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(54) **Title:** EXTRACTION CELL FOR A CENTRIFUGAL PARTITION CHROMATOGRAPH, A CENTRIFUGAL PARTITION CHROMATOGRAPH CONTAINING SUCH A CELL, AND A METHOD FOR PRODUCING SUCH AN EXTRACTION CELL

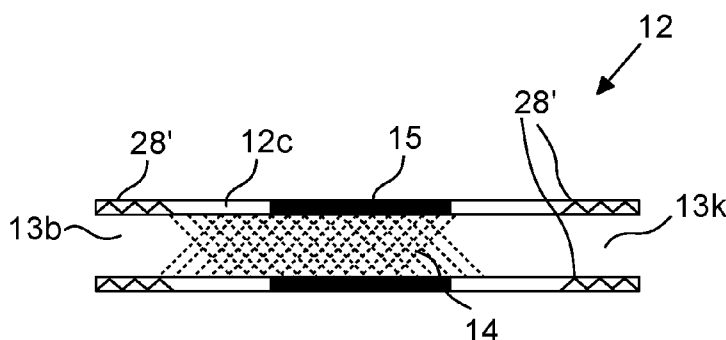


Fig. 2a

(57) **Abstract:** The object of the invention relates to an extraction cell for a centrifugal, partition chromatograph, which extraction cell contains an extraction chamber delimited by a cell wall and accommodates the liquid stationary phase, and it has a liquid inlet opening and a liquid outlet opening serving to let in and out the liquid mobile phase to be made to flow through the extraction cell. The essence of the extraction cell is that it contains an extraction chamber established as a tubular body, and a liquid inlet plug that includes a liquid inlet opening and a liquid outlet plug that includes a liquid outlet opening, that can be attached to the extraction chamber. An insert is included in the extraction cell chamber in order to overcome the effects of the Coriolis force on the mobile phase. The diameter of the passages of the insert is chosen dependant on the diameter of the droplets of the mobile phase. The object of the invention also relates to a centrifugal partition chromatograph containing such an extraction cell, and a ( method for producing such an extraction cell.



Extraction cell for a centrifugal partition chromatograph, a centrifugal partition chromatograph containing such a cell, and a method for producing such an extraction cell

5           The object of the present invention relates to an extraction cell for a centrifugal partition chromatograph, which extraction cell contains an extraction chamber delimited by cell walls, and has a liquid inlet opening and a liquid outlet opening.

          The object of the invention also relates to a centrifugal partition chromatograph containing such an extraction cell.

10           The object of the invention also relates to a method for producing such an extraction cell.

          Chromatography is the collective name for mixture separation methods based on multistage, high-efficiency, quasi-balance processes, which today, among separation technology processes, has become one of the most frequently used  
15   analytical methods. The fields of application include pharmaceutical analysis, foodstuff industry, toxicology and environmental analysis tests.

          The basis of the procedure is that the components in a mixture to be separated are distributed in different proportions between a stationary phase and a mobile phase (eluent) flowing through the stationary phase in a specific direction. Using this method  
20   the molecules, ions of the components may be selectively separated from each other from solutions with complex compositions. Separation is made possible by that the individual components travel at different speeds while the mobile phase is flowing. This speed depends on the degree of interaction between the component and the stationary phase. Therefore, the components of the mixture travel at different speeds because  
25   their distribution between the stationary phase and the mobile phase, in other words their partition coefficient is different.

          During centrifugal partition chromatography the liquid stationary phase is kept in place by a strong centrifugal field. In this technique, as seen in the block diagram in Figure 1a, the chromatograph contains a liquid pumping system 102 serving for  
30   feeding the mobile phase 30m, a sample feed unit serving for feeding the mixture

material 106 to be separated, a rotor 24 that rotates around an axis, a detector 110 and fraction collection system 112. A product 114 leaves the system as the final result of the separation process, which preferably contains a single component of the mixture 106. In the rotor 24 a network of serially connected extraction cells 10 connected to each other by connection tubes 18 ensuring liquid connection rotates around the axis of the rotor 24. The separation process takes place in the cascade of series-connected extraction cells containing an inlet and an outlet opening, which are rotated around a common axis at a given speed. As a result of the pumping the mobile phase enters the cell containing the stationary phase through the inlet opening and breaks up into tiny droplets. The resultant of the centrifugal force and the buoyancy will be exerted on the tiny droplets of the mobile phase, due to which the droplets will flow through the stationary phase. The two phases come into contact with each other over a large surface area within the cell. Near to the outlet opening the two phases are separated from each other and the mobile phase leaves the cell.

Coriolis force appears in the reference frame of the cells due to the rotation, as a result of which the path of the mobile phase is diverted. Using liquid simulation methods it can be demonstrated that the Coriolis force reduces the efficiency of the mixing of the two phases, as the diverted droplets run down the sidewall, so reducing the contact interface. The Coriolis force causes circular flow and remixing in the cell, which is a strongly degrading factor from the point of view of separation (see Figure 1b).

Various methods may be found in the literature for the production of extraction cells. The Partitron centrifugal partition chromatograph protected by the patent with registration number US6913692 consists of a titanium cylinder, in which the extraction cells and the channels connecting them are produced by milling. A special CNC milling machine is required as the device is milled inside and outside from a single titanium alloy cylinder. The titanium alloy used is very expensive and during machining a large part of the cylinder goes to waste. Therefore the manufacturing of the device is expensive and results in a great deal of waste. The milled channels and cells are connected by covering plates, with flat seals being used between them. The material of the flat seals according to the specification is fluoroelastomer (Viton), which, however, does not tolerate the organic solvents used for cleaning the device well.

