(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
06 January 2022 (06.01.2022)

WIPO | PCT

(10) International Publication Number
WO 2022/005781 A1

(51) International Patent Classification:
C03C 10/04 (2006.01) *C03C 29/00* (2006.01)
C03C 10/06 (2006.01)

(21) International Application Number:
PCT/US2021/038174

(22) International Filing Date:
21 June 2021 (21.06.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/045,489 29 June 2020 (29.06.2020) US

(71) Applicant: **CORNING INCORPORATED** [US/US]; 1 Riverfront Plaza, Corning, New York 14831 (US).

(72) Inventors: **COON, Erin**; 2602B Spencer Hill Road, Corning, New York 14830 (US). **FU, Qiang**; 7 Tara Place, Painted Post, New York 14870 (US). **WHITTIER, Alana Marie**; 5 Elmwood Lane, Painted Post, New York 14870 (US).

(74) Agent: **PATHAK, Shantanu C.**; Corning Incorporated, Intellectual Property Department, SP-TI-03-1, Corning, New York 14831 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,

(54) Title: GLASS-CERAMIC COMPOSITIONS AND METHODS OF MAKING THEREOF

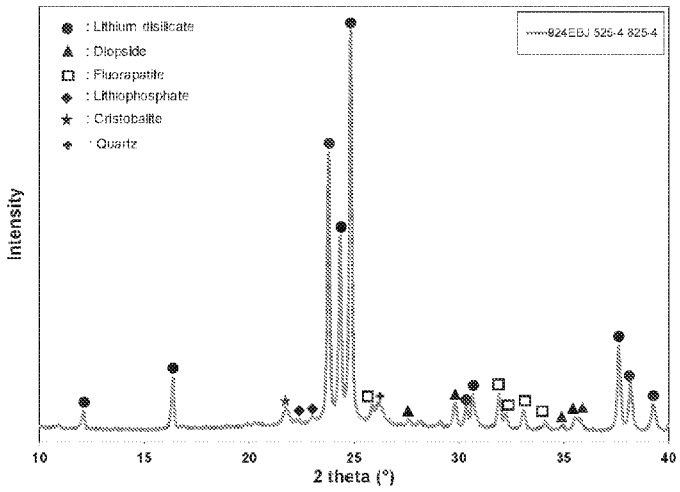


FIG. 1

(57) Abstract: A silicate-based composition includes: 40-80 mol% SiO_2, >0-25 mol% MO, 15-40 mol% R_2O, >0-10 mol% Al_2O_3, >0-10 mol% P_2O_5, and >0-5 mol% ZrO_2, such that MO is a sum of BeO, MgO, CaO, SrO, and BaO; and R_2O is a sum of Li_2O, Na_2O, K_2O, Rb_2O, Cs_2O.

[Continued on next page]

WO 2022/005781 A1

TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

GLASS-CERAMIC COMPOSITIONS AND METHODS OF MAKING THEREOF

[0001] This application claims the benefit of priority under 35 U.S.C. § 119 of U.S. Provisional Application Serial No. 63/045,489, filed on June 29, 2020, the content of which is relied upon and incorporated herein by reference in its entirety.

BACKGROUND

1. Field

[0002] The disclosure relates to glass-ceramic compositions and methods of making thereof for biomedical applications.

2. Technical Background

[0003] Bioactive materials 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 materials are able to bond with hard and soft tissues, thereby fostering growth (e.g., regeneration) of bone/teeth and cartilage cells.

[0004] Efforts have been made to produce bioactive materials to achieve high bioactivity and high strength. However, certain promising materials, such as diopside-containing bioactive materials, have been difficult to adopt in biomedical applications due to their lack of bulk nucleation, which is critical for producing porosity-free glass-ceramics with homogeneous microstructures. As a result, these glass-ceramics are prepared from powder sintering processes, which limit their forming capabilities and generate voids due to insufficient densification during sintering, thereby leading to weakened microstructures. Thus, there continues to be an unmet need for bioactive material compositions having an improved strength, while maintaining excellent bioactivity.

[0005] This disclosure presents improved biocompatible inorganic compositions for biomedical applications.

SUMMARY

[0006] In some embodiments, a silicate-based composition, comprises: 40-80 mol% SiO_2, >0-25 mol% MO, 15-40 mol% R_2O, >0-10 mol% Al_2O_3, >0-10 mol% P_2O_5, and >0-5 mol%

ZrO_2, wherein MO is a sum of BeO, MgO, CaO, SrO, and BaO; and wherein R_2O is a sum of Li_2O, Na_2O, K_2O, Rb_2O, Cs_2O.

[0007] In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: >0-5 mol% F^-. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: 15-30 mol% Li_2O; and >0-10 mol% a sum of Na_2O and K_2O. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: >0-5 mol% Na_2O; and >0-5 mol% K_2O. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: >0-15 mol% CaO; and >0-10 mol% MgO. In one aspect, which is combinable with any of the other aspects or embodiments, a sum of P_2O_5 and CaO is 1-15 mol%, or a ratio of CaO:P_2O_5 is 1:1 to 10:1. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: >0-10 mol% B_2O_3.

[0008] In some embodiments, a silicate-based composition, comprises: 50-70 mol% SiO_2, >0-25 mol% MO, 15-40 mol% R_2O, >0-5 mol% Al_2O_3, 0.5-5 mol% P_2O_5, and >0-5 mol% ZrO_2, wherein MO is a sum of MgO and CaO; and wherein R_2O is a sum of Li_2O, Na_2O, and K_2O.

[0009] In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: 15-30 mol% Li_2O, >0-5 mol% Na_2O, and >0-5 mol% K_2O. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: >0-10 mol% MgO, and >0-15 mol% CaO. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: 0.2-5 mol% F^-. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition comprises: >0-5 mol% B_2O_3.

[0010] In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition is a glass-ceramic composition comprising: at least a major phase including lithium disilicate, diopside, and apatite. In one aspect, which is combinable with any of the other aspects or embodiments, the glass-ceramic composition has a fracture toughness in a range of 2-4 $MPa•M^{1/2}$.

[0011] In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition is a glass-ceramic composition and is a particle, bead, particulate, short fiber, long fiber, woolen mesh, combination thereof. In one aspect, which is

combinable with any of the other aspects or embodiments, the glass-ceramic composition has at least one size dimension in a range of 1-100 μm. In one aspect, which is combinable with any of the other aspects or embodiments, the glass-ceramic composition has at least one size dimension in a range of 1-10 μm.

