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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61L 27/00, A61F 2/06

A1

(11) International Publication Number: WO 92/09311

(43) International Publication Date: 11 June 1992 (11.06.92)

(21) International Application Number: PCT/EP91/02258

(22) International Filing Date: 27 November 1991 (27.11.91)

(30) Priority data:
22228 A/90 29 November 1990 (29.11.90) IT

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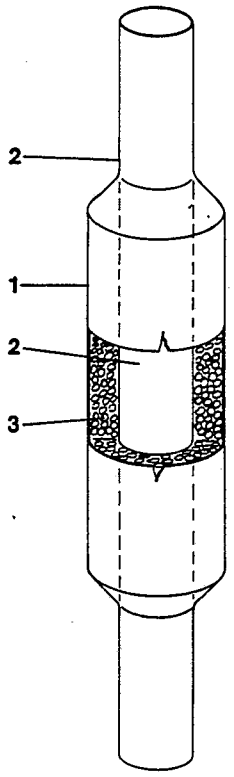
(81) Designated States: AT (European patent), BE (European patent), CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.

Published
With international search report.

(54) Title: BIOCOMPATIBLE SYNTHETIC DOUBLE-WALL VASCULAR PROSTHESIS CONTAINING HORMONE-SECRETING CELLS

(57) Abstract

Biocompatible synthetic double-wall vascular prostheses comprising an outer tubular element (1) made of low-porosity synthetic material and an internal tubular element (2) coaxial with the former and consisting of high porosity synthetic material imbued with polysaccharide material coated with polyaminoacids which impart to the element (2) the feature of a controlled permeability, the space comprised between said element (1) and said element (2) being filled with hormone-secreting cells (3).



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BIOCOMPATIBLE SYNTHETIC DOUBLE-WALL VASCULAR PROSTHESIS CONTAINING HORMONE-SECRETING CELLS

PRIOR ART

Microcapsules consisting of saccharide polymers and polyaminoacids, or other substances such as agarose polymers, suitable to contain hormone producing living cells are known.

Microcapsules of such a type are produced and commercialized for instance by the firm Damon Biotech of Boston under the Trade Mark Encapcell.

The features of said microcapsules allow the cells to be protected from possible rejection events, and enable the necessary cell metabolic supply and the release of the hormones secreted by the same cells.

However the implant of said microcapsules into the human body brings about problems among which the following are highlighted:

1) the microcapsules implanted in the body are surrounded by a connective reaction tissue which prevents both the cell metabolic supply and the release of the secreted hormones;

2) the microcapsules injected into a body cavity such as the peritoneal space tend to sediment and to concentrate in a deep limited area thus eliciting a strong connective reaction which wraps them.

SUMMARY OF THE INVENTION

It has now been found that the problems of the prior art may be avoided by employing biocompatible synthetic double-wall vascular

prostheses characterized in that they comprise an outer tubular element 1 made of low-porosity synthetic material and an internal tubular element 2 coaxial with the former and consisting of high porosity synthetic material imbued with polysaccharide material coated with polyaminoacids, the space comprised between said element 1 and said element 2 being filled with hormone-secreting cells 3.

The process for preparing said prostheses is characterized in that it comprises the following stages:

a) inside a tubular element 1 made of low-porosity synthetic material, a tubular web 2 of high-porosity synthetic material is placed;

b) within said tubular web, a mandrel is introduced of such a diameter that the web adheres to it;

c) the web is coated with a thin layer of saccharide polymer;

d) the mandrel is removed;

e) a further layer consisting of a polyaminoacid is sedimented upon said saccharide polymer layer ;

f) the space comprised between the element 1 and the element 2 is filled with hormone-secreting cells.

Thus obtained prosthesis exhibits the property of being biocompatible and moreover the element 2 shows a controlled permeability.

The prosthesis is employed to make arteriovenous fistulae in which the feasibility of the metabolic exchange between blood and cells 3 and the release into the blood stream of the hormones secreted

by the same cells is enabled.

DETAILED DESCRIPTION OF THE INVENTION

The features of, and the advantages implied by the vascular prostheses and by the process for manufacturing the same, according to the present invention, will be more clearly evident in the light of the following detailed description also with reference to the enclosed figure 1.

Figure 1 is a schematic illustration of a prosthesis according to the present invention.

Reference is made to the numbers in said figure. A tubular web 2, consisting of polyester fibres and including free spaces of size ranging from 10 to 100 μm within the fibres, is placed into a tubular element 1 consisting of PTFE or of low porosity tissue. Into the tubular web 2 there is located a mandrel of plastic material or glass having such a diameter that the web adheres to it.