When they come into contact with these they swell, soften and their sealing ability lessens.

Patent document with registration number US4968428 presents a stacked plate chromatograph in which the network of cells and channels is machined into a stainless steel plate. Teflon sealing plates are to be found between the stainless steel plates, which are punctured at the locations where flow is to take place between the plates. The greatest disadvantage of the arrangement is that the ratio of the useful volume as compared to the total mass of the device is very low, and the machining is expensive, as a great deal of waste is produced during machining. A further disadvantage of the plate arrangement is that due to the Teflon seals used its pressure resistance is low, and after time the Teflon plates become deformed, so reducing pressure tightness. In order to perfectly clean the device it must be completely disassembled, which is complicated and only possible with a press.

The aim of the invention is to provide an extraction cell, a centrifugal partition chromatograph containing such an extraction cell and a method for the production of such an extraction cell that is free of the disadvantages of the solutions according to the state of the art, in other words to be able to provide an extraction cell at a low cost in which the effect of the Coriolis force occurring may be effectively reduced. The aim of the invention is also to provide an extraction cell which may be manufactured so as to cause less waste than the solutions according to the state of the art.

The invention is based on the recognition that the extraction cell may be produced with the help of a tubular body shaped extraction chamber, and a liquid inlet plug and liquid outlet plug connected to its ends, during the production of which less waste is produced and the ratio of useful internal volume/mass is much greater as compared to the solutions according to the state of the art.

It was also recognised that an insert that liquid may flow through may be placed in the extraction cell, which effectively reduces the undesirable circular flow in the cell caused by Coriolis force, and the liquid jet of the mobile phase entering the cell more

effectively breaks up into droplets upon hitting the insert, due to which the interface between the two phases increases.

The task was solved in the sense of the invention with the extraction cell according to claim 1.

5           The task set for the invention was also solved with the centrifugal partition chromatograph according to claim x.

Individual preferable embodiments of the invention are specified in the dependent claims.

10           The details of the invention are presented in connection with embodiments, with the help of drawings. In the appended drawings

Figure 1a shows an outline block diagram of an exemplary embodiment of a centrifugal partition chromatograph,

15           Figure 1b is a simulated image of the liquid flow in an extraction cell not containing an insert, which illustrates the damaging remixing effect of the Coriolis force in the cell,

Figure 2a depicts an outline longitudinal cross-section image illustrating a preferable embodiment of the tubular shaped extraction chamber of the extraction cell according to the invention,

20           Figure 2b depicts an outline lateral cross-section image of the tubular shaped extraction chamber of the extraction cell according to figure 2a,

Figure 3 is a simulated image of the liquid flow in an extraction cell containing the insert according to the invention,

Figure 4a depicts a longitudinal cross-section of a preferable embodiment of the liquid inlet plug according to the invention,

25           Figure 4b depicts a lateral cross-section of a preferable embodiment of the liquid inlet plug according to figure 4a,

Figure 5a depicts a longitudinal cross-section of a preferable embodiment of the liquid outlet plug according to the invention,

30           Figure 5b depicts a lateral cross-section of the liquid outlet plug according to figure 5a,

Figure 6a depicts a longitudinal cross-section of another preferable embodiment of the liquid inlet plug according to the invention,

Figure 6b depicts a lateral cross-section of a preferable embodiment of the truncated cone element according to figure 6a,

Figure 7 depicts a longitudinal cross-section of another preferable embodiment of the liquid outlet plug according to the invention,

5        Figure 8 depicts a schematic image of a module containing the extraction cells according to the invention,

Figure 9 depicts a schematic image of a rotor containing the module presented in figure 9.

10       Figures 2a and 2b show outline longitudinal and lateral cross-sections illustrating a preferable embodiment of the tubular shaped extraction chamber 12 of the extraction cell 10 according to the invention.

The extraction cell 10 contains an extraction chamber 12 delimited by a cell wall 12c and accommodating the liquid stationary phase 30<sub>a</sub>, and on its opposing sides it has a liquid inlet opening 13b and a liquid outlet opening 13k serving to let in and out  
15       the liquid mobile phase 30<sub>m</sub> to be made to flow through the extraction cell 10. The material of the cell wall 12c delimiting the extraction chamber 12 is preferably stainless steel, but other materials are also conceivable, such as titanium alloy, aluminium, PEEK (polyether ether ketone), Teflon, etc.

20       In the case of a preferable embodiment the extraction chamber 12 is constructed as a tubular body. This embodiment of the extraction chamber 12 is preferably produced using a waste-free production technology, such as 3D printing or injection moulding or metal casting. PEEK is preferably used in 3D printing, but naturally other materials may also be used, as is known to a person skilled in the art.

25       An insert 14 through which liquid may pass is positioned in the extraction chamber 12 according to the invention between the liquid inlet opening 13b and the liquid outlet opening 13k. In the context of the present invention an insert 14 through which liquid may pass means an insert that has internal passages via which liquids are capable of flowing through the insert 14. The average diameter of the internal passages of the insert 14, in other words the average diameter of their cross-section is 1–30  
30       times, more preferably 1–20 times, and even more preferably 4–10 times the average diameter of the mobile phase 30<sub>m</sub> droplets created when the mobile phase 30<sub>m</sub> is made to flow in the stationary phase 30<sub>a</sub>. The cross-section of the internal passages is not necessarily circular. They may be square, rectangular, triangular or any other

irregular plane figure. In this case average diameter may be viewed as the diameter of a circle with an area equal to that of the area of the plane figure.

