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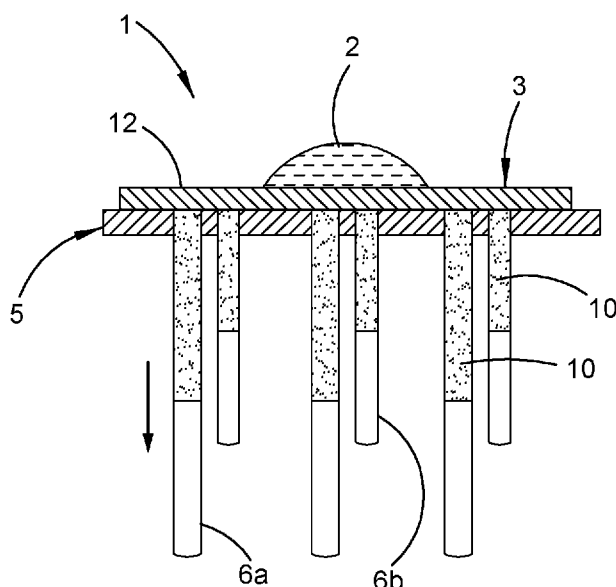


Fig. 2

(57) Abstract: A capillary system (5) for a blood separation device (1) having a blood separation membrane (3) with a plasma collection surface (4), the capillary system comprising: at least one support layer (7) having a receiving surface (8) for abutting the plasma collection surface (4), the or each support layer (7) supporting thereon at least one capillary conduit (6a, 6b, 26) for capturing blood plasma collected at the plasma collection surface.



"Capillary system for a blood separation device "

Technical Field

[1] The present disclosure is generally directed to blood separation devices, and in particular to a capillary system for a blood separation device suitable for use outside of a pathology laboratory.

Background

[2] Pathology laboratories typically use powered centrifuge equipment to separate large volumes blood samples. The plasma separated from the blood sample contains a variety of different proteins, many of which can be used as biomarkers indicating the presence of certain diseases in a patient. Various diagnostic tests have therefore been developed to identify relevant biomarkers within the separated plasma of the patient providing the blood sample.

[3] There is however a need within the healthcare industry for such tests to be conducted outside of a pathology laboratory, for example at the home of a patient. As it is impractical to have access to centrifuge equipment in such environments, it is necessary to conduct blood separation without such equipment. Plasma separation of small quantities of blood for point-of-care diagnosis has been a challenge to the healthcare industry, as well as to researchers in research institutions. Whole human blood contains 45% of red blood cells by volume and around 50% of plasma by volume. Conventional small volume blood collection methods using a finger or heel prick to collect the blood sample can typically only collect 5% to less than 20% of plasma from between 20 to 200 microlitres of whole blood. The rest of the plasma is absorbed in blood filtration media and is not recoverable by conventional methods. While a blood sample will naturally separate if left in a container for an extended period of time, this can lead to haemolysis of the red blood cells where the cytoplasm of the red blood cells is released into the surrounding plasma, thereby tainting any subsequent diagnostic test using the blood plasma from that sample.

[4] The blood separation devices that have been used with conventional small volume collection methods include devices utilising a plasma separation membrane to separate the plasma from a collected blood sample. The separated plasma is collected within an absorptive member held in contact with the plasma separation membrane. Such devices are for example shown in international patent application nos. PCT/FI2018/050272 (Ahlstrom-Munksjo OYJ) and PCT/US2015/045077 (Vivebio LLC). The plasma separated from the blood sample by the blood separation membrane is therefore collected and stored within the absorptive member. These devices cannot however separate and store the plasma in a liquid form as can be achieved using centrifuge equipment.

[5] It would be advantageous to be able to collect and store the separated liquid plasma for subsequent analysis, and to provide improved plasma separation efficiency over conventional plasma separation devices. It would also be preferable to be able to collect predetermined liquid plasma sample volumes which may be advantageous for certain tests. The collection of plasma in a liquid form and preferably with a predetermined sample volume would then facilitate ex-situ analysis of the separated liquid plasma, and would minimise the possibility of contamination of the collected plasma.

[6] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each of the appended claims.

Summary

[7] According to some embodiments, there is provided a capillary system for a blood separation device having a blood separation membrane with a plasma collection surface, the capillary system comprising:

at least one support layer having a receiving surface for abutting the plasma collection surface, the or each support layer supporting thereon at least one capillary conduit for capturing blood plasma collected at the plasma collection surface.

[8] The capillary conduit may comprise an elongate capillary tube having one end supported within the support layer, said end being located at or adjacent the receiving surface thereof. The capillary tube may have a circular cross section, and may preferably have a diameter within the range of between about 0.1 to about 4.0 millimetres. The use of capillary tubes having other cross sectional shapes such as rectangular or triangular shapes is also envisaged. A plurality of capillary tubes may extend from the support layer. The or each capillary tube may be of a uniform length and cross-sectional area to thereby define a uniform volume within which a predetermined volume of blood plasma can be captured. It is also envisaged that the capillary tubes of different (varying) lengths be provided to capture different volumes of blood plasma.

