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(54) **BIOACTIVE GLASS COMPOSITIONS**

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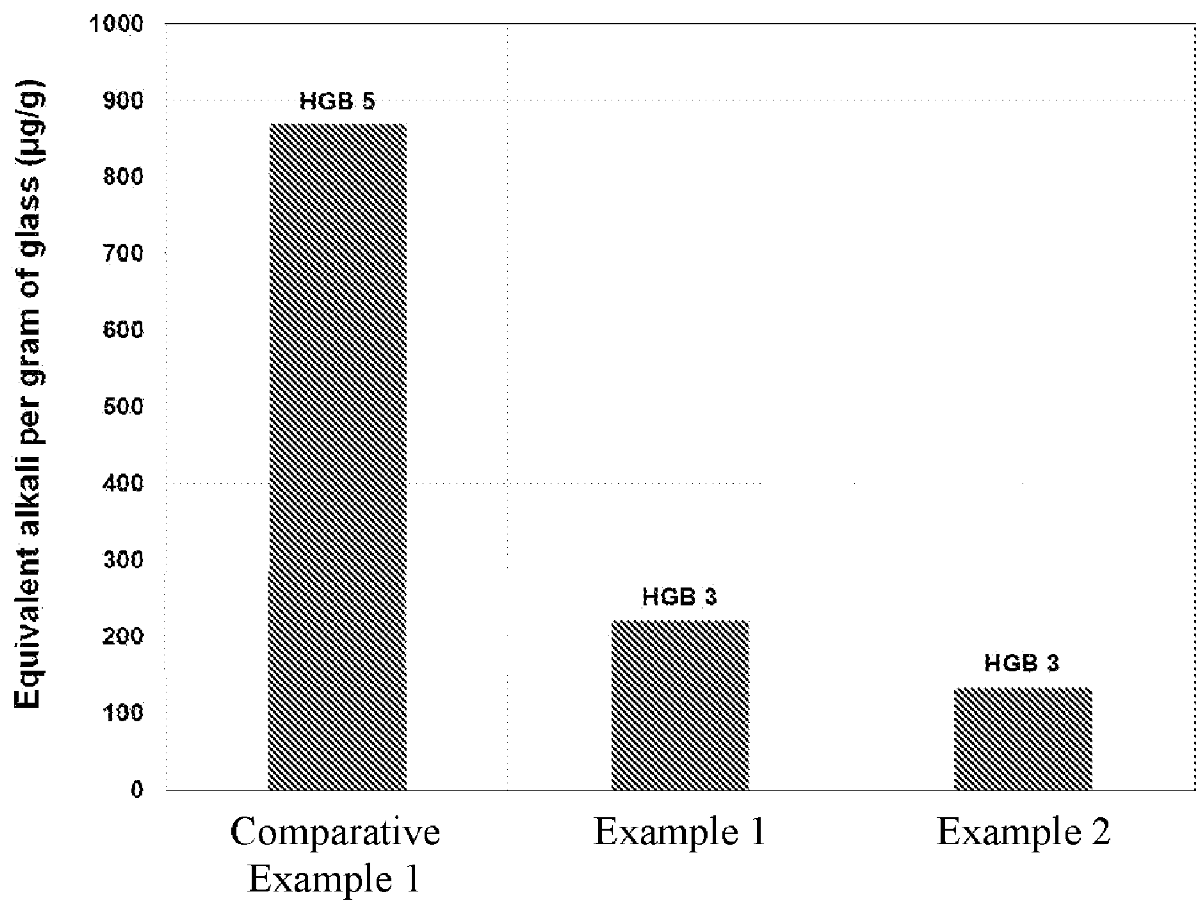
(57) **ABSTRACT**

A silicate-based glass composition includes 15-65 wt. % SiO_2, 2.5-25 wt. % MgO, 1-30 wt. % P_2O_5, and 15-50 wt. % CaO, such that the composition has a hydrolytic resistance of glass grains (HGB) of at most 3, when measured by International Organization for Standardization section 719 (ISO 719) and forms a bioactive crystalline phase in a simulated body fluid.



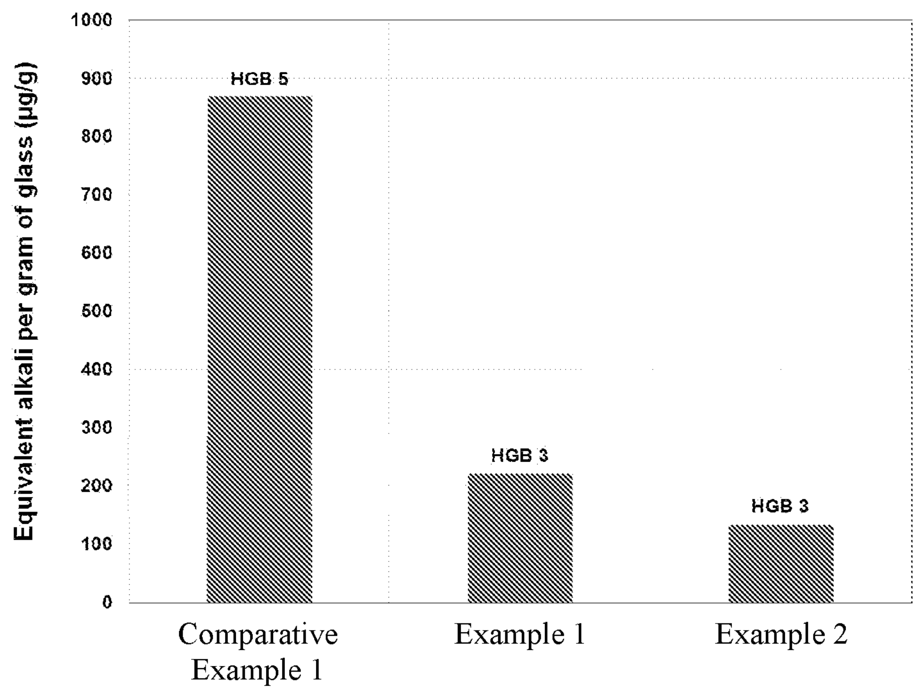

1000
900
800
700
600
500
400
300
200
100
0
Equivalent alkali per gram of glass (µg/g)
HGB 5
HGB 3
HGB 3
Comparative Example 1
Example 1
Example 2

FIG. 1

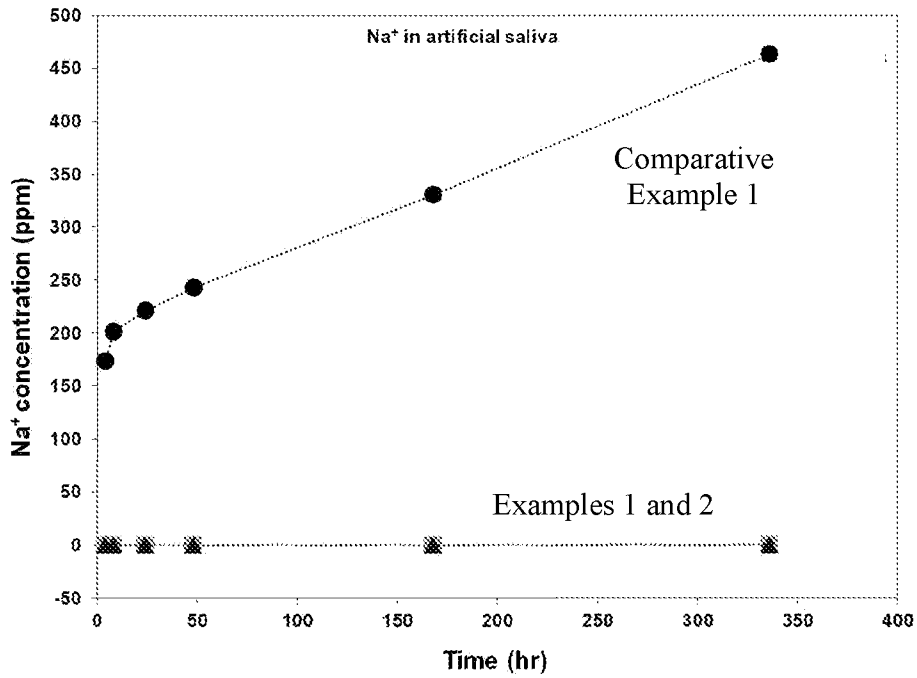

Na⁺ in artificial saliva
Comparative Example 1
Examples 1 and 2
Na⁺ concentration (ppm)
Time (hr)
500
450
400
350
300
250
200
150
100
50
0
-50
0
50
100
150
200
250
300
350
400

