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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 September 2005 (09.09.2005)

PCT

(10) International Publication Number
WO 2005/082283 A1

(51) International Patent Classification[7]: A61F 2/06

(21) International Application Number:
PCT/US2005/005630

(22) International Filing Date: 23 February 2005 (23.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/787,618 26 February 2004 (26.02.2004) US

(71) Applicant *(for all designated States except US)*: **BOSTON SCIENTIFIC SCIMED, INC.** [US/US]; Scimed Life Systems, Inc., One Scimed Place, Maple Grove, MN 55311-1566 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **COLEN, Fredericus, A.** [NL/US]; 7585 Blackoaks Lane North, Maple Grove, MN 55311 (US). **KNAPP, David** [US/US]; 640 Evergreen Circle, Shoreview, MN 55126 (US).

(74) Agent: **GAGEL, John, J.**; Fish & Richardson P.C., 225 Franklin Street, Boston, MA 02110-2804 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

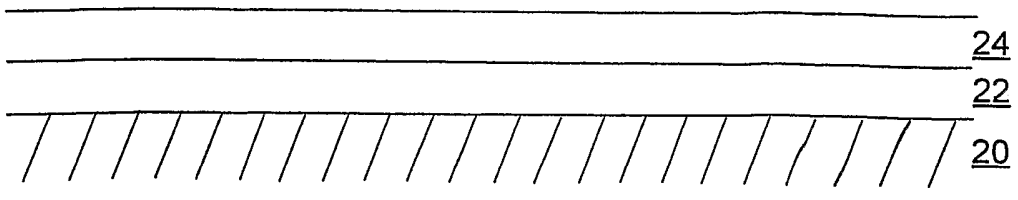
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/082283 A1

(54) Title: MEDICAL DEVICES



(57) Abstract: In some embodiments , medical devices, such as stents, can be suitable for drug delivery and can include a layer (24) of sugar, sugar derivative, inorganic ionic salt, polysaccharide, amino acid, amino acid derivative, polypeptide, surfactant, or combination thereof.

Medical Devices

TECHNICAL FIELD

This invention relates to medical devices, particularly endoprostheses.

BACKGROUND

The body includes various passageways such as arteries, other blood vessels, and other body lumens. For various treatments and diagnostic techniques, it is often desirable to deliver a medical device into these lumens. For example, these passageways sometimes become occluded or weakened. The passageways can be occluded by e.g. a tumor, restricted by plaque, or weakened by an aneurysm. When this occurs, the passageway can be reopened or reinforced, or even replaced, with a medical endoprosthesis. An endoprosthesis is typically a tubular member that is placed in a lumen in the body. Examples of endoprostheses include stents and covered stents, sometimes called "stent-grafts". An endoprosthesis can be delivered inside the body by a catheter that supports the endoprosthesis in a compacted or reduced-size form as the endoprosthesis is transported to a desired site. Upon reaching the site, the endoprosthesis is expanded, for example, so that it can contact the walls of the lumen. The expansion mechanism may include forcing the endoprosthesis to expand radially. For example, the expansion mechanism can include the catheter carrying a balloon, which carries the endoprosthesis. The balloon can be inflated to deform and to fix the expanded endoprosthesis at a predetermined position in contact with the lumen wall. The balloon can then be deflated, and the catheter removed.

In another delivery technique, the endoprosthesis is self-expanding. For example, the endoprosthesis can be formed of an elastic material that can be reversibly compacted and expanded. During introduction into the body, the endoprosthesis is restrained in a compacted condition. Upon reaching the desired implantation site, the restraint is removed, for example, by retracting a restraining device such as an outer sheath, enabling the endoprosthesis to self-expand by its own internal elastic restoring force. Another self-expansion technique uses shape memory metals which can "remember" a particular geometric configuration, e.g. an expanded condition, upon exposure to a trigger, such as an increase in temperature.

The endoprosthesis can carry a drug, such as an antiproliferative, to reduce the likelihood of restenosis, i.e., reclosure of the vessel due to immune reactions by the body at the treatment site.

SUMMARY

In one aspect, the invention features a medical stent with a generally tubular body. The medical stent also includes a therapeutic agent, and a sugar, sugar derivative, or inorganic ionic salt.

In another aspect, the invention features a stent delivery system that includes a catheter with a balloon and a medical stent device, and that has a generally tubular body, a therapeutic agent, and a sugar, sugar derivative, or inorganic ionic salt.

In another aspect, the invention features a stent delivery system that includes a catheter with a retractable sheath and a medical stent device, and that has a generally tubular body, a therapeutic agent, and a sugar, sugar derivative, or inorganic ionic salt.

In another aspect, the invention features a medical stent with a generally tubular body and a sugar, sugar derivative, or inorganic ionic salt.

In another aspect, the invention features a method of making a coated stent, the method including providing a stent, providing a therapeutic agent, and coating the stent with a layer of sugar, sugar derivative, or inorganic ionic salt.

In various aspects, the invention includes an implantable medical device (e.g., a stent) that includes an implantable body, a therapeutic agent and a sugar, sugar derivative, inorganic ionic salt, surfactant, polysaccharide, polypeptide, amino acid, amino acid derivative, or a combination thereof.

Embodiments can include one or more of the following features.

