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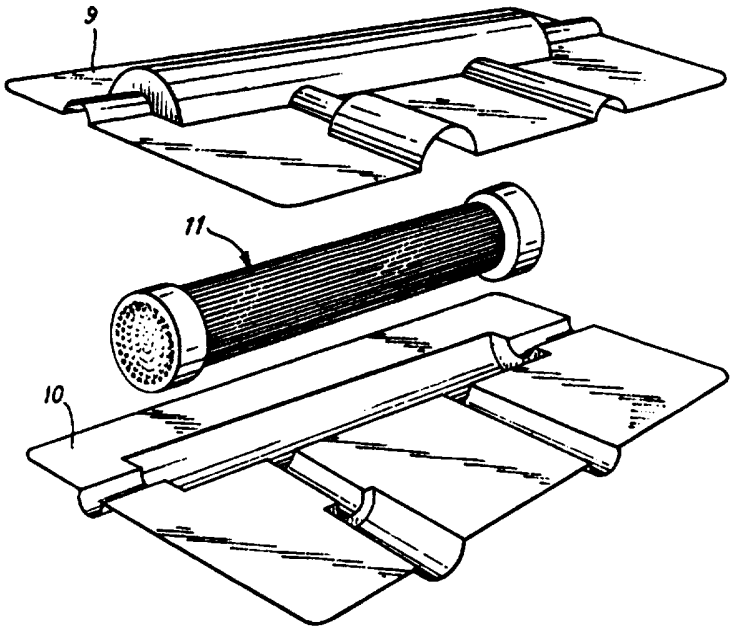

(57) Abstract

There is described a method of treating membranes which comprises exposing at least a portion of said membrane to a blocking moiety and then coating said membrane portion. Suitable blocking moieties include fluids (for example water) and small molecules (for example peptides, fatty acids or sugars). Suitable coatings include adhesive as well as antibodies, enzymes, lectins or other reactive molecules. Pre-treating of the membrane with the blocking moiety reduces the shear stresses on the membrane as the coating dries. In a preferred embodiment the membrane is pre-treated with water as a blocking moiety and coated with adhesive prior to insertion into an outer casing (9, 10) to form a sealed membrane unit (11).

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"Method of Treating Membranes"

The present invention is concerned with a process for producing sealed units which comprise a membrane.

Sealed membrane units are desirable for many purposes which require a filtration step. Generally, the membrane is sealed into the unit in such a way that the mother liquor (liquid to be processed) is separated from the filtrate by the membrane. Where the membrane unit is to be used for medical purposes, for example dialysis, it is of course particularly important for the unit to be sealed completely and for the membrane to be clean, preferably sterile.

Currently, sealed membrane units of this type are formed using a one-part (generally tubular) outer casing. The membrane fibres are threaded through the outer casing and the ends of the membrane are then fixed in place by adhesive. The adhesive is introduced into the outer casing and the whole unit is spun, so that the centrifugal forces created cause adhesive to locate at each end of the outer casing. The adhesive is then allowed to set. This process has the disadvantage that an adequate seal at each end of the

unit cannot be guaranteed and therefore careful testing of each unit is required. In addition, the ends of the hollow fibre membranes frequently become blocked by adhesive during the spinning process.

It is also possible to provide a sealed membrane unit by using two outer casing portions. In this methodology, the membrane is located within the casing portions which are then sealed together, for example with adhesive. Figs 1 to 3 illustrate this method of manufacture which is described in more detail in PCT/GB95/01836. Usually, a quick-setting adhesive is injected into the casing close to each end of the membrane, for example a membrane fibre bundle. Alternatively a bundle of membrane fibres may be placed into a mould and plugs of adhesive formed around each end, before transfer to an outer casing.

For all membrane units it is essential that the seal formed around the membrane by the adhesive is tight, so that communication between the two volumes described by the membrane only takes place by movement of material across the membrane itself.

Whichever method of unit formation is used there is always the necessity of using adhesive at each end of the membrane unit to provide a seal around the edge or end of the membrane. Preferably the adhesive is cured by exposure to UV light. Optionally, once the adhesive plugs have set the exterior of each plug may be trimmed, for example by use of a sharp knife or guillotine. The cut made may also slice through the membrane ensuring that, where hollow fibre membranes are used, the exposed end of each membrane fibre is free from cured adhesive.

However, it has now been found that setting or curing of adhesive causes the membrane material to experience shearing forces. Under certain circumstances the shearing forces can induce a tear within the membrane material. This problem is particularly noticeable where very small hollow fibre membranes (for example fibres having an external diameter of under 2mm, especially under 1mm) are used and under certain circumstances the forces can cause complete shearing of the membrane fibre. However, the problem is also noticeable where a flat sheet membrane is employed.

Surprisingly, it has been found that wetting the area of the membrane to be contacted by the adhesive prior to setting or curing eliminates the shearing stresses sufficiently to prevent membrane damage.

Whilst we do not wish to be bound by theoretical considerations, it is believed that wetting the membrane is a simple way of introducing small molecules (the molecules of which the liquid is comprised) into the interstices of the membrane material. The small molecules are believed to partially occlude the spaces present in the structure of the membrane material and prevents the adhesive from penetrating deeply. Thus, as the membrane itself is not saturated with adhesive it is less affected during the curing process by the chemical and physical alterations that occur in the adhesive composition during curing.

In a development of the invention it was then found that it is not essential for the membrane to be physically wet; it is necessary only for penetration of the adhesive (or any similar material coating the membrane) into the interstices of the membrane material to be hindered, preferably substantially prevented.

Thus, the undesirable shearing forces experienced when adhesive is applied directly to the membrane and then cured may be avoided if the membrane has been pre-treated with a blocking moiety.

In a further development of the process, it has been noted that the blocking moiety can be used to localise a coating onto one surface of the membrane, rather than simply applying the coating moiety and allowing it to penetrate through the membrane, and possibly even being lost from the membrane. This avoids the stresses on the membrane due to drying of the coating. Moreover the coating can be selected to alter the characteristics of the membrane.

In its widest aspect therefore the present invention provides a method of treating at least a portion of a membrane, said method comprising the following steps:

a. contacting a surface of said membrane portion with a blocking moiety; and

b. applying a coating to said surface of the treated membrane portion of step a).

Application of the blocking moiety should normally be sufficient to at least partially hinder entry of the coating into the interstices of the membrane portion.

Optionally, the blocking moiety may be generated on a surface of the membrane or within the porous structure of the membrane by chemical reaction.

The invention also includes coated membranes produced as described above.

Viewed from one aspect, the present invention provides a method of forming a (preferably sealed) membrane unit wherein a portion of the membrane is coated, said method comprising the step of pre-treating said membrane portion to be coated with a blocking moiety.

