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(54) Title: IMPLANT COATING

(57) Abstract: A coating for application to an orthopaedic implant to deliver a pharmaceutical composition. The coating comprises a polymeric matrix which acts as a carrier for the pharmaceutical composition. The matrix is formed from a polymer of at least one hydrophilic substituted or unsubstituted vinyl carbonyl monomer and at least one linking agent which has first and second reactive groups which can react with the vinyl carbonyl monomer so as to link them, spaced by from 3 to 30 repeating units whose chain length is from 2 to 10 atoms. The vinyl carbonyl monomer is present in an amount of from 20% to 90% by volume of the combined volume of the vinyl carbonyl monomer and the linking agent. The matrix also includes a particulate filler which is present in an amount of at least 3% by weight of the total weight of the matrix.

IMPLANT COATING

The present invention relates to a coating for application to an orthopaedic implant to deliver a pharmaceutical composition.

Orthopaedic implants can be used in elective surgery such as for example in joint replacement surgery, and in trauma surgery such as for example to repair a fracture. During surgery, an orthopaedic implant is inserted into an intramedullary cavity of the bone. An implant coating can be applied to the orthopaedic implant prior to insertion of the implant. The implant coating can be used to administer a pharmaceutical composition to the operative site. For example, the implant coating can contain antibiotics, analgesics, bone regenerating drugs, antimicrobials or antiseptics. During insertion of the coated orthopaedic implant, the implant coating will experience a number of adverse physical forces, including for example flexion and abrasion forces. Furthermore, movement of the bone relative to the implant will subject the implant coating to further flexion and abrasion forces. The implant coating must therefore have sufficient flexural properties, rigidity and wear resistance in order to withstand the adverse physical forces.

US-2002/0115985 discloses a system for treating infection in which an orthopaedic implant is coated with a drug delivery conforming film. Known drug delivery films for coating implants can lack sufficient rigidity and flexural properties that are required for the coatings to be suitable for long term implantation. Furthermore, the known drug delivery films for coating implants do not provide any control over the rate of elution of the drug from the film.

The present invention provides a coating for application to an orthopaedic implant to deliver a pharmaceutical composition, comprising a polymeric matrix which acts as a carrier for the pharmaceutical composition in which the polymeric matrix has the desired combination of flexural properties, rigidity, elution properties of the pharmaceutical composition and wear resistance.

CONFIRMATION COPY

Accordingly, in one aspect, the invention provides a coating for application to an orthopaedic implant to deliver a pharmaceutical composition, which comprises a polymeric matrix which acts as a carrier for the pharmaceutical composition and which comprises:

a. a polymer of at least one hydrophilic substituted or unsubstituted vinyl carbonyl monomer,

b. at least one linking agent which has first and second reactive groups which can react with the vinyl carbonyl monomer so as to link them, spaced by an average number of from 3 to 30 repeating units whose average chain length is from 2 to 10 atoms,

in which the vinyl carbonyl monomer is present in an amount of from 20% to 90% by volume of the combined volume of the vinyl carbonyl monomer and the linking agent, and

c. a particulate filler which is present in an amount of at least 3% by weight of the total weight of the matrix.

The hydrophilic linking agent forms a link between a first polymer chain of the vinyl carbonyl monomer and a second polymer chain of the vinyl carbonyl monomer. The first and second polymer chains can be separate polymer chains or separate sections of the same polymer chain. The chain length of the linking agent is the length of the hydrophilic linking agent which extends between the first and second polymer chains.

The chain length of the linking agent can be defined in terms of the average number of repeating units which form the chains of the linking agent. The average number of repeating units is equal to the total number of repeating units of the linking agent within the coating divided by the number of chains formed by the linking agent. The term "repeating unit" is used to refer to the smallest unit of the linking agent which is repeated along the chain of the linking agent. The linking agent can be a homopolymer containing a single type of repeating unit. Alternatively, the linking agent can be a copolymer containing a plurality of different types of repeating units in each chain. The "average number of repeating units" is therefore used to refer to the average of the total number of the one or more types of repeating units which form the chains of the linking agent.

The term "average chain length" of the repeating unit is used to refer to the average number of atoms within the one or more types of repeating unit which, when connected to other repeating units form the backbone of the chain of the linking agents.

It has been found that a number of properties of the coating, such as for example swellability, drug elution, rigidity and flexural properties, are effected by the chain length of the linking agent. The present invention therefore provides a coating having optimum properties for use as an implant coating.

The hydrophilic linking agent advantageously helps to control the rate of elution of the pharmaceutical composition from the polymeric matrix. It has been found that the degree of swelling of the polymeric matrix is directly related to the rate of elution of the pharmaceutical composition from the matrix. The chain length of the linking agent can effect the degree of swelling of the polymeric matrix and therefore effect the rate of elution of the pharmaceutical composition from the matrix. The degree of swelling of a polymeric matrix can be determined from the water uptake profile of the matrix.