[0012] In one aspect, which is combinable with any of the other aspects or embodiments, a matrix comprises the silicate-based composition disclosed herein wherein the matrix includes at least one of: dental bridges, dental enamel, dental filling material, bone filling material, orthopedic implants. In one aspect, which is combinable with any of the other aspects or embodiments, the silicate-based composition is a glass-ceramic composition attached to the matrix or mixed therein. In one aspect, which is combinable with any of the other aspects or embodiments, an antibacterial composition comprises the silicate-based composition disclosed herein.

[0013] In some embodiments, a bulk nucleation process, comprises: heating at temperatures ranging 600-1000°C for a predetermined time, a silicate-based composition comprising: 40-80 mol% SiO_2, >0-25 mol% MO, 15-40 mol% R_2O, >0-10 mol% Al_2O_3, >0-10 mol% P_2O_5, and >0-5 mol% ZrO_2, wherein MO is a sum of BeO, MgO, CaO, SrO, and BaO; and wherein R_2O is a sum of Li_2O, Na_2O, K_2O, Rb_2O, Cs_2O, to form a glass-ceramic article. In one aspect, which is combinable with any of the other aspects or embodiments, the glass-ceramic article includes a major phase comprising at least lithium disilicate, diopside, and apatite.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] The disclosure will become more fully understood from the following detailed description, taken in conjunction with the accompanying figures, in which:

[0015] FIG. 1 illustrates an x-ray diffraction (XRD) plot of a phase assemblage of Sample 1, according to some embodiments.

[0016] FIGS. 2A and 2B illustrate scanning electron microscopy (SEM) images of a microstructure of Sample 1, according to some embodiments. FIGS. 2C to 2F illustrates energy-dispersive x-ray spectroscopy (EDS) analysis of phases present in the microstructure of Sample 1, according to some embodiments.

[0017] FIG. 3A illustrates a magnified SEM image (5000x) of a microstructure of Sample 1, according to some embodiments. FIGS. 3B and 3C illustrate EDS elemental mapping of

calcium (FIG. 3B) and magnesium (FIG. 3C) in Sample 1 to analyze formation of diopside phase in the material.

[0018] FIG. 4 illustrates a comparison of fracture toughness for Sample 1 (having lithium disilicate, diopside, and fluorapatite main phases) and Comparative Sample 1 (having lithium disilicate and fluorapatite main phases), according to some embodiments.

DETAILED DESCRIPTION

[0019] 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. It also is understood that the various features disclosed in the specification and the drawings can be used in any and all combinations.

[0020] 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.”

[0021] Herein, compositions are expressed in terms of mol% 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 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.

[0022] Bioactive Material Compositions

[0023] Bioactive materials 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. As used herein, "bioactive material," "bioactive composition," "glass," "glass-ceramic," combinations thereof, or the like are used interchangeably. The biocompatibility and *in vivo* properties of the material are influenced by the composition. In the compositions described herein, SiO_2 serves as the primary forming oxide in combination with the bioactive oxides of calcium and phosphorous.

[0024] In the present application, novel bioactive material compositions (e.g., glass-ceramics) are disclosed which comprise multiple phases, including lithium disilicate, apatite and diopside in one system.

[0025] Lithium disilicate ($Li_2O•2SiO_2$), is an orthorhombic crystal based on corrugated sheets of Si_2O_5 tetrahedral arrays. The crystals are typically tabular or lath-like in shape (e.g., acicular, needle-like morphology), with pronounced cleavage planes. Glass-ceramics based on lithium disilicate offer highly desirable mechanical properties, including high body strength and fracture toughness, due to their microstructures of randomly-oriented interlocking crystals. Glass-ceramics with fracture toughness values of at least 2 $MPa•m^{1/2}$ are achievable in this composition system. Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$ may be used in medical bone and teeth healing applications. It is biocompatible with bone and can be used for orthopedic and dental implants and has found wide applications in biomedical fields. Diopside ($CaO•MgO•2SiO_2$) is another bioactive ceramic that possesses excellent *in vitro* apatite-forming ability, *in vivo* bioactivity and degradation, and improved mechanical strength. Fracture toughness as high as 3.5 $MPa.m^{1/2}$ may be achieved for diopside-containing ceramics.

[0026] Compositions disclosed herein (e.g., interlocking lithium silicate and coarse diopsides) are internally nucleated to produce glass-ceramics with homogeneous microstructures and high fracture toughness. The formation of apatite and diopside phases ensure a good biocompatibility for wide biomedical applications.

[0027] In some examples, the composition comprises a combination of SiO_2, alkaline earth oxides (MO, or the sum of BeO, MgO, CaO, SrO, BaO), and alkali oxides (R_2O, or the sum of Li_2O, Na_2O, K_2O, Rb_2O, Cs_2O). In some examples, the composition further comprises

Al_2O_3. In some examples, the composition may further comprise P_2O_5, ZrO_2, and fluorine. For example, the composition may comprise, in mol%: 40-80 SiO_2, >0-25 MO, and 15-40 R_2O. In some examples, the composition further comprises, in mol%, >0-10 Al_2O_3. In some examples, the composition may further comprise, in mol%, >0-10 P_2O_5, >0-5 ZrO_2, and 0-5 fluorine (F^-). The compositions disclosed herein are particularly suitable for biomedical or bioactive applications.

[0028] Silicon dioxide (SiO_2), which serves as the primary composition-forming oxide component of the embodiments, influences the mechanical strength, biocompatibility and degradation properties (e.g., temperature stability, chemical durability, etc.) of the bioactive compositions. For the compositions disclosed herein, SiO_2 functions to stabilize the networking structure of glass and glass-ceramics. Concentration of SiO_2 should be sufficiently high to form lithium disilicate crystal phase when the precursor glass is heat treated (i.e., cerammed) to convert to a glass-ceramic material. However, the precursor glass (and the resulting glass-ceramic after ceramming) cannot include too much SiO_2 (e.g., greater than 80mol%) since glass melting temperatures of pure SiO_2 or high-SiO_2 glasses is undesirably high (200 poise temperature), leading to decreased bioactivity.