The sugar, sugar derivative, or salt can have a solubility of at least 0.14 gram/mL of water, and/or a melting point of about 47°C or more. The stent can include a sugar or a sugar derivative (e.g., sucrose, sorbose, glucosamine, mannitol). The stent can include an inorganic ionic salt (e.g., sodium chloride, potassium chloride, sodium carbonate). The stent can have a layer that includes a therapeutic agent and the sugar, sugar derivative, or salt. The stent can have a layer of sugar, sugar derivative, or salt that covers a therapeutic agent-containing reservoir. The reservoir can be a layer of therapeutic agent. The reservoir can define pores in which the

therapeutic agent can be disposed. The reservoir can include metal that is integral with the stent body. The stent can further include a second therapeutic agent that is carried by the layer, and the second therapeutic agent can be different from the therapeutic agent that is carried by the reservoir. The therapeutic agent can be an antithrombogenic, an antioxidant, an anti-inflammatory, an antiproliferative, and/or an antibiotic. The stent can be a self-expanding stent or a balloon-expandable stent. The stent can be a vascular stent. Coating can include dip coating and/or spray coating. Coating can include forming a preform layer and fixing the preform layer to the stent. The perform layer can be fixed by applying a solution of, or a liquid form of, a sugar, sugar derivative, or to the stent.

Embodiments of the invention can have one or more of the following advantages. The protective layer can prevent the therapeutic agent from being exposed to or released into the body until it has reached its target site. The layer is highly bioerodible and water-soluble, such that it rapidly dissolves when the treatment site is reached. The layer can be flexible, such that it can be moved through a tortuous lumen and expanded as the strut expands without significant fracture, flaking, or disruption. Furthermore, the protective layer is the same as, or chemically analogous to, substances that are either commonly present in the body, or that the body regards as non-foreign. As a result, the protective layer generally is not of a material type that elicits an adverse reaction by the body, such as inflammation or an autoimmune response. The layer material typically is easily metabolized. In addition, the protective layer does not adversely interact with the drug during storage or during delivery. The layer can be relatively inexpensive and readily commercially available.

Still further aspects, features, and advantages follow.

DESCRIPTION OF DRAWINGS

FIGS. 1A and 1B are perspective views of a stent in the compressed and expanded condition, respectively.

FIG. 2 is a greatly enlarged cross-section through the side wall of a stent.

FIG. 3 is a greatly enlarged cross-section through a side wall of a stent.

FIGS. 4A-4C are a schematic representation of a stent delivery.

FIGS. 5A-5C are another schematic representation of a stent delivery.

DETAILED DESCRIPTION

Referring to FIGS. 1A and 1B, a stent 10 includes a generally tubular body 12. The tubular body includes aperture regions 14 provided in a pattern to facilitate stent functions, such as radial expansion and lateral flexibility. Referring particularly to FIG. 1A, for delivery into the body, the stent 10 is provided or maintained in a relatively small diameter condition corresponding to a diameter D_c. Referring to FIG. 1B, upon delivery to the treatment site, the stent 10 is expanded to a larger diameter, D_{exp}, so that the stent is in contact with the lumen wall. The stent may be expanded by a mechanical expander, such as an inflatable balloon, or it may be self-expanding. The body of the stent may be formed by a generally continuous sheet or by filaments that are wrapped, braided, knitted or otherwise configured to generally define a stent. The stent is delivered into the body on a catheter, such as a balloon catheter. The catheter can include a retractable sheath that concentrically surrounds the stent during delivery and is retracted during employment at the treatment site. Alternatively, the stent may be exposed to the body lumen during delivery. A suitable stent design is the Express stent, available from Boston Scientific, Natick, Mass. Balloon expandable and self-expanding stents and delivery systems are further discussed in Heath, U.S. 5,725,570, the entire contents of which are incorporated herein by reference.

Referring now to FIG. 2, a cross-section through the stent side wall, the stent 10 includes a body 20 onto which are provided a drug reservoir 22 and a protective layer 24. The body 20 is formed of material capable of performing the expansion function of the stent. For example, the body 20 may be a highly elastic metal, in the case of a self-expanding stent, or a plastically deformable metal, in the case of a balloon-expandable stent. The drug reservoir 22 contains a therapeutic agent to be released in the body during use of the stent. The protective layer 24 covers the drug reservoir prior to and, if desirable, during the delivery and implantation of the stent into the body. For example, the protective layer protects the reservoir from abrasion during packaging, shipping, unpacking, and delivery. The protective layer can be removed prior to delivery into the body. Alternatively, the protective layer can also protect the reservoir from premature exposure to body fluid during delivery.

The protective layer can be made of a sugar, a sugar derivative, a simple inorganic ionic salt, or a combination thereof. These material(s) are chemically the same as, or analogous to, substances that are commonly present in the body and material types that typically do not cause

adverse reactions, such as inflammation, or that do not interact adversely with the drug or reservoir. The protective layer preferably erodes at a relatively rapid rate, so that the therapeutic agent can be released into the body at the appropriate time, i.e., when the endoprosthesis reaches the target site. Preferably, the protective layer will dissolve within about 10 to 30 minutes after contact with bodily fluids. The protective layer preferably has a solubility of at least about 0.14 gram/mL of water at about 25°C (unless otherwise noted, all of the following solubility values are at about room temperature, i.e., about 25°C). Additionally, the protective layer preferably is flexible, such that it can be maneuvered within the lumen relatively easily. The protective layer preferably is a material that is relatively robust to abrasion, so that it can withstand friction created by contact with the lumen wall or the sheath of the catheter, for example. The protective layer maintains its structural integrity while it is passing through the body; i.e., the protective layer should not undergo substantial plastic or elastic deformation as it is dissolving. Deformation can be minimized by selecting protective layer materials with melting points substantially above, e.g. about 10°C or 50°C or more, normal body temperature (about 37°C).