FIG. 2A

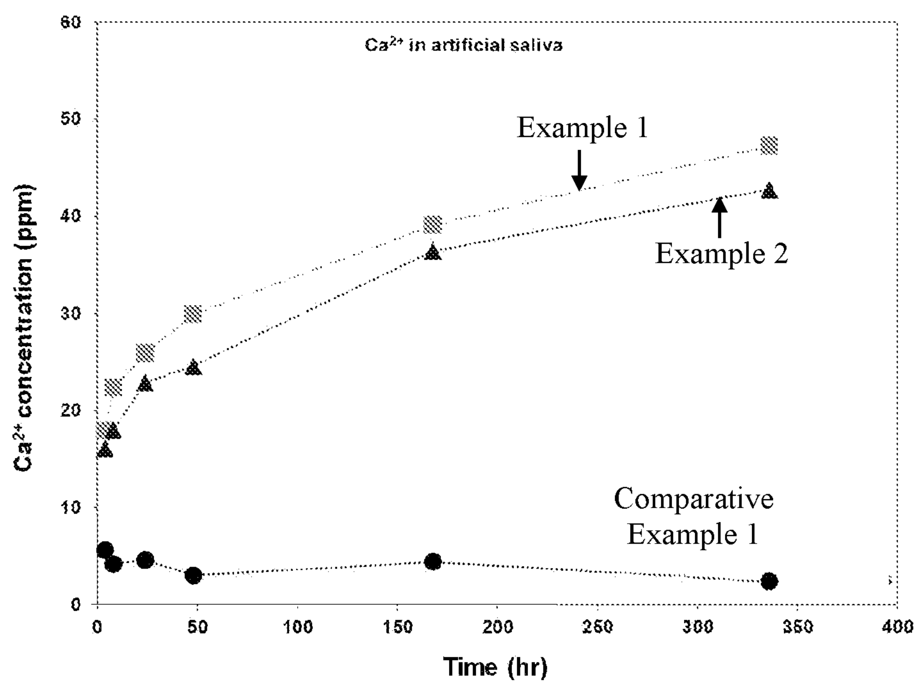
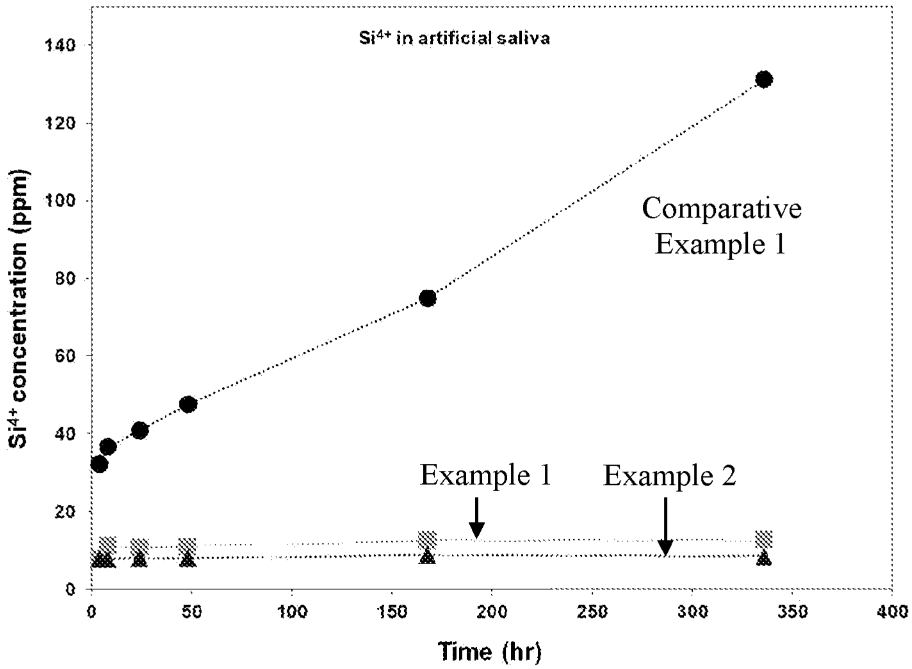
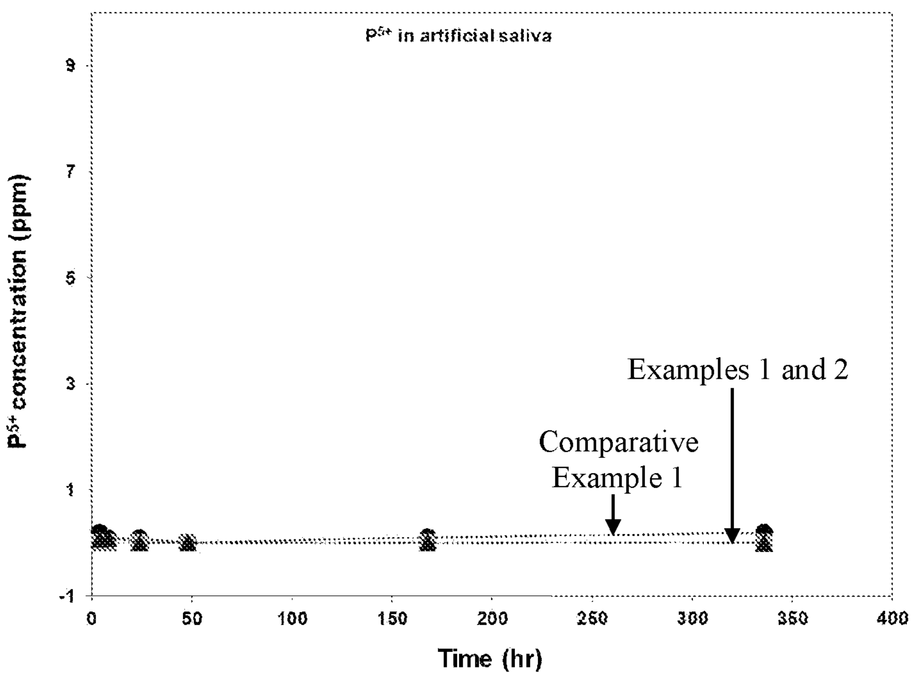

Ca²⁺ in artificial saliva
Example 1
Example 2
Comparative Example 1
Ca²⁺ concentration (ppm)
Time (hr)
60
50
40
30
20
10
0
0
50
100
150
200
250
300
350
400

FIG. 2B



Si4+ in artificial saliva
Si4+ concentration (ppm)
0
20
40
60
80
100
120
140
Comparative Example 1
Example 1
Example 2
0
50
100
150
200
250
300
350
400
Time (hr)

FIG. 2C



P5+ in artificial saliva
P5+ concentration (ppm)
-1
1
3
5
7
9
Examples 1 and 2
Comparative Example 1
0
50
100
150
200
250
300
350
400
Time (hr)

FIG. 2D

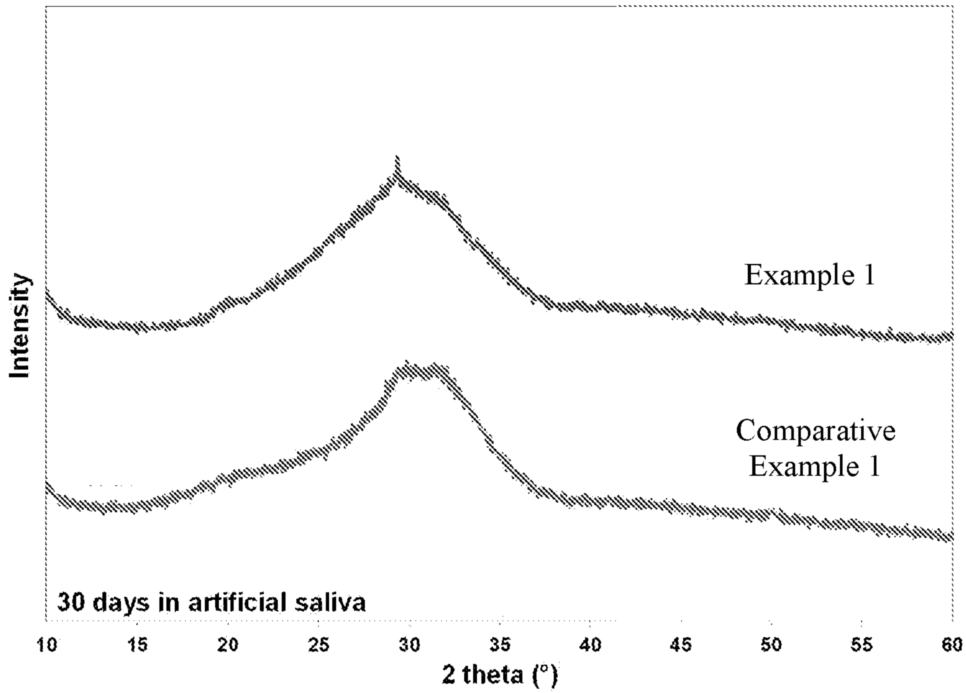

Intensity
Example 1
Comparative Example 1
30 days in artificial saliva
10 15 20 25 30 35 40 45 50 55 60
2 theta (°)