[0029] In some embodiments, the composition can comprise 40-80 mol% SiO_2. In some embodiments, the composition can comprise 50-70 mol% SiO_2. In some embodiments, the composition can comprise 40-80 mol%, or 40-60 mol%, or 45-65 mol%, or 50-70 mol%, or 55-75 mol%, or 60-80 mol% SiO_2, or any value or range disclosed therein. In some examples, the glass is essentially free of SiO_2 or comprises 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, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80 mol% SiO_2, or any value or range having endpoints disclosed herein.

[0030] Divalent cation oxides (such as alkaline earth oxides) are important for improvement of (1) melting behavior and bioactivity of the composition; (2) influencing the composition's Young's modulus and coefficient of thermal expansion. Particularly, CaO may react with P_2O_5 to form apatite (bioactive ceramic) 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.

[0031] In some examples, the compositions may comprise P_2O_5 and CaO with the sum of P_2O_5 and CaO being, in mol%, from 1-15%, or 3-12%, or 5-10%, or any value or range

disclosed therein. In some examples, the compositions comprise P_2O_5 and CaO with the sum of P_2O_5 and CaO being 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 mol%, or any value or range having endpoints disclosed herein. In some examples, the compositions comprise P_2O_5 and CaO with the ratio of CaO:P_2O_5 being in a range of 1-10, or 2-8, or 3-6 or any value or range having endpoints disclosed herein.

[0032] In some examples, the composition can comprise, in mol%, >0-25 alkaline earth oxides (MO, which is the sum of MgO, CaO, SrO, BeO, and BaO). In some examples, the composition can comprise, in mol%, 5-20 MO. In some examples, the composition can comprise, in mol%, >0-25, or >0-20, or 2-20, or 2-15, or 5-15, or 5-10, or 10-25, or 10-20, or >0-15, or >0-10 MO, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 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 MO, or any value or range having endpoints disclosed herein.

[0033] In some examples, the composition can comprise, in mol%, >0-15 CaO. In some examples, the composition can comprise, in mol%, 5-10 CaO. In some examples, the composition can comprise, in mol%, >0-15, or >0-14, or 1-14, or 1-13, or 2-13, or 2-12, or 3-12, or 3-11, or 4-11, or 4-10, or 5-10 CaO, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 CaO, or any value or range having endpoints disclosed herein.

[0034] In some examples, the composition comprises MgO, which is essential for diopside phase formation. In some examples, the composition can comprise, in mol%, >0-10 MgO. In some examples, the composition can comprise, in mol%, 1-7 MgO. In some examples, the composition can comprise, in mol%, >0-10, or >0-9, or 1-9, or 1-8, or 2-8, or 2-7, or 3-7 MgO, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 MgO, or any value or range having endpoints disclosed herein.

[0035] In some examples, the composition may comprise other alkaline earth oxides, either in combination or individually, such as BeO, SrO, and/or BaO. In some examples, the composition can comprise, in mol%, >0-15 BeO, SrO, and/or BaO, either alone or in combination. In some examples, the composition can comprise, in mol%, >0-15, or >0-14, or 1-14, or 1-13, or 2-13, or 2-12, or 3-12, or 3-11, or 4-11, or 4-10, or 5-10 BeO, SrO, and/or BaO, either alone or in combination, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13,

14, 15 BeO, SrO, and/or BaO, either alone or in combination, or any value or range having endpoints disclosed herein.

[0036] Alkali oxides are important for (I) reducing melting temperature and liquidus temperature of the glass; (II) shorten ceramming cycles; (III) increasing thermal expansion after ceramming of the resultant glass-ceramics, if desired; and (IV) improving bioactivity of the bioactive material.

[0037] In some examples, the composition can comprise, in mol%, 15-40 alkali oxides (R_2O, which is the sum of Li_2O, Na_2O, K_2O, Rb_2O, and Cs_2O). In some examples, the composition can comprise, in mol%, 20-35 R_2O. In some examples, the composition can comprise, in mol%, 15-40, or 15-35, or 20-35, or 20-30, or 15-25, or 25-40, or 20-25, or 25-30, or 30-35 R_2O, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, 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 R_2O, or any value or range having endpoints disclosed herein.

[0038] In some examples, the composition comprises Li_2O, which is essential for forming lithium disilicate crystal phases. In some examples, the composition can comprise, in mol%, 15-30 Li_2O. In some examples, the composition can comprise, in mol%, 20-30 Li_2O. In some examples, the composition can comprise, in mol%, 15-30, or 15-28, or 17-28, or 17-26, or 19-26, or 19-24 Li_2O, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 Li_2O, or any value or range having endpoints disclosed herein.

[0039] In some examples, the composition may comprise Na_2O and/or K_2O, which particularly affect (I) to (III) as described above, if present at low concentrations. In some examples, the composition can comprise, in mol%, >0-10 Na_2O and/or K_2O, either alone or in combination. In some examples, the composition can comprise, in mol%, >0-10, or >0-7, or >0-5, or >0-3, or 1-10, or 1-7, or 1-5, or 1-3, or 5-10, or 3-7 Na_2O and/or K_2O, either alone or in combination, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 Na_2O and/or K_2O, either alone or in combination, or any value or range having endpoints disclosed herein.

[0040] In some examples, the composition may comprise other alkali oxides, either in combination or individually, such as Rb_2O, and/or Cs_2O. In some examples, the composition can comprise, in mol%, >0-10 Rb_2O, and/or Cs_2O, either alone or in combination. In some examples, the composition can comprise, in mol%, >0-10, or >0-7, or >0-5, or >0-3, or 1-10, or 1-7, or 1-5, or 1-3, or 5-10, or 3-7 Rb_2O, and/or Cs_2O, either alone or in combination, or

any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 Rb_2O, and/or Cs_2O, either alone or in combination, or any value or range having endpoints disclosed herein.

[0041] In some examples, the composition further comprises network former alumina (Al_2O_3), which provides stabilization to the networking structure, as well as contributing to improved mechanical properties and chemical durability in silicate glasses while having no toxicity concerns. Above a certain content concentration, alumina generally increases viscosity of the melt and decreases the fraction of lithium disilicate crystals to an extent that no interlocking structure can be formed. The lack of interlocking structure leads to weakening mechanical state. Additionally, alumina also helps lower liquidus temperature and coefficient of thermal expansion, or, enhance the strain point. In some examples, the composition can comprise, in mol%, >0-10 Al_2O_3. In some examples, the composition can comprise, in mol%, >0-10, or >0-7, or >0-5, or >0-3, or 1-10, or 1-7, or 1-5, or 1-3, or 5-10, or 3-7 Al_2O_3, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 Al_2O_3, or any value or range having endpoints disclosed herein.

