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This paper comprises:

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LETTER FROM THE APPLICANT

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We are a small company doing research in inorganic materials. Our speciality is in the development of new glasses and ceramics. Rather unexpectedly, due to some research for a client of ours, we have entered the field of bioactive glasses.

We believe that the materials we describe in this letter may also be suitable for uses other than as bioactive materials. We are currently investigating this, but have not yet come to any conclusion. We know it is not possible to later add subject-matter to a patent application. However, we would nevertheless like you to draft claims in such a way that such products will also be covered. Please note that for financial reasons we will not pay any claim fees for this patent application.

Our research has primarily focused on bioactive glasses that can help in the formation of new bone tissue, which is very important in the field of orthopaedic surgery. This formation of new bone tissue is also known as ossification.

It is well known that stainless steel, titanium and alumina are used for prostheses or for the attachment of prostheses to the bone. These materials do not achieve bone bonding and are, therefore, prone to infection. These materials are also known as bio-inert materials. In contrast to this, bioactive glasses cannot only achieve contact with bone, but can also firmly attach to it. Several types of bioactive glasses are known, all of them based on inorganic materials containing calcium and phosphates.

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

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. We also believe this is not relevant for drafting the application.

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 reconstituted 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.

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.

A standard bioactive glass known in the art has the following composition:

Component	Amount (weight)
SiO_2	40-55%
P_2O_5	4-8%
CaO and/or MgO	10-40%
Na_2O	up to 30%

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 K_2O 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.

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

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 region of a bone.

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.

Preferably, however, a powder made from the glass composition according to the invention is intended to be applied as a coating to a permanent prosthesis. 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.

The composition can also be used to make implants for dental surgery. A very useful dental application is to coat the root of a dental implant with the composition.

We have performed the following experiments:

Examples

To show the benefits of our compositions, we have performed a large number of tests. In these tests three different compositions are used. We have also repeated some of the tests with prior art compositions.

If possible the compositions were formed into fibres. This was possible with all of our compositions, but good fibres could not be formed from the prior art compositions. Machines for drawing such fibres are very well known and can be bought commercially. They only need to be suitable for drawing fibres with the small diameters required. This can be seen from the specification of the machine. In our tests we have used a Glassfiber2000®.

The fibres were made into bundles, nets and gauzes. The fibres were also cut into particles. These particles were put into a paste using a binder consisting of equal amounts of dextran and water.

	Composition 1	Composition 2	Composition 3
SiO_2	46%	50%	54%
P_2O_5	7%	6%	5%
CaO	19%	16%	15%
Na_2O	20%	15%	19%
K_2O	3%	5%	1%
MgO	3%	2%	4%
Al_2O_3	2%	1%	2%
B_2O_3	-	5%	-

The following comparative compositions were made:

	Comparative Composition C1	Comparative Composition C2
SiO_2	46%	54%
P_2O_5	7%	5%
CaO	19%	15%
Na_2O	25%	22%
K_2O	-	-
MgO	3%	4%
Al_2O_3	-	-
B_2O_3	-	-

From Compositions 1 and 3, fibres of 15 μm diameter were formed at a temperature of 900°C.

In composition 2 some boron oxide (B_2O_3) is present. 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. Fibres of 20 μm diameter were drawn.

As already mentioned above, the comparative compositions were not suitable for forming good fibres. It was only possible to process these compositions into a rather irregular powder.

Example 1

In a first test, the fibres were cut into small particles. These particles were mixed with a binder to form a paste. The powders of the comparative mixtures were mixed with the same binder to make a similar paste.

Tests have been carried out on rats and rabbits using these pastes. X-ray microanalysis was carried out on the bones prior to insertion and directly after insertion.

During 4 months, the portions of bone concerned were regularly checked by X-ray microanalysis.