Suitable sugars are carbohydrates composed of polyhydroxy aldehydes and ketones and their derivatives. Examples of suitable sugars include sucrose ($C_{12}H_{22}O_{11}$), dextrose ($C_6H_{12}O_6$), and sorbose ($C_6H_{12}O_6$). Sucrose has a solubility of about 2 grams/mL of water and a melting point of about 185-186°C. Dextrose has a solubility of about 1 gram/mL of water and a melting point of about 146-150°C. Sorbose is freely soluble in water and has a melting point of about 162-165°C.

Suitable sugar derivatives include sugar alcohols, such as polyhydric alcohols having no more than one hydroxy group attached to each carbon atom, formed by the reduction of the carbonyl group of a sugar to a hydroxyl group. A suitable sugar alcohol is mannitol ($C_6H_{14}O_6$). Mannitol has a solubility of about 0.18 gram/mL of water and a melting point of about 168°C. Another example of a sugar derivative is glucosamine ($C_6H_{13}NO_5$), an amino derivative of glucose.

Suitable inorganic ionic salts include salts containing a cation and an anion, where the cation is an alkali or alkaline earth metal, and the anion is a halide or a polyatomic ion. Examples of suitable salts include sodium chloride (NaCl), potassium chloride (KCl), and sodium carbonate (Na_2CO_3). Sodium chloride has a solubility of about 0.36 gram/mL of water

and a melting point of about 804°C. Potassium chloride has a solubility of about 0.36 gram/mL of water and a melting point of about 773°C.

In embodiments, the protective layer can be made of a polysaccharide (e.g., starch, dextran, cyclodextrin), an amino acid, an amino acid derivative, a polypeptide, a surfactant (e.g., phosphatidylcholine, a Tween® surfactant, or a lipid), or a combination thereof.

The thickness of the protective layer can be selected on the basis of the protective layer's solubility and the desired dissolution time of the protective layer. Protective layers that are highly soluble can be thicker than those protective layers that are more insoluble. In embodiments, the protective layer has a thickness of from about 0.1 micron to about 20 microns. In embodiments, the protective layer dissolves en route to the target site or it may dissolve once the stent has reached the target site. In some cases, the protective layer partially dissolves en route to the target site, and finishes dissolution once the stent has reached the target site.

The protective layer can be applied to the stent by techniques including spraying and dip coating. The protective layer can also be preformed, e.g. by casting. The preformed protective layer can be applied to the stent by an adhesive layer, e.g. the molten or solubilized material of the protective layer itself (in the case of mannitol), or a heated syrup of fructose and sucrose which solidifies upon cooling, or syrups of other sugars or sugar derivatives (such as mannitol or sorbitol).

The drug reservoir can take several different forms. For example, the drug layer can be a layer of the drug itself, solidified on the surface of the stent. Alternatively or additionally, the drug can be contained in a reservoir defined by a different material, e.g. a polymer, that is also bioerodible and/or functions as a time-release membrane. For example, the reservoir can be formed of the materials suitable for the protective layer discussed above. A drug reservoir can be formed by a stent body that has an integral porous surface. The porous surface can be formed by machining, laser drilling, sintering or anodization. Sintering is a process by which metal particles are bonded together without being entirely melted. Rather, the particles are pressed together or molded into a certain shape via pressure. Then, the particles are heated to a point just below their melting point. The particles do not melt per se; instead, the particles bond together at their surfaces. The result is that spaces (i.e., "pores") remain between the bonded particles.

Anodization is an electrolytic oxidation of a metal. For certain metals, such as aluminum, anodization creates a morphology of post-shaped elements on the surface of the

metal, which can enhance strength. As a result, a porous structure can be formed generally without sacrificing the strength of the metal or impeding the function of the medical device. Referring to FIG. 3, greatly enlarged cross-section through a side wall of a stent, the stent side wall is composed of a base material 21, an intermediate layer 23, and a porous layer 26. The morphology of porous layer 26, which is formed by anodization, is a generally regular array of hollow post-shaped elements 30 defining internal volumes 27. Void regions 32 are defined between hollow post-shaped elements 30. A therapeutic agent 34 fills internal volumes 27 and void regions 32. A protective layer 36 covers porous layer 26 in order to prevent therapeutic agent 34 from being dispersed into the body before the stent has reached the target site. Anodization can be carried out directly on the stent body or a coating of a suitable anodizeable metal can be provided over the stent body. Anodization and stents with anodized surfaces are described, for example, in U.S. Patent Application No. 10/664,679, filed September 16, 2003, and entitled "Medical Devices", the entire contents of which are incorporated by reference herein.

The term "therapeutic agent" includes one or more "therapeutic agents" or "drugs". The terms "therapeutic agents" and "drugs" are used interchangeably and include pharmaceutically active compounds, nucleic acids with and without carrier vectors such as lipids, compacting agents (such as histones), virus (such as adenovirus, adeno-associated virus, retrovirus, lentivirus and a-virus), polymers, antibiotics, hyaluronic acid, gene therapies, proteins, cells, stem cells and the like, or combinations thereof, with or without targeting sequences. Specific examples of therapeutic agents include, for example, pharmaceutically active compounds, proteins, cells, stem cells, oligonucleotides, ribozymes, antisense oligonucleotides, DNA compacting agents, gene/vector systems (i.e., any vehicle that allows for the uptake and expression of nucleic acids), nucleic acids (including, for example, recombinant nucleic acids; naked DNA, cDNA, RNA; genomic DNA, cDNA or RNA in a noninfectious vector or in a viral vector and which further may have attached peptide targeting sequences; antisense nucleic acid (RNA or DNA); and DNA chimeras which include gene sequences and encoding for ferry proteins such as membrane translocating sequences ("MTS") and herpes simplex virus-1 ("VP22")), and viral, liposomes and cationic and anionic polymers and neutral polymers that are selected from a number of types depending on the desired application. Non-limiting examples of virus vectors or vectors derived from viral sources include adenoviral vectors, herpes simplex vectors, papilloma vectors, adeno-