As the polymer matrix swells the size of the pores provided by the polymer matrix increases. The rate of elution of a pharmaceutical composition from the polymeric matrix of a coating of the present invention can therefore increase as the size of the pores of the polymeric matrix increase. The degree of swelling, and therefore the size of pores provided by the polymer matrix, will depend on the chain length of the linking agent. For example, a polymeric matrix which includes a linking agent having a short chain length will restrict the degree of swelling of the matrix to a greater degree than a polymeric matrix which includes a linking agent which has a longer chain length. The polymeric matrix which includes a linking agent which has a longer chain length will therefore swell to provide larger pores than the polymeric matrix which includes a linking agent having a short chain length. The pharmaceutical composition will therefore be released through the pores of the matrix at a greater rate from a polymeric matrix which includes a linking agent having a long chain length than from a polymeric matrix which includes a linking agent which has a shorter chain length.

When the matrix of the coating of the invention includes a linking agent having a chain length of greater than a maximum limit, the matrix will be able to swell significantly and the pharmaceutical composition will be rapidly released from the matrix. In contrast, when the matrix of the coating of the invention includes a linking agent having a chain length of less than a minimum limit, the matrix will be unable to swell and the pore sizes of the matrix will be too small to enable the pharmaceutical composition to be released from the matrix. The coating of the present invention will therefore have optimum pharmaceutical composition elution properties when the chain length of the linking agent is within an optimum range.

During use, it is likely that the implant coating will be subjected to a number of adverse physical forces, including for example flexion and abrasion forces. It is therefore important that the coating has sufficient rigidity, flexural properties and wear resistance to withstand these stresses.

The rigidity of the polymeric matrix can be controlled by varying the chain length of the linking agent. As the chain length of the linking agent increases the first and second polymer chains which are attached to the linking agent have increased freedom to move relative to each other. The rigidity of the polymeric matrix can therefore decrease as the chain length of the linking agent increases. In order to provide a coating which has sufficient rigidity for use as an implant coating, the polymeric matrix should include a linking agent having a chain length below a maximum limit.

The coating of the present invention must also have sufficient flexural properties, such as the flexural strength and flexural modulus so that the coating does not tear or break during use as an implant coating. The chain length of the linking agent can effect the flexural strength and flexural modulus of the coating. In particular, when the chain length of the linking agent is below a minimum limit the first and second polymer chains which are attached to the linking agent have reduced freedom to move relative to each other. The coating can therefore become brittle if the polymeric matrix includes linking agents which have a chain length below a minimum limit. These coatings would not be suitable for use as implant coatings.

In order to provide coatings for use as an implant coating having optimum flexural properties, rigidity and controlled rate of elution of the pharmaceutical composition the coatings of the present invention have a polymeric matrix which comprises a linking agent having a chain length within a preferred range.

In order to provide a coating having the optimum properties, the maximum percentage of linking agent by volume that can be present in the polymeric matrix is no more than about 80%, preferably no more than about 70%, for example 60%. Coatings which have a matrix comprising greater than 80% by volume of a linking agent have been found to have poor flexural properties and can be brittle. These coatings are therefore not suitable as implant coatings.

The minimum percentage of linking agent by volume that can be present in the matrix of the coatings of the present invention is at least about 10%, preferably at least about 20%, more preferably at least about 30%, for example at least about 40% or at least about 50%. Coatings which have a polymeric matrix which comprise less than 10% by volume of a linking agent can be brittle and have poor rigidity. Furthermore, coatings which have a polymeric matrix with a relatively small amount of a linking agent can have poor drug elution properties and release the drug too quickly from the matrix.

The linking agent of the coating of the present invention can have an average number of less than 30 repeating units, preferably less than 25 repeating units, for example 20 repeating units. Preferably, the linking agent has an average number of more than 3 repeating units, preferably more than 5 repeating units, for example 10 repeating units.

The average chain length of the repeating unit of the linking agent is preferably at least 2 atoms, more preferably at least 3 atoms, for example 4 atoms. The average chain length of the repeating unit of the linking agent is preferably no more than 10 atoms, more preferably no more than 8 atoms, for example 6 atoms.

Coatings which have a polymeric matrix which comprises a linking agent which has less than 3 repeating units and/or has repeating units which have an average chain length of less

than two atoms can be rigid and/or have poor swellability characteristics. These coatings can therefore exhibit poor drug elution properties. These coatings are therefore not suitable as implant coatings.

Coatings which have a polymeric matrix which comprises a linking agent having more than 30 repeating units and/or includes repeating units which have an average chain length of more than ten atoms can have poor rigidity and control of the rate of elution of the pharmaceutical composition from the matrix. These coatings are therefore unsuitable as implant coatings.