[9] The one or more capillary tubes may extend generally laterally relative to a plane of the support layer. The one or more capillary tubes may be aligned at least substantially vertically and downwardly relative to the support layer.

[10] It is also envisaged that the capillary conduit may comprise a capillary groove provided within the receiving surface of the support layer. The capillary groove may have a 'V' or 'U' shaped or rectangular shaped cross section. The use of capillary grooves having other cross sections of other shapes such as semicircular or other concave shapes is also envisaged. A plurality of the capillary grooves may be provided within the receiving surface.

[11] The support layer may be formed from a chemically inert resilient material such as for example natural rubber or silicon rubber. The use of alternative materials for the support layer is however also envisaged. The capillary tubes may be made from glass or a rigid polymer, for example. Alternatively, the capillary tubes may be made from a soft polymer, for example.

[12] The plasma separation membrane may be a proprietary membrane sold under the 'Vivid™' brand (trademark of Pall Corporation), for example. The Vivid™ membrane is formed from highly asymmetric polysulfone, a thermoplastic polymer. The highly asymmetric nature of the membrane allows the cellular components of the blood (red cells, white cells, and platelets) to be captured in larger pores of the membrane located adjacent a blood sample receiving surface thereof without lysis, while the plasma flows through smaller pores thereof to the plasma collection surface of the membrane. The possible embodiment is not however restricted to the use of Vivid™ membranes, and use of alternative plasma separation membrane types is also envisaged.

[13] According to another possible embodiment, there is provided a blood separation device comprising a blood separation membrane having a plasma collection surface, and a capillary system as described above abutting the plasma collection surface.

[14] According to a further possible embodiment, there is provided a method of collecting blood plasma from a blood separation device as described above including releasing and drying the collected blood plasma on an absorbent substrate.

[15] According to yet another possible embodiment, there is provided a method of collecting blood plasma from a blood separation device as described above including releasing and collecting the blood plasma in a liquid form.

[16] The plasma captured within the or each capillary tube may be released therefrom by contacting an open end of the or each capillary tube with a woven or non-woven hydrophilic and porous material. Alternatively, the plasma captured within the or each capillary tube can be subdivided into smaller portions by inserting a small diameter capillary tube into the or each capillary tube to release plasma into the smaller diameter capillary tube. Alternatively, the plasma captured within the or each capillary tube can be released by mounting a pressurizing device to one end of the or each capillary tube to apply a pressure to the plasma to thereby release the plasma therefrom.

Alternatively, the plasma captured within the or each capillary tube can be released by touching an open end of the or each capillary tube with a surface carrying one or more surface capillaries for drawing the plasma therefrom.

[17] Advantageously, the possible embodiments therefore allow for liquid plasma to be collected using capillary forces and preferably gravitational forces without the need for pumps or volumetric micro pipettes. They may also allow for separate single or multiple aliquots of separated plasma to be quantitatively delivered.

[18] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

Brief Description of Drawings

[19] The accompanying drawings illustrate some possible embodiments of the capillary system for a blood separation device according to the present disclosure. Other embodiments are possible, and consequently, the particularity of the accompanying drawings is not to be understood as superseding the generality of the preceding description of the possible embodiments.

[20] In the drawings:

[21] Figures 1a and 1b respectively show top and side views of a capillary system for a blood separation device according to some possible embodiments;

[22] Figure 2 is a side view of a blood separation device incorporating the capillary system of Figure 1;

[23] Figure 3 is a side view of the blood separation device of Figure 2 wherein the capillary system is separated from the blood separation membrane; and

[24] Figure 4a is a schematic side view of a blood separation device with a capillary system according to another possible embodiment, and Figure 4b is an exploded schematic side view of the blood separation device shown in Figure 4a.

Description of Embodiments

[25] Referring initially to Figs 1a to 3, there is shown a blood separation device 1 including a first possible embodiment of a capillary system 5 according to the present disclosure. The capillary system 5 includes a planar support layer 7 formed from a chemically inert soft material such as rubber, and having a plasma receiving surface 8. The blood separation device 1 as shown in Fig. 2 and 3 further includes a blood separation membrane 3 having a plasma collection surface 4.

[26] In the experiments conducted by the inventors, a proprietary membrane sold under the 'Vivid™' brand (trademark of Pall Corporation) was used as the blood separation membrane 3. The Vivid™ membrane is formed from highly asymmetric polysulfone, a thermoplastic polymer. The highly asymmetric nature of the membrane allows the cellular components of the blood (red cells, white cells, and platelets) to be captured in larger pores of the membrane located adjacent a blood sample receiving surface 12 thereof without lysis, while the plasma flows through smaller pores thereof to the plasma collection surface 4 of the membrane 3. The present disclosure is not however restricted to the use of this proprietary membrane, and the use of alternative blood separation membranes is also envisaged.

[27] The support layer 7 includes a plurality of apertures 9 passing from the plasma receiving surface 8 and through to an underlying surface 11 of the support layer 7. While the apertures 9 are shown in a grid pattern in Fig. 1a, it is to be appreciated that the placement of the apertures 9 is not restricted to this pattern. The apertures 9 may for example be placed in a circular or other pattern as required. Each aperture 9 respectively supports an open end of a capillary tube 6a, 6b. The open end of each capillary tube 6a, 6b is located at or adjacent the plasma receiving surface 8 of the support layer 7. The capillary tubes 6a, 6b may be made from glass or a rigid polymer.