[0042] In some examples, the composition further comprises network former phosphorus pentoxide (P_2O_5), which serves as a nucleating agent for bulk nucleation in glass and glass-ceramic compositions disclosed herein. Inclusion and liberation of phosphate ions to the surface of bioactive glasses increases apatite formation rate and the binding capacity in physiological applications. Additionally, P_2O_5 increases glass viscosity, which expands the glass's range of operating temperatures and is advantageous to its manufacture and formation. If P_2O_5 concentration is too low, the precursor glass will not crystallize. If P_2O_5 concentration is too high, devitrification (occurring during cooling of the precursor glass) can be difficult to control. In some examples, the composition can comprise, in mol%, >0-10 P_2O_5. In some examples, the composition can comprise, in mol%, >0-10, or >0-7, or >0-5, or >0-3, or 1-10, or 1-7, or 1-5, or 1-3, or 5-10, or 3-7 P_2O_5, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 P_2O_5, or any value or range having endpoints disclosed herein.

[0043] In some examples, the composition further comprises network former/precursor glass intermediate zirconium oxide (ZrO_2), which helps to improve stability in Li_2O-Al_2O_3-SiO_2-P_2O_5 glasses by significantly reducing glass devitrification during the formation process and lowering liquidus temperature. Furthermore, ZrO_2 may also increase chemical durability of related glass-ceramics. Clear precursor glass patties can be formed from glasses containing

>0.2 mol% ZrO_2. In some examples, the composition can comprise, in mol%, >0-5 ZrO_2. In some examples, the composition can comprise, in mol%, >0-5, or >0-3, or >0-2, or >0-1.5, or >0-1 ZrO_2, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 ZrO_2, or any value or range having endpoints disclosed herein.

[0044] In some examples, the composition further comprises network former boron oxide (B_2O_3), which is beneficial for glass melting, if present at low concentrations. In some examples, the composition can comprise, in mol%, >0-10 B_2O_3. In some examples, the composition can comprise, in mol%, >0-10, or >0-7, or >0-5, or >0-3, or 1-10, or 1-7, or 1-5, or 1-3, or 5-10, or 3-7 B_2O_3, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 B_2O_3, or any value or range having endpoints disclosed herein.

[0045] In some examples, the composition further comprises a fluorine source (e.g., CaF_2), which can be batched in during composition formation. Fluorine (F^-) is essential for forming fluorapatite phases. In some examples, the composition can comprise, in mol%, >0-5 F^-. In some examples, the composition can comprise, in mol%, >0-5, or >0-3, or >0-2, or >0-1.5, or >0-1 F^-, or any value or range disclosed therein. In some examples, the composition can comprise, in mol%, >0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 F^-, or any value or range having endpoints disclosed herein.

[0046] Additional components can be incorporated into the composition to provide additional benefits or may be incorporated as contaminants typically found in commercially-prepared compositions. 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 compositions may comprise one or more compounds useful as ultraviolet radiation absorbers. In some examples, the composition can comprise 3 mol% 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 composition can comprise, in mol%, 0-3, or 0-2, or 0-1, or 0-0.5, or 0-0.1, or 0-0.05, or 0-0.01 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 compositions, according to some examples, can also include various contaminants associated with batch materials and/or introduced into the composition by the melting, fining, and/or forming equipment used to produce the

composition. For example, in some embodiments, the glass can comprise, in mol%, 0-3, or 0-2, or 0-1, or 0-0.5, or 0-0.1, or 0-0.05, or 0-0.01 SnO_2, Fe_2O_3, or combinations thereof.

EXAMPLES

[0047] The embodiments described herein will be further clarified by the following examples.

[0048] Non-limiting examples of amounts of oxides for forming the embodied compositions are listed in Table 1, along with the properties of the resulting compositions. Phase assemblage is analyzed by x-ray diffraction (XRD). XRD was conducted using a Bruker D4 Endeavor equipped with a LynxEye™ silicon strip detector. X-ray scanning was conducted from 5° to 80° (2θ) for data collection.

Oxide (mol%)	Comparative	1	2	3	4	5	6	7	8
SiO_2	61.2	61.6	61.2	60.8	60.1	62.1	62.3	62.5	61.6
Al_2O_3	1.5	1.4	1.3	1.3	1.2	1.4	1.4	1.4	1.4
Li_2O	24.5	22.4	21.6	20.9	19.5	22.5	22.6	22.7	22.4
Na_2O	2.0	1.8	1.8	1.7	1.6	1.8	1.8	1.8	1.8
MgO	0.0	3.0	3.8	4.5	5.8	3.0	3.0	3.0	4.1
CaO	6.5	5.9	6.6	7.2	8.3	6.0	6.0	6.0	5.9
P_2O_5	1.7	1.5	1.5	1.4	1.4	1.6	1.6	1.6	1.5
ZrO_2	1.0	0.9	0.9	0.8	0.8	0.9	0.9	0.9	0.9
F^-	1.6	1.5	1.4	1.4	1.3	0.7	0.4	0.0	0.4
Ceramming cycle	700°C-2hr 800°C-4hr	525°C-4hr 825°C-4hr	525°C-4hr 800°C-4hr	525°C-4hr 800°C-4hr	525°C-4hr 800°C-4hr	525°C-4hr 825°C-4hr	525°C-4hr 825°C-4hr	525°C-4hr 825°C-4hr	525°C-4hr 825°C-4hr
Appearance	White translucent, fine grain		White translucent, coarse grain		Surface crystallization	White translucent, fine grain			White translucent, coarse grain
Phase assemblage	(1)-(4)	(1)-(6)	(1)-(6)	(1)-(6)	(1)-(6)	(1), (2), (4)-(6)	(1)-(6)	(1), (3), (4), (6)	(1)-(6)

Table 1

Where, (1) is lithium disilicate; (2) is fluorapatite; (3) is quartz; (4) is lithiophosphate; (5) is diopside; and (6) is cristobalite.