The web is soaked with a polysaccharide gel, preferably sodium alginate, in order to fill up the free spaces within the fibres. The mandrel is thereafter removed and the thus obtained structure 2 is coated with a thin layer of a polyaminoacid, preferably polylysine or polyornithine.

The use of the mandrel is intended to prevent the polysaccharide material, or any other, from flowing into the lumen of the element 2, assuring in this way the result of a perfectly cylindrical internal surface free of any roughness.

The prosthesis manufactured according to the disclosed technique and making use of the described substances, exhibits structural properties, biocompatibility and porosity such as to allow it to be successfully employed as prosthesis for arteriovenous fistulae. Particularly the coating of the element 2 with polylysine (MW 15 000) imparts a good permeability for dextrane having MW 40 000 while maintaining the element 2 actually proof against dextrane having MW higher than 60 000. By making use of other polyaminoacids, the permeability may be changed in either direction.

Practically the permeability of the element 2 may be adjusted up to a MW of 70 000 thus allowing the transfer of metabolic products from the inside to the outside and vice versa, not however the exchange of immunoglobulins or any other high molecular weight substance.

The thickness of the element 2 needs in any case to be lower than 100 µm in order to allow the metabolic exchanges in both direction. The inner diameter of the element 2 is comprised between 4 and 8 mm while the inner diameter of the element 1 is comprised between 10 and 14 mm. According to an alternative embodiment, the tubular element 2 consists of a small tube of PTFE having a lamellar structure including free spaces of 10 to 100 µm, which impart to the same a high porosity.

The impregnation with polysaccharide material is achieved by dipping the small tube into the same material and then by submitting it to the vacuum in order to facilitate the filling of

the free spaces of the PTFE with the material itself.

The polyaminoacid is then sedimented on the thus obtained element.

Finally the space comprised between the tubular element 1 and the tubular element 2 is filled with hormone-secreting cells 3, which may be either free or microincapsulated.

Thus obtained prostheses, which are employed to make arteriovenous fistulae, allow the supply of oxygen and any other product necessary to the cellular metabolism from the blood stream to said cells and the release in opposite direction of the hormones secreted by the same cells.

Moreover because of the haematic flow, the inner surface of element 2 may be coated by a monolayer similar to an endothelial one. A specifically favourable application of the prostheses of the present invention is obtained when the microcapsules contain Langherans' islands cells which secret insulin.

Furthermore the disclosed technique can be applied for manufacturing any surface of synthetic material coated with biocompatible substances.

CLAIMS

1. Biocompatible synthetic double-wall vascular prosthesis characterized in that it comprises an outer tubular element (1) made of low-porosity synthetic material and an internal tubular element (2) coaxial with the former and consisting of high porosity synthetic material imbued with polysaccharide material coated with polyaminoacids, the space comprised between said element (1) and said element (2) being filled with hormone-secreting cells (3).

2. Prosthesis according to claim 1, characterized in that said tubular element (1) consists of PTFE.

3. Prosthesis according to claim 1, characterized in that said tubular element (2) consists of a tubular web of polyester fibres including free spaces of size comprised between 10 and 100 µm within the fibres.

4. Prosthesis according to claim 1, characterized in that said tubular element (2) consists of a small tube of PTFE with lamellar structure including free spaces of 10 to 100 µm.

5. Prosthesis according to claim 1, characterized in that said polysaccharide material is sodium alginate.

6. Prosthesis according to claim 1, characterized in that said polyaminoacid is polylysine or polyornithine.

7. Prosthesis according to claim 1, characterized in that said tubular element (2) has a thickness lower than 100 µm.

8. Prosthesis according to claim 1, characterized in that said tubular element (2) has a inner diameter comprised between 4 and 8

mm and that said tubular element (1) has an inner diameter comprised between 10 and 14 mm.

9. Prosthesis according to claim 1, characterized in that the treatment with the polysaccharide material and polyaminoacid adjusts the permeability of the tubular element (2) up to a MW of 70 000.

10. Prosthesis according to claim 1, characterized in that said cells (3) are microincapsulated.

11. Process for preparing biocompatible synthetic double-wall vascular prostheses containing hormone-secreting cells characterized in that:

a) inside a tubular element (1) made of low-porosity synthetic material, a tubular web (2) of high-porosity synthetic material is placed;

b) within said tubular web, a mandrel is introduced of such a diameter that the web adheres to it;

c) the web is coated with a thin layer of saccharide polymer;

d) the mandrel is removed;

e) a further layer consisting of a polyaminoacid is sedimented upon said saccharide polymer layer ;

f) the space comprised between the element (1) and the element (2) is filled with hormone-secreting cells.