In the case of a preferable embodiment the insert 14 contains one or more elements that liquid may pass through chosen from the following group: wound up net  
5 made from metal wire, fibrous woven textile, glass wool, steel wool, although other materials may also be used as is obvious for a person skilled in the art. In a given case the insert 14 may be fixed to the cell wall 12c, for example, by gluing, soldering, welding or by other mechanical fixing process. In the case of another exemplary embodiment the liquid inlet opening 13b and the liquid outlet opening 13k are dimensioned so that  
10 the insert cannot pass through, and due to this it is not necessary to fix the insert 14 within the extraction chamber 12.

With respect to its structure the insert 14 may have an irregular structure (glass wool, steel wool), a regular structure (metal wire, metal grid), or be a bulk insert. The latter may be realised by using a granulate, spheres, and/or other granular materials.

15 In the case of an especially preferable embodiment, with the extraction cell 10 in its position in the centrifugal partition chromatograph 20, the insert 14 is selected so as to reduce the effect of the Coriolis force occurring in the extraction cell 10 when in operation.

While providing the insert 14 through which liquid may pass, the extraction cell  
20 10 is filled with liquid stationary phase 30á, then liquid mobile phase 30m is made to flow through the stationary phase 30á in such a way that the mobile phase 30m breaks up into droplets when it penetrates the stationary phase 30á. Following this the average diameter of the droplets of the mobile phase 30m penetrating the stationary phase 30á and breaking up into droplets is determined. This make take place, for example, by  
25 experiment, on the basis of an image recorded of the inside of the extraction cell, or theoretically, with the help of formulae. In a given case the droplets may also have an irregular shape, in this case the diameter of a droplet may be defined as having the same diameter as sphere with the same volume as the droplet. In the case of a preferable embodiment the average diameter of the droplets of the mobile phase is  
30 determined on the basis of the Stokes' law. During this the droplets inside the

extraction cell 10 are considered to be spherical, the average diameter  $d$  of which may be calculated, with good approximation, using the following formula:

$$d = \frac{9 * v * \eta}{2 * \Delta\rho * \omega * \omega * R}$$

where  $v$  is the velocity of the mobile phase 30m penetrating the stationary phase 30a as compared to the stationary phase 30a,  $\eta$  is the viscosity of the stationary phase 30a,  $\Delta\rho$  is the absolute value of the difference in density between the stationary phase 30a and the mobile phase 30m,  $\omega$  is the angular velocity of the rotation of the extraction cell 10, and  $R$  is the distance of the extraction cell 10 from the axis of rotation. Naturally other relationships may be used to calculate the average diameter of the droplets apart from the above formula, as is obvious to a person skilled in the art.

By using the information obtained about the average diameter of the droplets, an insert 14 through which liquid may pass is provided that has internal passages, and the average diameter of the passages is 1–30 times, preferably 1–20 times, even more preferably 4–10 times the average diameter of the droplets.

In the case of a preferable embodiment an insert 14 is provided of a size so that its volume is 1–30%, preferably 1–20%, even more preferably 2–20% of the volume of the extraction cell 10. The volume that the insert 14 fills in the context of the present invention is the ratio of the net volume of the insert 14 and the internal volume of the extraction cell 10, where the net volume of the insert 14 is equal to that volume of liquid a completely immersed insert 14 would push out of a completely filled vessel.

The insert 14 presented above may be produced, for example, from a net (wound up) of metal wire, fibrous woven textile, glass wool, steel wool and from similar products, or a combination of them.

As a result of the effect of the insert 14 the circular flow of the liquid mobile phase 30m entering the extraction chamber 12 is reduced, as due to its viscosity a large amount of force is required for its to pass through the internal passages of the insert 14, which represent a braking resistance to the flow. This braking resistance is always opposite to the direction of movement of the liquid, and its extent is comparable to, or in a given case greater than, the extent of the Coriolis force occurring in the extraction cell 10, and in this way it reduces or completely extinguishes its effect. As the mobile phase 30m is driven by the difference between the centrifugal force and the buoyancy, which resultant force is greater than the Coriolis force, the mobile phase



30m entering the liquid inlet opening 13b can continue to flow through the extraction chamber 12 all the way to the liquid outlet opening 13k, through which it leaves the extraction chamber 12 (see Figure 3).

A further preferred characteristic of the insert 14 is that the liquid jet of the mobile phase 30m entering the extraction chamber 12 filled with stationary phase 30á more effectively breaks up into droplets when hitting the insert 14, and significantly ripples after passing through the insert 14. Due to this effect the mixing between the mobile phase 30m and the stationary phase 30á improves, and the transfer surface between the two liquids increases.

In the case of a preferable embodiment one or more pits 15 ensuring the securing of the extraction cell 10 to the external supporting structure 22 (see Figure 8) are established on the external surface of the cell wall 12c of the extraction chamber 12.

In the case of an especially preferable embodiment the extraction cell 10 can be attached to the extraction chamber 12, it contains the liquid inlet plug 16b according to figures 4a and 4b which includes in it the liquid inlet opening 13b and the liquid outlet plug 16k according to figures 5a and 5b which includes in it the liquid outlet opening 13k. In this case the liquid inlet opening 13b is established in the inlet plug 16b, and the liquid outlet opening 13k is established in the liquid outlet plug 16k. The liquid inlet plug 16b and/or the liquid outlet plug 16k are fixed to the cell wall 12c of the extraction chamber 12 preferably with a releasable connection, such as a screw thread. Naturally other releasable fixing methods (such as clasp fixing), or non-releasable fixing methods (such as welding, soldering, gluing, riveting, etc.) may be used, as is known to a person skilled in the art.