FIG. 3A

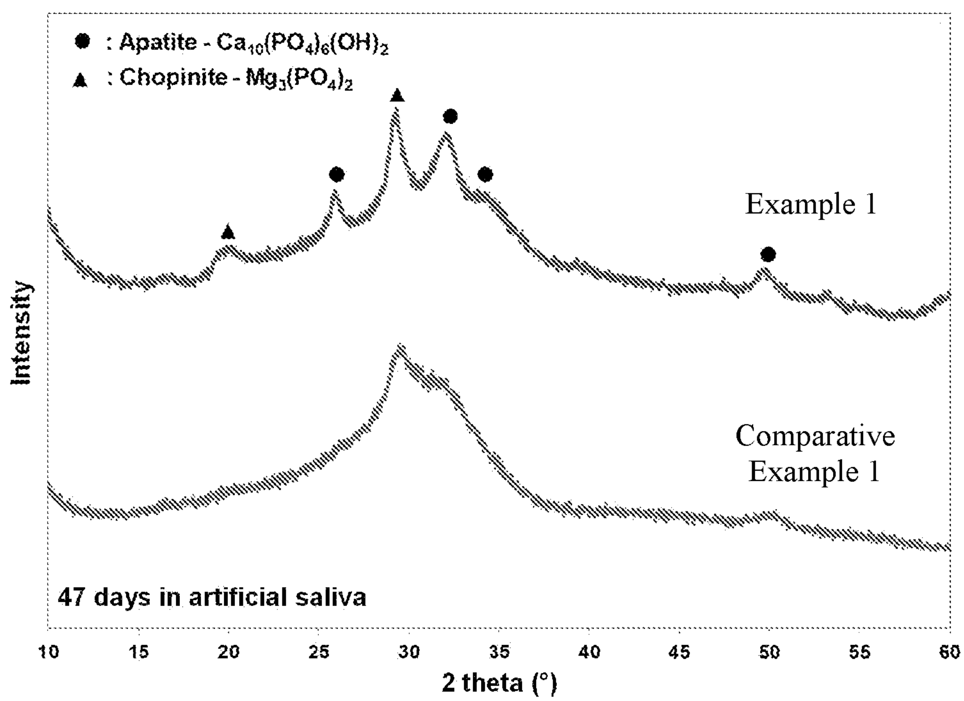

● : Apatite - $Ca_{10}(PO_4)_6(OH)_2$
▲ : Chopinite - $Mg_3(PO_4)_2$
Intensity
Example 1
Comparative Example 1
47 days in artificial saliva
10 15 20 25 30 35 40 45 50 55 60
2 theta (°)

FIG. 3B

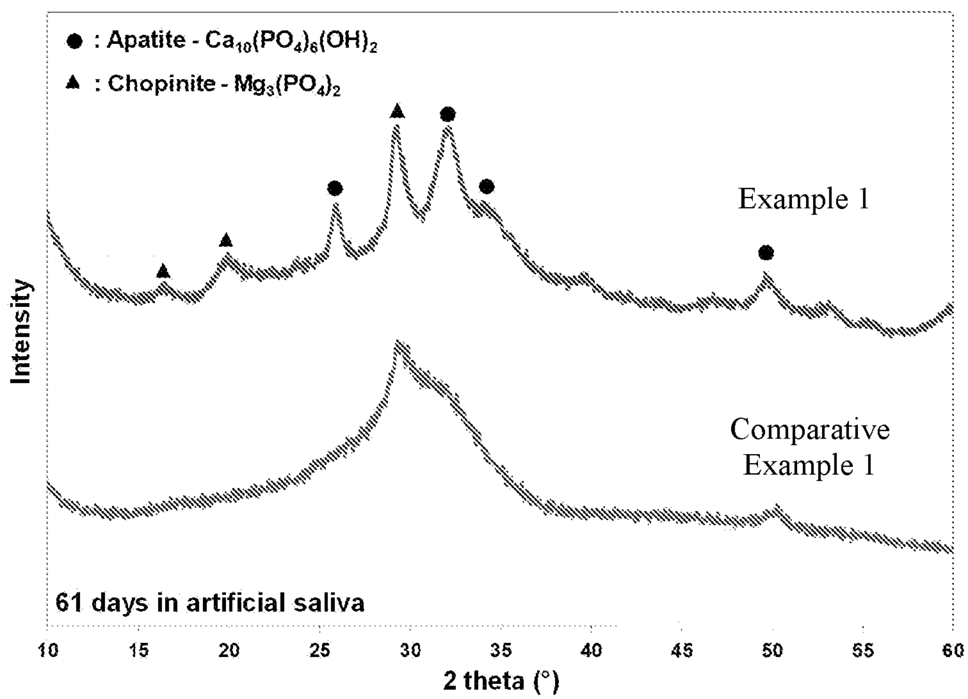

● : Apatite - $Ca_{10}(PO_4)_6(OH)_2$
▲ : Chopinite - $Mg_3(PO_4)_2$
Example 1
Comparative Example 1
Intensity
61 days in artificial saliva
10 15 20 25 30 35 40 45 50 55 60
2 theta (°)

FIG. 3C

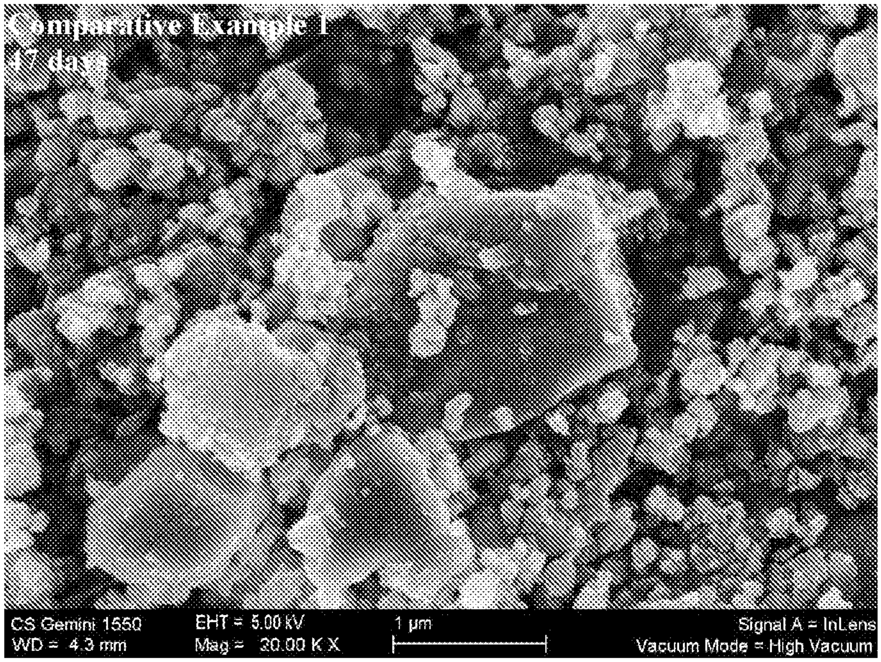

Comparative Example 1
47 days
CS Gemini 1550
WD = 4.3 mm
EHT = 5.00 kV
Mag = 20.00 K X
1 μm
Signal A = InLens
Vacuum Mode = High Vacuum