The term "coated" includes membranes coated with adhesive for fixing purposes, the adhesive being applied to a relatively small area of membrane to form a thick layer or "plug". More conventional coatings which cover substantially all of the membrane surface relatively thinly are also included within the term "coated".

Where the blocking moiety is a liquid (for example water) the part of the membrane to be coated may be wet.

Where the blocking moiety is a solid, it may be applied to the membrane in dissolved, colloidal or suspended form together with a delivery fluid. The coating may be applied whilst the membrane surface is still wet from the delivery fluid or alternatively the membrane may be allowed to dry before application of the coating.

In one embodiment the blocking protein is formed by precipitation in the interstices of the membrane when two separate fluids are allowed to flow down separate sides of the membrane; precipitation occurring when the two fluids come into contact with each other following migration through the membrane.

Examples of blocking moieties include liquids (ie the membrane is wet when the adhesive is applied) and also small inorganic or organic molecules. Particular

mention may be made of amino acids, peptides, proteins, sugars, fatty acids, and mixtures including these molecules. Serum albumins, for example bovine serum albumin and human serum albumen, are suitable as blocking proteins. Also suitable are milk proteins, such as caseins. Sugars include monosaccharides such as glucose, di-saccharides such as fructose, galactose etc and polysaccharides such as starches, cellulose, hemi-cellulose and the like. The size of the blocking moiety should of course be such to enable entry into the interstices of the membrane material. Generally, therefore the physical characteristics of the membrane will need to be considered when selecting a suitable blocking moiety.

Other coatings which may be applied to a membrane pre-treated according to the present invention include (but are not limited to) enzymes (such as hydrogen peroxidose, glucose oxidose etc), antibodies, lectins, epitopes, reactive groups (eg carboxyl groups, epoxides, amine groups) and the like.

Optionally the coated membrane may be incorporated into a membrane filter unit as described and illustrated in PCT/GB95/01834. In such a device, the coating applied may be used to determine the presence of a component of the mother liquor as described therein.

Viewed from a further aspect the present invention provides a method of forming a membrane unit wherein a part of the membrane is in contact with adhesive, said method comprising the step of wetting at least a portion of the part of said membrane prior to setting or curing of the adhesive.

Viewed from another aspect the present invention

provides a method of forming a membrane unit wherein the membrane is in contact with a set or cured adhesive, said method being characterised in that the adhesive setting or curing step is carried out whilst an area of membrane in contact with the adhesive is wet.

Where the blocking moiety is a fluid, it is not necessary for the whole surface of the membrane to be wet, but rather it is sufficient to wet only at least part of the area of the membrane which is to be in contact with the coating (for example adhesive), preferably substantially all of the area of the membrane which is to be coated or be in contact with the adhesive. In certain embodiments however it may be desirable or necessary for the whole surface area of the membrane to be wet. The membrane may be wet before insertion into the membrane unit casing, for example as in the case of the formation of membrane fibre bundles held at each end by an adhesive plug. Alternatively the membrane may be wet after insertion into the membrane unit casing. Likewise the membrane may be wet before or after introduction of the coating. For the purpose of convenience the membrane is generally wet before the coating is inserted either into the membrane unit or into the mould. Optionally, where the coating is an adhesive it may be introduced as a mixture with a suitable wetting fluid.

It is possible to wet the membrane with any fluid and mention may be made of water or other aqueous systems, including buffers (for example Tween). Organic fluids (such as for example ethanol, isopropanol, acetone, dichloroethane or mixtures containing them) may however also be used.

Generally, it is sufficient to simply dip the ends of the membrane into the fluid selected. Sufficient fluid will be sucked up into the membrane by capillary action. Alternatively, the membrane may be wet by dipping or soaking in fluid or by the deliberate introduction of the fluid into or onto the membrane, for example using a syringe to inject fluid down the lumen of the membrane. Optionally the fluid selected to wet the membrane prior to curing of the adhesive may be part of a pre-treatment process of the membrane, for example a process coating the membrane.

The membrane material may be any suitable membrane, and selection of the membrane will depend upon the intended end use of the filter unit. Examples of suitable membrane materials include polysulfone, cellulose, cellulose diacetate, polypropylene and/or ceramics materials. Nylon, cellulose nitrate, polytetrafluoro-ethylene (PTFE), polyvinylidene difluoride (PVDF) and glass fibres are also suitable membranes.

Generally, the adhesive used in the process may be any adhesive material which does not react with the membrane or outer casing materials in a dileterious manner. Preferably the adhesive material is quick-setting, ie cures within minutes, for example under five minutes. For certain embodiments adhesive material which cures on exposure to light is particularly desirable. For example, in medical applications, it may be preferred to use adhesive which cures upon exposure to blue light, especially UV light.

Suitable adhesive material is commercially available and mention may be made of polymers available from Ablestick Ltd (for example LCM 32, LCM 34 LCM 35), Bostick Ltd or Dynax Inc (eg 191M) as being suitable

curing adhesives.

Where the filter unit is intended for any medical or pharmaceutical end use, treatment of the membrane in accordance with the invention is preferably carried out under clean, preferably sterile, conditions, for example using sterilised water as the blocking moiety.

If the membrane used is a single hollow fibre (for example a hollow fibre having an external diameter of under 1.5mm, for example 500μm or less, such as 300μm or less), it has further been found that curing of the adhesive is sufficient to dry the fibre. Where a flat sheet membrane or bundle of hollow membrane fibres are used, however, a further drying step may be required. Additional drying may either take place by allowing the membrane to dry naturally in the atmosphere, or by application of heat or warm air. Again, if the membrane unit is for medical or pharmaceutical use any drying should be carried out under clean, preferably sterile, conditions.

Thus the present invention provides a method of treating a membrane, said method comprising the following steps:

a. exposing at least a part of the membrane portion which is to be coated to a blocking moiety;

b. coating said membrane portion;

c. optionally drying any wet area of said membrane.

In a further aspect the present invention provides a method of forming a membrane unit, said method comprising the following steps:

a. exposing at least a part of the membrane area which is to be in contact with adhesive to a blocking moiety;

b. applying said adhesive to said membrane area;

c. curing the adhesive or allowing the adhesive to set;

d. optionally drying any wet area of said membrane.

By way of illustration filter units which may comprise a membrane treated as described above are shown in Figs 1-8.

Figs 1 to 3 show exploded views of membrane filter units in which the membrane is treated accorded to the invention to avoid shear during setting of the adhesive;

Figs 4 to 8 show filter units which may comprise a membrane treated according to the invention.

Figure 1 shows general detail of the construction of a filter unit having a casing constructed from two portions. Moulded casing halves 9 and 10 are sealed together with a UV-activated acrylic sealant to enclose a hollow fibre bundle membrane unit 11. The membrane unit 11 is bonded to the outer casing in such a way that a seal is formed at the ends of the whole filter cell. To form membrane unit 11 the bundle of membranes is pretreated by wetting with water or a buffer solution. The pretreated membrane is then placed into a mould, into which adhesive is inserted. The adhesive is then cured. The presence of the blocking agent on the membranes ensures that the membranes are not

sheared during the curing of the adhesive.