The coating of the present invention is preferably able to withstand repeated wear due to localised stresses. The particulate filler preferably improves the wear resistance of the coating. The particle size and concentration of the particulate filler can effect the wear resistance of the coating. In order to have sufficient resistance to wear, the coating of the present invention can contain at least about 3%, preferably at least about 4%, for example at least about 5% by weight of a particulate filler. The wear resistance of the coating can however be increased by including more than about 10% by weight of the particulate filler. The coating of the present invention can contain not more than about 10%, preferably not more than about 8%, for example not more than about 7% by weight of a particulate filler.

The coating preferably contains a particulate filler having an average particle size of at least about 0.1 μm, preferably at least about 0.2 μm, for example about 0.5 μm. The coating preferably contains a particulate filler having an average particle size of less than about 20 μm, preferably less than about 10 μm, for example about 1 μm. Average particle size is used to refer to the average particle diameter. When the particles of the particulate filler are generally round but not necessarily circular, an estimate of their diameters might be made by measuring the maximum diameter and the minimum diameter, and calculating the mean of the two. It will be appreciated that it will usually be preferable to employ the same measurement and/or estimation technique to derive the diameters of the particles in a sample in order to minimise errors.

The linking agent can include a single linking agent or a mixture of a plurality of different linking agents. The linking agent is formed by the polymerization of monomer units. Each monomer unit preferably comprises two or more polymerisable groups which are each capable of reacting with a polymerisable group of another monomer unit to form the repeating units of the linking agent. The linking agent is preferably formed by the polymerization of one or more different hydrophilic polyvinyl monomers. Preferably, the linking agent is formed from one or more hydrophilic monomers comprising at least one polymerisable group selected from carboxylic acids, carboxylic amides, alcohols, amides, amines and allyl groups. Preferably, the at least one polymerisable group is selected from acrylic acid or methacrylate.

Suitable hydrophilic linking agents for use with the coating of the present invention include methacrylates such as ethylene glycol dimethacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, tetraethylene glycol dimethacrylate, polyethylene glycol dimethacrylates, 1,3-butanediol dimethacrylate, 1,4-butanediol dimethacrylate, glycerol dimethacrylate, glycerol dimethacrylate and trimethylolpropane trimethyacrylate.

Preferably, the polymeric matrix includes a linking agent comprising polyethylene glycol dimethacrylate having a number average molecular weight in the range of at least 300 $g.mol^{-1}$, more preferably at least about 400 $g.mol^{-1}$, for example 500 $g.mol^{-1}$. Preferably, the polymeric matrix includes polyethylene glycol dimethacrylate having a number average molecular weight of not more than about 1000 $g.mol^{-1}$, for example not more than about 900 $g.mol^{-1}$, for example not more than about 800 $g.mol^{-1}$.

More preferably, the polymeric matrix includes a linking agent comprising polyethylene glycol dimethacrylate having a number average molecular weight of 330, 550 or 875 $g.mol^{-1}$. Coatings having a polymeric matrix which includes a linking agent comprising polyethylene glycol dimethacrylate having a number average molecular weight of 330, 550 or 875 $g.mol^{-1}$ as a linking agent have been found to have improved rigidity, flexural properties and swellability of the polymeric matrix.

The vinyl carbonyl monomer of the coating of the present invention can include methyl methacrylate monomers, methacrylate monomers, hydroxyester acrylates, aminofunctional methacrylate monomers, methacrylamides and ethermethyacrylate

Examples of methacrylate monomers include methyl methacrylate, ethyl methacrylate, butyl methacrylate, hexyl methacrylate, 2-ethylhexyl methacrylate and methacrylic acid.

Examples of methacrylate monomers include 2-hydroxyethyl methacrylate, hydroxypropyl methacrylate and tetrahydrofurfuryl methacrylate.

Examples of hydroxyester acrylates include 2-hydroxyethyl acrylate and hydroxypropyl acrylate.

Examples of aminofunctional methacrylate monomers include 2-dimethylaminoethyl methacrylate, 3-dimethylaminopropyl methacrylamide, 2-trimethylammonioethyl methacrylate chloride, 3-trimethylammoniopropyl methacrylamide chloride, 2-ter. butylaminoethyl methacrylate and diethylaminoethyl methacrylate.

Examples of methacrylamides include methacrylamide and N-methyl methacrylamide.

Examples of ethermethacrylate include ethyltriglycol methacrylate and methoxypolyethylene glycol-methacrylate.

Examples of particulate fillers include glass particles, metal oxide particles such as alumina, polymer particles such as polyamide and UHMWPE, and inorganic fillers such as nano silica particles and clay.

The coating preferably comprises a polymeric matrix including 2-hydroxyethyl methacrylate monomer (HEMA) as the vinyl carbonyl monomer and polyethylene glycol dimethacrylate (PEGDMA) as the linking agent.