The following table shows the results of these tests. In this table we show the bone index for the several bones. The bone index is an index that we have devised that takes into account several properties of the growing bone. It takes into account the amount of growth, the taking up of the glass phase in the bone etc. When the material has completely converted to bone material, the index is 10. When the bone index is 8 or higher, the new bone is very good and strong.

	Composition 1	Composition 2	Composition 3	Comparative Composition C1	Comparative Composition C2
7 days	1	1	1	1	1
14 days	3	4	4	2	1
28 days	5	6	5	3	2
56 days	8	9	8	4	4
112 days	9	9	9	4	5

Example 2

This example tests the suitability of the compositions in dental applications. The root of dental implant was coated with cut fibres of Composition 3. The coating was applied using plasma spraying. For comparison, dental implants were made using Comparative Composition C2.

The implants were tested on a group of volunteers in a dental clinic specialising in dental implants. Also, non-coated implants were tested. The patients were checked twice with X-ray microanalysis. The bone index was determined as described in example 1. The results can be seen in the following table:

	Composition 3	Comparative Composition C2	No Coating
1 month	6	3	1
4 months	9	5	3

As can be seen from this table, the dental implant is taken up very well in the jaw. The new composition exhibits a clear advantage over the comparative coating composition and has the advantage that there is less chance that the implant will be lost by the patient.

Example 3

In a third test, hip prostheses were coated with cut fibres of Compositions 1 and 2 and particles of Comparative Composition C1. These prostheses were implanted in volunteers who required hip prosthesis. Again, X-ray examination was used to determine the effect of the coatings. It was clear from this X-ray examination that, when using Compositions 1 and 2 much better adhesion was obtained than when using Comparative Composition C1 (prior art).

The current letter describes only three compositions that were tested for their bioactivity. We made many more different compositions within the limits that we have described and that could all easily be formed into fibres. However, for financial reasons, it was impossible to test these compositions for their bioactivity. However, it is believed that these compositions will have similar bioactivity to the compositions of the examples.

DOCUMENT D1

Bioactive glasses were discovered by Larry Hench at the University of Florida. Since then, much research has been performed to make these glasses suitable for bone treatments.

These glasses have turned out to be useful in quite a number of applications. The first application is the coating of prostheses. Especially, the coating of hip and knee prostheses has found major application in routine surgery. The result of using these coated prostheses is that less and less of them are rejected by the body. Another type of prosthesis that has been greatly improved by these bioactive glasses is a dental implant. The root to be implanted in the jaw is also coated with the bioactive glass. Further in this case, better fixation of the implant is obtained. The compositions used for dental application usually contain a fluorine compound, for example calcium fluoride.

Most glass compositions that have been used in the literature fall within the following ranges:

Component	Amount (weight)
SiO_2	40-55%
P_2O_5	4-8%
CaO and/or MgO	10-40%
Na_2O	up to 30%

Often, these bioactive glasses will be used in the form of a paste. Such pastes are usually made by mixing the bioactive glass powder with a mixture of dextran and water. The dextran should have an average molecular weight of 10 000 to 100 000 Daltons. The dextran should be used in a concentration of 1 g/ml water. To 1 g of such a solution about 1 g of bioactive glass is usually added.

DOCUMENT D2

GLASS TIMES

In our bimonthly feature on surprising glass compositions we have an entry from Washington State, USA. Dr. William I. Neglas has made the following glass compositions:

	Composition 1	Composition 2	Composition 3
SiO_2	46%	50%	54%
P_2O_5	7%	6%	5%
CaO	19%	16%	15%
Na_2O	20%	15%	19%
K_2O	3%	5%	1%
MgO	3%	2%	4%
Al_2O_3	2%	1%	2%
B_2O_3	-	5%	-

Dr. Neglas reports that he was able to make a nice glass from these compositions and he is currently experimenting with compositions around compositions 1 to 3. He does not know anything about possible applications of these glass compositions. Anyone who finds any useful application for these interesting compositions can e-mail us at surprising@glasstimes.com.

As usual, the most interesting idea will be rewarded with a set of 6 wine glasses.