associated vectors, retroviral vectors, and the like. Non-limiting examples of biologically active solutes include anti-thrombogenic agents such as heparin, heparin derivatives, urokinase, and PPACK (dextrophenylalanine proline arginine chloromethylketone); antioxidants such as probucol and retinoic acid; angiogenic and anti-angiogenic agents and factors; agents blocking smooth muscle cell proliferation such as rapamycin, angiopeptin, and monoclonal antibodies capable of blocking smooth muscle cell proliferation; anti-inflammatory agents such as dexamethasone, prednisolone, corticosterone, budesonide, estrogen, sulfasalazine, acetyl salicylic acid, and mesalamine; calcium entry blockers such as verapamil, diltiazem and nifedipine; antineoplastic/antiproliferative/anti-mitotic agents such as paclitaxel, 5-fluorouracil, methotrexate, doxorubicin, daunorubicin, cyclosporine, cisplatin, vinblastine, vincristine, epothilones, endostatin, angiostatin and thymidine kinase inhibitors; antimicrobials such as triclosan, dephalosporins, aminoglycosides, and nitorfurantoin; anesthetic agents such as lidocaine, buplvacaine, and ropivacaine; nitrix oxide (NO) donors such as lisidomine, molsidomine, L-argine, NO-protein adducts, NO-carbohydrate adducts, polymeric or oligomeric NO adducts; anti-coagulants such as D-Phe-Pro-Arg chloromethyl ketone, an RGD peptide-containing compound, heparine, antithrombin compounds, platelet receptor antagonists, anti-thrombin antibodies, anti-platelet receptor antibodies, enoxaparin, hirudin, Warafin sodium, Dicumarol, aspirin, prostaglandin inhibitors, platelet inhibitors and tick antiplatelet factors; vascular cell growth promoters such as growth factors, growth factor receptor antagonists, transcriptional activators, and translational promoters; vascular cell growth inhibitors such as growth factor inhibitors, growth factor receptor antagonists, transcriptional repressors, translational repressors, replication inhibitors, inhibitory antibodies, antibodies directed against growth factors, bifunctional molecules consisting of a growth factor and a cytotoxin, bifunctional molecules consisting of an antibody and a cytotoxin; cholesterol-lowering agents; vasodilating agents; agents which interfere with endogenous vascoactive mechanisms; survival genes which protect against cell death, such as anti-apoptotic Bcl-2 family factors and Akt kinase; and combinations thereof. Cells can be of human origin (autologous or allogenic) or from an animal source (xenogeneic), genetically engineered if desired to deliver proteins of interest at the injection site. The delivery mediated is formulated as needed to maintain cell function and viability.

In some cases, the protective layer may contain a drug, which may be the same as or different from the drug in the reservoir. For example, the protective layer may include one type of drug, e.g. an antithrombogenic agent which is released quickly during delivery and deployment, while the reservoir may contain a different type of drug, e.g. an anti-inflammatory which is released more slowly at the site.

As discussed above, the stent body may be made out of any of a number of different materials. Referring to FIGS. 4A-4C, the delivery of a self-expanding stent is illustrated. The stent 10 is deployed on a catheter 38 and covered by a sheath 40. When the target site is reached, the sheath is retracted and the stent self-expands into contact with the body lumen. Referring now to FIGS. 5A-5C, the delivery of a balloon-expandable stent is illustrated. The stent 10 is carried on a catheter 42 over a balloon 44. When the treatment site is reached, the balloon is expanded to expand the stent into contact with the lumen wall. The stent body may be made of, for example, Nitinol, a nickel-titanium alloy that can provide stent with superelasticity and shape memory properties. In some cases, the stent body may be made of stainless steel (e.g., 300 series stainless steel), or aluminum. The stent body may be made of composite materials as described in Heath, U.S. 5,725,570, and Mayer, U.S. 5,800,511. A stent as described above has many different possible applications. For example, the stent may be used in the vascular system (e.g., in the coronary arteries), or in the gastrointestinal tract. The stent may be an esophageal stent. The stent may be used in the biliary duct, or in other body lumens.

While a stent has been described above, a protective layer and a drug-containing reservoir may be applied to other implantable medical devices, and particularly to implantable medical devices that are suitable for drug delivery. For example, they may be used in guidewires, catheters (including balloon angioplasty catheters), or filters (including vena cava filters).

Still other embodiments are possible. For example, where the protective layer material itself has a desirable therapeutic effect, e.g. if delivery of a sugar or salt to a treatment site is desired, the protective layer material can be applied to a stent that does not include a drug reservoir.

All publications, applications, references, and patents referred to above are incorporated by reference in their entirety.

Other embodiments are within the following claims.

WHAT IS CLAIMED IS:

1. A medical stent, comprising:
a generally tubular body;
a therapeutic agent; and
a sugar, sugar derivative, or inorganic ionic salt.

2. The medical stent of claim 1 wherein the sugar, sugar derivative, or salt has a solubility of at least 0.14 gram/mL of water.