The coating can include one or more pharmaceutical composition selected from antibiotics, analgesics, bone regenerating drugs, antimicrobials and antiseptics. The pharmaceutical composition is preferably present within the polymeric matrix at a concentration of at least about 0.5%, preferably at least about 2%, for example at least about 3% by volume of the combined volume of the vinyl carbonyl monomer, the linking agent and the pharmaceutical composition. The pharmaceutical composition is preferably present within the polymeric matrix at a concentration of no more than about 10%, preferably not more than about 8%, for example not more than about 5%, by volume of the combined volume of the vinyl carbonyl monomer, the linking agent and the pharmaceutical composition.

The coating can be applied to an orthopaedic implant for use in a surgical procedure, such as joint replacement or fracture treatment. The coating can be applied over the whole length of the implant. The coating can be applied over the whole of the outer surface of the implant. The coating can be applied to the implant so as to cover a selected area of the outer surface of the implant. The coating can be positioned on the implant so that when the implant is positioned within the intramedullary cavity of the bone, the coating is positioned adjacent to the area of the bone which is to be treated with the pharmaceutical composition. The coating can be applied to a sheath which is dimensioned and configured to receive at least a part of the implant. The sheath can be positioned on the implant so that on implantation the sheath is adjacent to the area of the bone which is to be treated with the pharmaceutical composition.

The thickness of the coating will depend on a number of factors including the separation between the bone and the implant, the required rate of elution of the pharmaceutical composition from the coating and the amount of pharmaceutical composition present within the coating. The coating preferably has a minimum thickness of at least about 0.1 mm, preferably at least about 0.2 mm, for example at least about 0.3 mm. The coating preferably has a thickness of not more than about 2 mm, preferably not more than about 1 mm, for example not more than about 0.5 mm.

Orthopaedic implants to which the invention is applicable can include the components of joint protheses having a stem which can be positioned inside an intramedullary cavity. For

example, the implant might be the femoral component of a hip joint prosthesis or the humeral component of a shoulder joint prosthesis. It might by the tibial component of a knee joint prosthesis. Then the implant has a stem, the coating can be applied to the stem. The coating can be applied to other surfaces of such an implant. For example, it can be applied to the surface of the implant which sits against the surface of the resected bone. The implant to which the implant of the invention can be one which does not have a stem which can be positioned inside the intramedullary cavity of a bone. For example, the implant might be an acetabular cup component of a hip joint prosthesis, or it might be the femoral component of a knee joint prosthesis.

The implant of the invention might be for use in a trauma application, for example in the treatment of a fracture. Such an implant might include a nail which is positioned in the intramedullary cavity to bridge the fracture site.

EXAMPLES

Tables 1, 2 and 3 illustrate various properties such as the flexural strength (MPa), the flexural modulus (MPa), water uptake properties and wear testing of three coatings of the present invention comprising a polymeric matrix including 2-hydroxyethyl methacrylate as the vinyl carbonyl monomer and varying percentages (by volume) of PEGDMA 330, PEGDMA 550 and PEGDMA 875 as the linking agents. The percentages given are percentages of the total monomer concentration. PEGDMA 330 has approximately 4 repeating units. PEGDMA 550 has approximately 9 repeating units. PEGDMA 875 has approximately 16 repeating units.

Flexural strength and flexural modulus

Bending tests were carried out on samples of the coatings using an Instron 5544 mechanical tester to determine the flexural strength and the flexural modulus of the coatings. Cylindrical samples of the coatings were used having a length of 5 cm and an average diameter of 0.5 cm. The Instron 5544 mechanical tester was fitted with a 3-point bend test rig having a cross-head speed of 5 $mm.min^{-1} \pm 1$ $mm.min^{-1}$. The Instron 5544

mechanical tester was equipped with a device for measuring and recording the deflection of the centre of the specimen to an accuracy of ±0.05 mm.

The flexural strength is equal to the maximum strength of the sample material in bending. The flexural strength can be expressed as the tensile stress of the outermost region of the bent sample at the instant of failure of the sample. The flexural modulus is the ratio, within the elastic limit, of the applied stress on a sample in flexure, to the corresponding strain in the outermost region of the sample.

Table 1 illustrates the flexural strength (MPa) of three coating samples of the present invention.

% Linking agent	PEGDMA 330	PEGDMA 550	PEGDMA 875
0	304	304	304
10	338	323	132
32	361	198	155
52	334	132	11
76	262	18	7
100	228	17	9

An implant coating should preferably have a flexural strength of at least about 100 MPa. Table 1 shows that coating having a polymeric matrix comprising up to 32% of PEGDMA 875 as the linking agent have a flexural strength of at least 155 MPa and therefore has sufficient flexural strength to be used as an implant coating. Coatings having a polymeric matrix comprising at least 52% of PEGDMA 875 have a flexural strength of up to 11 MPa and are therefore not suitable for use as an implant coating.