However, as such rigid capillary tubes could be considered a hazardous 'sharp', it is also envisaged that coiled capillary tubes may be used, or that the capillary tubes may be made from a flexible soft polymer material.

[28] Figs 1b to 3 show the capillary tubes 6a being of a greater length than capillary tubes 6b. It is however also envisaged that the capillary tubes 6a, 6b be all of the same length. The length and cross-sectional area of each capillary tube 6a, 6b define the maximum potential volume of plasma that can be captured within each capillary tube 6a, 6b. While Figs 1a to 3 show six capillary tubes being used, it is to be appreciated that a greater or smaller number of capillary tubes could be fitted to the support layer 7 depending on the design requirement.

[29] The plasma receiving surface 8 of the support layer 7 is adapted to be held in an abutting relationship with the plasma collection surface 4 of the plasma separation membrane 3 when in use as shown in Fig. 2. The capillary tubes 6a, 6b are ideally positioned vertically when the blood separation device 1 is in use to allow both gravitational forces and capillary forces to be used to draw the plasma collected at the plasma collection surface 4 into the capillary tubes 6a, 6b using principles that will be subsequently discussed. When a blood sample 2 is applied to the blood sample receiving surface 12 of the plasma separation membrane 3, the red cells of the blood sample 2 are trapped within the membrane 3, with the liquid plasma 10 passing through the membrane 3 and collecting on the blood collection surface 4 of the membrane 3. A separated liquid plasma 10 is then captured by capillary action within the capillary tubes 6a, 6b as shown in Fig. 2. The capillary system 5 can then be separated from the blood separation membrane 3 once the capillary tubes 6a, 6b are filled with an amount of separated liquid plasma 10 as shown in Fig. 3. Each capillary tube 6a, 6b can then be separated from the support layer 7, with each capillary tube 6a, 6b acting as a storage vial for each separated liquid plasma sample 10. The length and cross-sectional area of each capillary tube 6a, 6b defines the maximum volume of separated liquid plasma 10 that can be stored therein.

[30] Without wishing to be bound by theory, the following principles of the transportation of the plasma in a capillary tube was used by the inventors. The following computations specifically relate to a circular capillary tube, but may also be indirectly applicable for capillary tubes having non circular cross-sections.

[31] If the circular capillary tube is horizontal, the gravity effect could be neglected, the Laplace pressure P_1 can be described as below.

$$P_1 = \frac{2\gamma \cos \theta}{r} \quad (1)$$

[32] If the capillary tube is upright as that in the blood separation device 1 shown in Figs. 1a to 3, both the gravity and the capillary action contribute to the driving force F , which can be presented as below.

$$F = 2\pi r \gamma \cos \theta + \rho \pi r^2 h g \quad (2)$$

[33] On the other hand,

$$F = P_1^* \pi r^2 \quad (3)$$

[34] From equation (2) and (3), the driving pressure P_1^* is deduced as below.

$$P_1^* = \frac{2\gamma \cos \theta}{r} + \rho g h \quad (4)$$

[35] Where, γ is liquid's surface tension, θ is the liquid-solid contact angle, r is the radius of the tube. ρ is the liquid density, g is the gravitational constant, h is the height of the liquid in the capillary tube.

[36] These equations show that holding the capillary tubes in a vertical orientation during use will allow gravitational force to contribute to the capillary action to thereby reinforce the driving force for collecting the liquid plasma provided by each capillary tube of the capillary system.

[37] The inventors have found that circular capillary tubes having a diameter range of between 0.1 to 4.0 millimetres are the optimum size based on the above noted computations and experiments that were conducted on experimental capillary systems.

[38] Figs. 4a and b show an alternative blood separation device 21 using another possible embodiment of the capillary system 25 according to the present disclosure. The capillary system 25 shares some of the features of the earlier described embodiment shown in Fig. 1a to 3, in having a support layer 27 formed of a chemically inert soft material having a plasma receiving surface 28 for abutting a plasma collection surface 24 of a blood separation membrane 23. The blood sample 22 can be supported within an open ended reservoir 29 located over the blood sample receiving surface 31 of the blood separation membrane 23. The capillary system 25 however differs by instead using capillary grooves (not shown) within the plasma receiving surface 28 of the support layer 27 in place of the capillary tubes 6a, 6b of the previously described possible embodiment. The capillary grooves may for example be “V”, “U” or rectangular in cross-sectional shape and may also draw liquid plasma collected at the plasma collection surface 24 using capillary force. The capillary grooves may allow for a predetermined amount of liquid plasma to be captured therein. The liquid plasma can then be drained from the capillary grooves to a collection cavity 30, shown as a square hole, within the support layer 27. The collected liquid plasma can then be drained from the collection cavity 30 to the side of the support layer 27 through a drain capillary tube 26 using appropriate means such as cellulose paper, nitrocellulose paper or other suitable porous material, for subsequent analysis.

[39] Without wishing to be bound by theory, the driving force provided by each capillary groove placed horizontally can be determined using the following principles.

