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(21) International Application Number: PCT/US96/03362 (22) International Filing Date: 12 March 1996 (12.03.96) (30) Priority Data: 08/422,274 13 April 1995 (13.04.95) US (71) Applicant (for all designated States except US): TRAVENOL LABORATORIES (ISRAEL) LTD. [IL/IL]; P.O. Box 2, 77100 Ashdod (IL). (72) Inventors; and (75) Inventors/Applicants (for US only): KRAUS, Menahem, A. [US/IL]; 25 Pashosh, 76100 Rehovot (IL). GAMLIELI, Yephet [IL/IL]; 25 Smilchanski, 75233 Rishon Lezion (IL). YONATH, Jacob [IL/IL]; 43 Gordon, 76287 Rehovot (IL). HAZAN, Roni [IL/IL]; 73 Moshe Dayan, 67420 Tel Aviv (IL). (74) Agent: FRIEDMAN, Mark, M.; c/o Sheinbein, Robert, 2940 Birchtree Lane, Silver Spring, MD 20906 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: LEUKOCYTE FILTRATION METHOD AND APPARATUS		
(57) Abstract A method for selectively removing leukocytes from a suspension which also contains platelets, such as a platelet concentrate or whole blood. The method includes passing the suspension through a filter which includes a polysaccharide-type coating. The coating may include one or more of hydroxypropylmethyl cellulose, hydroxybutylmethyl cellulose, dextran and hydroxyethyl starch. Also provided is a filter for selectively removing leukocytes from a suspension which also contains platelets. The filter includes a substrate which is coated with a polysaccharide-type composition.		

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LEUKOCYTE FILTRATION METHOD AND APPARATUS

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FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to methods of removing leukocytes from whole blood or platelet concentrates.

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It is widely known that for the vast majority of transfusion therapies it is desirable to remove the leukocytes from donated blood, typically by filtration, prior to the transfusion of the various blood components into a patient.

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It is desirable to remove the leukocytes since their presence may have adverse effects on the patient. For example, leukocytes may cause non-hemolytic febrile reactions and/or HLA allo-immunization. Leukocytes may also induce graft versus host reactions. In addition, leukocytes present in contaminated blood may harbor various viruses. At the same time, the removal of the leukocytes does not generally have negative implications for the recipient since the leukocytes serve no useful purpose in the vast majority of transfusions.

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The current practice is to remove the leukocytes from the various blood components after these have been separated from whole blood. Thus, each portion of whole blood is typically first separated, e.g., by centrifuging and/or filtration, into a number of components or fractions, principally (1) packed erythrocytes (red blood cells); (2) platelet concentrate; and (3) plasma. Each of the fractions then undergoes separate treatment, typically filtration, to remove the leukocytes present in that fraction.

For example, in PCT/US94/01413 the present inventors describe unique, membrane-based filters for removing leukocytes from packed red blood cells or for removing both leukocytes and platelets from whole blood. The filters described in PCT/US94/01413 capture platelets and are thus unsuitable for the removal of leukocytes from platelet concentrates or from whole blood.

A difficulty with filters such as those disclosed in PCT/US94/01413 is that they are limited to treatment of specific blood fractions rather than to whole blood. This limitation makes it necessary to carry out a number of separate filtrations, each using a specific filter, to separately remove the leukocytes from each of the blood fractions.

It would be advantageous to have an efficient filter capable of selectively removing leukocytes from whole blood, i.e., a filter which would effectively capture leukocytes while effectively passing the other blood components, including the plasma, red blood cells and the platelets.

The ability of selectively removing leukocytes from whole blood with the attendant recovery of red cells and platelets would have significant operational and cost advantages. In practice, whole blood would then be filtered to remove leukocytes only once, preferably in the blood bank. Following this filtration, the leukocyte-free blood would be separated, as by centrifugation, into leukocyte-free fractions and processed in the usual manner.

The removal of leukocytes from whole blood requires a special filter which captures leukocytes but passes red blood cells and platelets.

Currently, no such filter is commercially available, although at least one such filter is described in the literature. Specifically, a whole blood leukocyte filter is disclosed in U.S. Patent No. 4,985,153. However the performance of that filter, as described in the above-referenced patent, is far from satisfactory, considering current internationally accepted standards. Current international standards call for residual leukocytes of no more than 5×10^6 per unit of blood. Platelet recovery is expected to be no less than 70%.