FIG. 4A

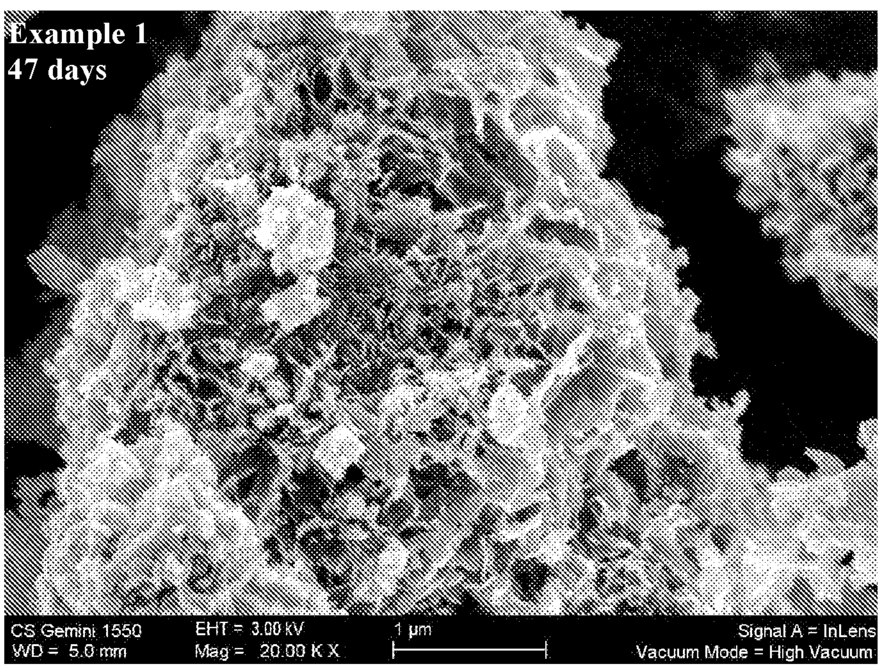

Example 1
47 days
CS Gemini 1550
WD = 5.0 mm
EHT = 3.00 kV
Mag = 20.00 K X
1 μm
Signal A = InLens
Vacuum Mode = High Vacuum

FIG. 4B

BIOACTIVE GLASS COMPOSITIONS

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of priority under 35 U.S.C. § 119 of U.S. Provisional Application No. 63/156,530, filed on Mar. 4, 2021, the content of which is relied upon and incorporated herein by reference in its entirety.

BACKGROUND

1. Field

[0002] The disclosure relates to biocompatible inorganic compositions for consumer and dental applications.

2. Technical Background

[0003] Bioactive glasses are a group of glass and glass ceramic materials that have shown biocompatibility or bioactivity, which has allowed them to be incorporated into human or animal physiology. Generally speaking, bioactive glasses are able to bond with hard and soft tissues, thereby fostering growth of bone and cartilage cells. Moreover, bioactive glasses may also enable release of ions which activate expression of osteogenic genes and stimulate angiogenesis, as well as promote vascularization, wound healing, and cardiac, lung, nerve, gastrointestinal, urinary tract, and laryngeal tissue repair.

[0004] Currently available bioactive glasses are being investigated for their ability to convert to apatite; however, the low chemical durability of these traditional bioactive glasses are problematic for compositions requiring prolonged shelf times in aqueous environments. For example, 45S5 Bioglass® requires development of a non-aqueous environment for glass particulates to be used in toothpaste applications. Other glass compositions (e.g., alkali-free glasses) do not exhibit the bioactivity of alkali-containing compositions. Thus, there continues to be an unmet need for bioactive glass compositions having high bioactivity while remaining chemically durable in aqueous environments.

[0005] This disclosure presents improved biocompatible inorganic compositions for consumer and dental applications.

SUMMARY

[0006] In some embodiments, a silicate-based glass composition, comprises 15-65 wt. % SiO_2, 2.5-25 wt. % MgO, 1-30 wt. % P_2O_5, and 15-50 wt. % CaO, wherein the composition: has a hydrolytic resistance of glass grains (HGB) of at most 3, when measured by International Organization for Standardization section 719 (ISO 719), and forms a bioactive crystalline phase in a simulated body fluid.

[0007] In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition further comprises >0-5 wt. % F^-. In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition further comprises one of >0-10 wt. % Li_2O, >0-10 wt. % Na_2O, or >0-10 wt. % K_2O. In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition further comprises >0 to 10 wt. % ZrO_2. In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition further comprises 0-10 wt. % Al_2O_3, 0-10 wt. % SrO, 0-10 wt. % ZnO, and 0-5 wt. % B_2O_3. In one aspect, which is combinable with any of the other aspects or embodiments, the glass comprises 15-50 wt. % MO, and 0-30 wt. % R_2O, wherein MO is the sum of MgO, CaO, SrO, BeO, and BaO, and R_2O is the sum of Na_2O, K_2O, Li_2O, Rb_2O, and Cs_2O. In one aspect, which is combinable with any of the other aspects or embodiments, the bioactive crystalline phase comprises apatite. In one aspect, which is combinable with any of the other aspects or embodiments, a sum of P_2O_5 and CaO is from 25-65 wt. %.

[0008] In some embodiments, a silicate-based glass composition, comprises 30-50 wt. % SiO_2, 10-20 wt. % MgO, 5-15 wt. % P_2O_5, and 25-40 wt. % CaO, wherein the composition has a hydrolytic resistance of glass grains (HGB) of at most 3, when measured by International Organization for Standardization section 719 (ISO 719), and forms a bioactive crystalline phase in a simulated body fluid.

[0009] In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition further comprises >0-3 wt. % F. In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition further comprises >0-10 wt. % Li_2O, >0-10 wt. % Na_2O, or >0-10 wt. % K_2O. In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition further comprises >0 to 10 wt. % ZrO_2. In one aspect, which is combinable with any of the other aspects or embodiments, the bioactive crystalline phase comprises apatite. In one aspect, which is combinable with any of the other aspects or embodiments, a sum of P_2O_5 and CaO is from 25-65 wt. %.

[0010] In one aspect, which is combinable with any of the other aspects or embodiments, a matrix comprising a glass composition described herein, wherein the matrix includes at least one of: a toothpaste, mouthwash, rinse, spray, ointment, salve, cream, bandage, polymer film, oral formulation, pill, capsule, or transdermal formulation. In one aspect, which is combinable with any of the other aspects or embodiments, the glass composition is attached to the matrix or mixed therein. In one aspect, which is combinable with any of the other aspects or embodiments, an aqueous environment comprises a glass composition described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] The disclosure will become more fully understood from the following detailed description, taken in conjunction with the accompanying figures, in which:

[0012] FIG. **1** illustrates equivalent alkali per gram of Examples 1 and 2 and Comparative Example 1, when tested in water at 98° C. for 2 hrs, according to ISO 719 standard procedure, according to some embodiments.

[0013] FIGS. **2**A-**2**D illustrate inductively coupled plasma (ICP) analysis of released Na^+ (FIG. **2**A), Ca^{2+} (FIG. **2**B), Si^{4+} (FIG. **2**C), and P^{5+} (FIG. **2**D) ion concentrations in artificial saliva solutions after soaking glass powder samples of Examples 1 and 2 and Comparative Example 1 therein, according to some embodiments.

[0014] FIGS. **3**A-**3**C illustrate powder x-ray diffraction (XRD) analysis on Example 1 and Comparative Example 1 after immersion in artificial saliva (maintained at 37° C.) for 30 days (FIG. **3**A), 47 days (FIG. **3**B), and 61 days (FIG. **3**C), according to some embodiments. Samples were dried and ground before XRD analysis.

[0015] FIGS. **4**A and **4**B illustrate scanning electron microscopy (SEM) images of Comparative Example 1 (FIG.

4A) and Example 1 (FIG. 4B) after immersion in artificial saliva (maintained at 37° C.) for 47 days, according to some embodiments. Samples were dried before SEM analysis.

DETAILED DESCRIPTION

[0016] In the following description, whenever a group is described as comprising at least one of a group of elements and combinations thereof, it is understood that the group may comprise, consist essentially of, or consist of any number of those elements recited, either individually or in combination with each other. Similarly, whenever a group is described as consisting of at least one of a group of elements or combinations thereof, it is understood that the group may consist of any number of those elements recited, either individually or in combination with each other. Unless otherwise specified, a range of values, when recited, includes both the upper and lower limits of the range as well as any ranges therebetween.

[0017] Where a range of numerical values is recited herein, comprising upper and lower values, unless otherwise stated in specific circumstances, the range is intended to include the endpoints thereof, and all integers and fractions within the range. It is not intended that the scope of the claims be limited to the specific values recited when defining a range. Further, when an amount, concentration, or other value or parameter is given as a range, one or more preferred ranges or a list of upper preferable values and lower preferable values, this is to be understood as specifically disclosing all ranges formed from any pair of any upper range limit or preferred value and any lower range limit or preferred value, regardless of whether such pairs are separately disclosed. Finally, when the term "about" is used in describing a value or an end-point of a range, the disclosure should be understood to include the specific value or end-point referred to. When a numerical value or end-point of a range does not recite "about," the numerical value or end-point of a range is intended to include two embodiments: one modified by "about," and one not modified by "about."