[40] In a ‘V’ shaped groove, Rye’s model is utilized to describe the liquid wicking data (see: R. R. Rye, J. A. Mann, F. G. Yost, The flow of liquids in surface grooves. *Langmuir*, 12 (1996) 555-565). In this model the Laplace pressure P_2 can be related to the geometry of V-groove to yield.

$$P_2 = \gamma \frac{\sin(\alpha - \theta) \tan \alpha}{h(l)} \quad (4)$$

[41] Where, θ is the liquid-solid contact angle and α is the model variable angle (Fig 1). $h(l)$ is the height of the liquid of the wicking front, it varies along the wicking front. The Laplace pressure P (Eqn (4)) will drive the liquid to wick along the groove. In this model, θ should be lower than α in order to ensure wicking occurs in groove.

[42] In a rectangular groove placed horizontally, Ichikawa et al. estimated the capillary force in a rectangular channel based on the Young-Laplace equation (see N. Ichikawa, K. Hosokawa, R. Maeda, Interface motion of capillary-driven flow in rectangular microchannel, Journal of colloid and interface science, 280 (2004) 155-164). They simplified the force with constant curvature (i.e., a circular interface shape) and constant contact angle on the inner surface of the channel. Pressure difference P_3 at the interface in a rectangular channel can be described as below.

$$P_3 = \gamma(1/R_w + 1/R_h) \quad (5)$$

[43] Where, R_w and R_h are interface curvature in width and height directions, respectively. The relations between curvature, channel size and contact angle is as below.

$$R_w = w/(2 \cos \theta), \quad R_h = h/(2 \cos \theta) \quad (6)$$

[44] Then, the pressure difference is calculated as below.

$$P_3 = \gamma((2 \cos \theta)/w + (2 \cos \theta)/h) \quad (7)$$

[45] Where w is the width and h is the height of the rectangular channel.

[46] The inventors also conducted a comparison of the driving forces provided by different capillary systems. To simplify the comparison, based on the assumption that the cross section area of the V-groove is approximately equal to that of the circular

capillary tube, it was assumed that $\alpha=60^\circ$, $\theta=30^\circ$, $h(l)=2r$, $w \approx h \approx 2r$. Then the pressure could be respectively calculated in circular capillary tube, V-groove and rectangular channel, respectively.

$$P_1=(\sqrt{3} \gamma)/r, P_1^*=(\sqrt{3} \gamma)/r+\rho gh, P_2=(\sqrt{3} \gamma)/4r, P_3=(\sqrt{3} \gamma)/r$$

[47] Therefore, $P_1^* > P_1 = P_3, P_3 > P_2$. In other words, the driving force of an upright capillary tube is greater than a horizontal capillary tube, which equals to a “rectangular-cross-sectioned” capillary groove, which is greater than a “V cross-sectioned” capillary groove.

[48] As for P_1^* , it is composed of two parts. The first part is $(\sqrt{3} \gamma)/r$ contributed by capillary pressure and the second part ρgh is contributed by gravity. If $r=0.35\text{mm}$, $h=3\text{cm}$, $\gamma=0.05\text{N/m}$, then, $(\sqrt{3} \gamma)/r=247.4\text{ pa}$, $\rho gh=294\text{ pa}$. Therefore, the gravity force could make a significant contribution, in addition to that provided by the curved liquid meniscus, to drive the transport of plasma in the capillary. In comparison, the “V” and rectangular shaped surface grooves on horizontal surfaces could only provide the same (as for rectangular groove) or a fraction (i.e. 25% for “V” groove) of the driving force of that by an upright capillary, and having no benefit from gravity. It can then be concluded that the upright capillary design would provide the maximum pressure in the plasma separation compared with other designs. It is however envisaged that the capillary grooves designs may be used in applications where capillary tubes cannot be used, for example in situations where the capillary tubes could be considered as potentially hazardous ‘sharps’.

[49] The liquid plasma collected by the blood separation device 1 may be released as a liquid, or may be released on and dried within an absorbent substrate.

[50] In the exemplary embodiments, the liquid plasma is collected within the capillary tubes 6a, 6b of the blood separation device 1 shown in Figs 1 to 3, or within the drain capillary tube 26 of the blood separation device 21 shown in Figure 4a and b.

The liquid plasma can be released or subdivided into multiple portions via one or more of the following example methods:

a) An open end of the capillary tubes 6a, 6b, 26 filled with liquid plasma is made to contact with a woven or non-woven hydrophilic and porous material such as fabric, paper, wound-dressing gauze, compressed power discs, thread, and so on.

The plasma will then be released into the porous material by capillary action within the porous material.

b) The plasma collected within the capillary tube 6a, 6b, 26 can be subdivided into smaller portions by using a small diameter capillary tube. The smaller diameter capillary tube can be inserted into the capillary tube 6a, 6b, 26 on the blood separation device 1, 21 to thereby release plasma into the smaller diameter capillary tube. This method of plasma release can be quantitative, provided that the smaller diameter capillary tube is completely filled by plasma.

c) A pressurising device such as a rubber teat or bulb can be mounted to one end of a capillary tube 6a, 6b, 26 in the same manner as an eyedropper for example. Squeezing of the teat or bulb will apply an air pressure to the plasma contents of the capillary tube 6a, 6b, 26 resulting in the release of plasma therefrom.

d) The plasma could be released from a capillary tube 6c, 6b, 26 by touching the open end of the capillary tube filled with plasma to a solid surface that carries natural or manufactured surface capillaries such as the previously described capillary grooves, or cut through slots.

