenous dentin, autogenous cement, autogenous enamel usable in air abrasion devices. The use of these products alone or in different combinations provides an important innovation. With the invention, gradual applications are also made possible. For example, first the surface is cleaned mechanically and then the surface is sprayed with antibacterial boron compounds and/or silver nanoparticles. Decontamination of implant surfaces is a prerequisite for treatment success in both surgical and non-surgical treatment of peri-implantitis. While substances such as boron/silver in our invention provide these antibacterial properties, calcium phosphate components will increase new bone formation. Thus, a serious contribution will be made to the success of the treatment. The invention can also be used in implants and tissues in dentistry, orthopedics, plastic surgery and other medical fields.

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to air abrasion powder to be used in air abrasion devices; The feature of the powder is that it is “highly biocompatible, osteogenic and antibacterial”:

¬ Air abrasion powder contains nano-titanium and nano-sized calcium phosphate-based bioceramic material for high biocompatibility and osteogenic effect; At least one of the nanoscale hydroxyapatite, tricalcium phosphate, octacalcium phosphate, biphasic calcium phosphate, autogenous dentin, cement, enamel and bone powders will be used as matrix material (main material).

¬ If increased osteogenic properties are desired, at least one of the “boron components, cerium components or stronium components” will be added to the main material as an additive material.

¬ For antibacterial property, at least one of "silver nanoparticles, titanium dioxide nanoparticles, boron additive, cerium additive and stronium additive" will be added to the main material.

Solid state method or wet chemical method can be used for doping to the main material; Different from these methods, the additives determined can also be used directly by mixing them with the main material in certain proportions.

Example 1: Hydroxyapatite in nanosize (95% wt.) as base material (matrix material) for high biocompatibility and osteogenic effect, cerium additive in nanosize (CeO_2, 4% wt.) to increase osteogenic effect, silver additive ($AgNO_3$, wt. . %one).

Example 2: Nanosized α-tricalcium phosphate (98% wt.) as base material (matrix material) for high biocompatibility and osteogenic effect, boron additive (H_3BO_3, 2% wt.) to both increase osteogenic effect and impart antibacterial effect.

The technical effects of our invention that distinguish it from the known technique are as follows;

1. Osteogenic potential

Octocalcium phosphate (OCP) materials have a positive effect on bone-forming cells, similar to autogenous bone. It has been suggested that OCP is a precursor to biological apatite crystals in bone and teeth. Calcium phosphate compounds positively support osteogenesis with their osteoinductive properties. OCP increases the activity of various bone cells, including osteoblasts, osteocytes, osteoclasts, and macrophages, during conversion to Hydroxy Apatite (HA). Changes in the physicochemical properties of OCP affect osteoclast formation, differentiation of osteocytes, and proliferation of osteoblasts. OCPs remodel (remodel) with bone. Up-regulation of osteoblast differentiation markers such as

alkaline phosphatase (ALP) and osterix and RANKL is induced by OCP crystals. The conversion process from OCP to HA happens very slowly and gradually. Meanwhile, it causes physicochemical changes, including the consumption of Calcium (Ca 2+) and the release of inorganic phosphate (P) ions, and the high adsorption affinity of serum proteins such as a2HS-glycoproteins. Thus, it contributes to the formation of new bone.

2. Antibacterial property

Adding an antimicrobial agent to small particles not only removes bacterial biofilm, but also reduces the occurrence of future biofilm-associated infections. Due to the reduced bacterial colonization, the success of surgical treatments is also increased. Antibacterial properties are gained by adding at least one of the silver nanoparticles and boron compounds. Thus, the development of infection in the region during and after the treatment is significantly reduced.

3. Ability to increase clot adhesion

Nanohydroxyapatite (NHA) application increases free surface energy and wettability. It is also associated with platelet activation and increased bone formation.

4. Synergistic effect of NHA + boron

When Boron and Nanohydroxyapatite are used together, they increase the osteogenic activity more than when they are used alone.

Boron-containing nano-hydroxyapatite composites increase the osteogenic differentiation of mesenchymal stem cells by increasing alkaline phosphatase activity compared to nano-hydroxyapatite composite or boric acid alone. When the molecular mechanism of the effective dose of boron-containing hydroxyapatite is evaluated by transcriptomic analysis; Wnt appeared to affect TGF-related genes in response to stress signaling pathways compared to nano-hydroxyapatite composite, boric acid.