[0018] As used herein, the term "about" means that amounts, sizes, formulations, parameters, and other quantities and characteristics are not and need not be exact, but may be approximate and/or larger or smaller, as desired, reflecting tolerances, conversion factors, rounding off, measurement error and the like, and other factors known to those of skill in the art. It is noted that the terms "substantially" may be utilized herein to represent the inherent degree of uncertainty that may be attributed to any quantitative comparison, value, measurement, or other representation. These terms are also utilized herein to represent the degree by which a quantitative representation may vary from a stated reference without resulting in a change in the basic function of the subject matter at issue. Thus, for example, a glass that is "free" or "essentially free" of Al_2O_3 is one in which Al_2O_3 is not actively added or batched into the glass, but may be present in very small amounts as a contaminant (e.g., 500, 400, 300, 200, or 100 parts per million (ppm) or less or).

[0019] Herein, glass compositions are expressed in terms of wt. % amounts of particular components included therein on an oxide bases unless otherwise indicated. Any component having more than one oxidation state may be present in a glass composition in any oxidation state. However, concentrations of such component are expressed in terms of the oxide in which such component is at its lowest oxidation state unless otherwise indicated.

[0020] Oral diseases pose a major health burden worldwide, causing pain, discomfort, disfigurement, and even death. The dissolution of apatite crystals and the net loss of calcium, phosphate, and other ions from the tooth (i.e., demineralization) leads to dental caries formation. Caries can be managed non-invasively through a remineralization process, in which calcium and phosphate ions are supplied from an external source to the tooth to promote crystal deposition into voids in demineralized enamel. Calcium phosphate phases in both crystalline form (brushite, β-tricalcium phosphate, octocalcium phosphate, hydroxyapatite, fluorapatite and enamel apatite) and amorphous form have been used in remineralization processes. Use of amorphous calcium phosphate (e.g., bioactive glass) in remineralization processes has shown promising results. There is a strong desire to develop new glass compositions that promote the remineralization process to prevent or repair tooth caries.

[0021] Glass Compositions

[0022] Bioactive glasses are a group of glass and glass ceramic materials that have shown biocompatibility or bioactivity, which has allowed them to be incorporated into human or animal physiology. In the glass compositions described herein, SiO_2 serves as the primary glass-forming oxide in combination with the bioactive oxides of calcium and phosphorous.

[0023] In some examples, the glass comprises a combination of SiO_2, MgO, P_2O_5, and CaO. In some examples, the glass further comprises Li_2O, Na_2O, K_2O, F^-, and/or ZrO_2. In some examples, the glass may further comprise Al_2O_3, SrO, ZnO, and/or B_2O_3. For example, the glass may comprise a composition including, in wt. %: 15 to 65% SiO_2, 2.5 to 25% MgO, 1 to 30% P_2O_5, and 15 to 50% CaO. In some examples, the glass may further comprise in wt. %: 0 to 10% Li_2O, 0 to 10% Na_2O, 0 to 10% K_2O, 0 to 5% F, and/or 0 to 10% ZrO_2. In some examples, the glass may further comprise, in wt. %: 0 to 10% Al_2O_3, 0 to 10% SrO, 0 to 10% ZnO, and/or 0 to 5% B_2O_3. In some examples, the glass comprises, in wt. %: 15 to 50 MO and 0-30 R_2O, wherein MO is the sum of MgO, CaO, SrO, BeO, and BaO and R_2O is the sum of Li_2O, Na_2O, K_2O, Rb_2O, and Cs_2O. The silicate glasses disclosed herein are particularly suitable for consumer, dental, or bioactive applications.

[0024] Silicon dioxide (SiO_2), which serves as the primary glass-forming oxide component of the embodied glasses, may be included to provide high temperature stability and chemical durability. For the glasses disclosed herein, compositions including excess SiO_2 (e.g., greater than 60 wt. %) suffer from decreased bioactivity. Moreover, glasses containing too much SiO_2 often also have too high melting temperatures (e.g., greater than 200 poise temperature).

[0025] In some embodiments, the glass can comprise 15-65 wt. % SiO_2. In some examples, the glass may comprise 20-55 wt. % SiO_2. In some examples, the glass can comprise 15-65 wt. %, or 15-55 wt. %, or 20-55 wt. %, or 20-50 wt. %, or 25-50 wt. %, or 25-45 wt. %, or 30-45 wt. %, or 30-40 wt. %, or any value or range disclosed therein. In some examples, the glass comprises 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, or 65 wt. % SiO_2, or any value or range having endpoints disclosed herein.

[0026] In some examples, the glasses comprise MgO. In some examples, the glass can comprise 2.5-25 wt. % MgO.

In some examples, the glass can comprise 5-20 wt. % MgO. In some examples, the glass can comprise from 2.5-25 wt. %, or 2.5-22.5 wt. %, or 5-22.5 wt. %, or 5-20 wt. %, or 7.5-20 wt. %, or 7.5-17.5 wt. %, or 10-17.5 wt. %, or 10-15 wt. % MgO, or any value or range disclosed therein. In some examples, the glass can comprise 2.5, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 wt. % MgO, or any value or range having endpoints disclosed herein.

[0027] Phosphorus pentoxide (P_2O_5) also serves as a network former. Furthermore, the liberation of phosphate ions to the surface of bioactive glasses contributes to the formation of apatite. Apatite is an inorganic mineral in bone and teeth, and formation of apatite in a simulated body fluid is one criteria for a material to be bioactive, according to ASTM F1538-03 (2017). In some examples, simulated body fluid may include a salt solution comprising NaCl, $NaHCO_3$, KCl, K_2HPO_4, $MgCl_2$-$6H_2O$, $CaCl_2$, $NaSO_4$, $(CH_2OH_3)CNH_2$ in nano-pure water, with pH adjusted with acid, such as HCl. In some examples, the simulated body fluid comprises artificial saliva. The inclusion of phosphate ions in the bioactive glass increases apatite formation rate and the binding capacity of the bone tissue. In addition, P_2O_5 increases the viscosity of the glass, which in turn expands the range of operating temperatures, and is therefore an advantage to the manufacture and formation of the glass. In some examples, the glass can comprise 1-30 wt. % P_2O_5. In some examples, the glass can comprise 5-25 wt. % P_2O_5. In some examples, the glass can comprise 1-30 wt. %, or 3-30 wt. %, or 3-27 wt. %, or 5-27 wt. %, or 5-25 wt. %, or 7-25 wt. %, or 7-23 wt. % P_2O_5, or any value or range disclosed therein. In some examples, the glass can comprise about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 wt. % P_2O_5, or any value or range having endpoints disclosed herein.

[0028] In some examples, the glass can comprise 15-50 wt. % CaO. In some examples, the glass can comprise 25-45 wt. % CaO. In some examples, the glass can comprise from 15-50 wt. %, or 20-50 wt. %, or 20-45 wt. %, or 25-45 wt. %, or 25-40 wt. % CaO, or any value or range disclosed therein. In some examples, the glass can comprise 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50 wt. % CaO, or any value or range having endpoints disclosed herein.

[0029] Alkaline earth oxides may improve other desirable properties in the materials, including influencing the Young's modulus and the coefficient of thermal expansion. In some examples, the glass comprises from 15-50 wt. % MO, wherein MO is the sum of MgO, CaO, SrO, BeO, and BaO. In some examples, the glass comprises 15-45 wt. %, or 20-45 wt. %, or 20-40 wt. %, or 25-40 wt. % MO, or any value or range disclosed therein. In some examples, the glass can comprise about 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 wt. % MO, or any value or range having endpoints disclosed herein.

[0030] Divalent cation oxides (such as alkaline earth oxides and ZnO) also improve the melting behavior, chemical durability, and bioactivity of the glass. Particularly, CaO is found to be able to react with P_2O_5 to form apatite when immersed in a simulated body fluid (SBF) or in vivo. The release of Ca^{2+} ions from the surface of the glass contributes to the formation of a layer rich in calcium phosphate. Thus, the combination of P_2O_5 and CaO may provide advantageous compositions for bioactive glasses. In some examples, the glass compositions comprise P_2O_5 and CaO with the sum of P_2O_5 and CaO being from 25-65 wt. %, or 25-60 wt. %, or 30-60 wt. %, or 30-55 wt. %, or 35-55 wt. %, or any value or range disclosed therein. In some examples, the glass compositions comprise P_2O_5 and CaO with the sum of P_2O_5 and CaO being 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, or 65 wt. %, or any value or range having endpoints disclosed herein.