3. The medical stent of claim 1 wherein the sugar, sugar derivative, or salt has a melting point of about 47°C or more.

4. The medical stent of claim 1 wherein the stent comprises a sugar or sugar derivative.

5. The medical stent of claim 4 wherein the sugar or sugar derivative comprises sucrose, sorbose, glucosamine, or mannitol.

6. The medical stent of claim 1 wherein the stent includes an inorganic ionic salt.

7. The medical stent of claim 6 wherein the salt comprises sodium chloride, potassium chloride, or sodium carbonate.

8. The medical stent of claim 1 including a layer including a therapeutic agent and said sugar, sugar derivative, or salt.

9. The medical stent of claim 1 including a layer of sugar, sugar derivative, or salt that covers a therapeutic agent-containing reservoir.

10. The medical stent of claim 9 wherein the reservoir is a layer of therapeutic agent.

11. The medical stent of claim 9 wherein the reservoir defines pores and the therapeutic agent is disposed within the pores.

12. The medical stent of claim 9 wherein the reservoir comprises metal integral with the stent body.

13. The medical stent of claim 9 further comprising a second therapeutic agent, carried by the layer, wherein the second therapeutic agent is different from the therapeutic agent carried by the reservoir.

14. The medical stent of claim 1 wherein the therapeutic agent is selected from an antithrombogenic, antioxidant, anti-inflammatory, antiproliferative, or antibiotic.

15. The medical stent of claim 1 wherein the stent is a self-expanding stent.

16. The medical stent of claim 1 wherein the stent is a balloon-expandable stent.

17. The medical stent of claim 1 wherein the stent is a vascular stent.

18. A stent delivery system including a catheter with a balloon and a medical stent device, comprising:

a generally tubular body;

a therapeutic agent; and

a sugar, sugar derivative, or inorganic ionic salt.

19. A stent delivery system including a catheter with a retractable sheath and a medical stent device, comprising:

a generally tubular body;

a therapeutic agent; and

a sugar, sugar derivative, or inorganic ionic salt.

20. A medical stent comprising a generally tubular body and a sugar, sugar derivative or inorganic ionic salt.

21. The medical stent of claim 20 wherein the stent comprises a sugar or a sugar derivative.

22. The medical stent of claim 20 wherein the sugar or sugar derivative comprises sucrose, sorbose, glucosamine or mannitol.

23. The medical stent of claim 20 wherein the stent comprises an inorganic ionic salt.

24. The medical stent of claim 23 wherein the salt comprises sodium chloride, potassium chloride, or sodium carbonate.

25. A method of making a coated stent, comprising:

providing a stent;

providing a therapeutic agent; and

coating the stent with a layer of sugar, sugar derivative, or inorganic ionic salt.

26. The method of claim 25 wherein coating comprises dip coating or spray coating.

27. The method of claim 25 wherein coating comprises forming a preform layer and fixing the preform layer to the stent.

28. The method of claim 27 wherein the perform layer is fixed by applying a solution of, or a liquid form of, a sugar, sugar derivative, or salt to the stent.

29. An implantable medical device, comprising:

an implantable body;

a therapeutic agent; and

a sugar, sugar derivative, or inorganic ionic salt.

30. A medical stent, comprising:

a generally tubular body;

a therapeutic agent-containing reservoir; and

a layer that covers the reservoir, the layer selected from the group consisting of sugars, sugar derivatives, inorganic ionic salts, surfactants, polysaccharides, polypeptides, amino acids, amino acid derivatives, and combinations thereof.

31. A medical stent, comprising:

a generally tubular body;

a therapeutic agent; and

a surfactant.