THE PLACE AND IMPORTANCE OF CALCIUM PHOSPHATE IN BIOLOGY

It has been suggested that early stages of mineralization of skeletal tissues involve the accumulation of OCP, Ca8H2 (PO4.5H2O (OCP)) as a precursor phase of the more thermodynamically stable, carbonate apatite. Most of the biomaterials used in hard tissue treatments involve the use of calcium orthophosphates (CaP) due to their chemical and structural similarity to the

inorganic phase of vertebrate biomineralized tissues. In this area, hydroxyapatite (HA), which is the most similar to the mineral component of bone and a derivative of CaP, plays an important role. However, the excellent biocompatibility and bioactivity of HA is shared by other CaPs. Octacalcium phosphate (OCP), which is thought to be a deposit that accumulates in the first stage in the biological environment, is of increasing interest for biomedical applications. The protein binding ability of octacalcium phosphate surfaces has been demonstrated in rat serum. In the extraction of adsorbed proteins and identification by mass spectrometry, a total of 138 proteins were detected in OCP and 103 proteins in HA with similar surface area. Therefore, only proteins adsorbed on OCP surfaces were detected.

Thus, although most of the literature on Calcium phosphates has focused on HA, there is a high interest in other phases for their incorporation into the mineral phase of bones and teeth and their use in the preparation of biomaterials for hard tissue replacement/repair.

BORON COMPOUNDS

Boron (B), the fifth element in the periodic table, is the only nonmetal in the elements in group 3A, but contains properties of both metals and nonmetals. Boron is a bioactive element that positively affects bone formation, composition and physical properties and central nervous system function, relieves joint symptoms, facilitates hormone action, and is associated with a reduced risk for some types of cancer. Boron affects the production and activity of steroid hormones, the actions of this trace mineral in the prevention of calcium loss and bone demineralization. However, Boron plays an important role in osteogenesis and its deficiency has been shown to negatively affect bone development and regeneration. Especially due to its positive effects on bone, studies have been carried out on its use as a scaffold-scaffold in bone tissue engineering.

Boron has proven to be an important trace mineral because

(1) It is necessary for the development and maintenance of bone health;

(2) It has positive contributions to wound healing;

(3) beneficially affects the body's use of estrogen, testosterone, and vitamin D;

(4) Increases magnesium absorption;

(5) Reduces the levels of inflammatory biomers;

(6) Increases antioxidant enzymes;

(7) Protects against pesticide-induced oxidative stress and heavy metal toxicity;

(8) Improves brain electrical activity, cognitive performance and short-term memory in the elderly.

(9) Affects the formation and activity of key biomolecules such as S-adenosyl methionine (SAM-e) and nicotinamide adenine dinucleotide (NAD+);

(10) It has shown preventive and therapeutic effects in a number of cancers such as prostate, cervical and lung cancers, and multiple and non-Hodgkin lymphomas. It can help improve the negative effects of traditional chemotherapeutic agents.

SILVER NANOPARTICLES

Silver nanoparticles have a broad spectrum of antibacterial, antifungal and antiviral properties. Silver nanoparticles have the ability to penetrate bacterial cell walls, alter the structure of cell membranes and even result in cell death. Thanks to its electrostatic attraction and its affinity for sulfur proteins, silver ions can adhere to the cell wall and cytoplasmic membrane. Adhering ions increase the permeability of the cytoplasmic membrane and cause disruption of the bacterial membrane. After the free silver ions are taken into the cells, respiratory enzymes are deactivated to form reactive oxygen species and interrupt the production of adenosine triphosphate. Denaturation of the cytoplasmic membrane can degrade organelles and even cause cell lysis. Their effectiveness is due not only to their nanoscale size, but also to their large surface area/volume ratio. Silver nanoparticles can increase the permeability of cell membranes by secreting silver ions, produce reactive oxygen species and interrupt the replication of deoxyribonucleic acid (DNA). Silver nanoparticles can be used in dentistry as an antibacterial agent in the structure of removable dentures, in composite filling materials, as irrigation solution and obturation material in endodontic treatment, in adhesive materials in orthodontic treatment, in membranes used for directed tissue regeneration in periodontal treatment, and in the production of titanium coating in dental implant treatments.

Periodontitis is a chronic inflammatory disease in which various types of microorganisms are common. Infection control through biofilm degradation and suppression of inflammation is essential for periodontal treatment. Compared with

conventional antibiotics, silver nanoparticles are advantageous because they have antibacterial properties without creating bacterial resistance. Silver nanoparticles loaded up to about 8.2% by weight provide systems that can promote osteoblast viability and differentiation and inhibit the growth of multidrug resistant bacteria. The smaller size silver nanoparticles offer a higher antibacterial property against oral anaerobic pathogenic bacteria. When the membrane containing silver nanoparticles is used in tissue regeneration, it can increase clinical success in the treatment of intraosseous defects, since it reduces the adhesion and penetration of bacteria. However, even at low concentration, silver nanoparticles reduce some inflammatory cytokines and angiogenesis parameters. However, silver nanoparticles can also increase anti-inflammatory cytokine synthesis. It is biocompatible with fibroblasts and keratinocytes. The silver accumulated in the organs is cleared in 8 weeks. It is phagocytosed by macrophages. However, systemic toxicity of ingested silver nanoparticles has not been reported.