Figure 2 shows a unit having a coated membrane according to the present invention. The unit illustrated has outer casing portions 1, 2 and 2'. Upper outer casing portions 2 and 2' are alternatives allowing flexible manufacturing capacity. A membrane bundle 3 is manufactured with cured adhesive plugs 4, 5 at each end thereof as described above for Fig. 1. The plugs 4, 5 have been trimmed at their outer edges so that the end of each hollow membrane fibre is fully exposed. The adhesive plugs 4, 5 fit snugly into corresponding indentations 6 in the outer casing portions 1, 2, 2'. To seal the unit adhesive is smeared onto lip 7 of either or both upper and lower outer casing portions. Curing of this adhesive does not create stress in the treated membrane fibres. Optionally indentations 6 may also receive adhesive. The membrane bundle 3 is located in the outer casing portions so that the plugs 4, 5 are both correctly located in indentations 6. The outer casing portions 1 and 2 (or 1 and 2' as appropriate) are then aligned and held together whilst the adhesive sets firmly. The unit is shaped so that a tight seal around each plug 4, 5 is produced.

Inlet and outlet ports 8, 9 are also illustrated and optionally connectors may be adfixed thereto. Likewise side ports 10 are also shown; these enable sampling of the mother liquor during the process or addition of a second fluid to the mother liquor, for example to control the trans-membrane pressure. Alternatively the side ports may be used to hold a sensor which monitors the filtration process.

Figure 3 illustrates an alternative unit which

comprises a membrane bundle treated according to the present invention. This unit is formed as described for the unit of Figure 2 but the membrane bundle is bent into a "U"-shape to fit into the outer casing portions.

Figure 4 shows a filter unit device indicated generally at 100 having a flat sheet membrane filter 12 which separates the flow-through cell 13 from the filtrate chamber 14. The membrane may be treated according to the invention on one or both surfaces. In use process liquor is pumped at pressure through the cell in the direction shown by the arrow and the filtrate may leave the filtrate chamber 14 by a port 15 which may be fitted with a tap (not shown). Alternatively a further fluid may be input via port 15 and be filtered across membrane 12. A reactive or binding agent may be located on the membrane filter 12, cell 13 and/or in chamber 14. The blocking moiety and, subsequently, the coating may be sequentially introduced into a device (eg as illustrated in Fig. 4) having an untreated membrane. Thus, the membrane may be treated in situ when part of the device. This may allow easier handling of the membrane.

Figure 5 illustrates a device similar to that shown in Figure 4 and described above. In the device of Figure 5 (shown generally at 100) the filter membrane 12 is in the form of a tube 16. Either the internal or external surfaces (or both) of the hollow fibre membrane may be treated as described for the present invention. For example, the blocking agent used may be a sugar solution, which is then followed by an antibody or lectin coating. The mother liquor is passed through the lumen of tube 16 (which forms flow-through cell 13), preferably at a controlled pressure, in the

direction of the arrow. The filtrate will collect in chamber 14 and may be taken off via port 15 which again may if desired be fitted with a tap. Alternatively port 15 may be used to input a second fluid, either to react with the filtrate of the mother liquor (ie the agent may be present in the second fluid) or to control the pressure within the device. Reaction of the coating on the membrane with a component of the mother liquor may result in a detectable change, for example in fluorescene or other photometric change.

Figure 6 illustrates a further embodiment, similar to those previously described with respect to Figures 4 and 5. In the embodiment of Figure 6 the membrane filter (shown generally at 12) is in the form of hollow fibre membranes 17 of which two are illustrated for simplicity. The number of hollow fibre membranes may be adjusted from 1 to several hundred depending upon the size of the device. Each or any of the hollow fibre membranes may be coated. The coatings used may be the same, or may vary. Likewise the blocking moieties required may be varied as required. The lumen of the individual fibres are used to transport the mother liquor into the device and thus act as the flow-through cell. The filtrate collects in chamber 14. The ends of the hollow fibres are sealed into the device to prevent the mother liquor entering the filtrate chamber 14 by any means other than by passing across the membrane.

Figure 7 depicts a further embodiment of device 100 with tubular filter membrane 12 as depicted in Figure 5 but with the addition of a direct sensor 18. The sensor 18 may be, for example, a pH sensor, a conductivity sensor or a biosensor. The sensor may detect the reaction of the component of interest with

the coating on the membrane. In use the component of interest passes across the membrane filter 12 into the filtrate chamber 14. The pressure differential across the membrane may be controlled via port 15 which may contain a tap or valve. The component of interest may react with the coating on the membrane and then be detected by sensor 18 which then generates production of an output signal, preferably an electrical, audible or visual output signal.

Figure 8 illustrate three further embodiments of a device having a membrane treated according to the present invention. In general the embodiments shown are similar to those described above for Figures 4 to 7, especially Figure 6. In Figure 8A, the membrane 12 consists of a single hollow fibre membrane, having an internal lumen of approximately 1mm. The membrane is coated on its outer surface. The whole of the volume between the exterior surface of the membrane and the interior surface of the outer casing 19 is filled with a material 110, such as LCM 32 or LCM 35 from Ablestick, which contains an agent able to react with a component of interest in the mother liquor. In use the mother liquor is passed down the lumen of the hollow fibre membrane 17 and filtrate moves across the membrane surface by cross-flow filtration. The component of interest present in the filtrate then encounters the agent held within the material 110. In the illustrated embodiment the material is solid and the agent is uniformily distributed therein. However a porous material encapsulating the agent could equally be used. The component may either be modified by reacting with the agent or may be simply detected by the agent which may not alter it physically or chemically. For example the agent could be light emitting, photosensitive or photoreactive.

In Figure 8B the material 110 does not entirely fill the volume between the exterior surface of the membrane and the interior surface of the outer casing 19, but leaves a pre-determined volume able to accept filtrate. The agent may be present either in the free volume or else be held within material 110 as described for Figure 8A above. Alternatively two different agents may be present in these separate physical locations.

Although not illustrated, the device of Figure 8B could also be produced having two or more (for example three, four or five) volumes separately filled with material 110 (or with different types of material 110) and separated or abutting each other. Again different agents or different concentrations of agents could be contained in each.

In Figure 8C, the device is as shown in Figure 8B, except that the device further includes a additional port 15. Port 15 may be used to draw off filtrate, to introduce a second fluid, optionally containing an agent to modify or detect the component of interest or simply to adjust the pressure and thus the flow across the membrane.

Example 1

Forming a Sealed Membrane Unit and Coating the Lumen Surface of the Membrane Fibre with Enzyme

A membrane in the form of a hollow fibre was taken. Before encapsulation of the membrane fibre into a sealed outer casing, the fibre was treated with a solution of buffered bovine serum albumen (BSA). Treatment occurred by controlled flow of the buffered BSA through the lumen of the fibre with slight resistance to the flow.