[51] A series of tests were conducted by the inventors to determine the average plasma separation efficiency of the blood separation device according to the present disclosure. Each test used an initial test volume of whole blood of 200 microlitres, and measured the percentage of the volume of plasma separated from the initial volume of whole blood. Four sets of test results were obtained of 31.0%, 32.5%, 34.2% and 28.6% respectively, giving an average plasma separation efficiency of 31.6%.

[52] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the above-described embodiments, without departing from the broad general scope of the present disclosure. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

CLAIMS:

1. A capillary system for a blood separation device having a blood separation membrane with a plasma collection surface, the capillary system comprising:

at least one support layer having a receiving surface for abutting the plasma collection surface, the or each support layer supporting thereon at least one capillary conduit for capturing blood plasma collected at the plasma collection surface.

2. A capillary system for a blood separation device according to claim 1, wherein the capillary conduit comprises an elongate capillary tube having one end supported within the support layer, said end being located at or adjacent the receiving surface thereof.

3. A capillary system for a blood separation device according to claim 2, wherein the capillary tube has a circular cross section.

4. A capillary system for a blood separation device according to claim 3, wherein the capillary tube has a diameter within the range of between about 0.1 to about 4.0 millimetres.

5. A capillary system for a blood separation device according to claim 2, wherein the capillary tube has a non-circular cross sectional shape.

6. A capillary system for a blood separation device according to any one of claims 2 to 5, wherein a plurality of the capillary tubes extends from the support layer.

7. A capillary system for a blood separation device according to claim 6, wherein each capillary tube is of a uniform length and cross-sectional area to thereby define a uniform volume within which a predetermined volume of blood plasma can be captured.

8. A capillary system for a blood separation device according to claim 6, wherein each capillary tube is of a varying length and/or cross-sectional area to thereby define different volumes within which a predetermined volume of blood plasma can be captured.
9. A capillary system for a blood separation device according to any one of claims 2 to 8, wherein the or each capillary tube extends generally laterally relative to a plane of the support layer.
10. A capillary system for a blood separation device according to claim 9, wherein the one or more capillary tubes are aligned at least substantially vertically and downwardly relative to the support layer when in use.
11. A capillary system for a blood separation device according to any one of claims 2 to 10, wherein the or each capillary tube is made of glass or a rigid polymer.
12. A capillary system for a blood separation device according to any one of claims 2 to 10, wherein the or each capillary tube is made of a soft polymer.
13. A capillary system for a blood separation device according to claim 1, wherein the capillary conduit comprises at least one capillary groove provided within the receiving surface of the support layer.
14. A capillary system for a blood separation device according to claim 13, wherein the or each capillary groove has a 'V' or 'U' shaped cross section.
15. A capillary system for a blood separation device according to claim 13, wherein the or each capillary groove has a rectangular shaped cross section.
16. A capillary system for a blood separation device according to any one of claims 13 to 15, further comprising at least one collection cavity within the support layer for receiving the plasma from the or each capillary groove and/or the plasma

collection surface, and one or more drain capillary tubes for collecting the plasma receive in the or each collection cavity.

17. A capillary system for a blood separation device according to any one of the preceding claims, wherein the support layer is formed from a chemically inert resilient material.

18. A capillary system for a blood separation device according to claim 17, wherein the support layer is formed from natural rubber or silicon rubber.

19. A capillary system for a blood separation device according to any one of the preceding claims, wherein the plasma separation membrane is formed from an asymmetric polysulfone.

20. A capillary system for a blood separation device according to any of claims 2 to 12, wherein the plasma captured within the or each capillary tube is released therefrom by contacting an open end of the or each capillary tube with a woven or non-woven hydrophilic and porous material.

21. A capillary system for a blood separation device according to any one of claims 2 to 12, wherein the plasma captured within the or each capillary tube is subdivided into smaller portions by inserting a small diameter capillary tube into the or each capillary tube to release plasma into the smaller diameter capillary tube.

22. A capillary system for a blood separation device according to any one of claims 2 to 12, wherein the plasma captured within the or each capillary tube is released by mounting a pressurizing device to one end of the or each capillary tube to apply a pressure to the plasma to thereby release the plasma therefrom.

23. A capillary system for a blood separation device according to any one of claims 2 to 12, wherein the plasma captured within the or each capillary tube is

released by touching an open end of the or each capillary tube with a surface carrying one or more surface capillaries for drawing the plasma therefrom.

24. A blood separation device comprising a blood separation membrane having a plasma collection surface, and a capillary system as claimed in any one of the preceding claims abutting the plasma collection surface.

25. A blood separation device according to claim 24, wherein the plasma separation membrane is formed from an asymmetric polysulfone.