Table 1 also illustrates that coatings having a polymeric matrix comprising up to 52% of PEGDMA 550 as the linking agent have a flexural strength of at least 132 MPa and therefore have sufficient flexural strengths to be used as an implant coating. Coatings

having a polymeric matrix comprising at least 76% of PEGDMA 875 have a flexural strength of up to 18 MPa and are therefore not suitable for use as an implant coating.

Table 1 also illustrates that coatings having a polymeric matrix comprising up to 100% of PEGDMA 330 as the linking agent have a flexural strength of at least 228 MPa and therefore have sufficient flexural strengths to be used as an implant coating.

From these results, it appears that on average a coating of the present invention having PEGDMA as a linking agent should have sufficient flexural strength to be used as an implant coating provided the polymeric matrix comprises less than about 80% of the linking agent by volume.

Table 2 illustrates the flexural modulus (MPa) of three coatings of the present invention.

% Linking agent	PEGDMA 330	PEGDMA 550	PEGDMA 875
0	33849	33849	33849
10	29427	22800	20930
32	24959	17320	13054
52	22841	11754	390
76	15728	538	201
100	13937	452	266

An implant coating should have a flexural modulus of at least 10000 MPa. Table 2 illustrates that coatings having a polymeric matrix comprising up to 32% of PEGDMA 875 as the linking agent have flexural moduli of at least 13054 MPa and therefore have sufficiently high flexural moduli to be used as implant coatings. The flexural moduli of coatings having a polymeric matrix comprising at least 52% of PEGDMA 875 are however too low (less than or equal to 390 MPa) for the coatings to be useful as implant coatings.

Table 2 also shows that coatings having a polymeric matrix comprising up to 52% of PEGDMA 550 as the linking agent have flexural moduli of at least 11754 MPa and therefore have sufficiently high flexural moduli to be used as implant coatings. The flexural moduli of coatings having a polymeric matrix comprising at least 76% of PEGDMA 550 are however too low (538 MPa) for these coatings to be useful as implant coatings.

Table 2 also illustrates that coatings having a polymeric matrix comprising up to 100% of PEGDMA 330 as the linking agent have flexural moduli of at least 13937 MPa and therefore have sufficiently high flexural moduli to be used as implant coatings.

From these results, it appears that on average a coating of the present invention having PEGDMA as a linking agent should have a sufficiently high flexural modulus to be used as an implant coating provided the polymeric matrix comprises less than about 80% of the linking agent.

Water Uptake Data

The water uptake of samples of the coatings were determined. The samples were disk-shaped having a diameter of about 2.5 cm and a thickness of about 1.5 mm. Each sample was placed in a plastic jar containing distilled water at a temperature of 37°C. The jars were then placed in an oven at 37°C. After a pre-determined amount of time, the disks were removed from the solution and blotted dry with a paper towel. Each sample was weighed to the nearest 0.0001 g and returned to the solution.

The samples were each weighed after time periods of 5, 10, 20, 40 and 60 minutes from immersion of the sample in the distilled water. The samples were then each weighed hourly for a over a period of at least four hours. Each sample was then weighed twice a day after being immersed in the distilled water between 24 hours and 96 hours. After 96 hours, the samples were each weighed once a day for a minimum of one day a week.

The percentage of swelling, S, of the sample was calculated using the following equation:

$$S = \left(\frac{M_t - M_o}{M_o} \right) \times 100$$

where M_0 is the initial dry weight and M_t is the weight of the swollen gel at time t. S is presented as a function of time.

Once the weight of the sample reached an equilibrium and no significant changes in sample weight were recorded the study ended.

The results given relate to the percentage water uptake of the coatings of the present invention.

% Linking agent	PEGDMA 330	PEGDMA 550	PEGDMA 875
0	55.6	55.6	55.6
10	30	46.7	45
32	22.5	46.4	35.9
52	18.7	45	32.2
76	10.7	50.845	27.3
100	2.5	40.3	32.8

It has been found that coatings having water uptake properties of less than 20% have very slow drug elution profiles. Therefore, coatings which can be used as implant coatings should have water uptake properties of at least 20%. Table 3 illustrates that coatings comprising a polymeric matrix having up to 100% PEGDMA 875 have water uptake properties of at least 27.3%. Therefore, these coatings have suitable water uptake properties to be used as implant coatings.

Table 3 also illustrates that coatings comprising a polymeric matrix having up to 100% PEGDMA 550 have water uptake properties of at least 40.3%. Therefore, these coatings have suitable water uptake properties to be used as implant coatings.

Table 3 also shows that coatings having a polymeric matrix comprising up to 32% of PEGDMA 330 as the linking agent have a water uptake property of at least 22.5% and therefore have suitable water uptake properties for use as implant coatings. Table 3 does however show that coatings having at least 52% of PEGDMA 330 as the linking agent have water uptake properties of less than 20% and are therefore unsuitable as implant coatings.