[0031] Alkali oxides (Na_2O, K_2O, Li_2O, Rb_2O, or Cs_2O) serve as aids in achieving low melting temperature and low liquidus temperatures. Meanwhile, the addition of alkali oxides can improve bioactivity. In some examples, the glass can comprise a total of 0-30 wt. % Na_2O, K_2O, Li_2O, Rb_2O, and Cs_2O combined. In some examples, the glass can comprise from 0-10 wt. % Li_2O and/or Na_2O and/or K_2O. In some examples, the glass can comprise >0-10 wt. % Li_2O and/or Na_2O and/or K_2O. In some examples, the glass can comprise about 0, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 wt. % Li_2O and/or Na_2O and/or K_2O, or any value or range having endpoints disclosed herein.

[0032] Fluorine (F^-) may be present in some embodiments and in such examples, the glass can comprise from 0-5 wt. % F^-. In some examples, the glass can comprise from >0-5 wt. % F^-. In some examples, the glass can comprise from 0-5 wt. %, >0-5 wt. %, >0-4 wt. %, >0-3 wt. %, >0-2.5 wt. %, >0-2 wt. %, F^-, or any value or range disclosed therein. In some examples, the glass can comprise about 0, >0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, or 5 wt. % F^-, or any value or range having endpoints disclosed herein. F^- can combine with CaO and P_2O_5 to form fluorapatite to improve the bioactivity of the claimed compositions. Fluorapatite is an inorganic mineral in dental enamel. The ability to form fluorapatite can help regeneration the enamel due to cavities.

[0033] Zirconium dioxide (ZrO_2) may be present in some embodiments and serves to function as a network former or intermediate in precursor glasses, as well as a key oxide for improving glass thermal stability by significantly reducing glass devitrification during forming and lowering liquidus temperature. In certain aspects, ZrO_2 may play a similar role as alumina (Al_2O_3) in the composition. Alumina may influence (i.e., stabilize) the structure of the glass and, additionally, lower the liquidus temperature and coefficient of thermal expansion, or, enhance the strain point. In addition to its role as a network former, Al_2O_3 (and ZrO_2) help improve the chemical durability and mechanical properties in silicate glass while having no toxicity concerns. Too high a content of Al_2O_3 or ZrO_2 (e.g., >10 wt. %) generally increases the viscosity of the melt and decreases bioactivity. In some examples, the glass can comprise 0-10 wt. % ZrO_2 and/or Al_2O_3. In some examples, the glass can comprise from 0-10 wt. %, 0-8 wt. %, 0-6 wt. %, 0-4 wt. %, 0-2 wt. %, >0-10 wt. %, >0-8 wt. %, >0-6 wt. %, >0-4 wt. %, >0-2 wt. %, 1-10 wt. %, 1-8 wt. %, 1-6 wt. %, 1-4 wt. %, 1-2 wt. %, 3-8 wt. %, 3-6 wt. %, 3-10 wt. %, 5-8 wt. %, 5-10 wt. %, 7-10 wt. %, or 8-10 wt. % ZrO_2 and/or Al_2O_3, or any value or range disclosed therein. In some examples, the glass can comprise 0, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 wt. % ZrO_2 and/or Al_2O_3, or any value or range having endpoints disclosed herein.

[0034] Strontium oxide (SrO) may be present in some embodiments and in such examples, the glass can comprise from 0-10 wt. % SrO. In some examples, the glass can comprise from >0-10 wt. % SrO. In some examples, the glass can comprise from 3-10 wt. %, 5-10 wt. %, 5-8 wt. % SrO, or any value or range disclosed therein. In some examples, the glass can comprise from 0-10 wt. %, 0-8 wt. %, 0-6 wt. %, 0-4 wt. %, 0-2 wt. %, >0-10 wt. %, >0-8 wt. %, >0-6 wt. %, >0-4 wt. %, >0-2 wt. %, 1-10 wt. %, 1-8 wt. %, 1-6 wt. %, 1-4 wt. %, 1-2 wt. %, 3-8 wt. %, 3-6 wt. %, 3-10 wt. %, 5-8 wt. %, 5-10 wt. %, 7-10 wt. %, or 8-10 wt. % SrO, or any value or range disclosed therein. In some examples, the glass can comprise about >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 wt. % SrO, or any value or range having endpoints disclosed herein.

[0035] In some examples, the glasses comprise ZnO. In some examples, the glass can comprise 0-10 wt. % ZnO. In some examples, the glass can comprise from 0-5 wt. % ZnO. In some examples, the glass can comprise from >0-10 wt. %, 3-10 wt. %, or 3-8 wt. % ZnO, or any value or range disclosed therein. In some examples, the glass can comprise from 0-10 wt. %, 0-8 wt. %, 0-6 wt. %, 0-4 wt. %, 0-2 wt. %, >0-10 wt. %, >0-8 wt. %, >0-6 wt. %, >0-4 wt. %, >0-2 wt. %, 1-10 wt. %, 1-8 wt. %, 1-6 wt. %, 1-4 wt. %, 1-2 wt. %, 3-8 wt. %, 3-6 wt. %, 3-10 wt. %, 5-8 wt. %, 5-10 wt. %, 7-10 wt. %, or 8-10 wt. % ZnO, or any value or range disclosed therein. In some examples, the glass can comprise about 0, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 wt. % ZnO, or any value or range having endpoints disclosed herein.

[0036] In some examples, the glass can comprise 0-5 wt. % B_2O_3. In some examples, the glass can comprise >0-5 wt. % B_2O_3. In some examples, the glass can comprise from 0-5 wt. %, or >0-5 wt. %, or 2-5 wt. % B_2O_3, or any value or range disclosed therein. In some examples, the glass can comprise 0, >0, 1, 2, 3, 4, or 5 wt. % B_2O_3, or any value or range having endpoints disclosed herein.

[0037] Additional components can be incorporated into the glass to provide additional benefits or may be incorporated as contaminants typically found in commercially-prepared glass. For example, additional components can be added as coloring or fining agents (e.g., to facilitate removal of gaseous inclusions from melted batch materials used to produce the glass) and/or for other purposes. In some examples, the glass may comprise one or more compounds useful as ultraviolet radiation absorbers. In some examples, the glass can comprise 3 wt. % or less ZnO, TiO_2, CeO, MnO, Nb_2O_5, MoO_3, Ta_2O_5, WO_3, SnO_2, Fe_2O_3, As_2O_3, Sb_2O_3, Cl, Br, or combinations thereof. In some examples, the glass can comprise from 0 to about 3 wt. %, 0 to about 2 wt. %, 0 to about 1 wt. %, 0 to 0.5 wt. %, 0 to 0.1 wt. %, 0 to 0.05 wt. %, or 0 to 0.01 wt. % ZnO, TiO_2, CeO, MnO, Nb_2O_5, MoO_3, Ta_2O_5, WO_3, SnO_2, Fe_2O_3, As_2O_3, Sb_2O_3, Cl, Br, or combinations thereof. The glasses, according to some examples, can also include various contaminants associated with batch materials and/or introduced into the glass by the melting, fining, and/or forming equipment used to produce the glass. For example, in some embodiments, the glass can comprise from 0 to about 3 wt. %, 0 to about 2 wt. %, 0 to about 1 wt. %, 0 to about 0.5 wt. %, 0 to about 0.1 wt. %, 0 to about 0.05 wt. %, or 0 to about 0.01 wt. % SnO_2 or Fe_2O_3, or combinations thereof.

Examples

[0038] The embodiments described herein will be further clarified by the following examples.

[0039] Non-limiting examples of amounts of precursor oxides for forming the embodied glasses are listed in Table 1, along with the properties of the resulting glasses. The annealing point (° C.) may be measured using a beam bending viscometer (ASTM C598-93).