There is thus a need for, and it would highly advantageous to have, a universal filter exhibiting high platelet recovery and very high leukocyte retention.

SUMMARY OF THE INVENTION

According to the present invention there is provided a method for selectively removing leukocytes from a suspension which also contains platelets, comprising passing the suspension through a filter which includes a polysaccharide-type coating.

Also according to the present invention there is provided a filter for selectively removing leukocytes from a suspension which also contains platelets, comprising: (a) a substrate; and (b) a coating on the substrate which includes a polysaccharide-type composition.

Finally according to the present invention there is provided a process for preparing a filter for selectively removing leukocytes from a suspension which also contains platelets, comprising the steps of: (a) providing a coating

solution including a polysaccharide-type composition and a solvent; (b) applying the coating solution to a substrate; and (c) drying the coated substrate to form a dry coated substrate.

According to further features in preferred embodiments of the invention described below, the polysaccharide-type composition includes one or more of hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropylmethyl cellulose, hydroxybutylmethyl cellulose, dextran and hydroxyethyl starch.

The present invention successfully addresses the shortcomings of the presently known configurations by providing a method and apparatus for efficiently selectively removing leukocytes from suspensions, such as blood and blood fractions, which also contain platelets.

The method and apparatus involves use of a membrane and/or non-woven material coated with a polysaccharide-type composition through which a suspension containing both leukocytes and platelets is passed. It has been found that this method and apparatus are effective in passing the platelets while retaining the leukocytes.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of a method and apparatus for efficiently selectively removing leukocytes from whole blood or from a blood fraction which contains platelets.

The principles and operation of the present invention will be better understood with reference to the following description and examples.

It is known in the literature that filtration can be used to recover platelets from leukocyte-free blood through the use of very specific surface treatments of the filter medium. In the absence of these treatments the filter will retain a large proportion of the platelets.

5 Two types of such surface treatments are described in the literature. U.S. Patent 4,936,998 discloses the surface coating of preformed acrylic copolymers, such as copoly(hydroxyethyl methacrylate-diethylaminoethyl methacrylate). U.S. Patent 4,880,548 discloses the grafting of certain monomers, such as acrylate, onto the surface. It is noted parenthetically
10 that U.S. Patent No. 4,880,548 asserts that in order to obtain efficient platelet filtration a filter is required which features critical wetting surface tension of 90 dyn/cm or more.

None of the commercially available platelet concentrate leuko-depletion filters is suitable for recovery of platelets from whole blood since
15 the presence of red blood cells along with platelets serves to rapidly clog these filters.

It has been unexpectedly found that coating of a suitable filter media using simple commercially available polysaccharides and polysaccharide derivatives (referred to herein singly and collectively as a "polysaccharide-type composition") makes it possible to construct highly efficient platelet
20 filters which operate to remove leukocytes from platelet concentrates. Similar treatments can be used to make a highly efficient universal filter which efficiently removes leukocytes from whole blood. Thus, methods and filters according to the present invention are suitable for the removal of

leukocytes, with minor modifications, for both platelet and whole blood filtration.

Various polysaccharide-type compositions are suitable in a method and filter according to the present invention. Examples include various cellulose derivatives, including but not limited to, hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), hydroxybutylmethyl cellulose, hydroxypropylmethyl cellulose dextran and hydroxyethyl starch. Preferred polysaccharide-type compositions include hydroxypropyl cellulose, hydroxypropylmethyl cellulose and hydroxybutylmethyl cellulose. The most preferred polysaccharide-type composition is hydroxypropyl cellulose. The various polysaccharide-type compositions are generally soluble in water and a number of other solvents, such as ethanol.

A dilute solution, typically in water, of one or more of these polymers is used as a coating solution to coat the surface of the filter substrate or medium. A preferred solution is an aqueous HPC solution with an HPC concentration of from about 0.1 to about 10% wt/vol. Most preferred is a concentration of from about 0.5 to about 3% wt/vol.

The filter substrate may be any suitable medium, preferably one or more non-woven sheets or one or more membranes. Most preferably, the filter substrate includes both one or more non-woven sheets and one or more membranes. As used herein, the term 'membrane' is intended to include a continuous, nonfibrous porous matrix.