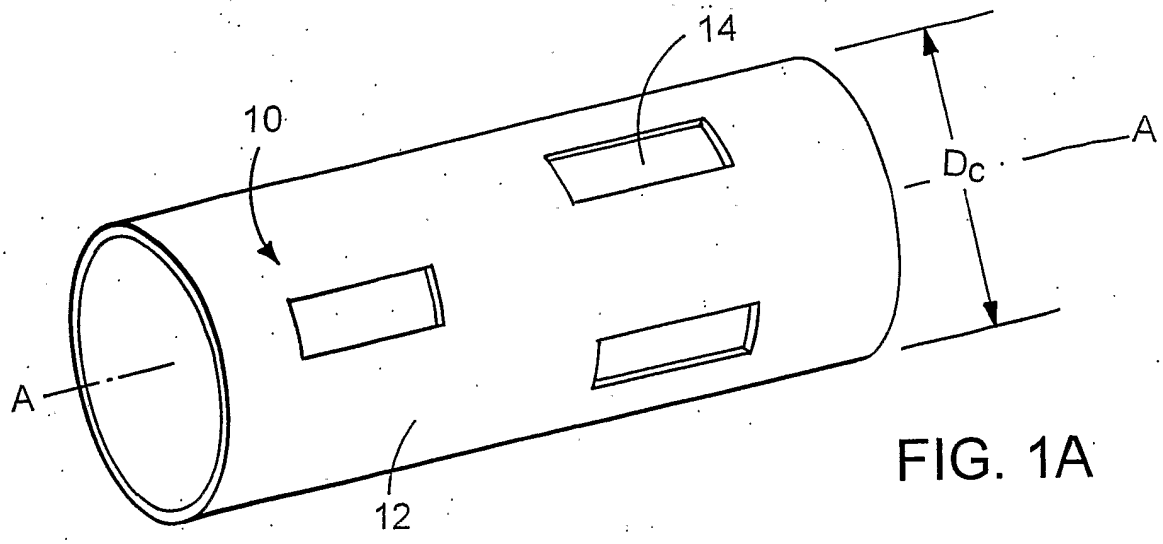


FIG. 1A

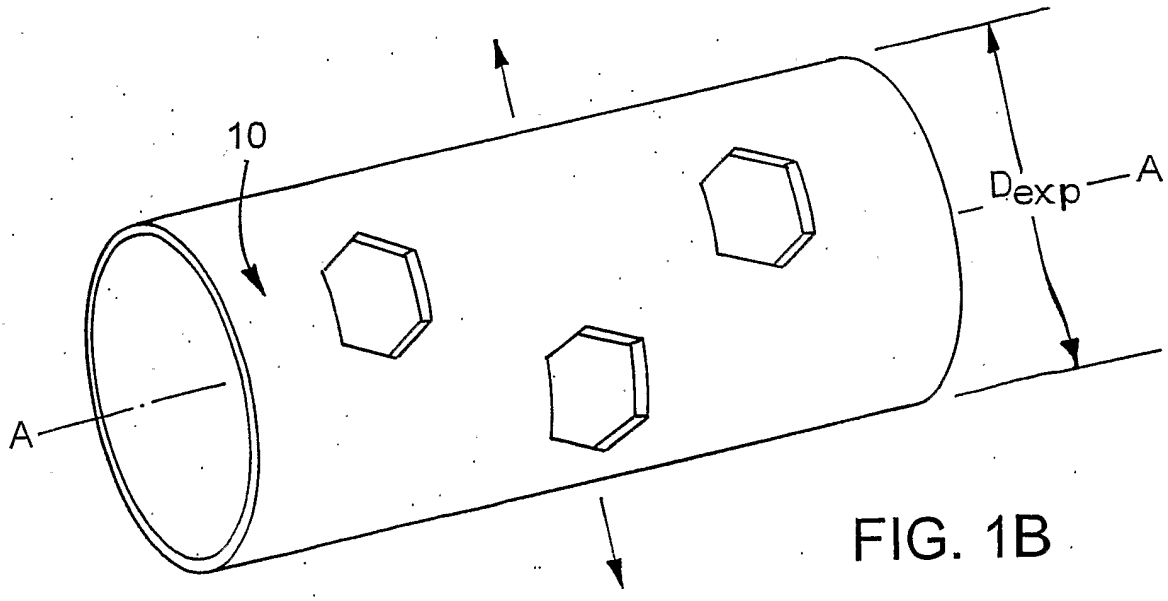


FIG. 1B

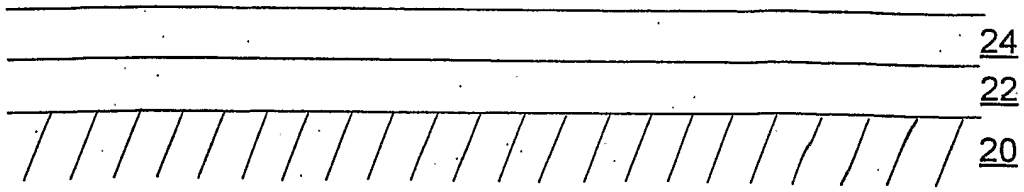


FIG. 2

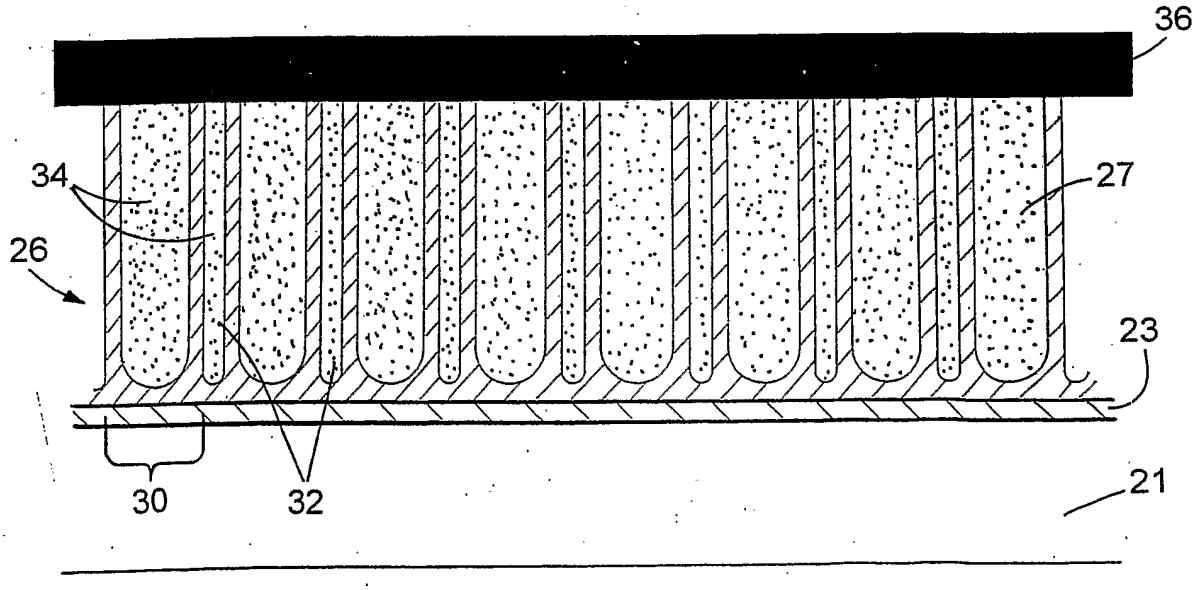


FIG. 3

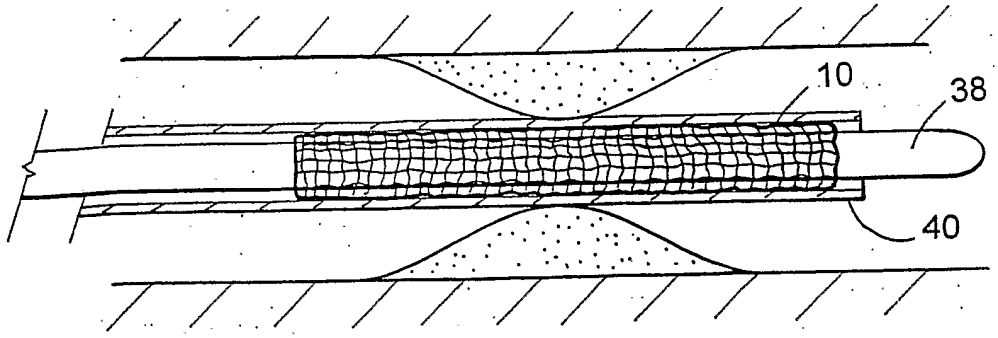


FIG. 4A

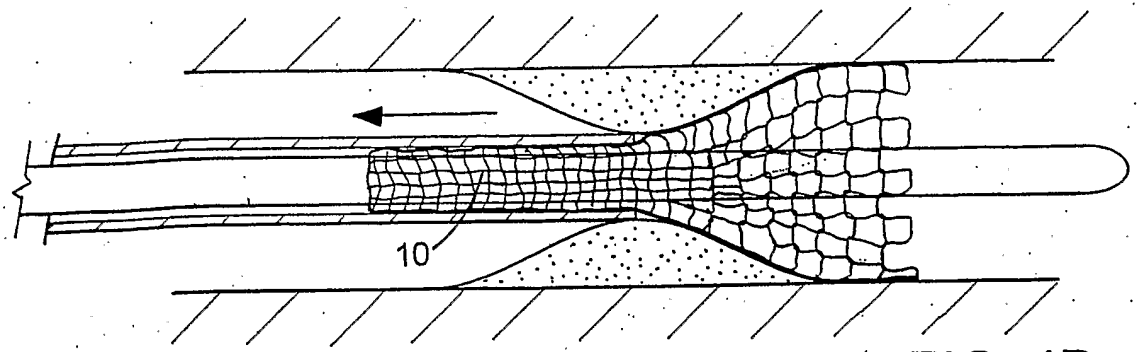


FIG. 4B

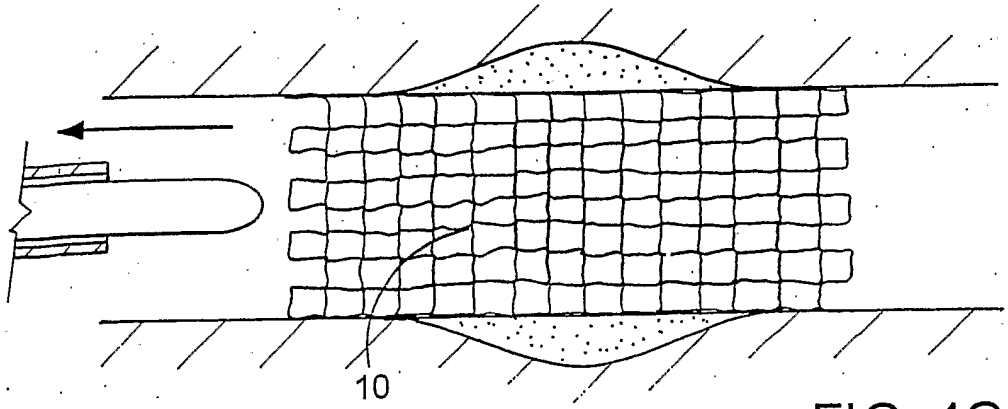


FIG. 4C

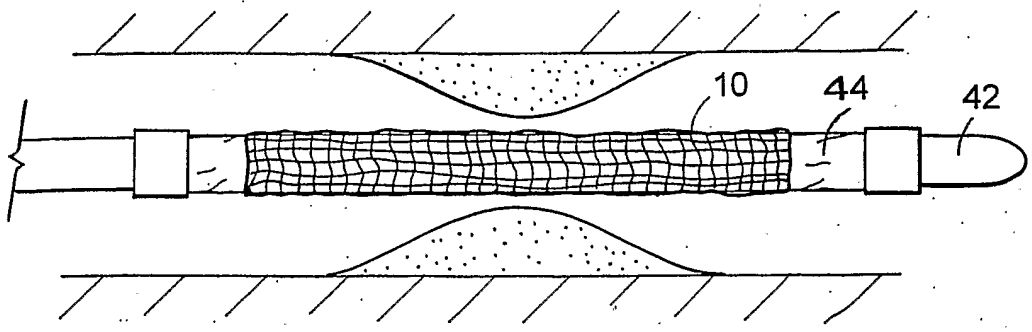


FIG. 5A

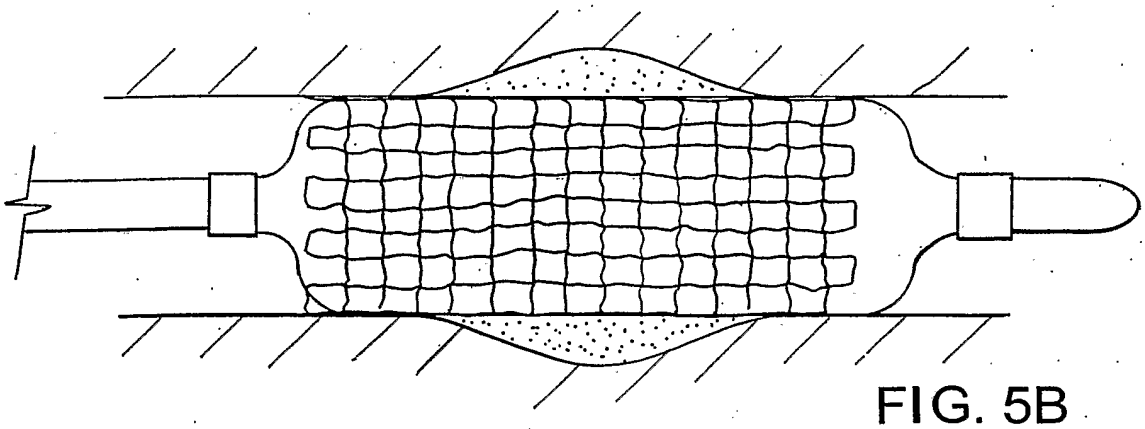


FIG. 5B

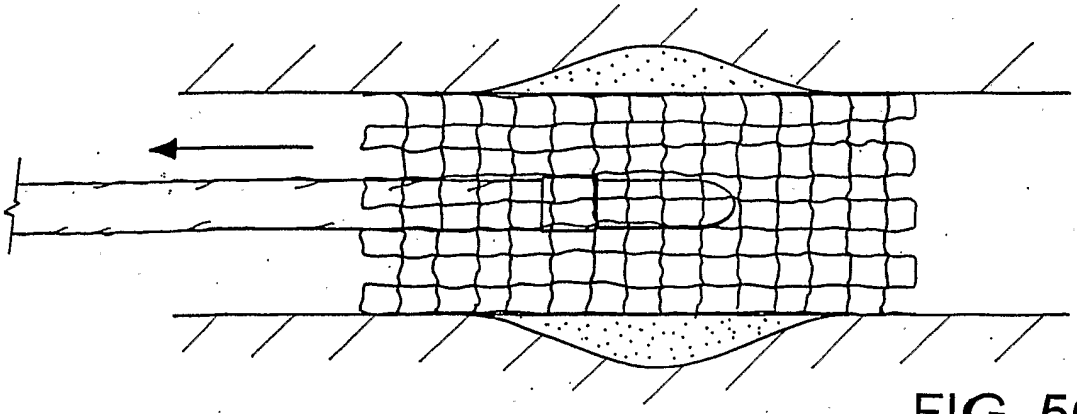


FIG. 5C

INTERNATIONAL SEARCH REPORT

Int...al Application No
PCT/US2005/005630

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/06

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)
IPC 7 A61F

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 273 314 A (TERUMO KABUSHIKI KAISHA) 8 January 2003 (2003-01-08)	1-3, 6-10, 13-20, 23-31
Y	page 1, line 7 - page 13, line 40; figures 1-9	11,12