On average it appears that coatings of the present invention having up to 80% PEGDMA as the linking agent have suitable water uptake properties for use as implant coatings.

Wear Testing

Cylindrical samples of the coatings were tested. The cylindrical samples had an average diameter of 2 cm and a length of 1.5 cm. The wear testing of the samples was determined using an Elcometer (trade mark) wear testing equipment model 1720 machine. The samples were mounted on the support rig. The samples were repeatedly contacted with and moved along an abrasive surface. The abrasive surface was fine sand paper, grade P1200 from Norton. The samples were tested after being contacted with the abrasive material for 2000 cycles at a speed of 37 cycles per minute on a track length of about 27 cm. The water flow rate was about 8 ml per minute.

The sample wear was calculated using the following equation:

$$Wear = M_o - M_t$$

where M_0 is the initial weight of the sample and M_t is the final dry weight of the sample.

Figures 1 and 2 illustrate the weight loss of coatings of the present invention which include 0%, 5% or 10% by weight of a particulate filler when subjected to 2000 cycles of repeated

wearing. Figure 1 illustrates the weight loss of coatings of the present invention having a polymeric matrix which includes 10% by volume of linking agent. Figure 2 illustrates the weight loss of coatings of the present invention having a polymeric matrix which includes 32% by volume of linking agent. The general trend that can be seen from these diagrams is that the weight loss of the coatings is significantly reduced when a particulate filler is included in the coating. Figure 1 however shows that for coatings comprising 10% PEGDMA 330 there is an optimum range for the amount of particulate filler present within the coating. The weight loss for a coating comprising 10% PEGDMA 330 and 10% silicate is approximately equal to the weight loss for a coating which does not include the particulate filler. By extrapolating the data, the optimum range for the amount of particulate filler present within a coating comprising 10% PEGDMA appears to be between about 3 and 8% by weight.

Elution Properties

Figure 3 illustrates the relationship between the percentage release of the pharmaceutical composition (sodium fusidate) from the polymeric matrix of the coating over time and the percentage of linking agent present in the matrix.

In order for the coatings to be able to provide sustained release of the pharmaceutical composition, it is preferable that the coating does not release more than about 50% of the pharmaceutical composition from the polymeric matrix within the first 50 days of immersion of the sample within the solution. It is also preferable that the coating does not release more than about 60% of the pharmaceutical composition within 150 days of immersion of the sample within the solution.

Figure 3 illustrates that samples of the coatings comprising a polymeric matrix without a linking agent release over 70% of the pharmaceutical composition within 50 days of immersion of the sample in solution. The pharmaceutical composition is therefore released from the coatings too quickly for the coatings to be suitable for use with an orthopaedic implant. Coatings which do not include a polymeric matrix having a linking agent are therefore unable to provide sustained release of the pharmaceutical composition over time.

Figure 3 also illustrates that coatings having at least 10% linking agent have suitable pharmaceutical composition release profiles for use as coatings for orthopaedic implants. Coatings comprising a polymeric matrix having 10% linking agent release less than 50% of the pharmaceutical composition within the first 50 days of immersion of the coating within the solution. Furthermore, coatings comprising a polymeric matrix having 10% linking agent release less than 60% of the pharmaceutical composition within 150 days of immersion of the coating within the solution. Coatings comprising a polymeric matrix having 10% linking agent therefore have suitable elution properties for use with an implant coating. These coatings are therefore able to provide sustained release of the pharmaceutical composition over time.

Figure 3 also illustrates that as the percentage of linking agent present in the polymeric matrix increases the rate of elution of the pharmaceutical composition decreases. Figure 3 shows that coatings comprising a polymeric matrix having 32% linking agent release less than 20% of the pharmaceutical composition within the first 50 days of immersion of the coating within the solution. Furthermore, coatings comprising a polymeric matrix having 32% linking agent release less than 30% of the pharmaceutical composition within 150 days of immersion of the coating within the solution. It therefore appears that the rate of release of the pharmaceutical composition from the polymeric matrix can decrease as the percentage of linking agent in the matrix increases.

CLAIMS:

1. A coating for application to an orthopaedic implant to deliver a pharmaceutical composition, which comprises a polymeric matrix which acts as a carrier for the pharmaceutical composition and which comprises:

a. a polymer of at least one hydrophilic substituted or unsubstituted vinyl carbonyl monomer,

b. at least one linking agent which has first and second reactive groups which can react with the vinyl carbonyl monomer so as to link them, spaced by from 3 to 30 repeating units whose chain length is from 2 to 10 atoms,

in which the vinyl carbonyl monomer is present in an amount of from 20% to 90% by volume of the combined volume of the vinyl carbonyl monomer and the linking agent, and

c. a particulate filler which is present in an amount of at least 3% by weight of the total weight of the matrix.