Membranes for use in the present invention may be made of any suitable material, including but not limited to, polycarbonate, acrylic

copolymer, polyvinyl chloride, nylon and nitrocellulose. Preferably, the membrane features a pore size of from about 2 to about 20 μ .

Non-woven materials for use in the present invention may be made of any suitable material, including but not limited to, polyester, cellulose, nylon and polypropylene.

To produce a properly coated filter medium, typically membrane and/or non-woven, a coating solution, typically in water or ethanol, which includes a polysaccharide composition is provided. The filter substrate is then coated, as by dipping, with the coating solution. The filter is then dried at any suitable temperature, such as near room temperature or at elevated temperatures to evaporate the solvent and form a dry coated substrate.

To provide for better bonding between the polysaccharide-type composition and the substrate it may be desirable to provide a cross-linking agent in the coating solution. Any suitable cross-linking agent may be used, including but not limited to a melamine, such as hexamethoxymethyl melamine, a polyepoxide, or a polyaldehyde. Upon drying the cross-linking agent reacts with the polysaccharide-type composition and renders it insoluble. Depending on the substrate chemistry, the cross-linking agent may also react with the substrate serving to bind the polysaccharide-type composition tightly to the substrate so as to preclude the possibility of the separation of the coating from the substrate.

Optionally, regardless of whether curing is used, it may be desirable to wash the dry coated substrate with a suitable washing medium, such as

water or ethanol, and subsequently re-dry the washed coated substrate. Even in the absence of cross-linking, sufficient coating material may remain on the substrate to be effective.

5 The coating of the filter substrate as described above has been found to have a dramatic beneficial effect on platelet passage through the filter despite the fact that the coated substrate has a surface tension of only about 70 dyn/cm.

10 Whereas many untreated filter media, such as polyester, nylon, nitrocellulose, with pore size of 2-20 μm retain all or a very significant fraction of the platelets, following treatment with a polysaccharide-type composition, platelet recovery is typically from about 80 to about 100%. While at times the retention of white cells is also slightly reduced by the treatment, the effect is not nearly as pronounced as the increase in platelet recovery. In this way, a good separation between leukocytes and platelets
15 can be achieved.

Because of their flexible membrane and poor adhesion, red cells pass easily through filters of the present invention. Thus, a universal filter, which is able to selectively remove leukocytes from all other blood components is achieved.

20 As demonstrated in the examples below, with the appropriate number and porosity of layers of filter media, highly efficient leukocyte-removing filters for platelet concentrates and for whole blood can be constructed.

The most preferred filter configuration includes two layers: (1) a non-woven filter layer and a membrane filter layer. Each of the layers may

include multiple filter sheets. Both layers are treated with the polysaccharide-type composition as described above. A typical filter, made as described, yields platelets recovery of greater than 70% and leukocyte retention of greater than 99% in both platelet concentrate filtration and whole blood filtration.

EXAMPLES

Examples 1-23 relate to the filtration of platelet concentrates while Examples 24-28 relate to the filtration of whole blood.

Examples 1-6: Effect of Coating on Membrane Performance

Various membranes were treated by dipping into a solution of 1% hydroxypropyl cellulose (HPC) in water. The membranes were then allowed to dry at ambient conditions. The treated membranes and untreated controls were tested for passage of platelets and white blood cells from standard platelet concentrates. The results are summarized in Table 1. As can be clearly seen, the treatment dramatically improves platelet passage and flow rate.

Table 1: Filtration of Platelet Concentrates (PC) Through Coated Membrane Filters

Ex.	Membrane	Pore size (μm)	Treatment	No. of Layers	Flow Rate ml/min	Cell Passage	
						PLT%	WBC%
1	Polycarbonate (PC, Poretics)	2	Untreated	1	0	0	0
			Coated	1	0.3	100	30
2	Acrylic copolymer (Versapore, Gelman)	3	Untreated	1	0	1	0
			Coated	1	0.5	75	17
3	PVC (GLA-5000, Gelman)	5	Untreated	1	0	0	0
			Coated	1	0.3	32	0
4	Nylon (Magna-Nylon, MSI)	10	Untreated	1	0.1	13	0
			Coated	1	0.8	75	14
5	Nylon (Magna-Nylon, MSI)	20	Untreated	1	0.9	77	32
			Coated	2	3.8	96	11
6	Nitrocellulose (NC, AE100, S&S)	12	Untreated	2	0.7	32	18
			Coated	2	9.0	92	13

Examples 7-10: Effect of Coating on Non-woven Filter Performance

Various Polyester non-woven filters were treated by dipping the filter substrate in 1% aqueous or ethanol HPC solution and drying.

