Candidate's answer

Bioactive glass compositions

Field of invention

The present invention relates to glass compositions. More specifically, it relates to bioactive glass compositions.

Background

Since the early seventies of the previous century, research has been done on bioactive glasses after their discovery by Larry Hench at the University of Florida.

D1 describes the use of bioactive glasses in bone treatments, for example the coating of prostheses. D1 mentions the use of the glasses in the form of pastes, usually made by mixing glass powder with a mixture of dextran and water.

D1 does not describe the use of bioactive glass compositions in any other form.

D2 discloses a glass composition similar to those described by D1, with the addition of K_2O, Al_2O_3 and in some examples B_2O_3.

However, D2 does not contain any suggestion as to the possible use of such compositions. D2 also does not indicate the form in which the glass compositions described may be formed.

When a bioactive glass is put into a human or animal body, ossification or bone formation takes place. This ossification is a rather complicated process that is not yet completely understood.

When forming bones inside the body, it is desirable for the prosthetic glass implant to degrade until it disappears completely as the bone gradually reforms. The only way to use the known glasses for prosthetic implants is to grind them to produce a powder. These powders are made into a paste with a binder and are then packed in the place where bone-growth is needed. The particles of the powder are far from uniform in size and some are too large. Large particles are not usually taken up completely in the bone structure. Furthermore, the particles of the powder are irregular in shape with dimensions ranging from a few micrometers to several hundreds of micrometers. Due to the non-uniformity of the particle sizes, most of the smallest particles are absorbed completely during the bone reconstitution process, whilst the largest particles are not

absorbed or degraded and cause undesirable glassy inclusions in the recon bone. The reconstituted bone therefore has a discontinuous structure.

Furthermore, the random arrangement of the particles of different sizes encourages the bone tissue to grow in a similarly random arrangement when, for the purposes of the mechanical strength of the bone, it is much more desirable for the tissue to be reconstituted in a regular arrangement. The bone produced using these bioactive glasses is therefore irregular in structure and not as strong as might be expected.

In certain applications, the use of a powder in a prosthetic implant is even dangerous since, on the one hand, the blood can form a mixture with the powder which constitutes a barrier against the growth of bone and, on the other hand, the powder particles may be entrained in the bloodstream and form thromboses.

Glass fibres have also been made of these compositions, but these fibres were very difficult to make and were not very well absorbed.

Summary of invention

The present invention provides a composition as defined in claim 1.

In our labs we have now discovered a glass composition that can be easily drawn into fibres of small diameters. The fibres are also very regular in size. The use of these fibres has several advantages. They can be used as bundles or other shapes in which the fibres are positioned in a certain direction. Even when cut into smaller particles, the advantage is that the particles can be much more regular in shape and particle size.

It has been found experimentally that both K_2O and Al_2O_3 can be used to make higher quality glass fibres of a bioactive glass. If these two components are used instead of some of the Na_2O, the glass can be kept in an amorphous condition when it is drawn into a filament thus preventing a crystalline ceramic from being formed. This amorphous condition then persists during the life of the filament.
The presence of K_2O in a bioactive glass is beneficial for the bioactivity. In this regard, K_2O is also interesting as a substitute for Na_2O, especially for patients suffering from hypertension.

However, one cannot continue to increase the K_2O concentration, because increasing the amount of K_2O makes the composition more soluble in water. This means that a glass composition containing too high a percentage of K_2O will soften or even be converted to a gel if it is kept under ambient conditions, due to hydrolysis of K_2O by interaction with humidity from the atmosphere. Thus, filaments of glass compositions having too high a percentage of K2O can be stored and handled, e.g. woven, only in a

perfectly dry atmosphere, but this would be quite impractical from an industrial point of view.

The undesirable effects of K_2O can be successfully compensated for by the addition of Al_2O_3 to the glass composition. However, compositions with higher amounts of Al_2O_3 have a lower reactivity with bone tissue.

It has been found that a glass composition including amounts of K_2O and Al_2O_3 within a certain ratio and within certain concentration ranges performs well under both aspects of fully preventing crystallisation of the drawn filaments and fully preserving their affinity to the bone tissues.

The composition can be formed into fibres with diameters of the order of 10-50 µm. From these fibres, different products can be made, like bundles of fibres, gauzes and nets. Furthermore, powders can be made by cutting the fibres into lengths of at most 100 µm. It is not technically possible to cut fibres to a length shorter than 10 µm.

In order to be able to draw fibres from the composition, the composition needs between 2 and 9 wt.% of the combination of K_2O and Al_2O_3. The amount of Al_2O_3 should be at least 0.5 wt.% and not more than 2.5 wt.%, based on the weight of the composition.

The small diameter of the filaments or fibres of below 50 µm is essential to ensure that they are completely absorbed. This means they are completely replaced by bone tissue.

In addition, it has been found that the *presence of B_2O_3 widens the temperature range within which the composition can be drawn into fibres without becoming crystalline to between 800°C and 1050°C. Boron oxide is useful in amount of 2 to 7 weight percent.*

Thus, a composition according to claim 2 is also provided.