26. A method of collecting blood plasma from a blood separation device according to claim 24 or 25, including releasing and drying the collected blood plasma on an absorbent substrate.

27. A method of collecting blood plasma from a blood separation device according to claim 24 or 25 including releasing and collecting the blood plasma in a liquid form.

28. A method of collecting blood plasma from a blood separation device according to claim 26, wherein the plasma captured within the or each capillary tube of the capillary system is released therefrom by contacting an open end of the or each capillary tube with a woven or non-woven hydrophilic and porous material.

29. A method of collecting blood plasma from a blood separation device according to claim 27, wherein the plasma captured within the or each capillary tube of the capillary system is subdivided into smaller portions by inserting a smaller portions by inserting a small diameter capillary tube into the or each capillary tube to release plasma into the smaller diameter capillary tube.

30. A method of collecting blood plasma from a blood separating device according to claim 26 or 27, wherein the plasma captured within the or each capillary tube of the capillary system is released by mounting a pressurizing device to one end of

the or each capillary tube to apply a pressure to the plasma to thereby release the plasma therefrom.

31. A method of collecting blood plasma from a blood separation device according to claim 26 or 27, wherein the plasma captured within the or each capillary tube is released by touching an open end of the or each capillary tube with a surface carrying one or more surface capillaries for drawing the plasma therefrom.