In a given case, an embodiment may be conceived in the case of which the liquid inlet opening 13b is established in the liquid inlet plug 16b and the liquid outlet opening 13k is established in the cell wall 12c, or vice versa, in other words the liquid outlet opening 13k is established in the liquid outlet plug 16k and the liquid inlet opening 13b is established in the cell wall 12c. The liquid inlet plug 16b and the liquid outlet plug 16k are preferably made from one or more of the following list of materials: stainless steel, titanium alloy, aluminium, PEEK, Teflon. The liquid inlet plug 16b and the liquid outlet plug 16k may also be made using one of the previously presented

waste-free production technologies, and/or using other material working technologies (such as milling, grinding, drilling, etc.).

The longitudinal and lateral cross-sections of a liquid inlet plug 16b that consists of a single part can be seen in Figures 4a and 4b. In the case of a preferable embodiment the inlet plug 16b leading the mobile phase 30m into the extraction chamber 12 is established as a cylindrical body, on the side of which facing the internal space of the extraction chamber 12 there is a thread 28 formed on the outside, such as an external NPT(F) 3/8" thread. In the case of this embodiment the extraction chamber 12 is established in the form of a tubular body, and at least at the one end of the tube on the internal surface there is also a thread 28' established, such as an NPT(F) 3/8" thread, into which the NPT(F) 3/8" thread 28 of the inlet plug 16b may be screwed. An external thread 29 is established at the other end of the inlet plug 16b, such as a 5/16-20 UN thread. Preferably a hexagonal nut formation may be found between the NPT(F) 3/8" and the 5/16-20 UN threads 28, 29, which when held with a standard fork spanner the thread 28 of the inlet plug 16b may be easily driven into the thread 28' of the extraction chamber 12.

In the case of a preferable embodiment the liquid inlet opening 13b of the inlet plug 16b contains one or more slanted bores 17f that divides the liquid flowing through it into several liquid jets (see Figures 4a and 4b). In the case of an exemplary embodiment the diameters of the bores 17f are between 0.1 mm and 1 mm, but naturally different diameters may also be conceived. The role of the bores 17f is to divide the jet of mobile phase 30m liquid into several parts and to spray it evenly into the extraction chamber 12. The division may take place into any optional number of branches, however, when producing the bores it is preferable if the following aspects are taken into consideration:

- when divided the flowing liquid should be divided in equal proportions,
- the liquid flowing in the various bores should take equally long paths.

According to liquid simulation tests dividing the mobile phase 30m into several liquid jets has a positive effect on the flow pattern, as atomisation is improved, or, in other words, the interface between the two phases increases, which is especially desirable from a chromatography point of view.

In the case of an exemplary embodiment the outlet plug 16k is also tubular, which, however, preferably contains a single branched liquid outlet opening 13k, and

conical machining 17k is formed on its side facing the internal space of the extraction chamber 12 (see Figures 5a and 5b).

Similarly to the inlet plug 16b, on the side of the outlet plug 16k facing the internal space of the extraction chamber 12 there is an external thread 28 formed on the outside, such as an NPT(F) 3/8" thread, and on the other side there is an external thread 29 formed on the outside, such as a 5/16-20 UN thread. The outlet plug 16k may also be fixed into the thread 28' of the extraction chamber 12 using the external NPT(F) 3/8" thread 28. The connection tube 18 visible in Figure 9 may be connected to the external 5/16-20 UN thread 29 of the inlet plug 16b and outlet plug 16k, with the help of which a liquid connection may be realised between the liquid outlet opening 13k of an extraction cell 10 and the liquid inlet opening 13b of another extraction cell 10 connected in series with it.

The purpose of the conical machining 17k is for the droplets of the mobile phase breaking up into droplets which pass through the extraction chamber 12 to easily combine, and due to this only the mobile phase 30m leaves through the liquid outlet opening 13k.

In the case the extraction chamber 12 has a larger tube diameter, the liquid inlet plug 16b and/or the liquid outlet plug 16k are constructed from several parts that may be separated from each other, as can be seen in Figures 6a and 7. In the case of this embodiment the liquid inlet plug 16b contains an inlet truncated cone element 19b responsible for the division of the liquid jet of the mobile phase 30m and for sealing, a cylindrical body 19h fitted to it, and a threaded cap 19m fixing the cylindrical body 19h to the extraction chamber 12. The material of the inlet truncated cone element 19b is preferably PEEK, but apart from this it may be made of Teflon, HDPE or other material that is easily machined. The cylindrical body 19h is preferably made from ANSI 316 stainless steel, but it may also be from titanium alloy, aluminium, PEEK, Teflon, etc., as is obvious for a person skilled in the art.

In the case of a preferable embodiment four branches are formed by milling in the inlet truncated cone element 19b, and three bores 17f branch off each branch, as can be seen in Figure 6b. Therefore, there are a total of twelve bores 17f located in the inlet truncated cone element 19b, through which the mobile phase 30m gets into the extraction chamber 12 after being evenly divided. A section of internal surface of the cell wall 12c at the side towards the liquid inlet opening 13b is etched, which is followed

by a conically shaped machined section into which the inlet truncated cone element 19b fits so as to form a seal.

The cylindrical body 19h contains a base part 19t that is drilled through in the centre and fits into the internal machining of the extraction chamber 12 and a hollow stem 19sz fixed to the base part 19t, as can be seen in Figure 6a. The inside of the stem 19sz includes a 45 degree conical part 119 and a 6.45 mm depression, a thread 27 is preferably formed on its exterior surface, such as a 7/16-20 UNC thread, with the help of which the connection tube 18 may be fixed to the stem 19sz.