The present invention also provides bundles of glass fibres, nets of glass fibres and gauzes of glass fibres as defined in claims 3, 4 and 5 respectively.

A bundle of fibres of the described composition can be used as an implant by being inserted in a bone defect with the filaments oriented in the direction in which it is envisaged that the bone tissue will grow. In this way, the mechanical strength of the bone is much higher than in the prior art.

The fabrics, particularly the nets and gauzes produced from the glass fibres of the invention, behave in the same way as the bundles of fibres as regards absorption but enable the growth of bone in several preferred directions. Thus, a net or a gauze can encourage the bone tissue to form a network similar to that of the original bone tissue.

Nets and gauzes can be used in the form of bandages for binding the broken reg... bone.

The present invention also provides a powder as defined in claim 6. As described above, the powder is formed by cutting the fibres into lengths of not more than 100 µm.

The present invention also provides a paste as described in claims 7 to 10.

A particulate product obtained by cutting the fibres and optionally made into a paste with a binder, can be implanted using known techniques. As the powder is made of uniformly sized particles, it degrades and is completely replaced by bone tissue over a period of time. A suitable binder is formed by a solution of dextran in water. The paste is made by adding the bioactive glass to this solution of dextran in water. The dextran must have an average molecular weight of 10 000 to 100 000 Daltons and be used in a concentration of 0.5 g/ml water to 2.0 g/ml water. To 1 g of such a solution about 1 g of bioactive glass is usually added, but this can be varied slightly dependent on the use. Bioactive glass can be added in amounts of 0.5 to 1.5 g per gram of dextran solution. Dextran, a branched polysaccharide, is very suitable for use in the body, since the body can absorb it in a few days.

Naturally, as already mentioned in relation to the prior art, this application is justified only if there is no danger of thrombosis, that is when there is no danger of blood clotting and/or of the entrainment of the powder particles by the blood.

The present invention also provides a prosthesis as defined in claim 11.

In preferred embodiments the prosthesis is as defined in claim 12.

The prostheses have at least a partial coating of the powder defined by claim 6.

Such a coating can, for example, be applied by plasma spraying. For example, a hip prosthesis made of titanium is coated with the glass composition. The prosthesis is more readily accepted by the surrounding bone because the glass coating eventually becomes completely replaced by bone tissue. Since the current glass fibres can be made into uniform powders, the coating can also be very uniform. This results in much better anchorage to the surrounding bone.

Since the compositions of the present invention are new and inventive, their use in therapy is claimed as defined in claim 13.

In particular, their use in the treatment of bone defects as defined in claim 14 is also claimed.

The present invention also provides a process for making the glass fibres de claim 2 (i.e., containing B_2O_3) as defined in claim 15.

(Examples omitted as per instructions to candidates).

1. A composition comprising glass fibres having a diameter of less than or equal to 50 µm, the glass comprising:

    - 40 to 55 wt.% S_1O_2;
    - 4 to 8 wt.% P_2O_5;
    - 10 to 40 wt.% CaO and/or MgO;
    - up to 30 wt.% NaO; and
    - 2 to 9 wt.% K_2O and Al_2O_3

    wherein the amount of Al_2O_3 is at least 0.5wt.% and not more than 2.5 wt.%.

2. The composition according to claim 1, wherein the glass additionally comprises from 2 to 7 wt.% B_2O_3.

3. A bundle of glass fibres formed from the glass fibres defined in claim 1.

4. A net of glass fibres formed from the glass fibres defined in claim 1.

5. A gauze of glass fibres formed from the glass fibres defined in claim 1.

6. A powder formed from the glass fibres defined in claim 1 cut into lengths not greater than 100 µm.

7. A paste formed by mixing the powder of claim 6 with a binder.

8. The paste according to claim 8, wherein the binder is a solution of dextran in water, the dextran having an average molecular weight of 10,000 to 100,000 Daltons.

9. The paste according to claim 8, wherein the dextran has a concentration of from 0.5 g/ml water to 2.0 g/ml water.

10. The paste according to either claim 8 or claim 9, comprising from 0.5 g to 1.5 g of powder per gram of dextran solution.

11. A prosthesis at least partially coated with a powder as defined in claim 6.

12. The prosthesis according to claim 11, wherein the prosthesis is a prosthesis having a root coated with the powder as defined in claim 6.

13. A composition as defined in claim 1 for use in therapy.

14. A composition as defined in claim 1 for the treatment of bone defects.

15. A process for preparing a composition as defined in claim 2, comprising drawing the glass into fibres at a temperature of from 800 to 1050 °C.

EXAMINATION COMMITTEE I

Candidate No.

Paper A (Chemistry) 2010 - Marking Sheet

Category		Maximum possible	Marks awarded	
			Marker	Marker
Independent claims	Glass Fibre	25	20	20
	Derived Products	30	26	26
	Medical Uses	15	15	15
Dependent claims		15	10	10
Description		15	12	12
Total		**100**	**83**	**83**

Examination Committee I agrees on 83 marks and recommends the following grade to the Examination Board:

☒ PASS (50-100) ☐ COMPENSABLE FAIL (45-49) ☐ FAIL (0-44)

01 July 2010

Chairman of Examination Committee I