12. Process according to claim 11, characterized in that said tubular element (1) consists of PTFE.

13. Process according to claim 11, characterized in that said

tubular web (2) consists of polyester fibres and includes free spaces within the fibres of size comprised between 10 and 100 µm.

14. Process according to claim 11, characterized in that said polysaccharide material is sodium alginate.

15. Process according to claim 11, characterized in that said polyaminoacid is polylysine or polyornithine.

16. Process according to claim 11, characterized in that said tubular web (2) has a inner diameter comprised between 4 and 8 mm and that said tubular element (1) has an inner diameter comprised between 10 and 14 mm.

17. Process according to claim 11, characterized in that said tubular web (2) is replaced by a small tube of PFTE with lamellar structure including free spaces of 10 to 100 µm.

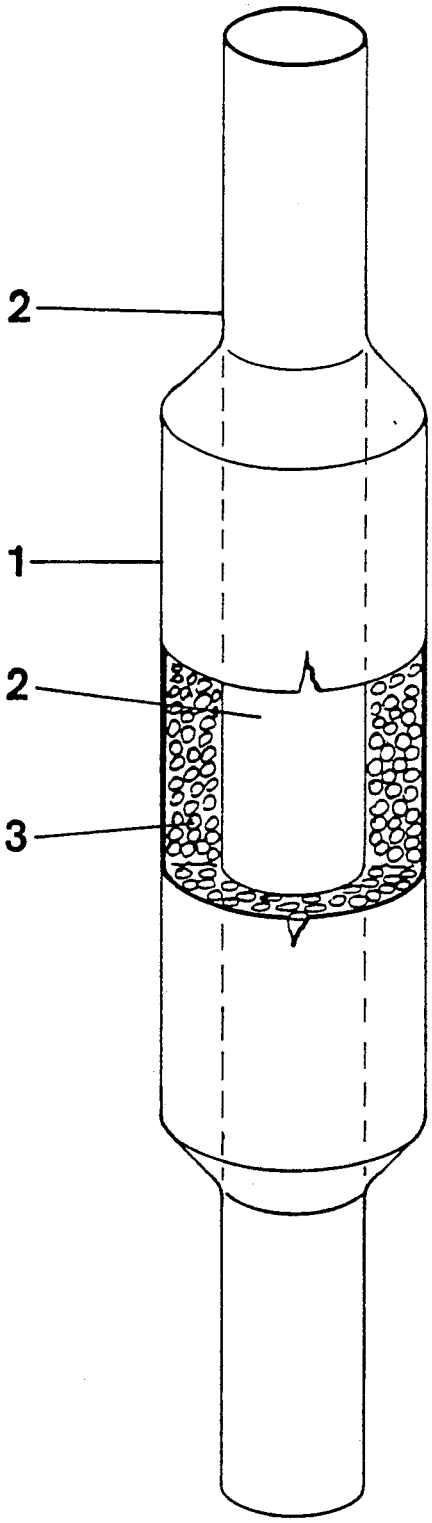

FIG 1

INTERNATIONAL SEARCH REPORT

International Application No PCT/EP 91/02258

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61L27/00; A61F2/06

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	A61L ; A61F

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
P,X	EP,A,0 406 665 (BROTZU, GIOVANNI) 9 January 1991 see claims 1-9	1-17
P,X	WO,A,9 100 119 (BAXTER INTERNATIOONAL,INC.) 10 January 1991 see abstract; figure 1	1
Y	WO,A,8 203 764 (MASSACHUSETS INSTITUTE OF TECHNOLOGY) 11 November 1982 see claims 1-18; figure 1	1-17
Y	CA,A,1 215 922 (CONNAUGHT LABORATORIES LIMITED) 30 December 1986 see the whole document	1-17
A	US,A,4 487 758 (MATTHEUS F. A. GOOSEN ET AL.) 11 December 1984	

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
11 FEBRUARY 1992	20. 02. 92
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	M. ESPINOSA

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	EP,A,0 147 939 (JOHNSON & JOHNSON) 10 July 1985 ---	

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. EP 9102258 SA 53486

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on
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WO-A-9100119	10-01-91	None	
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