In the case of this embodiment a fine M60x3 metric thread is formed on the external surface of the cell wall 12c, at both ends of the cylindrical body shaped extraction chamber 12, onto which the threaded cap 19m may be screwed. The edge of the threaded cap 19m screwed onto the extraction chamber 12 fixes the inlet truncated cone element 19b and the cylindrical body 19h located in the extraction chamber 12. The material of the threaded cap 19m is preferably strong steel.

An embodiment is also conceivable in which the inlet truncated cone element 19b and the cylindrical body 19h are fixed to the extraction chamber 12 with the thread formed on the external surface of the cylindrical body 19h and the thread formed on the internal surface of the cell wall 12c. In this case it is unnecessary to use a threaded cap 19m. The screwing in of the cylindrical body 19h preferably takes place using the hexagonal nut formation established on the cylindrical body.

The construction of the liquid outlet plug 16k according to figure 7 differs from that presented above to the extent that instead of an inlet truncated cone 19b it contains an outlet truncated cone 19k, on which a single branch liquid outlet opening 13k and conical machining 17k facing towards the internal space of the extraction chamber 12 are formed.

Figure 8 illustrates a module 40 of a rotor 24 according to the invention, which contains several extraction cells 10 connected in series with connection tubes 18. In the case of this embodiment the module 40 also includes in itself the supporting structure 22 that fixes the extraction cells 10 to the module 40. The module 40 is preferably fixed to the rotor 24 in a releasable way, such as by using screws. The supporting structure 22 is preferably of high strength and has a light, grid-like or net-like structure. The supporting structure 22 may be constructed from, for example, metal, metal alloy, plastic, other composite, etc., as is obvious for a person skilled in

the art. The extraction chamber 12 is fixed to the supporting structure 22 using one or more pits 15 formed in the external surface of the cell wall 12c, preferably in a releasable way. Naturally, the extraction cells 10 may be fixed to the supporting structure 22 in other releasable or non-releasable ways, apart from the fixing with the pits 15.

Figure 9 illustrates a disc rotor 24 with an annular cross-section constructed using the modules 40 presented in Figure 8. This embodiment of the centrifugal partition chromatograph 20 has a modular structure made up of substantially identical modules, in the case of which each of the modules 40 contains one or more extraction cells 10 connected with connection tubes 18 ensuring a liquid connection between them.

Around the circumference of the rotor 24 the modules 40 are connected in series with connection tubes 18 in such a way that the liquid input of a selected module 40 is preferably connected to the liquid input at the main axis of the rotor 24 through a feed tube 26, while the liquid output of the neighbouring module 40 is preferably connected to the liquid output at the main axis of the rotor 24 through a discharge tube 26'.

In the following the operation of the extraction cell according to the invention and of the centrifugal partition chromatograph 20 containing the extraction cell 10 is presented.

Before separation the extraction cells 10 are at least partially filled with liquid stationary phase 30<sub>a</sub>, then the rotation of the rotor 24 along with the extraction cells 10 is started. Following this the pumping of the mobile phase 30<sub>m</sub> through the series-connected extraction cells 10 is started and as a consequence of the rotation centrifugal force occurs in them. This centrifugal force immobilises the stationary phase 30<sub>a</sub>, in other words it keeps the stationary phase 30<sub>a</sub> in the cells. Subsequently, the

mixture to be separated is added to the mobile phase 30m with the sample input unit, preferably in impulse-like doses.

The direction of the pumping is selected as follows depending on the relationship between the densities of the stationary phase 30a and the mobile phase

5 30m:

- if the stationary phase 30a is the denser phase (ascendant mode), then the mobile phase 30m is made to flow in the direction of the axis of rotation of the rotor 24;

- if the stationary phase 30a is the less dense phase (descendent mode), then the mobile phase 30m is made to flow from the centre of rotation in the direction of the rotational circumference.

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Due to the pumping the mobile phase 30m enters the extraction cell 10 via the liquid inlet opening 13b, then breaks up into tiny droplets in the stationary phase 30a. In an ideal case the distribution of the droplets is homogenous inside the extraction chamber 12. The insert 14 placed in the extraction chamber 12 further improves the homogenisation.

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Coriolis force is created in the extraction cells 10 of the rotating rotor 24 as a result of the rotation, which endeavours to displace the flow of the mobile phase 30m entering the extraction chamber 12 in the sideways direction. The insert 14 exerts resistance with respect to the flow, which resistance is comparable to the extent of the

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Coriolis force, thereby significantly reducing its effect. As the difference between the centrifugal force and the buoyancy is exerted on the mobile phase 30m, which resultant force is greater than the Coriolis force, the mobile phase 30m entering through the liquid inlet opening 13b is able to flow through the extraction chamber 12 containing the insert 14. In an ideal case the two phases are in contact with each other from the

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liquid inlet opening 13b all the way to the liquid outlet opening 13k. The mobile phase 30m and the stationary phase 30a become separated in the proximity of the liquid outlet opening 13k due to the conical machining 17k and the effect of the difference in density between the two phases. The phase with lower density is driven by buoyancy towards the liquid inlet opening 13b, while the denser phase continues to be moved towards the liquid outlet opening 13k due to the greater centrifugal force being exerted on it. In an ideal case only the mobile phase leaves the extraction cell 10. The

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processes presented above are carried out and repeated in each of the series-connected cells 10. If the mixture to be separated is added to the mobile phase 30m

(preferably intermittently), then the components characterised by different partition coefficients are separated from each other in the extraction cells 10.