[0049] The compositions disclosed herein can be in any form that is useful for the medical and dental processes disclosed, for example: particles, powder, microspheres, fibers, sheets, beads, scaffolds, woven fibers, etc.

[0050] Table 1 represents glass-ceramic compositions (cerammed from their glass counterparts) having multiple crystalline phases, including lithium disilicate, diopside, and fluorapatite. Additional phases can include lithiophosphate, quartz, and cristobalite.

[0051] Example 1—Precursor Glass Composition Formation

[0052] Glasses having the oxide contents listed in Table 1 can be made via traditional methods (e.g., rolling, molding, and float processes). In some examples, the precursor glasses can be formed by thoroughly mixing the requisite batch materials (for example, using a tubular 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 below 1500°C or below 1400°C (e.g., 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.

[0053] 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.

[0054] 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.

[0055] Example 2—Glass-Ceramic Composition Formation

[0056] After forming the precursor glasses as described in Example 1, the precursor glasses were subjected to a heat treatment (i.e., ceramming) as follows: (a) a first temperature ramp from room temperature (RT) to a nucleation step temperature at 5°C/min; (b) a first isothermal hold at the nucleation step temperature for a first predetermined time; (c) a second temperature ramp from the nucleation step temperature to a crystallization step temperature at 5°C/min; (d) a second isothermal hold at the crystallization step temperature for a second predetermined time; and (e) a final cooling from the crystallization step temperature to room temperature at the natural rate of cooling within the furnace. Table 1 shows properties (appearance, phase assemblage) of the glass-ceramics formed as a result of the ceramming treatment.

[0057] Example 3—Characterization

[0058] Turning now to the figures, FIG. 1 illustrates an x-ray diffraction (XRD) plot of a phase assemblage of Sample 1 from Table 1. As is explained above in Examples 1 and 2, precursor glasses are cerammed into glass-ceramic articles with high crystallinity (typically over 50%). FIG. 1 shows that this ceramming process does indeed lead to high crystalline structures. For example, Sample 1 includes multiple crystalline phases, such as major phases lithium disilicate, diopside and fluorapatite and minor phases lithiophosphate, quartz, and

cristobalite can also be formed. Low peak intensities for diopside and fluorapatite major phases correspond to low weight percentiles of the phases.

[0059] FIGS. 2A and 2B illustrate scanning electron microscopy (SEM) images of a microstructure of Sample 1 while FIGS. 2C to 2F illustrate energy-dispersive x-ray spectroscopy (EDS) analysis of phases present in the microstructure of Sample 1.

[0060] Specifically, FIG. 2A and 2B provide SEM images of the microstructure of Sample 1 at magnifications of 1000x and 10000x, respectively. FIG. 2A shows glass-ceramic articles composed of interlocking lithium disilicate embedded with coarse diopside grains obtained by ceramming precursor glasses at temperatures ranging at 600-1000°C for a predetermined time. FIG. 2B marks the locations of EDS analysis of FIGS. 2C-2F. Magnesium and calcium peaks from the coarse white phase of the microstructure of Sample 1 indicate the presence of a diopside phase (FIG. 2C) while silicon peaks from the acicular black phase confirms the presence of a lithium disilicate phase (FIG. 2D). FIG. 2E indicates a partitioning of Na, Zr, P, Si, Al, Mg and CaO in a glassy phase of Sample 1 while an association of fluorine, phosphorus, and calcium in FIG. 2F suggests formation of fluorapatite. Thus, by EDS analysis, Sample 1 is confirmed to have lithium disilicate, diopside and fluorapatite major phases.

[0061] Formation of apatite and diopside phases (bioactive ceramics) ensures good biocompatibility of the compositions for biomedical applications. Residual glass in the disclosed glass-ceramics (post-ceramming) may be ion-exchanged to create a compressive stress layer in a surface of the ware to further improve its mechanical strength.

[0062] FIG. 3A illustrates another magnified SEM image (5000x) of a microstructure of Sample 1. EDS elemental mapping of the microstructure of FIG. 3A provides further evidence of diopside crystals in the glass-ceramic, with majority of calcium (FIG. 3B) and magnesium (FIG. 3C) present in the white coarse grains.

[0063] FIG. 4 illustrates a comparison of fracture toughness for Sample 1 (having lithium disilicate, diopside, and fluorapatite main phases) and Comparative Sample 1 (having lithium disilicate and fluorapatite main phases). Sample 1 was cerammed using a cycle of 525°C for 4hrs and 825°C for 4hrs with a ramp rate of 5°C/min; Comparative Sample 1 was cerammed using a cycle of 700°C for 2hrs and 800°C for 4hrs. Fracture toughness was measured using a chevron-notched short beam method according to ASTM. A significantly higher fracture toughness was observed in Sample 1.

[0064] Interlocking crystals as a result of multiple phases helps develop toughening mechanisms (e.g., including crack deflection and tortuous crack path) which contribute to high fracture toughness. A K_{ic} value ranging between about 2.65-2.9 $MPa•M^{1/2}$ was observed in Sample 1 while for Comparative Sample 1, the K_{ic} value varied between about 2-2.35 $MPa•M^{1/2}$, which is significantly lower than that for Sample 1.

[0065] Without being bound by theory, the improved toughness in Sample 1 is believed to result from the presence of coarse diopside grains within the microstructure. Thus, fracture toughness in a range of 2-4 $MPa•M^{1/2}$ is achievable in the novel glass-ceramic compositions disclosed herein.

[0066] Example 4—Composition Bioactivity

[0067] Aspects are related to compositions or matrices containing embodied bioactive compositions and the methods of using the matrices to treat medical conditions. The matrices can be dental bridges, dental enamel, dental filling material, bone filling material, orthopedic implants. The bioactive compositions claimed can be physically or chemically attached to matrices or other matrix components, or simply mixed in. As noted above, the bioactive compositions 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.

[0068] Thus, as presented herein, biocompatible inorganic compositions for biomedical applications are described having improved bioactivity.

[0069] 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.

[0070] 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.

[0071] 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.

[0072] 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.

[0073] 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. In other words, the terms "about," "approximately," and the like, mean 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.

[0074] Thus, a composition that is "free" or "essentially free" of a component is one in which that component 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).

[0075] 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.

[0076] 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.