The membrane fibre was air dried under sterile conditions at ambient temperature for approximately 1½ hours.

The treated membrane fibre was placed within an outer casing and was sealed into the outer casing by application of an adhesive at each end of the membrane fibre. Upon curing of the adhesive using UV light no tear in the fibre was observed.

A buffered enzyme solution was pushed through the lumen of the membrane fibre using a syringe. The enzyme adhered to the inner surface of the membrane and excess enzyme was washed off with buffer.

A substrate of the enzyme was introduced into the lumen of the membrane fibre and the enzymic reaction was observed optically. It was noted that only the inner surface of the membrane fibre had been coated with enzyme.

Example 2

Materials and Media

1. The immunoassay reader detected chemiluminescence by a photon counter which was developed by A.D.L Ltd, and was used for these experiments.

2. **Filter Unit** The filers used were 5mm FSM Technologies Ltd Glowgrub™ hollow fibre membrane filter units. These units comprise a single hollow fibre membrane having a diameter of approximately 280μm up to 1mm outer diameter pre-blocked in blocking buffer, and potted at either end with adhesive so that the volume described by the outer surface of the fibre and the inner surface of the casing is completely enclosed. The lumen of the hollow fibre is not blocked by the adhesive and the sample flows along the lumen of the fibre and undergoes cross-flow filtration, the filtrate collecting in the volume between the outer fibre surface and inner wall of the casing. Details of the blocking buffer are given at Item 6 below.

3. **Antigen** A formalin fixed culture of virulent *Staphylococcus aureus* at a concentration of 10^7 cellsml^{-1} supplied by FAS Medical Ltd.

4. **Primary Antibody** An IgG anti-*Staphylococcus aureus* monoclonal antibody (1° Ab) at a concentration of 1mgml^{-1} as determined by OD 280mm and purified by column chromatography. The antibody was reported to show no cross reactivity with E.coli, Streptococcus Group G, Strep. faecalis, Strep. bovis, Strep. uberis, Strep.

agalactiae, Mycoplasma bovis or M. bovigenitalium. The antibody was prepared for use at a titre equivalent to $1\mu gml^{-1}$ and $10\mu gml^{-1}$ in buffer.

5. **Secondary Antibody** (2° Ab) An anti-mouse IgG raised in goat, labelled with Alkaline Phosphatase with whole molecule affinity. The recommended titre dot blot assay was 1:30000 and the titre chosen for this experiment was 1:150000.

6. **Buffers** The wash buffer and antibody diulation buffer was 20mM Tris pH 8.0 with 0.05% (v/v) Tween 20 and 0.5% v/v Casein/Maleic acid buffer. The buffers were freshly prepared and sterilised by autoclaving. The blocking buffer used to pretreat the membranes was 20mM Tris pH 8.0 with 0.05% (v/v) Tween 20 and 1.0% (v/v) Casein/Maleic Acid.

7. **Substrate** Disodium 3-(4-methoxyspiro{1,2-dioxetans-3,2'-tricyclo[3.3.1.1^{3,7}]decan}-4-yl)phenyl phosphate (AMPPD), is a non-isotopic, stable substrate which can detect 4.0pg enzyme after 5 min reaction time. The substrate used was a pre-prepared working strength solution in DEA buffer at pH 10.0.

Test Methods

For each test the method was the same. The filter unit was fitted into a holder with a 75% restrictor and Luer fitment. 1 ml of antigen solution was passed through. This was followed with approximately 500μ 1° Ab, the filter unit was laid aside for 1 min to allow antigen/antibody interaction then $500\mu l$ of 2° Ab applied. The filter unit was laid aside for a further minute after which time it was washed with 1ml wash

buffer. This was repeated minus antigen for the negative control. When all filter units had been treated each in turn received 500µl AMPPD at timed intervals. A count was made after 5 min reaction time.

Example Results

	Sample	RLU
1.	Instrument blank	13087
2.	Negative control (No1)	13429
3.	Test 10^5 ml^{-1} (No1)	517451
4.	Negative control (No2)	9052
5.	Test 10^5 ml^{-1} (No2)	13786
6.	Sample 7.30 sec later (No2)	33160
7.	Negative control	49331
8.	Test 10^5 ml^{-1}	83467

RLU = Relative light units, being the relative difference in light emitted due to the presence of the filter unit, compared to the background reading of the instrument alone.

The test indicated the background is shown to be very small and consistent.

Little or no non-specific binding of the secondary antibody for the membrane of the filter unit was observed even with only one wash step in the procedure.

Non-specific binding has caused significant problems and multiplied the wash steps by many times with other systems.

The test over control readings indicate a significant increase in count. Even with high debris high

turbidity samples a 30% increase over background is normal.

Example 3

Adhesive curing with and without a Blocking Agent

Membrane - Polysulphone or Polypropylene

Size(μm) - 280 and 660 and 1000 (outer diameter)

Adhesive - LCM 32 and LCM 35 (Ablestick Ltd)

Block Agents - Sterile Water, Ethanol or Glycol

Test Procedure Twenty samples of each (given in percentage by volume with respect to the weight of the membrane) filter unit were tested for compliance and fracture at the adhesive membrane interphase. All samples were checked immediately after curing of the adhesive and 5 minutes later.

Results

Membrane Type	Size	% Blocking Agent	Time (mins)	Results
Polysulphone	280	100% Water	5	OK
Polysulphone	280	10% Water	5	OK
Polysulphone	280	Dry	Instant	Fail
Polysulphone	660	100% Water	5	OK
Polysulphone	660	10% Water	5	OK
Polysulphone	660	Dry	Instant	Fail
Polypropylene	1000	10% Water	5	OK
Polysulphone	280	10% Ethanol	5	OK
Polysulphone	660	10% Ethanol	5	OK
Polypropylene	1000	10% Glycol	5	OK

"OK" indicates that no fracture of the membrane occurred.

Example 4

Coating with Acridine Orange

Polypropylene hollow fibre membranes were obtained and the lumen washed with Tween buffer as blocking agent, by injecting the Tween buffer down the lumen using a syringe. The exact concentration of the Tween buffer will be selected in accordance with the characteristics of the membrane, but generally a concentration of 0.01% to 1.0% (v/v) is sufficient. The membrane was then dried by hot air in a drying oven. The treated membrane was immersed in a solution of acridine orange and dried in a hot air oven.

The coated membrane was inserted and sealed into a membrane unit and then challenged with a sample containing bacteria, the sample being introduced down the lumen of the membrane. A UV response was observed from the acridine orange coated membrane, indicating that bacteria had been detected in the sample.

The outer surface of the hollow fibre membrane can likewise be treated as described above. Where only the outer surface is to be treated, the blocking agent and/or the coating may be sprayed on to the fibre surface.