5 In the case of a preferable embodiment several series-connected extractions cells 10 form modules 40 that may be individually removed from the centrifugal partition chromatograph 20. One of the greatest advantages of the modular construction is that in the case of a single extraction cell 10 becoming faulty (blocked, for example) the extraction cell 10 can be easily repaired or replaced, furthermore, the periodical cleaning of the extraction cells 10 is also simpler to perform. In the case of those  
10 embodiments in which the liquid inlet opening 13b and the liquid outlet opening 13k are formed in the inlet plug 16b and the outlet plug 16k, the cleaning of the extraction cells can be simply performed by unscrewing the plugs, as opposed to the solutions according to the state of the art, in which the entire device has to be dismantled to do this.

15 It is clear that alternative solutions will be apparent to a person skilled in the art as compared to the embodiments presented here, which, however, fall within the scope of protection determined by the claims.

## Claims

1. Extraction cell for a centrifugal partition chromatograph, which extraction cell contains an extraction chamber delimited by a cell wall and accommodates a liquid stationary phase, and it has a liquid inlet opening and a liquid outlet opening serving to let in and out the liquid mobile phase to be made to flow through the extraction cell, **characterised by** that it contains an extraction chamber established as a tubular body, and a liquid inlet plug that includes a liquid inlet opening and a liquid outlet plug that includes a liquid outlet opening, that can be attached to the extraction chamber.

2. The extraction cell according to claim 1, **characterised by** that an insert through which liquids may pass is positioned in the extraction chamber between the liquid inlet opening and the liquid outlet opening, which has internal passages, and the average diameter of the passages is 1–30 times, preferably 1–20 times, even more preferably 4–10 times the average diameter of the mobile phase droplets created when the mobile phase is made to flow in the stationary phase.

3. The extraction cell according to claim 1 or 2, **characterised by** that it is made using waste-free production technology, such as 3D printing or extruding or drawing or welding or injection moulding or metal casting.

4. The extraction cell according to any of claims 1 to 3, **characterised by** that the insert has an irregular structure, or a regular structure, or is created as a bulk insert.

5. The extraction cell according to any of claims 1 to 4, **characterised by** that the insert contains one or more components that liquid may pass through chosen from the following group: (wound up) net made from metal wire, fibrous woven textile, glass wool, steel wool.

6. The extraction cell according to any of claims 1 to 5, **characterised by** that the porosity of the insert is selected to reduce the effect of the Coriolis force occurring



in the extraction cell as a result of the rotational movement of the extraction cell when it is in the centrifugal partition chromatograph in operation.

5        7. The extraction cell according to any of claims 1 to 6, **characterised by** that the material of the cell wall delimiting the extraction chamber is selected from one or more elements of the following group: stainless steel, titanium alloy, aluminium, PEEK, Teflon.

10      8. The extraction cell according to any of claims 1 to 7, **characterised by** that the liquid inlet plug and/or the liquid outlet plug are fixed to the cell wall of the extraction chamber with a releasable connection, preferably with a screw thread.

15      9. The extraction cell according to any of claims 1 to 8, **characterised by** that one or more pits are formed on the external surface of the cell wall of the extraction chamber to ensure the fixing of the extraction cell to the external supporting structure.

20      10. The extraction cell according to any of claims 1 to 9, **characterised by** that the liquid inlet plug contains one or more bores that divide the liquid made to flow through it into several liquid jets.

25      11. The extraction cell according to any of claims 1 to 10, **characterised by** that conical machining is formed on the side of the liquid outlet plug facing the internal space of the extraction chamber.

30      12. The extraction cell according to any of claims 1 to 11, **characterised by** that the liquid inlet plug and/or the liquid outlet plug are constructed from several parts that may be separated from each other.

35      13. The extraction cell according to any of claims 1 to 12, **characterised by** that the material of the liquid inlet plug and the liquid outlet plug is selected from one

or more of the following elements: stainless steel, titanium alloy, aluminium, PEEK, Teflon.

14. Centrifugal partition chromatograph, **characterised by** that it contains at least one extraction cell according to any of claims 1 to 15.

15. Centrifugal partition chromatograph according to claim 14, **characterised by** that it contains several extraction cells that are connected in series with channels that ensure a liquid connection.

10

16. Centrifugal partition chromatograph according to claim 15, **characterised by** that several series-connected extraction cells form individually removable modules.

17. Centrifugal partition chromatograph according to claim 16, **characterised by** that it has a modular structure made up of substantially identical modules, where each of the modules contains one or more extraction cells connected with connection tubes ensuring a liquid connection between them, furthermore, the individual modules are connected to each other in series via tubes.

18. Method for producing extraction cell that maybe used in a centrifugal partition chromatograph, during which:

- the extraction cells are filled with liquid stationary phase,
  - liquid mobile phase is made to flow through the stationary phase,
- characterised by** that:
- the average diameter of the droplets of the mobile phase breaking up into droplets and penetrating the stationary phase is determined,
  - an insert through which liquid may pass through is arranged in the extraction cell that has internal passages and the average diameter of the passages is 1–30

times, preferably 1–20 times, even more preferably 4–10 times the average diameter of the droplets.

5 19. The method according to claim 18, **characterised by** that the average diameter of the droplets of the mobile phase is determined on the basis of Stokes' law.

10 20. The method according to claim 18 or 19, **characterised by** that an insert is provided of a size so that its volume is 1–30%, preferably 1–20%, even more preferably 2–20% of the internal volume of the extraction chamber.

15 21. The method according to any of claims 18 to 20, **characterised by** that an insert is provided in the extraction chamber containing a net (wound up) of metal wire, fibrous woven textile, glass wool, steel wool or from similar products, or a combination of them.