1/3

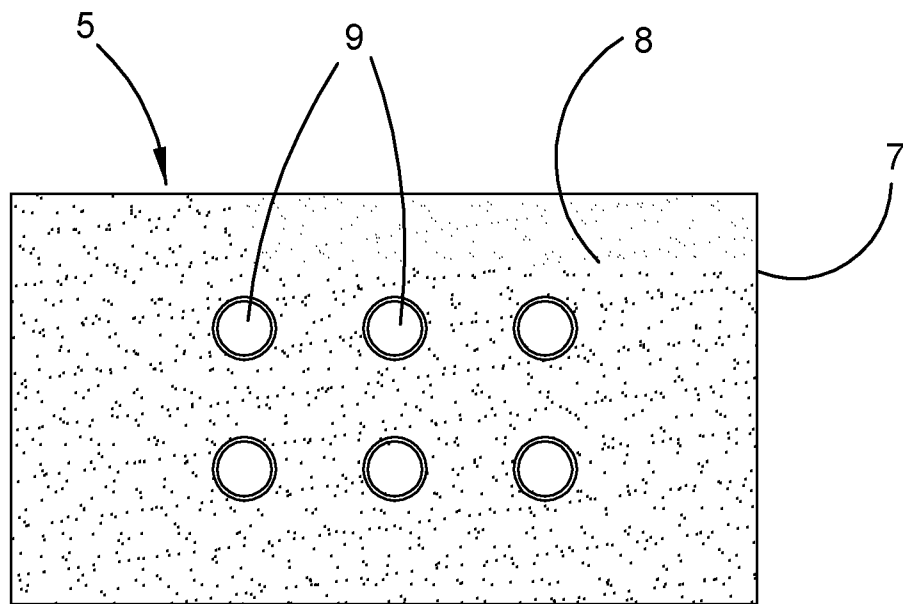


Fig. 1a

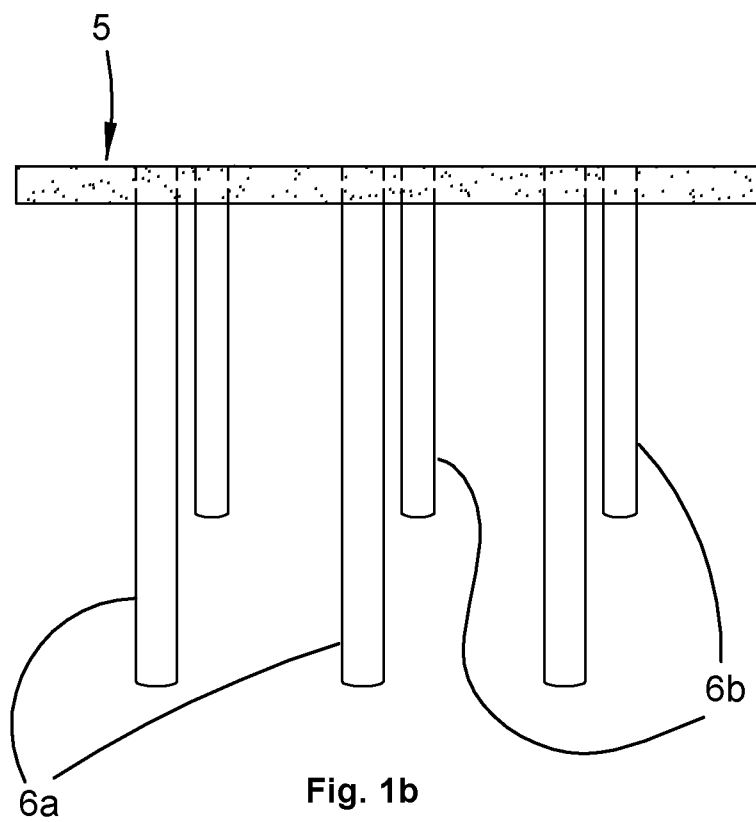


Fig. 1b

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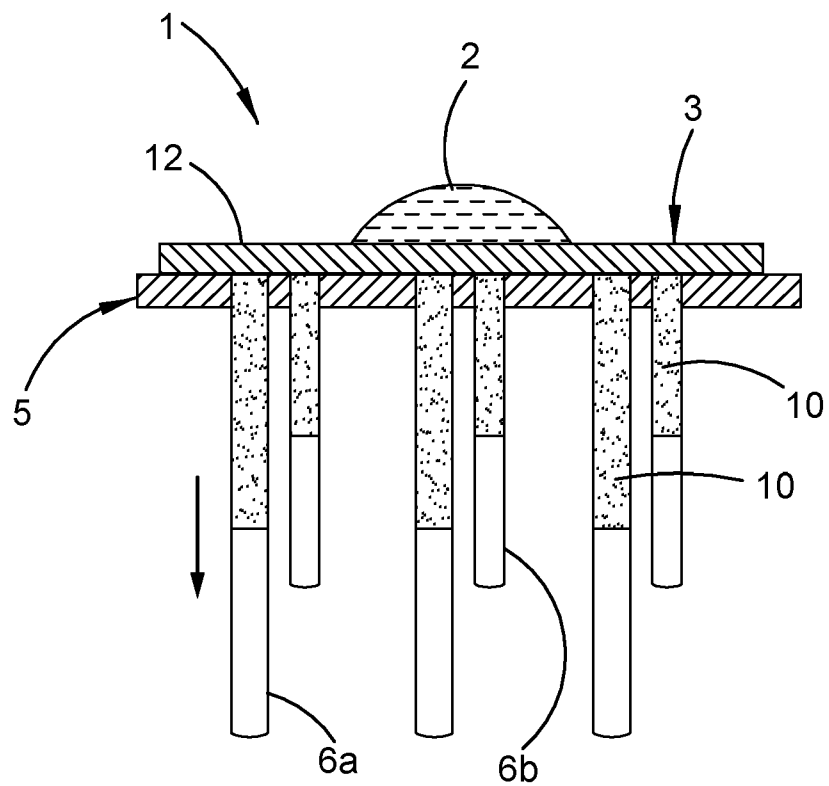