The treated membrane described above may likewise be used to detect the presence of virus in a sample, since the acridine orange coating binds to nucleic acids to give a UV detectable response.

The Example described above may be repeated using Bisbenzimide H33258 of Hoechst to replace the acridine orange as coating. Bisbenzimide H33258 gives a fluorescent staining of DNA in cells (see Kim et al, Anal Biochem 174:168 (1988)).

CLAIMS

1. A method of treating at least a portion of a membrane, said method comprising:

   a. contacting a surface of said membrane portion with a blocking moiety; and

   b. applying a coating to said surface of the treated membrane portion of step a.

2. A method as claimed in Claim 1 wherein said blocking moiety is a fluid.

3. A method as claimed in Claim 2 wherein said blocking moiety is water.

4. A method as claimed in Claim 1 wherein said blocking moiety is an amino acid, peptide, protein, sugar, fatty acid or a mixture thereof.

5. A method as claimed in Claim 4 wherein said blocking moiety includes a serum albumin or a milk protein.

6. A method as claimed in any one of Claims 1 to 5 wherein said coating is an adhesive, an antibody, an enzyme, a lectin, an epitope, or a reactive molecule.

7. A method as claimed in Claim 6 wherein said coating is an adhesive.

8. A method as claimed in Claim 6 wherein said coating is an antibody, epitope or lectin.

9. A method as claimed in any one of Claims 1 to 8 wherein said blocking moiety at least partially fills the interstices of the membrane portion.

10. A method as claimed in any one of Claims 1 to 9 wherein said blocking moiety is formed in or on said membrane portion by a chemical reaction.

11. A method of forming a membrane unit, said method comprising:

a. exposing at least a part of the membrane portion which is to be in contact with adhesive to a blocking moiety;

b. applying said adhesive to said membrane portion;

c. curing the adhesive or allowing the adhesive to set;

d. optionally drying any wet area of said membrane.