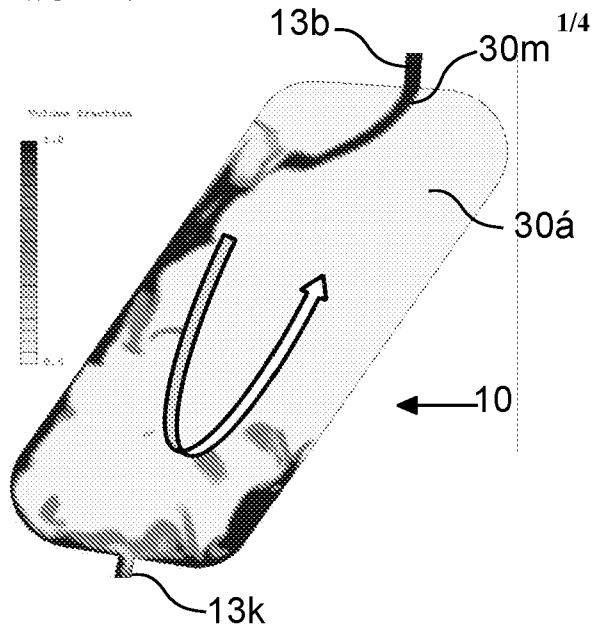


Fig. 1b

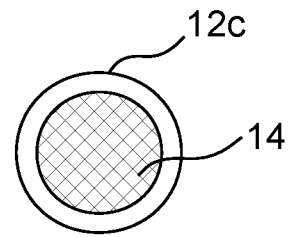


Fig. 2b

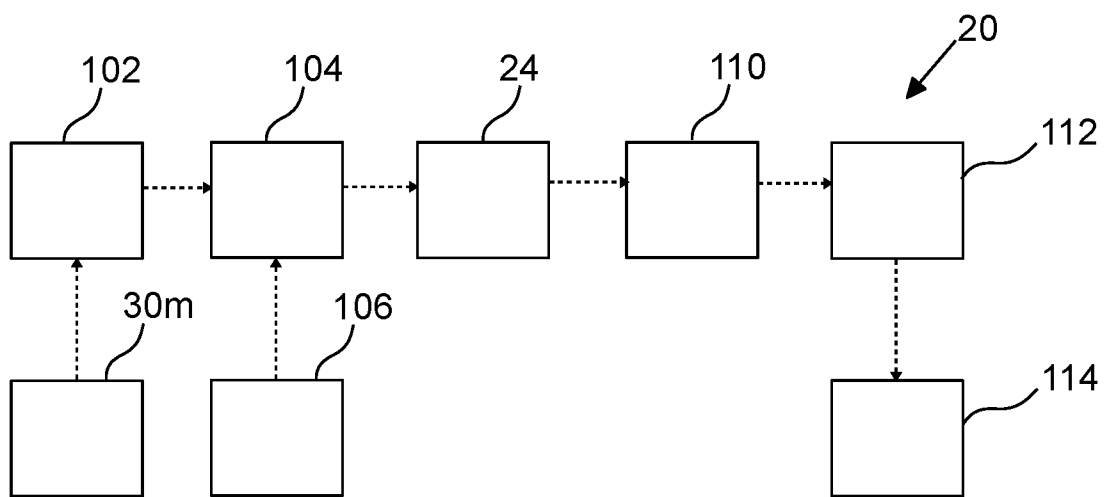


Fig. 1a

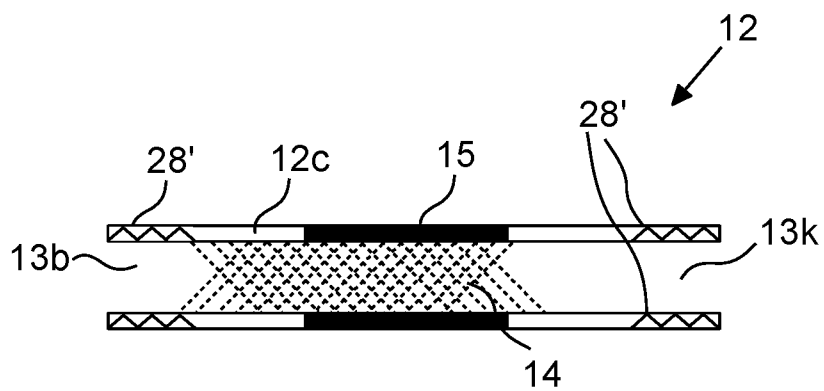


Fig. 2a

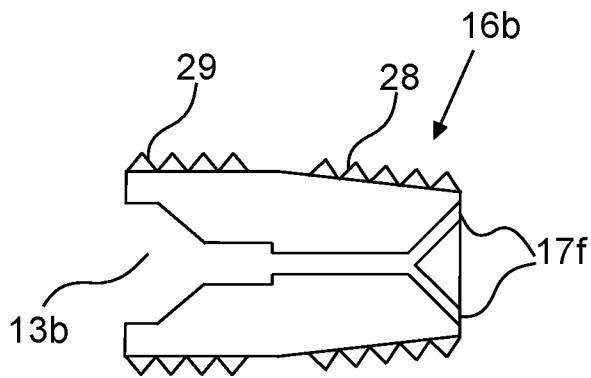


Fig. 4a

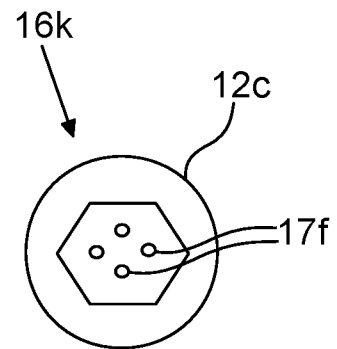