[0077] Unless otherwise specified, all compositions are expressed in terms of as-batched mole percent (mol%). 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 mole percent values used in relation to such constituents are intended to encompass values within ±0.5 mol% of these constituents in final, as-melted articles. With the forgoing in mind, substantial compositional equivalence between final articles (glass-ceramic compositions) and as-batched compositions (precursor glasses) is expected. For example, substantial compositional equivalence is expected between the precursor glass and glass-ceramic after the step of heat treatment (ceramming).

[0078] 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.

WHAT IS CLAIMED IS:

1. A silicate-based composition, comprising:
40-80 mol% SiO_2,
>0-25 mol% MO,
15-40 mol% R_2O,
>0-10 mol% Al_2O_3,
>0-10 mol% P_2O_5, and
>0-5 mol% ZrO_2,
wherein MO is a sum of BeO, MgO, CaO, SrO, and BaO; and
wherein R_2O is a sum of Li_2O, Na_2O, K_2O, Rb_2O, Cs_2O.

2. The silicate-based composition of claim 1, further comprising:
>0-5 mol% F^-.

3. The silicate-based composition of claim 1 or claim 2, comprising:
15-30 mol% Li_2O; and
>0-10 mol% a sum of Na_2O and K_2O.

4. The silicate-based composition of claim 3, comprising:
>0-5 mol% Na_2O; and
>0-5 mol% K_2O.

5. The silicate-based composition of any one of claims 1-4, comprising:
>0-15 mol% CaO; and
>0-10 mol% MgO.

6. The silicate-based composition of claim 5, wherein:
a sum of P_2O_5 and CaO is 1-15 mol%, or
a ratio of $CaO:P_2O_5$ is 1:1 to 10:1.

7. The silicate-based composition of any one of claims 1-6, further comprising:
>0-10 mol% B_2O_3.

8. A silicate-based composition, comprising:
50-70 mol% SiO_2,
>0-25 mol% MO,
15-40 mol% R_2O,
>0-5 mol% Al_2O_3,
0.5-5 mol% P_2O_5, and
>0-5 mol% ZrO_2,
wherein MO is a sum of MgO and CaO; and
wherein R_2O is a sum of Li_2O, Na_2O, and K_2O.

9. The silicate-based composition of claim 8, comprising:
15-30 mol% Li_2O,
>0-5 mol% Na_2O, and
>0-5 mol% K_2O.

10. The silicate-based composition of claim 8 or claim 9, comprising:
>0-10 mol% MgO, and
>0-15 mol% CaO.

11. The silicate-based composition of any one of claims 8-10, further comprising:
0.2-5 mol% F^-.

12. The silicate-based composition of any one of claims 8-11, further comprising:
>0-5 mol% B_2O_3.

13. The silicate-based composition of any one of claims 1-7, wherein the silicate-based composition is a glass-ceramic composition comprising:
at least a major phase including lithium disilicate, diopside, and apatite.

14. The silicate-based composition of claim 13, wherein the glass-ceramic composition has a fracture toughness in a range of 2-4 $MPa \cdot M^{1/2}$.

15. The silicate-based composition of any one of claims 8-12, wherein the silicate-based composition is a glass-ceramic composition comprising:

at least a major phase including lithium disilicate, diopside, and apatite.

16. The silicate-based composition of claim 15, wherein the glass-ceramic composition has a fracture toughness in a range of 2-4 $MPa•M^{1/2}$.

17. The silicate-based composition of any one of claims 1-7, wherein the silicate-based composition is a glass-ceramic composition and is a particle, bead, particulate, short fiber, long fiber, woolen mesh, combination thereof.

18. The silicate-based composition of claim 17, wherein the glass-ceramic composition has at least one size dimension in a range of 1-100 μm.

19. The silicate-based composition of claim 17, wherein the glass-ceramic composition has at least one size dimension in a range of 1-10 μm.

20. A matrix comprising the silicate-based composition of any one of claims 1-7, wherein:

the matrix includes at least one of: dental bridges, dental enamel, dental filling material, bone filling material, orthopedic implants.

21. The matrix of claim 20, wherein the silicate-based composition is a glass-ceramic composition attached to the matrix or mixed therein.

22. An antibacterial composition comprising the silicate-based composition of any one of claims 1-7.

23. A bulk nucleation process, comprising:

heating at temperatures ranging 600-1000°C for a predetermined time, a silicate-based composition comprising:

40-80 mol% SiO_2,

>0-25 mol% MO,

15-40 mol% R_2O,

>0-10 mol% Al_2O_3,

>0-10 mol% P_2O_5, and

>0-5 mol% ZrO_2,

wherein MO is a sum of BeO, MgO, CaO, SrO, and BaO; and

wherein R_2O is a sum of Li_2O, Na_2O, K_2O, Rb_2O, Cs_2O,

to form a glass-ceramic article.

24. The bulk nucleation process of claim 23, wherein the glass-ceramic article includes a major phase comprising at least lithium disilicate, diopside, and apatite.

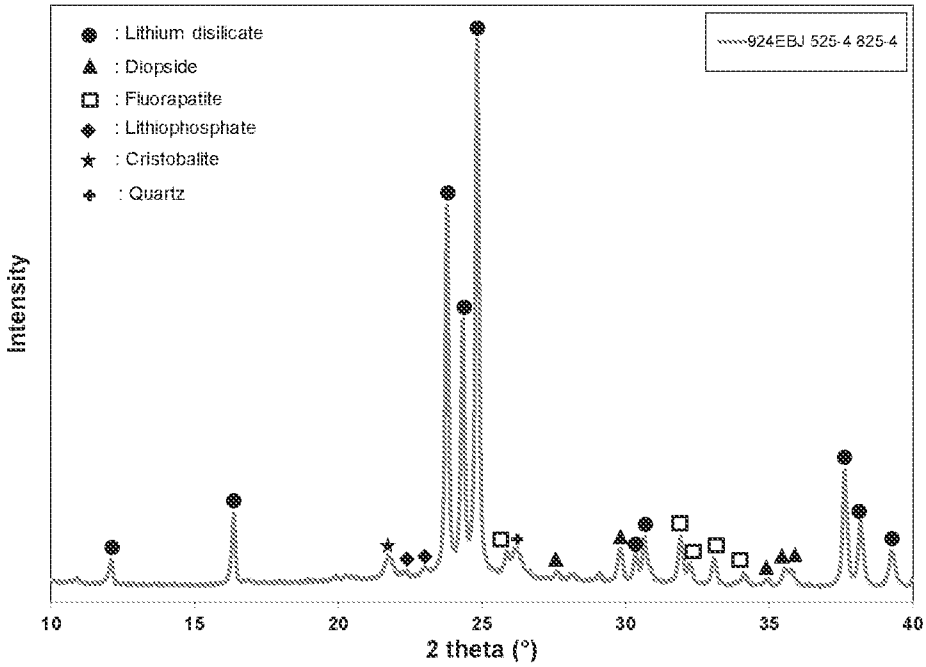

: Lithium disilicate
: Diopside
: Fluorapatite
: Lithiophosphate
: Cristobalite
: Quartz
924EBJ 525-4 825-4
Intensity
10
15
20
25
30
35
40
2 theta (°)