X	WO 02/47739 A (MD3, INC; STEINKE, THOMAS, A) 20 June 2002 (2002-06-20)	1-5,9, 10, 14-22, 25-30
	page 1, line 6 - page 8, line 19; figures 1-4	

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document 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
14 June 2005	22/06/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Skorovs, P

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/005630

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 071 305 A (BROWN ET AL) 6 June 2000 (2000-06-06) column 9, line 43 - column 10, line 55; figures 5,7	1-9, 11-24,29
X	EP 1 260 214 A (SCHNEIDER INC) 27 November 2002 (2002-11-27) page 1, line 5 - page 21, line 12	31
Y	WO 03/035131 A (ADVANCED CARDIOVASCULAR SYSTEMS, INC) 1 May 2003 (2003-05-01) page 29, line 1 - line 7; figure 2a	11,12
Y	US 6 506 437 B1 (HARISH SAMEER ET AL) 14 January 2003 (2003-01-14) column 10, line 54 - column 11, line 16; figure 9a	11,12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2005/005630

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
EP 1273314	A	08-01-2003	EP	1273314 A1	08-01-2003
			EP	1413327 A1	28-04-2004
			WO	03004089 A1	16-01-2003
			JP	2003093520 A	02-04-2003
			US	2003033004 A1	13-02-2003
			US	2003181975 A1	25-09-2003
WO 0247739	A	20-06-2002	US	2002103526 A1	01-08-2002
			AU	3092702 A	24-06-2002
			WO	0247739 A2	20-06-2002
US 6071305	A	06-06-2000	AU	5266698 A	22-06-1998
			WO	9823228 A1	04-06-1998
			ZA	9710342 A	10-06-1998
EP 1260214	A	27-11-2002	US	5879697 A	09-03-1999
			EP	1260214 A1	27-11-2002
			AT	269055 T	15-07-2004
			AT	231718 T	15-02-2003
			CA	2236182 A1	30-10-1998
			DE	69810986 D1	06-03-2003
			DE	69810986 T2	30-10-2003
			DE	69824648 D1	22-07-2004
			EP	0879595 A2	25-11-1998
			JP	10305105 A	17-11-1998
			US	6042875 A	28-03-2000
			US	6316018 B1	13-11-2001
WO 03035131	A	01-05-2003	US	6753071 B1	22-06-2004
			WO	03035131 A1	01-05-2003
			US	2004234737 A1	25-11-2004
US 6506437	B1	14-01-2003	NONE		