Multilayer arrays of treated filters and untreated controls were used to filter platelet concentrates. The results are summarized in Table 2.

It is clearly seen that the passage of platelets is very substantially improved following treatment, while the passage of white cells increases to a much smaller extent.

Table 2: Filtration of Platelets Concentrates Through Coated Non-wovens

Example	Filter	Treatment	No. of Layers	Flow Rate ml/min	Cell Passage	
					PLT%	WBC%
7	Polyester 80 g/m ² , Sodoca	Untreated	10	86	55	15
		Coated	10	40	100	35
		Coated	30	6	94	5
8	Polyester 100 g/m ² , Sodoca	Untreated	10	7	24	9
		Coated	10	3	100	29
9	Polyester 120 g/m ² , Freudenberg	Untreated	10	3*	19	0
		Coated	10	3*	86	9
10	Cellulose 11 μ (Whatman)	Untreated	6	0.7	83	20
		Coated	6	2	96	40

* Flow adjusted to 3 ml/min.

Examples 11-15: Effect of the Concentration of the Coating Solution

The coating effect is concentration dependent as shown in Table 3. The model filters used were a combination of membranes and non-woven sheets. As shown, HPC concentration of 0.5% (wt/vol) and higher ensures good flow, good platelet passage and little white cell leakage.

Table 3: Effect of HPC Coating Concentration on Filter Performance

Filter Composition: Polyester 120g/m² Sheets (6 layers)

Nitrocellulose membrane: AE100 (3 layers)

Filter treatment: HPC coating

Flow Rate: Adjusted to 1.0-1.5 ml/min

Example	HPC Concen. (%)	Vol. (ml) Filtered Before Clogging	Cell Passage	
			PLT%	WBC%
11	0	< 6	9	2
12	0.25	< 23	79	4
13	0.5	> 30	84	5
14	1.0	> 30	85	3
15	2.0	> 30	89	5

Examples 16-18: Effect of Coating Cross Linking

The filter coating was cross-linked for improved stability. The cross-linking agent used was hexamethoxymethyl melamine. Table 4 summaries results from a number of treatment variables.

It is shown that cross-linking, alone or in conjunction with subsequent washing, apparently has little effect on either platelet or white cell passage. However, the amount of extractable material lost upon washing is substantially reduced.

Table 4: Cell Separation Following Various Filter Treatments

Filter composition: Polyester 120g/m² sheet (8 layers) and AE (3 layers)

Example	Filter and Treatment	Cell Passage	
		PLT%	WBC%
16	2% HPC	89	3
17	2% HPC + Cross Linking	87	2
18	2% HPC + Cross Linking + Washing	88	2

Examples 19-23: Full Scale Platelet Filters

Full scale platelet filters, suitable for 4 to 5 pooled units, were constructed from a layered structure of surface treated non-woven materials and treated membranes. Construction and performance data are summarized in Table 5.

Table 5: Performance of Full Scale Platelet Filters

Ex.	Filter Composition	No. of Layers	Vol. Filtered (ml)	Platelet Recovery (%)	WBC Removal (%)	Residual WBC	
						per μ l	Total
19	Polyester 80g/m ²	32	200	98	99.95	0.25	0.1x10 ⁶
	AE-100 (12 μ)	3					
20	Polyester 100g/m ²	20	250	94	99.83	1.1	0.25x10 ⁶
	AE-100 (12 μ)	4					
21	Polyester 100g/m ²	16	200	95	99.74	1.4	0.27x10 ⁶
	AE-100 (12 μ)	5					
22	Polyester 100g/m ²	20	200	100	99.70	1.6	0.32x10 ⁶
	AE-100 (12 μ)	5					
23	Polyester 100g/m ²	20	230	88	99.81	1.1	0.25x10 ⁶
	AE-100 (12 μ)	5					

- Treatment
- Filters 19 and 21 - coating (1% HPC)
 - Filters 20 and 22 - coating and cross-linking (0.025% melamine)
 - Filter 23 - coating, cross-linking and washing

Example 24: Hydroxypropyl Cellulose Coating (Whole Blood)

A 0.1% aqueous solution of hydroxypropyl cellulose (HPC) of 370000

MW was used. The filter materials included nitrocellulose membranes of
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nominal pore size 12 and 8 microns, and a 120g/m² non-woven polyester fabric.