TABLE 1

Oxide (wt. %)	Comparative Example 1	1	2	3	4	5	6	7
SiO_2	45	42.9	41.2	43.5	37.7	37.7	37.7	37.7
Al_2O_3	0	0	0	0	0	0	0	0
Li_2O	0	0	0	0	5	0	0	0
Na_2O	24.5	0	0	0	0	5	0	0
K_2O	0	0	0	0	0	0	5	0
MgO	0	14.5	13.9	14.5	14.5	14.5	14.5	14.5
CaO	24.5	32.4	31.2	32.5	32.5	32.5	32.5	32.5
SrO	0	0	0	0	0	0	0	0
ZnO	0	0	0	0	0	0	0	0
F^-	0	0.8	0.8	0	0.8	0.8	0.8	0.8
P_2O_5	6	9.5	9.1	9.5	9.5	9.5	9.5	9.5
ZrO_2	0	0	3.8	0	0	0	0	2
Anneal Pt (° C.)	500	400	400	375	400	400	400	400

[0040] The bioactive glass compositions disclosed herein exhibit high chemical durability and excellent bioactivity and can be in any form that is useful for the medical and dental processes disclosed. The compositions can be in the form of, for example, particles, powder, microspheres, fibers, sheets, beads, scaffolds, woven fibers, or other form depending on the application. The compositions of Table 1 may be melted at temperatures below 1300° C., or at temperatures below 1250° C., or at temperatures below 1200° C., thereby making it possible to melt in relatively small commercial glass tanks.

[0041] In some embodiments, the compositions of Table 1 demonstrate significantly higher chemical durability and bioactivity over Comparative Example 1 (45S5 glass).

[0042] FIG. **1** illustrates equivalent alkali per gram of Examples 1 and 2 and Comparative Example 1, when tested in water at 98° C. for 2 hrs, according to ISO 719 standard procedure, according to some embodiments. In other words, equivalent alkali release in FIG. **1** was measured using a titration method of 50 mL of DI water containing glass grains for 2 hrs at 98° C., as specified by ISO 719. The solution is titrated with 0.01 M HCl using methyl red as an indicator and reported as g neutralized alkali per gram of grains, as described in ISO 719. A higher alkali release indicates a lower water durability of the glass composition. Thus, because the equivalent alkali release from Example 1 and Example 2 is about one fifth to one tenth of that from Comparative Example 1 (45S5), Comparative Example 1 has a lower water durability than either Example 1 or Example 2. The improved hydrolytic resistance of Examples 1 and 2 (and by extension, Examples 3-7) may be attributed to their lower alkali (i.e., Na_2O, K_2O, Li_2O) content as compared with Comparative Example 1.

[0043] Moreover, from FIG. **1**, Examples 1 and 2 fall within HGB 3 category, while Comparative Example 1 falls within HGB 5 based on ISO 719 testing in water. HGB stands for hydrolytic resistance of glass grains under a boiling water test. A smaller number HGB indicates a higher resistance (greater durability), according to ISO 719. This suggests a significant improvement in water durability in the Example compositions.

[0044] What FIG. **1** indicates is that glass compositions with higher durability ensures a longer shelf time when being used in an aqueous solution. With respect to Comparative Example 1, dental applications using this compositions are currently formulated with a non-aqueous solution. The current Examples of Table 1, which have improved water durability, allow flexibility in formulating with both aqueous and non-aqueous solutions, making them better candidates in dental or oral care or beauty product applications.

[0045] FIGS. **2A**-**2D** illustrate inductively coupled plasma (ICP) analysis of released Na^{+} (FIG. **2A**), Ca^{2+} (FIG. **2B**), Si^{4+} (FIG. **2C**), and P^{5+} (FIG. **2D**) ion concentrations in artificial saliva solutions after soaking glass powder samples of Examples 1 and 2 and Comparative Example 1 therein. ICP analysis was conducted with an Agilent 5800 ICP-OES device to analyze the ion concentration in the artificial saliva. From FIG. **2A**, ICP data confirms that a much lower Na^{+} ion concentration was detected for Examples 1 and 2 than for Comparative Example 1. Similarly, from FIG. **2C**, a much lower Si^{4+} ion concentration was detected for Examples 1 and 2 than for Comparative Example 1, suggesting that the novel compositions exhibit higher resistance to water corrosion than 45S5 glass, given that silicon dioxide serves as the primary glass-forming oxide component of the tested glasses. Higher Ca^{2+} ion concentrations were measured in Examples 1 and 2 than in Comparative Example 1, which is consistent with higher CaO content in those Examples than in 45S5. In other words, higher calcium content in glass compositions may result in a higher released Ca amount. For Examples 1 and 2 and Comparative Example 1, not all calcium may be bonded with phosphorus to form apatite. There is excess calcium released in the saliva, as detected by ICP in higher CaO compositions. From FIG. **2D**, there is no measurable P^{5+} in the saliva, suggesting a reaction of phosphorus with calcium to form apatite. These results provide additional support of the improved durability of the exemplified compositions over 45S4 glass. Higher apatite was formed in Example compositions, as confirmed by XRD in FIGS. **3A**-**3C** (high peak intensity and sharper peaks indicate a higher amount of apatite).

[0046] FIGS. **3A**-**3C** illustrate powder x-ray diffraction (XRD) analysis on Example 1 and Comparative Example 1 after immersion in artificial saliva (maintained at 37° C.) for 30 days (FIG. **3A**), 47 days (FIG. **3B**), and 61 days (FIG. **3C**). Samples were dried and ground before XRD analysis. Samples were prepared for XRD analysis by grinding to a fine powder using a Rocklabs ring mill. The powder was then analyzed using a Bruker D4 Endeavor device equipped with a LynxEye™ silicon strip detector. X-ray scanning was conducted from 5° to 800 (2θ) for data collection. As explained above, apatite is an inorganic mineral in bone and teeth, and the formation thereof in a simulated body fluid is one criteria for a material to be bioactive. The XRD data in FIGS. **3A**-**3C** shows that although no crystalline phases were detected in Example 1 or Comparative Example 1 (45S5 glass) after 30 days (FIG. **3A**) in artificial saliva, apatite was identified in Example 1 after 47 days (FIG. **3B**), with the peaks growing more pronounced by 61 days (FIG. **3C**). In contrast, no well-developed apatite phase was detected in Comparative Example 1 even after soaking in artificial saliva after 61 days. This suggests that Example 1 has a higher crystallinity and better bioactivity than Comparative Example 1. Because calcium is a key component in apatite, a higher CaO concentration favors faster apatite formation. Example 1 has higher concentrations of CaO than Comparative Example 1.

[0047] FIGS. **4A** and **4B** illustrate scanning electron microscopy (SEM) images of Comparative Example 1 (FIG. **4A**) and Example 1 (FIG. **4B**) after immersion in artificial saliva (maintained at 37° C.) for 47 days. Samples were dried before SEM analysis. A conductive carbon coating was applied to the glass powder to reduce surface charging and then observed in a Zeiss Gemini 500 SEM. The SEM images provide further evidence of the needle-like apatite phase on the surface of Example 1 versus spherical nuclei in Comparative Example 1. Results from XRD and SEM provide additional support of a higher bioactivity in the exemplified compositions than in 45S5 glass.

[0048] Glass Bioactivity

[0049] Aspects are related to compositions or matrices containing embodied bioactive glass compositions and the methods of using the matrices to treat medical conditions. The matrices can be a toothpaste, mouthwash, rinse, spray, ointment, salve, cream, bandage, polymer film, oral formulation, pill, capsule, transdermal formulation, and the like. The bioactive glass compositions claimed can be physically or chemically attached to matrices or other matrix components, or simply mixed in. As noted above, the bioactive glass can be in any form that works in the application, including particles, beads, particulates, short fibers, long fibers, or woolen meshes. The methods of using the glass-containing matrices to treat a medical condition can be simply like the use of matrix as normally applied.

[0050] Glass Making Processes

[0051] Glasses having the oxide contents listed in Table 1 can be made via traditional methods. For example, in some examples, the precursor glasses can be formed by thoroughly mixing the requisite batch materials (for example, using a turbular mixer) in order to secure a homogeneous melt, and subsequently placing into silica and/or platinum crucibles. The crucibles can be placed into a furnace and the glass batch melted and maintained at temperatures ranging from 1100° C. to 1400° C. for times ranging from about 6 hours to 24 hours. The melts can thereafter be poured into steel molds to yield glass slabs. Subsequently, those slabs can be transferred immediately to an annealer operating at about 400° C. to 700° C., where the glass is held at temperature for about 0.5 hour to 3 hours and subsequently cooled overnight. In another non-limiting example, precursor glasses are prepared by dry blending the appropriate oxides and mineral sources for a time sufficient to thoroughly mix the ingredients. The glasses are melted in platinum crucibles at temperatures ranging from about 1100° C. to 1400° C. and held at temperature for about 6 hours to 16 hours. The resulting glass melts are then poured onto a steel table to cool. The precursor glasses are then annealed at appropriate temperatures.