Fig. 2

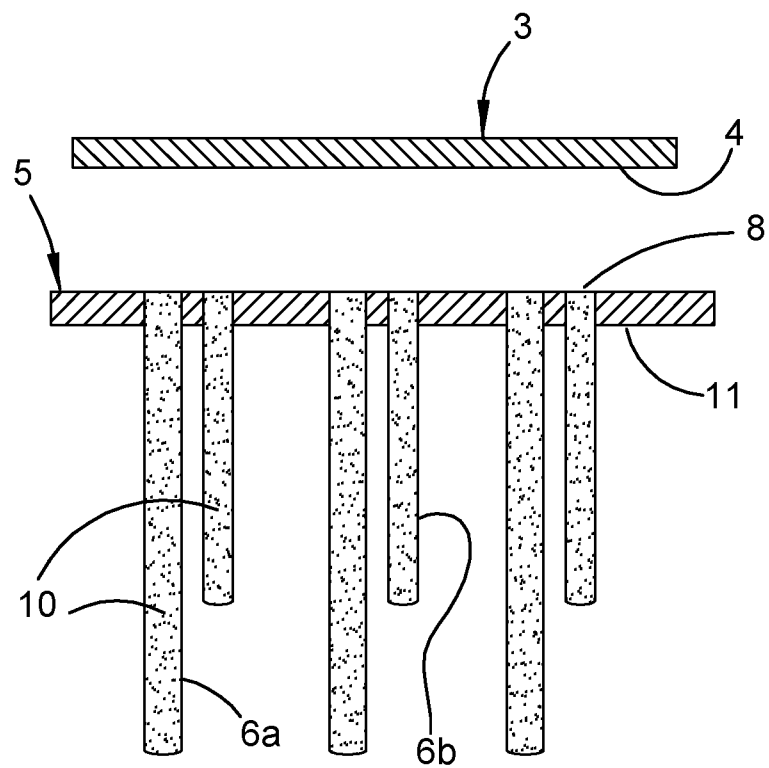


Fig. 3

3/3

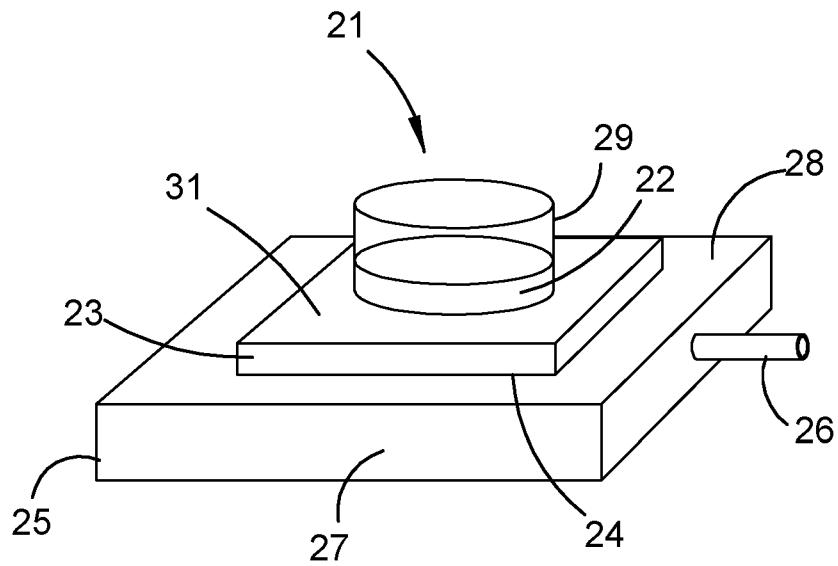


Fig. 4a

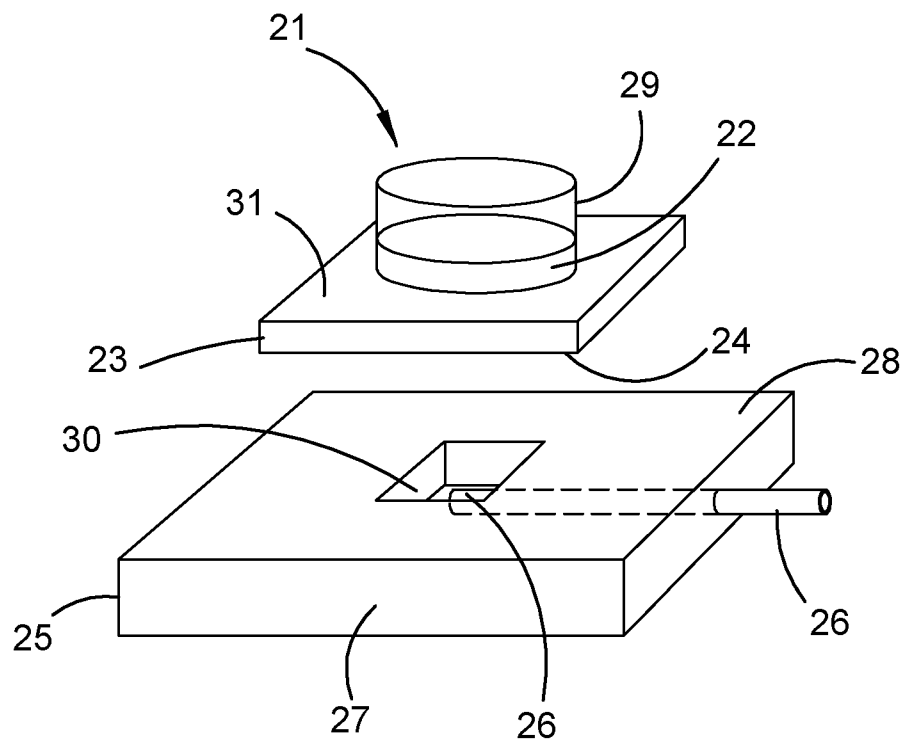


Fig. 4b

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2020/050091

A. CLASSIFICATION OF SUBJECT MATTER

B01L 3/00 (2006.01) G01N 33/49 (2006.01) A61B 5/00 (2006.01)

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)

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)

PATENW, INSPEC, Espacenet, Google Patents and Google Scholar with IPC: B01L3/00, B01L2400/0406, G01N33/49 and A61B5/00 ; and keywords: Capillary, separation, blood plasma, microfluidics and similar terms.

Applicant(s) and Inventor(s) names searched in Espacenet and internal databases provided by IP Australia

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	



Further documents are listed in the continuation of Box C



See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"D" document cited by the applicant in the international application	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search 30 March 2020	Date of mailing of the international search report 30 March 2020
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustalia.gov.au	Authorised officer Leo Lai AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. +61262832781

INTERNATIONAL SEARCH REPORT		International application No.
C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		PCT/AU2020/050091
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Durc, Pavol et al., "Fast Blood Plasma Separation Device for Point-of-Care Application", Talanta, 2018, 183, pages 55-60 (DOI: https://doi.org/10.1016/j.talanta.2018.02.004) Abstract, figure 1, section 2.2.1 and section 2.2.3	1-4, 9-11, 13-19, 21, 22, 24-27, 29 and 30
X	WO 2001/024931 A1 (ROCHE DIAGNOSTIC GMBH) 12 April 2001 Abstract, figure 1 and 3, examples 1 and 2, pages 10 to 11, page 19 paragraph 2 and page 21	1, 2, 4-9, 11, 12 and 17-31
A	US 2017/0095190 A1 (THERANOS, INC.) 06 April 2017 Whole Document	1-31
A	US 2011/0005341 A1 (NEIJZEN et al.) 13 January 2011 Whole Document	1-31
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P,X	WO 2019/025914 A1 (GUPTA) 07 February 2019 Abstract, figures 2 and 6, [0069] and [0071]	1-31

INTERNATIONAL SEARCH REPORT		International application No.	
Information on patent family members		PCT/AU2020/050091	
This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.			
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WO 2019/025914 A1	07 February 2019	WO 2019025914 A1	07 Feb 2019
End of Annex			
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.			