12. A method as claimed in Claim 11 wherein said blocking moiety is water.

13. A treated membrane produced by the method of any one of Claims 1 to 10.

14. A membrane unit produced by the method of either one of Claims 11 and 12.

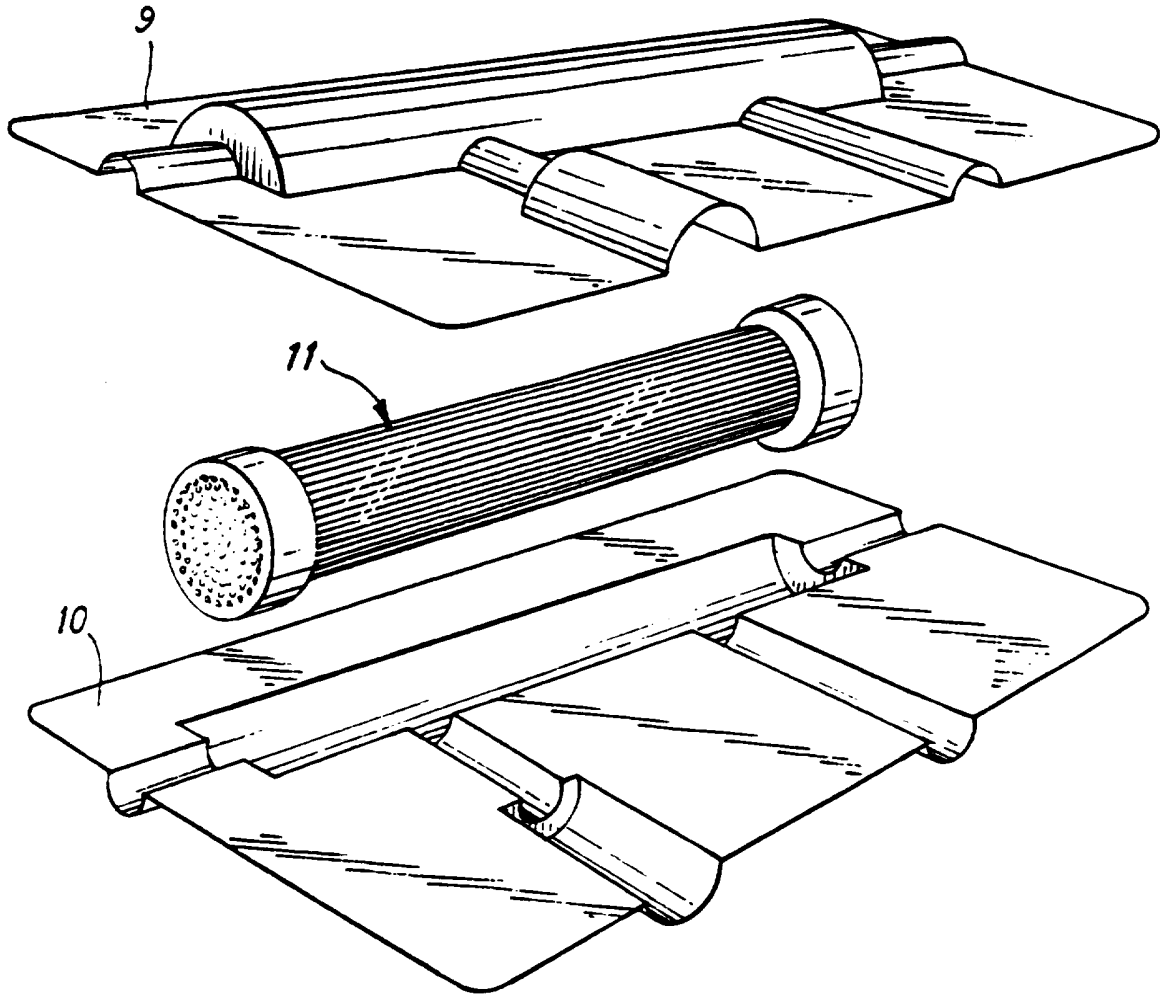

FIG.1

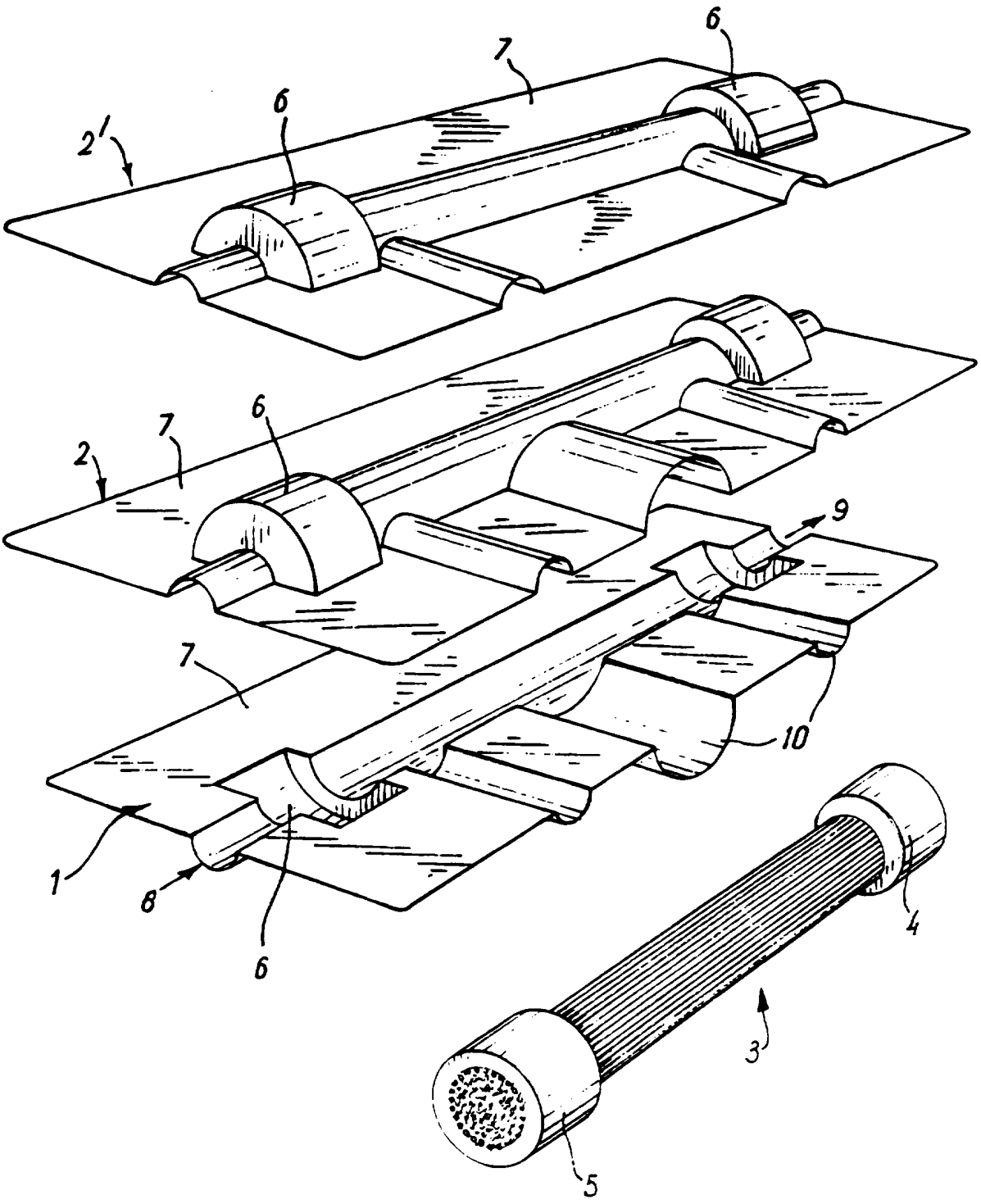

FIG 2

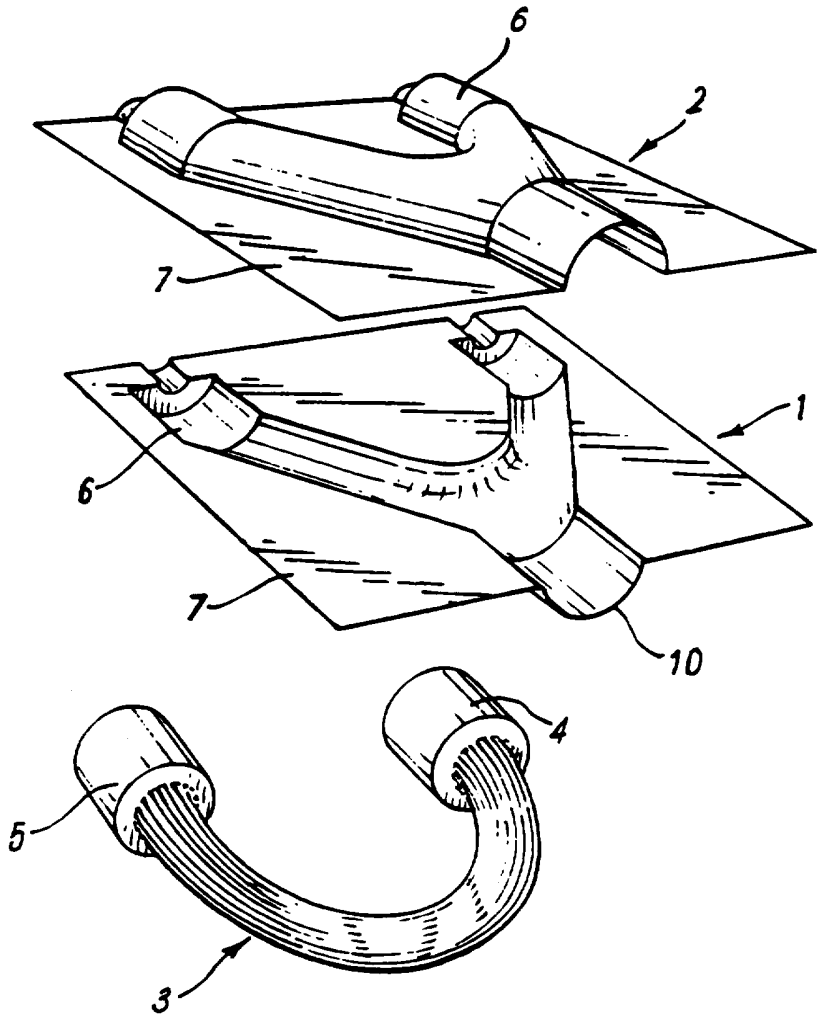

FIG. 3

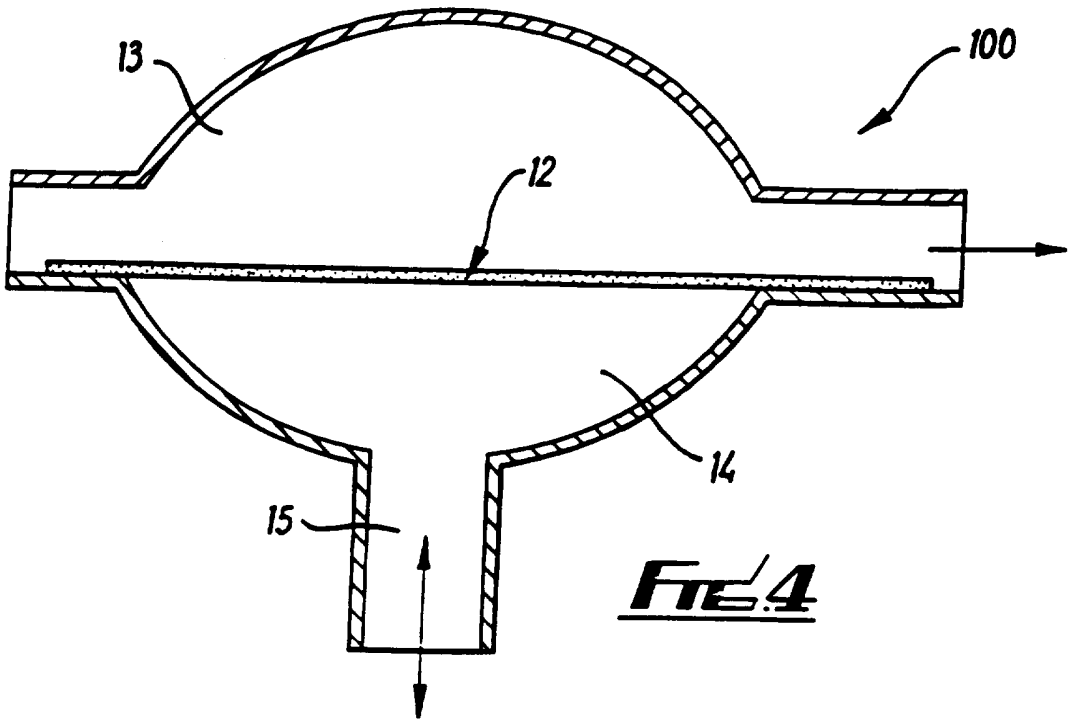

FIG.4

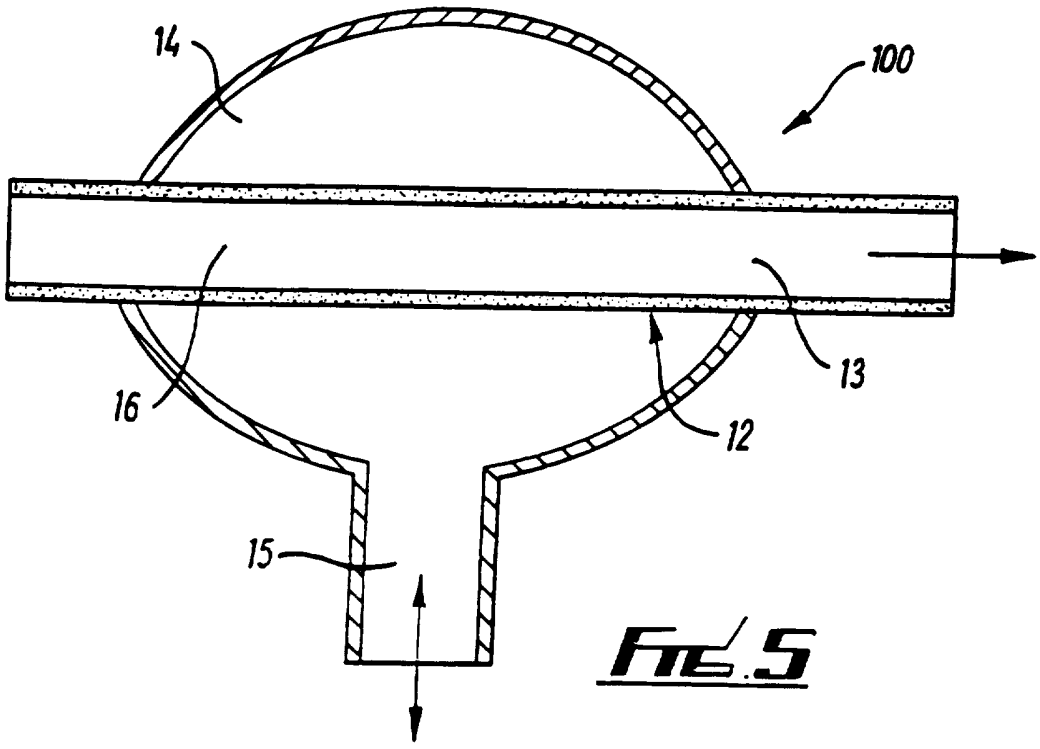

FIG.5