IMPORTANCE IN BIOMOMETHICS

Bone is a nano-apatite composite, a mostly natural nanostructured calcium phosphate (CaP) ceramic composed of approximately 60% mineral by dry weight. CaP materials most closely mimic the mineral phase of bone and due to its high osteoinductivity, CaP is a common material of choice for bone grafts. Calcium phosphate is a family of minerals. It contains calcium phosphate, orthophosphate, metaphosphate or pyrophosphate and especially calcium ions with hydrogen ions or hydroxide. Calcium phosphates have a very important place in biology. For example, tooth enamel is largely calcium phosphate. Calcium phosphate based materials, Ca/P ratios, chemical formulas and abbreviations are presented in Table 1.

Tricalcium phosphate and Hydroxyapatite are the most well-known calcium phosphate compounds. It is important that these two calcium compounds occur in skeletal structure, similar crystallographic structure and chemical composition. Calcium phosphate compounds are used as graft material, scaffold scaffolding (roof and carrier) or to increase implant osseointegration. However, Biphasic calcium phosphate is a good alternative to bone grafts for use around implants and replaces living bone as it is absorbable.

CaP-based materials	Ca/P molar ratio	Chemical formula	Abbreviation
Monocalcium phosphate monohydrate	0.5	$Ca(H_2PO_4)_2 \cdot H_2O$	MCPM
Monocalcium phosphate anhydrous	0.5	$Ca(H_2PO_4)_2$	MCPA or MCP
Dicalcium phosphate dihydrate, mineral brushite	1.0	$CaHPO_4 \cdot 2H_2O$	DCPD
Dicalcium phosphate anhydrous, mineral monotite	1.0	$CaHPO_4$	DCPA or DCP
Octacalcium phosphate)	1.33	$Ca_8(HPO_4)_2(PO_4)_4 \cdot 5H_2O$	OCP
α-tricalcium phosphate	1.50	α-$Ca_3(PO_4)_2$	α-TCP
β-tricalcium phosphate	1.50	β-$Ca_3(PO_4)_2$	β-TCP
Amorphous calcium phosphates	1.20-2.20	$Ca_xH_y(PO_4)_z \cdot nH_2O$ n=3-4.5; %15-%20 H_2O	ACP
Calcium-deficient hydroxyapatite	1.50-1.67	$Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$	CDHA or Ca-def HA
Hydroxyapatite	1.67	$Ca_{10}(PO_4)_6(OH)_2$	HA, HAp or OHAp
Fluorapatite	1.67	$Ca_{10}(PO_4)_6F_2$	FA or FAp
Oxyapatite	1.67	$Ca_{10}(PO_4)_6O$	OA, OAp or OXA
Tetracalcium phosphate	2.0	$Ca_4(PO_4)_2O$	TetCP

Table 1. CaP-based materials, Ca/P ratios, chemical formulas and abbreviations

In air abrasion powder in the form of nanoparticles, the effect of contributing to the stabilization of osteogenic/clots that will be displayed by the particles remaining on the tooth/implant surface after the application is also important. On Titanium surfaces treated with CaP, nanoparticles reduce proinflammatory

cytokines such as IL1 β and TNF-α, while increasing the adhesion of osteoblasts to the surface.

Calcium is the most abundant mineral found in the body. It is the main component of bones and teeth. Adequate calcium intake is a critical factor for a healthy skeletal system. It is known that calcium phosphate is biocompatible and non-toxic to the body due to its chemical similarity to bones and teeth. In addition, calcium is very important as a coagulation factor in hemostasis and clot formation. In order for physiological functions to be performed, calcium levels in the blood must be within a certain concentration range.

TITANIUM AND ITS COMPOUNDS

Titanium shows excellent surface reactivity with high in vitro/vivo osteoconductivity when in contact with biological fluids. The nano topography produced by the deposition of nano-structured TiO2 on Titanium alloy surfaces increases corrosion resistance, biocompatibility and cell integration for implants made of Ti alloys. The high biocompatibility and bioactivity of nano-structured TiO2 increases bone formation with its osteoconductive properties. Ag – TiO2 nanoparticles exhibit excellent antimicrobial activity against Gram-positive and Gram-negative bacterial cultures and Candida albicans. Complete inhibition of microorganisms was achieved at a very low Ag – TiO2 concentration. Its mesoporous nature and antimicrobial activity at low concentrations without photoactivation make this material an excellent potential candidate for application as a disinfectant and/or antimicrobial agent.