The filter materials were dipped in the HPC solution for 5 minutes at room temperature. The non-woven fabric was squeezed to remove excess solution. The membranes were treated similarly, but were not squeezed. After 24 hours of drying at room temperature a filter was constructed in a plastic holder of 43 cm² filtration area. The filter was made up of two layers of 8 μ membrane, two layers of 12 μ membrane and 20 layers of non-woven fabric serving as a pre-filter. Another four layers of the same non-woven fabric were introduced between adjacent membranes to serve as separators. Four hundred seventy ml of whole blood were collected into a standard collection bag using CPD anticoagulation solution and filtered 6 hours after donation. Filtration time was 27 minutes at a pressure head of 0.09 atm. Leukocyte content was reduced from 6300/ μ l in the original blood to 4/ μ l in the filtered blood. Seventy two percent of the original platelets (185000/ μ) were recovered. The erythrocyte content of the filtered blood was reduced by only 0.5%. When the same experiment was repeated without applying HPC coating to the filter layers only 1-5% of the platelets were recovered.

Example 25: Effect of Washing (Whole Blood)

The procedure of Example 24 was repeated except that the 8 μ membrane was omitted, and a 1% solution of HPC was used. In addition, after the dip-coated membranes and pre-filters were dried, they were washed by soaking in water at 22°C for 20 min. Twenty hours old whole

blood was filtered in this system at a rate of 485 ml/11 min. Leukocyte reduction was from 5000/ μ l to 15/ μ l. Platelet recovery was 216000/ μ l out of 282000/ μ l in the original blood.

Repeating this experiment without applying the HPC coating resulted in only a 1-5% platelet recovery.

Example 26: Hydroxypropyl-methyl Cellulose Coating (Whole Blood)

The same filter structure as in Example 24 was used for filtration of 6 hours old whole blood. Coating was performed using a 0.6% aqueous solution of hydroxypropyl-methyl cellulose (M.W. 86000; hydroxypropyl content: 10%, methyl content: 30%) containing 0.016% glyoxal as cross-linking agent. After dipping, membranes and pre-filters were baked at 108-115°C for 40 minutes, washed and dried as per Example 25.

Filtration rate was 470ml/33min. Leukocytes were reduced from 5600/ μ l to 7/ μ l and platelet recovery was 182000/ μ l out of 216000/ μ l in the original blood.

Example 27: Hydroxybutyl-methyl Cellulose Coating (Whole Blood)

The procedure of Example 26 was repeated except that four 12 μ membranes were used and a 0.5% hydroxybutyl-methyl cellulose solution in a 9:1 water ethanol mixture was used as coating solution. No cross-linking agent was used, and the baking and washing steps were omitted. Four hundred forty ml of whole blood were filtered in 25 minutes. Platelet recovery was 73%, and leukocyte content was reduced from 7800/ μ l to 300/ μ l.

Example 28: Hydroxyethyl Cellulose Coating (Whole Blood)

5 The procedure of Example 26 was repeated using four 12 μ membranes and a coating solution made up of a 1% hydroxyethyl cellulose aqueous solution containing 0.04% glyoxal as cross-linking agent. 530 ml of 6 hours old whole blood were filtered in 19 minutes. The leukocyte count was reduced from 6200/ μ l to 300/ μ l and platelet recovery was 45%.

10 While the invention has been described with respect to a limited number of embodiments, it will be appreciated that many variations, modifications and other applications of the invention may be made.

WHAT IS CLAIMED IS:

1. A method for selectively removing leukocytes from a suspension which also contains platelets, comprising:

passing the suspension through a filter which includes a polysaccharide-type coating.
2. The method of claim 1, wherein said polysaccharide-type coating includes one or more species selected from the group consisting of hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropylmethyl cellulose, hydroxybutylmethyl cellulose, dextran and hydroxyethyl starch.
3. The method of claim 1, wherein said polysaccharide-type coating includes hydroxypropyl cellulose.
4. A filter for selectively removing leukocytes from a suspension which also contains platelets, comprising:
 - (a) a substrate; and
 - (b) a coating on said substrate which includes a polysaccharide-type composition.
5. The filter of claim 4, wherein said polysaccharide-type composition includes one or more species selected from the group consisting of hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropylmethyl cellulose, hydroxybutylmethyl cellulose, dextran and hydroxyethyl starch.