[0052] The embodied glass compositions can be ground into fine particles in the range of 1-10 microns (μm) by air jet milling or short fibers. The particle size can be varied in the range of 1-100 μm using attrition milling or ball milling of glass frits. Furthermore, these glasses can be processed into short fibers, beads, sheets or three-dimensional scaffolds using different methods. Short fibers are made by melt spinning or electric spinning; beads can be produced by flowing glass particles through a hot vertical furnace or a flame torch; sheets can be manufactured using thin rolling, float or fusion-draw processes; and scaffolds can be produced using rapid prototyping, polymer foam replication and particle sintering. Glasses of desired forms can be used to support cell growth, soft and hard tissue regeneration, stimulation of gene expression or angiogenesis.

[0053] Continuous fibers can be easily drawn from the claimed composition using processes known in the art. For example, fibers can be formed using a directly heated (electricity passing directly through) platinum bushing. Glass cullet is loaded into the bushing, heated up until the glass can melt. Temperatures are set to achieve a desired glass viscosity (usually <1000 poise) allowing a drip to form on the orifice in the bushing (Bushing size is selected to create a restriction that influences possible fiber diameter ranges). The drip is pulled by hand to begin forming a fiber. Once a fiber is established it is connected to a rotating pulling/collection drum to continue the pulling process at a consistent speed. Using the drum speed (or revolutions per minute RPM) and glass viscosity the fiber diameter can be manipulated—in general the faster the pull speed, the smaller the fiber diameter. Glass fibers with diameters in the range of 1-100 μm can be drawn continuously from a glass melt. Fibers can also be created using an updraw process. In this process, fibers are pulled from a glass melt surface sitting in a box furnace. By controlling the viscosity of the glass, a quartz rod is used to pull glass from the melt surface to form a fiber. The fiber can be continuously pulled upward to increase the fiber length. The velocity that the rod is pulled up determines the fiber thickness along with the viscosity of the glass.

[0054] Thus, as presented herein, biocompatible inorganic compositions for consumer and dental applications are described having a combination of improved bioactivity and chemical durability in aqueous environments.

[0055] As used herein, the term "and/or," when used in a list of two or more items, means that any one of the listed items can be employed by itself, or any combination of two or more of the listed items can be employed. For example, if a composition is described as containing components A, B, and/or C, the composition can contain A alone; B alone; C alone; A and B in combination; A and C in combination; B and C in combination; or A, B, and C in combination.

[0056] References herein to the positions of elements (e.g., "top," "bottom," "above," "below," "first," "second," etc.) are merely used to describe the orientation of various elements in the FIGURES. It should be noted that the orientation of various elements may differ according to other exemplary embodiments, and that such variations are intended to be encompassed by the present disclosure. Moreover, these relational terms are used solely to distinguish one entity or action from another entity or action, without necessarily requiring or implying any actual such relationship or order between such entities or actions.

[0057] Modifications of the disclosure will occur to those skilled in the art and to those who make or use the disclosure. Therefore, it is understood that the embodiments shown in the drawings and described above are merely for illustrative purposes and not intended to limit the scope of the disclosure, which is defined by the following claims, as interpreted according to the principles of patent law, including the doctrine of equivalents.

[0058] It will be understood by one having ordinary skill in the art that construction of the described disclosure, and other components, is not limited to any specific material. Other exemplary embodiments of the disclosure disclosed herein may be formed from a wide variety of materials, unless described otherwise herein.

[0059] As utilized herein, the terms "approximately," "about," "substantially", and similar terms are intended to have a broad meaning in harmony with the common and accepted usage by those of ordinary skill in the art to which the subject matter of this disclosure pertains. It should be understood by those of skill in the art who review this disclosure that these terms are intended to allow a description of certain features described and claimed without restricting the scope of these features to the precise numerical ranges provided. Accordingly, these terms should be interpreted as indicating that insubstantial or inconsequential modifications or alterations of the subject matter described and claimed are considered to be within the scope of the invention as recited in the appended claims.

[0060] As utilized herein, "optional," "optionally," or the like are intended to mean that the subsequently described event or circumstance can or cannot occur, and that the description includes instances where the event or circumstance occurs and instances where it does not occur. As used herein, the indefinite articles "a," "an," and the corresponding definite article "the" mean "at least one" or "one or more," unless otherwise specified. It also is understood that the various features disclosed in the specification and the drawings can be used in any and all combinations.

[0061] With respect to the use of substantially any plural and/or singular terms herein, those having skill in the art can translate from the plural to the singular and/or from the singular to the plural as is appropriate to the context and/or application. The various singular/plural permutations may be expressly set forth herein for the sake of clarity.

[0062] Unless otherwise specified, all compositions are expressed in terms of as-batched weight percent (wt. %). As will be understood by those having ordinary skill in the art, various melt constituents (e.g., silicon, alkali- or alkaline-based, boron, etc.) may be subject to different levels of volatilization (e.g., as a function of vapor pressure, melt time and/or melt temperature) during melting of the constituents. As such, the as-batched weight percent values used in relation to such constituents are intended to encompass values within ±0.5 wt. % of these constituents in final, as-melted articles. With the forgoing in mind, substantial compositional equivalence between final articles and as-batched compositions is expected.

[0063] It will be apparent to those skilled in the art that various modifications and variations can be made without departing from the spirit or scope of the claimed subject matter. Accordingly, the claimed subject matter is not to be restricted except in light of the attached claims and their equivalents.

1. A silicate-based glass composition, comprising:

15-65 wt. % SiO_2,

2.5-25 wt. % MgO,

1-30 wt. % P_2O_5, and

15-50 wt. % CaO,

wherein the composition:

has a hydrolytic resistance of glass grains (HGB) of at most 3, when measured by International Organization for Standardization section 719 (ISO 719), and

forms a bioactive crystalline phase in a simulated body fluid.

2. The glass composition of claim **1**, further comprising:
>0-5 wt. % F^-.

3. The glass composition of claim **1**, further comprising one of:
>0-10 wt. % Li_2O,
>0-10 wt. % Na_2O, or
>0-10 wt. % K_2O.

4. The glass composition of claim **1**, further comprising:
>0 to 10 wt. % ZrO_2.

5. The glass composition of claim **1**, further comprising:
0-10 wt. % Al_2O_3,
0-10 wt. % SrO,
0-10 wt. % ZnO, and
0-5 wt. % B_2O_3.

6. The glass composition of claim **1**, wherein the glass comprises:
15-50 wt. % MO, and
0-30 wt. % R_2O,
wherein MO is the sum of MgO, CaO, SrO, BeO, and BaO, and
R_2O is the sum of Na_2O, K_2O, Li_2O, Rb_2O, and Cs_2O.

7. The glass composition of claim **1**, wherein the bioactive crystalline phase comprises apatite.

8. The glass composition of claim **1**, wherein a sum of P_2O_5 and CaO is from 25-65 wt. %.

9. A silicate-based glass composition, comprising:
30-50 wt. % SiO_2,
10-20 wt. % MgO,
5-15 wt. % P_2O_5, and
25-40 wt. % CaO,
wherein the composition:
has a hydrolytic resistance of glass grains (HGB) of at most 3, when measured by International Organization for Standardization section 719 (ISO 719), and
forms a bioactive crystalline phase in a simulated body fluid.

10. The glass composition of claim **9**, further comprising:
>0-3 wt. % F^-.

11. The glass composition of claim **9**, further comprising one of:
>0-10 wt. % Li_2O,
>0-10 wt. % Na_2O, or
>0-10 wt. % K_2O.

12. The glass composition of claim **9**, further comprising:
>0 to 10 wt. % ZrO_2.

13. The glass composition of claim **9**, wherein the bioactive crystalline phase comprises apatite.

14. The glass composition of claim **9**, wherein a sum of P_2O_5 and CaO is from 25-65 wt. %.

15. A matrix comprising the glass composition of claim **1**, wherein:
the matrix includes at least one of: a toothpaste, mouthwash, rinse, spray, ointment, salve, cream, bandage, polymer film, oral formulation, pill, capsule, or transdermal formulation.

16. The matrix of claim **15**, wherein the glass composition is attached to the matrix or mixed therein.

17. An aqueous environment comprising the glass composition of claim **1**.

* * * * *