AUTOGENE DENTIN/CEMENT/ENNA/BONE/LYOPHYLIZED PRF

Dentine; Dentin is covered by a crown made of highly mineralized and protective enamel and is covered by cementum, a structure at the root that plays a role in the attachment of teeth to the bone socket. 70% of its weight consists of minerals. The remaining 30% consists of organic matrix and water. Its inorganic material is calcium and phosphate ions, which form hydroxyapatite crystals, as in enamel, but the crystals are 30 times smaller, which makes dentin slightly softer than enamel.

Cement; It covers the root dentin, its structure is similar to bone, but without Haversian system and blood vessels. Mesenchymal is calcified tissue. The organic matrix of cement consists of 90% Type I and 5% Type III collagen. Sharpey's

fibers, which make up most of the cement volume, are mostly composed of Type I collagen. Considering the inorganic component of cement, it is seen that it contains less hydroxyapatite than bone, enamel or dentin. Hydroxyapatite ratios: Cement 45-50%, bone 65%, enamel 97%, dentin 70%.

Bone; 2/3 of the bone is inorganic and the remaining 1/3 is organic matter. The main component of the mineralized matrix is hydroxy apatite crystals. Type 1 collagen fibrils constitute the majority of the intercellular fibrillar matrix.

Enamel; It is the hardest and most durable tissue in the human body. Enamel contains morphologically parallel, ~50 nm wide, nanocrystals. About 95% to 98% of enamel is made up of calcium and phosphate ions that form strong hydroxyapatite crystals. However, they are not pure crystals because they are carbonated and contain trace minerals such as strontium, magnesium, lead and fluoride. Millions of carbonated hydroxyapatite crystals are arranged in long, slender structures from 4 μm to 8 μm in diameter. These factors make “biological hydroxyapatite” more soluble than pure hydroxyapatite.

Lyophilized PRF; Platelet-rich fibrin (PRF) is a second generation platelet concentrate developed for tissue repair and regeneration. PRF is used in many tissue engineering fields as a highly biocompatible and inductive bioscaffold. As a fresh plasma preparation, PRF was originally developed for immediate autologous use. It is especially important to apply on the same day to keep the release of growth factors at the highest level. Freeze-drying (lyophilization) is a commonly used process for the long-term storage of proteins used for increasing stability and tissue regeneration. Freeze-dried, protein-based materials not only have the advantage of better stability and storage potential, but are also important for the immediate access of new growing cells and tissues to growth factors. Lyophilized PRF can be used as a biomimetic scaffold for bone regeneration and mineralized tissue engineering. When PRF is applied as lyophilized, it has better tissue integration and increased osteogenic benefit to the wound area compared to fresh PRF.

In our invention, it is aimed to apply the autogenous products by pulverizing (freeze drying, grinding, etc.) by spraying on the dental implant/tooth root surface and to obtain a biologically compatible surface that will support regeneration.

CLAIMS

1. It is air abrasion treatment powder and is characterized by;

- Octocalcium Phosphate (OCP), which has a positive effect on bone-forming cells, similar to autogenous bone,
- Nanohydroxyapatite (NHA), which increases free surface energy and wettability,
- at least one of the silver nanoparticles and boron compounds that provide antibacterial properties,
- nanotitanium with high biocompatibility and bioactivity, which together with osteoconductive properties increases bone formation,
- autogenous dentin,
- cement,
- enamel,
- bone,
- containing at least one of the lyophilized PRF.

2. It is air abrasion treatment powder according to claim 1 and is characterized by; it is contained at least one of Nanohydroxyapatite (NHA) and boron compounds, which increase the osteogenic differentiation of mesenchymal stem cells by increasing alkaline phosphatase activity.

3. It is air abrasion treatment powder according to claim 1 and is characterized by; it is contained at least one of boron components, cerium components and stronium components in order to increase the osteogenic effect.

4. It is abrasion treatment powder an antibacterial air according to claim 1, and and is characterized by; it is contained at least one of silver nanoparticles, titanium dioxide nanoparticles, boron additive, cerium additive and stronium additive, exhibiting antibacterial/antimicrobial activity against gram-positive, gram-negative bacterial cultures, *Candida albicans*.