2. A coating as claimed in claim 1, in which the vinyl carbonyl monomer is a vinyl carboxylic acid or a salt or an ester thereof.

3. A coating as claimed in claim 2, in which the carboxylic acid comprises acrylic acid or methacrylic acid.

4. A coating as claimed in claim 1, in which the vinyl carbonyl monomer is a methacrylate.

5. A coating as claimed in claim 1, in which the particulate filler is present in an amount of not more than 10% by weight of the total weight of the matrix.

6. A coating as claimed in claim 1, in which the repeating groups in the linking agent include an ether linkage.

7. A coating as claimed in claim 1, in which at least one of the reactive groups in the linking agent is a vinyl carbonyl group.

8. A coating as claimed in claim 1, in which the polymeric matrix contains between 1 and 10% by weight of the pharmaceutical composition.

9. An orthopaedic implant coated with a coating as claimed in any one of the preceding claims.

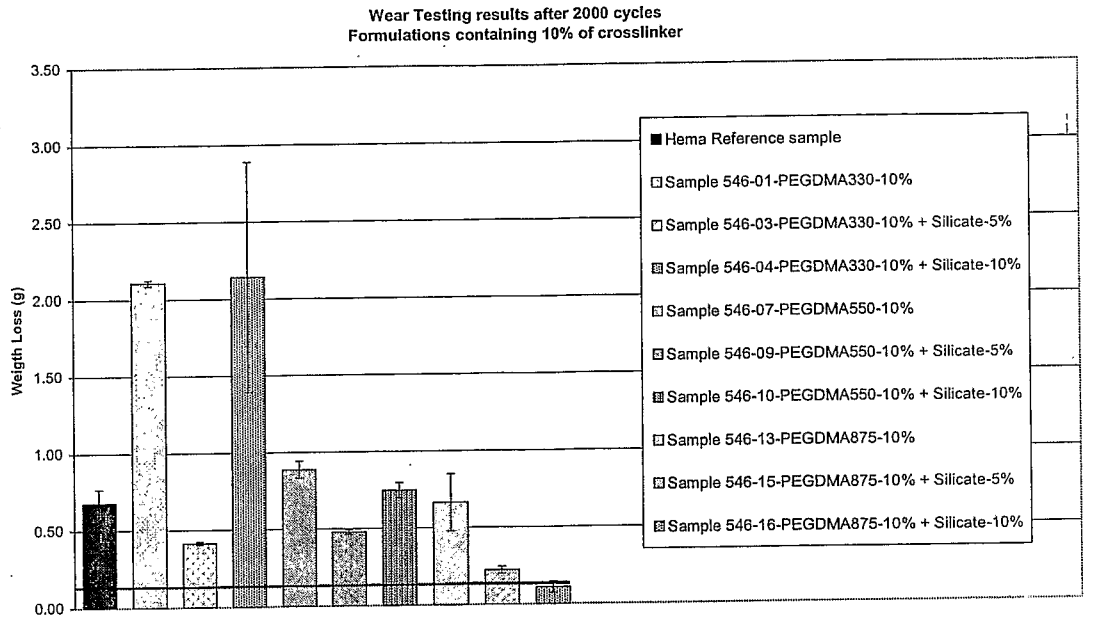

FIGURE 1

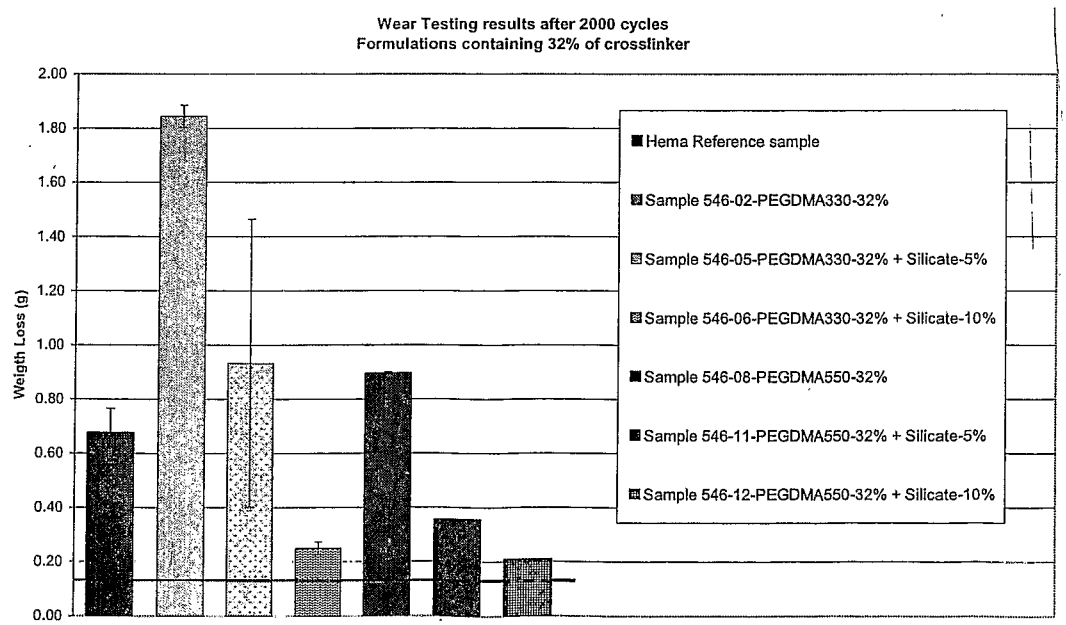

FIGURE 2

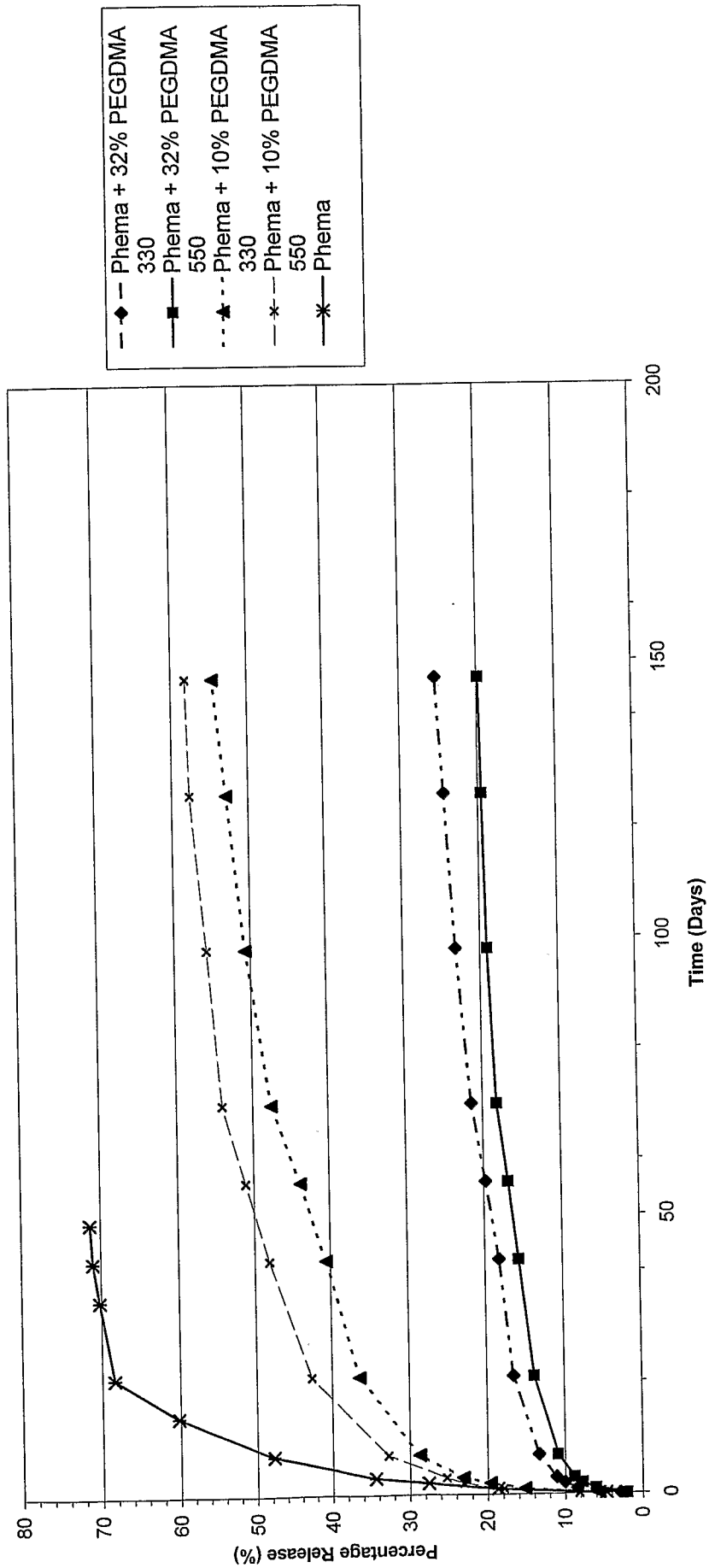
Phema + 32% PEGDMA 330
Phema + 32% PEGDMA 550
Phema + 10% PEGDMA 330
Phema + 10% PEGDMA 550
Phema
Percentage Release (%)
0
10
20
30
40
50
60
70
80
Time (Days)
0
50
100
150
200

Figure 3