6. The filter of claim 4, wherein said polysaccharide-type composition includes hydroxypropyl cellulose.
7. The filter of claim 4, wherein said substrate includes at least one membrane.
8. The filter of claim 4, wherein said substrate includes at least one non-woven material.
9. The filter of claim 8, wherein said substrate further includes at least one membrane.
10. The filter of claim 7, wherein said membrane has a pore size of from about 2 to about 20μ .
11. The filter of claim 7, wherein said membrane includes material selected from the group consisting of polycarbonate, acrylic copolymer, polyvinyl chloride, nylon, nitrocellulose and cellulose esters.
12. The filter of claim 8, wherein said non-woven material is a polyester.

13. A process of preparing a filter for selectively removing leukocytes from a suspension which also contains platelets, comprising the steps of:

- (a) providing a coating solution including a polysaccharide-type composition and a solvent;
- (b) applying said coating solution to a substrate; and
- (c) drying said coated substrate to form a dry coated substrate.

14. The process of claim 13, wherein said coating solution further includes a cross-linking agent.

15. The process of claim 14, wherein said cross-linking agent is selected from the group consisting of melamine, polyepoxide and polyaldehyde.

16. The process of claim 13, wherein said polysaccharide-type composition includes one or more of the species selected from the group consisting of hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropylmethyl cellulose, hydroxybutylmethyl cellulose, dextran and hydroxyethyl starch.

17. The process of claim 13, wherein said polysaccharide-type composition includes hydroxypropyl cellulose.

18. The process of claim 13, wherein the concentration of said hydroxypropyl cellulose in said solvent is from about 0.1 to about 10% (wt/vol).

19. The process of claim 13, wherein the concentration of said hydroxypropyl cellulose in said solvent is from about 0.5 to about 3% (wt/vol).

20. The process of claim 13, wherein said substrate includes at least one membrane.

21. The process of claim 13, wherein said substrate includes at least one non-woven material.

22. The process of claim 21, wherein said substrate further includes at least one membrane.

23. The process of claim 20, wherein said membrane has a pore size of from about 2 to about 20 μ .

24. The process of claim 20, wherein said membrane includes material selected from the group consisting of polycarbonate, acrylic copolymer, polyvinyl chloride, nylon and nitrocellulose.

25. The process of claim 21, wherein said non-woven material is a polyester.

26. The process of claim 13, further comprising:

- (d) washing said dry coated substrate; and
- (e) drying said washed coated substrate.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US96/03362

A. CLASSIFICATION OF SUBJECT MATTER		
IPC(6) :Please See Extra Sheet. US CL :Please See Extra Sheet. 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) U.S. : 210/483, 488, 490, 496, 500.24, 503, 504, 506, 508, 650, 651, 767; 427/243, 244, 331, 372.2		
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 practicable, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 5,091,086 A (F.F. STENGAARD) 25 FEBRUARY 1992 (25.02.92), see entire document.	4-9 ----- 1-3
X -- Y	US 5,053,133 A (E. KLEIN ET AL) 01 OCTOBER 1991 (01.10.91), see entire document.	4-5, 7-10, 11 ----- 1-2, 13-14, 16, 20-24
Y	US 4,416,777 A (T. KURODA ET AL) 22 NOVEMBER 1983 (22.11.83), see entire document.	4, 8, 12-13, 21, 25
A	US 4,880,548 A (D.B. PALL ET AL) 14 NOVEMBER 1989 (14.11.89), see entire document.	1-2, 4-5, 8, 10, 11-16, 21, 23-26
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:	"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
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Date of the actual completion of the international search 13 JUNE 1996	Date of mailing of the international search report 02 JUL 1996	
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INTERNATIONAL SEARCH REPORT

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4,744,907 A (R.J. KLIMCHAK) 17 MAY 1988 (17.05.88), see entire document.	1-6, 16-19

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/03362

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (6):

B01D 24/00, 37/00, 39/00, 39/16, 61/00, 69/12, 71/08, 71/48, 71/78; B05D 1/00, 1/18, 3/00, 3/02

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

210/483, 488, 490, 496, 500.24, 503, 504, 506, 508, 650, 651, 767; 427/243, 244, 331, 372.2