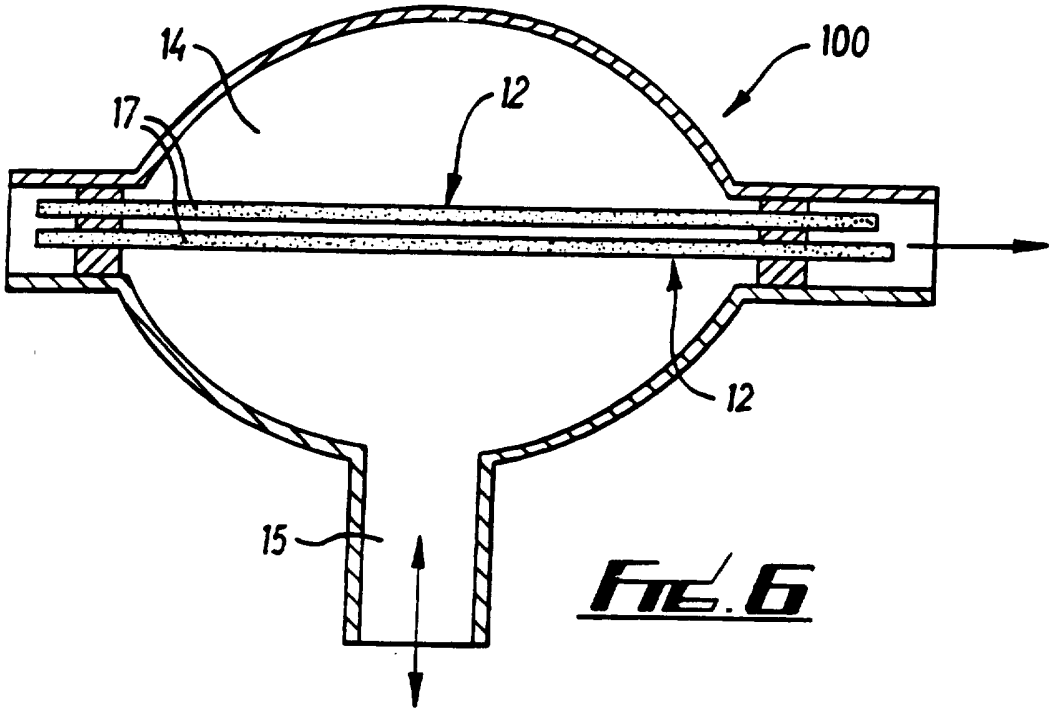

FIG. 6

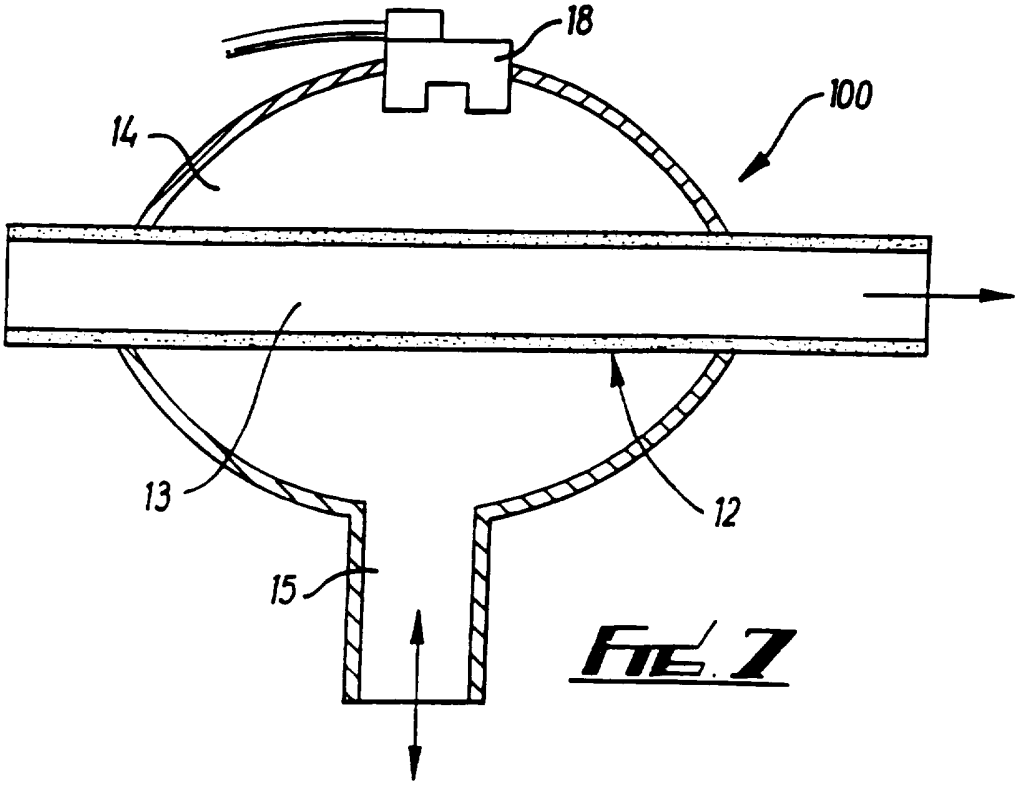

FIG. 7

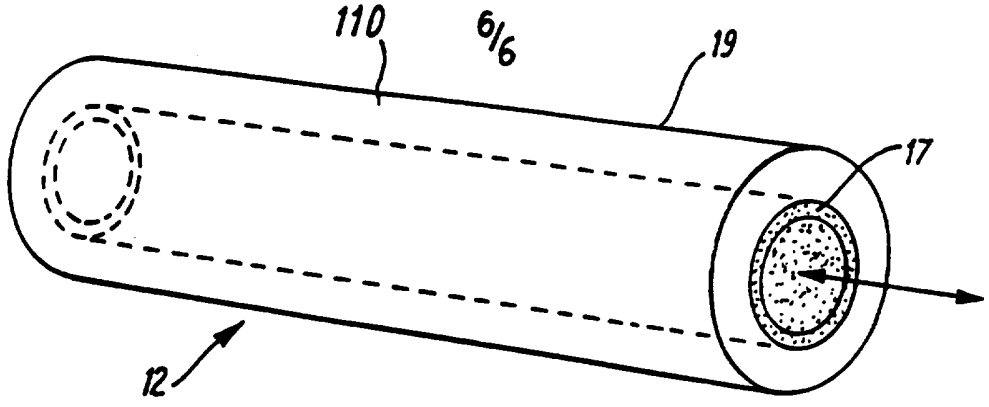

FIG. 8A

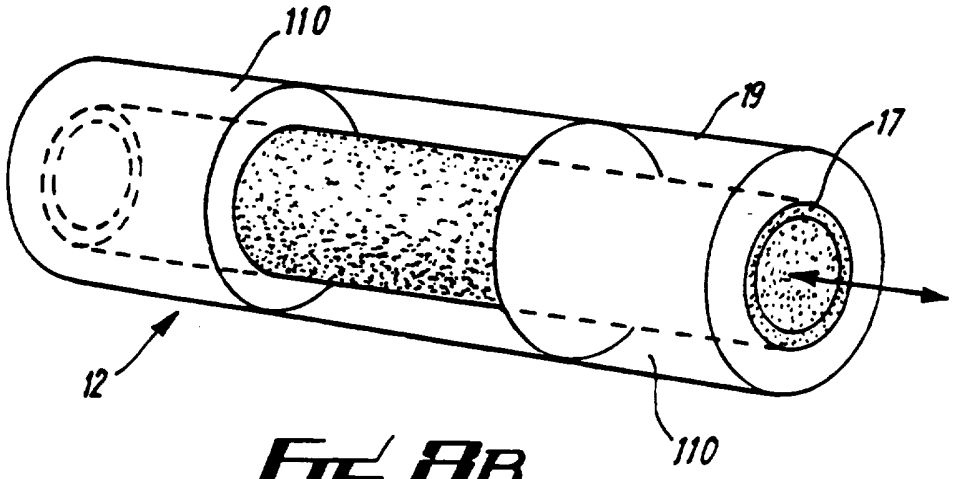

FIG. 8B

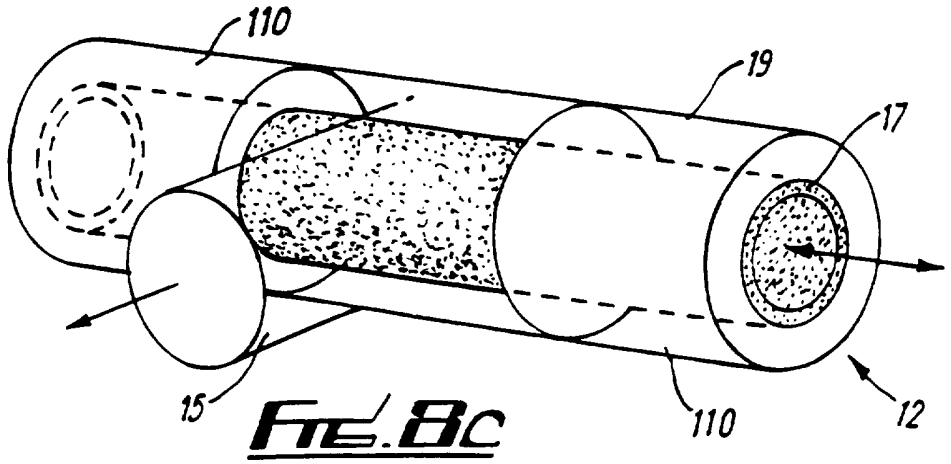

FIG. 8C