FIG. 1

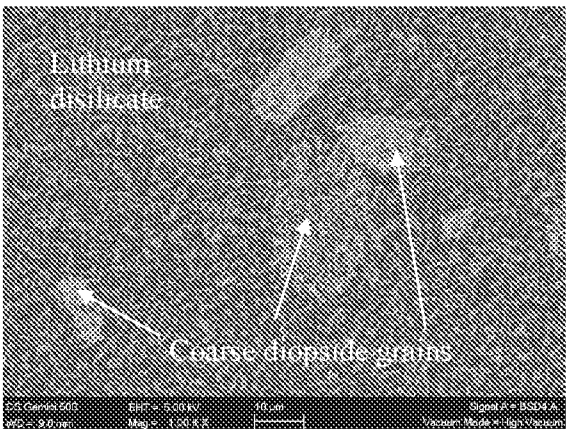


FIG. 2A

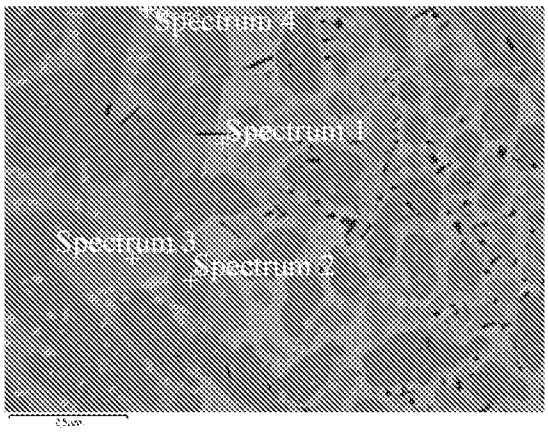


FIG. 2B

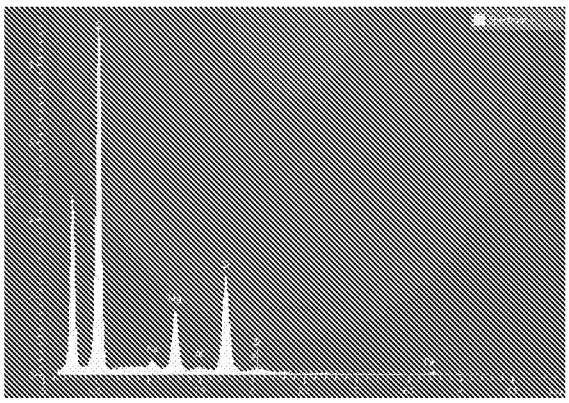


FIG. 2C

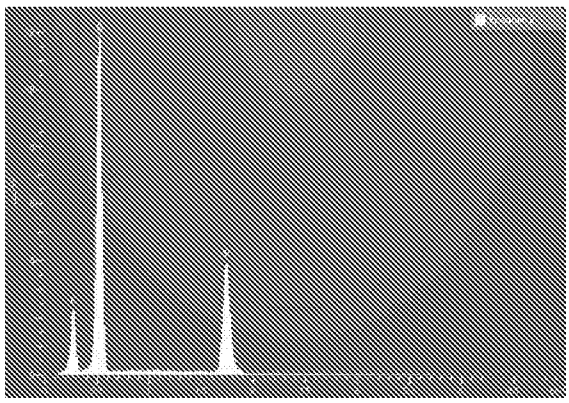


FIG. 2D

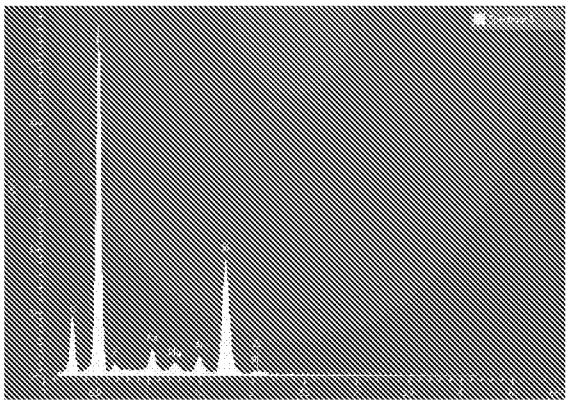


FIG. 2E

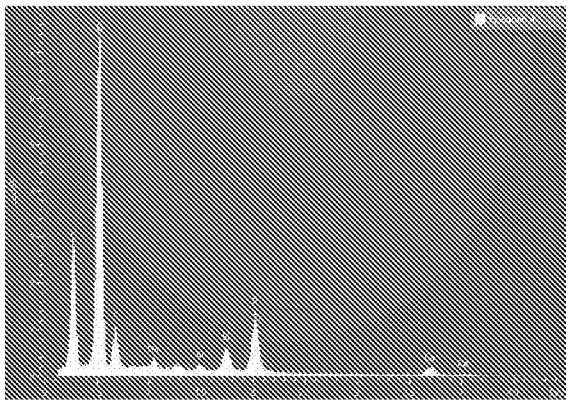


FIG. 2F

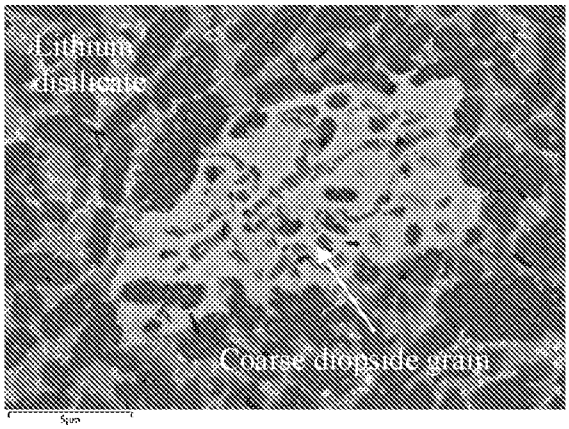


FIG. 3A

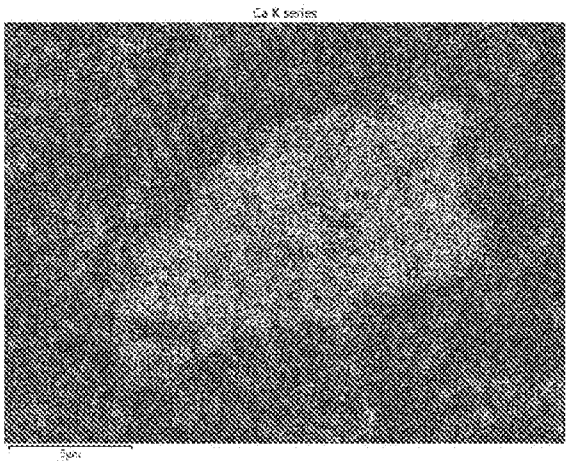


FIG. 3B

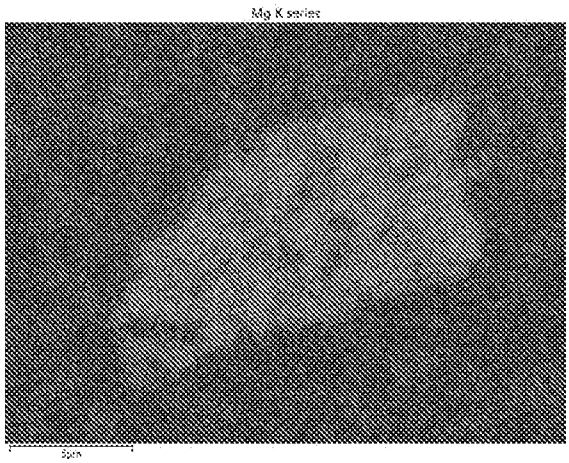


FIG. 3C

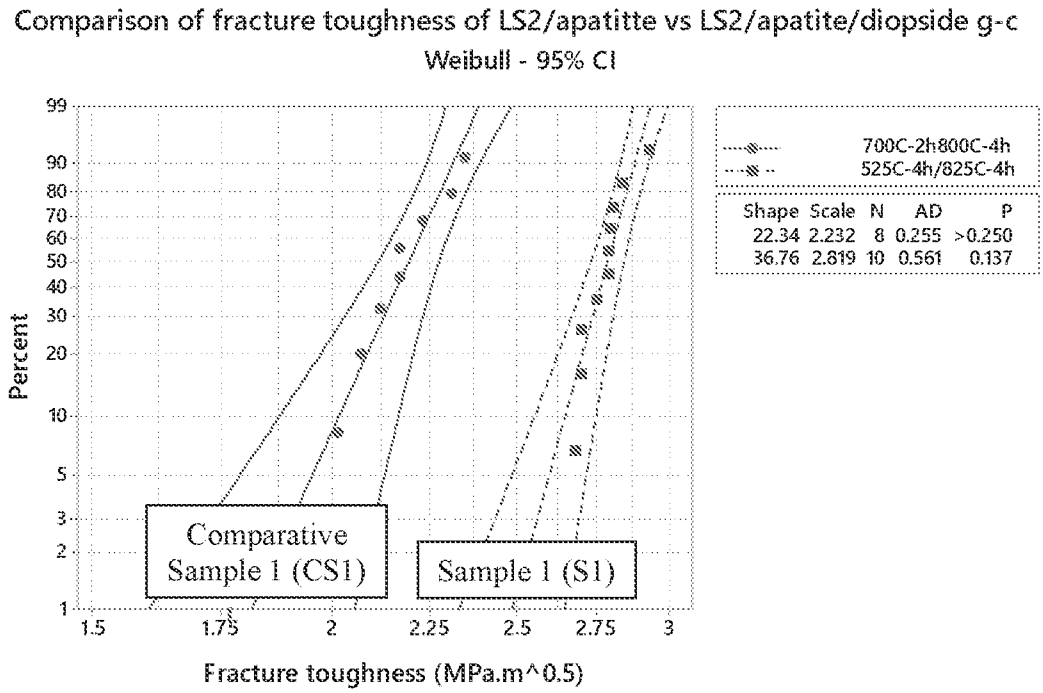

Comparison of fracture toughness of LS2/apatitte vs LS2/apatite/diopside g-c
Weibull - 95% CI
Percent
99
90
80
70
60
50
40
30
20
10
5
3
2
1
1.5
1.75
2
2.25
2.5
2.75
3
Fracture toughness (MPa.m^0.5)
Comparative Sample 1 (CS1)
Sample 1 (S1)
700C-2h800C-4h
525C-4h/825C-4h
Shape Scale N AD P
22.34 2.232 8 0.255 >0.250
36.76 2.819 10 0.561 0.137

FIG. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/38174

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C03C 10/04; C03C 10/06; C03C 29/00 (2021.01)

CPC - C03C 10/0036; C03C 29/00; C03C 3/062; C03C 3/066

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7,867,930 B2 (Apel et al.) 11 January 2011 (11.01.2011) Entire document, especially Abstract, col 2 ln 49-52; col 4 ln 46-55; col 5 ln 42-44; col 10 Table 1; col 12 ln 31-44	1-4, 8-10, 23-24
A	US 8,071,493 B2 (Yagi) 6 December 2011 (06.12.2011) Entire document	1-4, 8-10, 23-24
A	US 6,802,894 B2 (Brodkin et al.) 12 October 2004 (12.10.2004) Entire document	1-4, 8-10, 23-24
A	US 9,745,218 B2 (James R. Glidewell Dental Ceramics, Inc.) 29 August 2017 (29.08.2017) Entire document	1-4, 8-10, 23-24
A	US 2014/0322503 A1 (3M Innovative Properties Company) 30 October 2014 (30.10.2014) Entire document	1-4, 8-10, 23-24

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 August 2021 (25.08.2021)	SEP 29 2021
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Kari Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

Form PCT/ISA/210 (second sheet) (July 2019)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 21/38174

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 5-7 ,11-22
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.