Fig. 4b

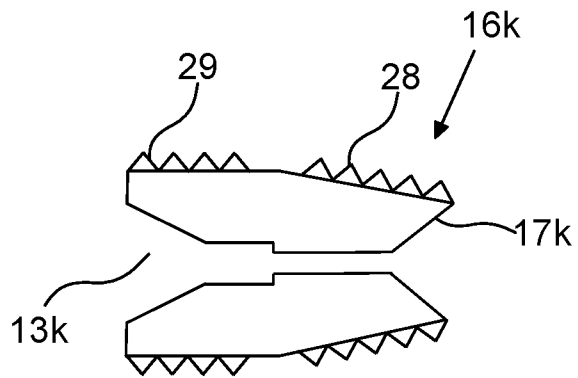


Fig. 5a

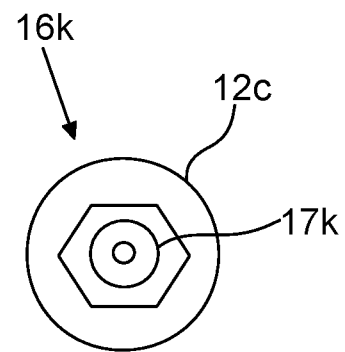


Fig. 5b

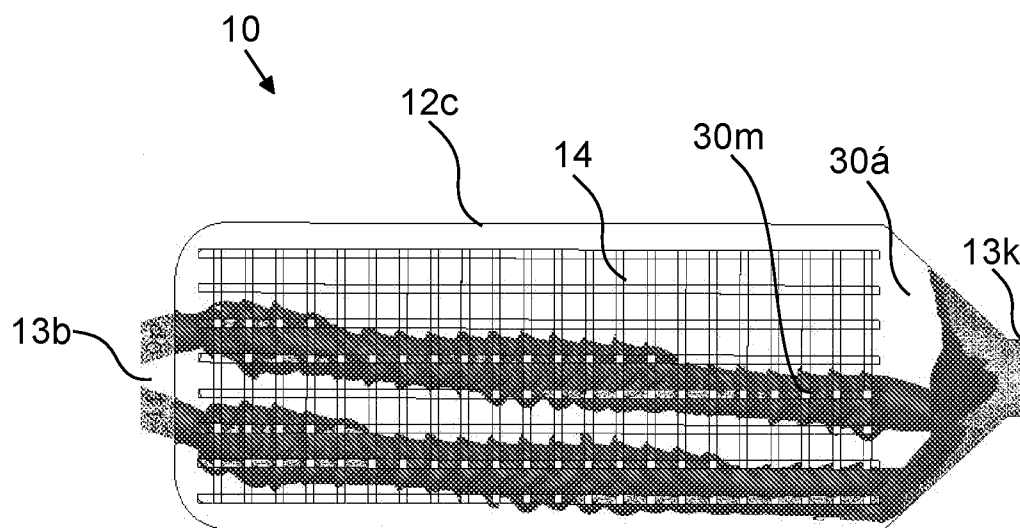


Fig. 3

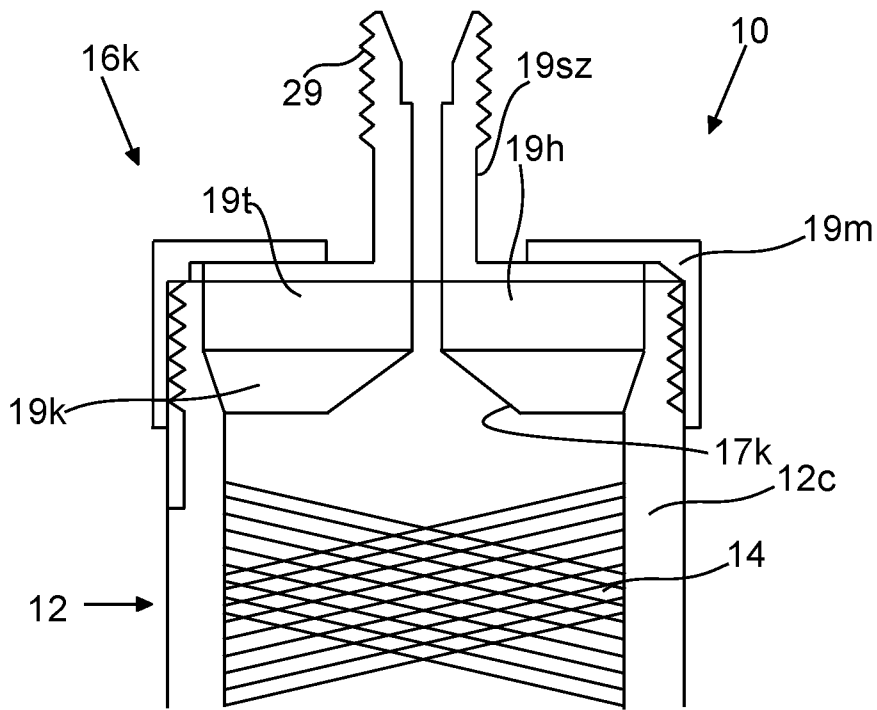


Fig. 7

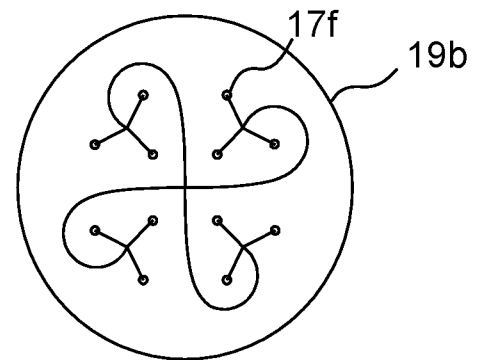


Fig. 6b

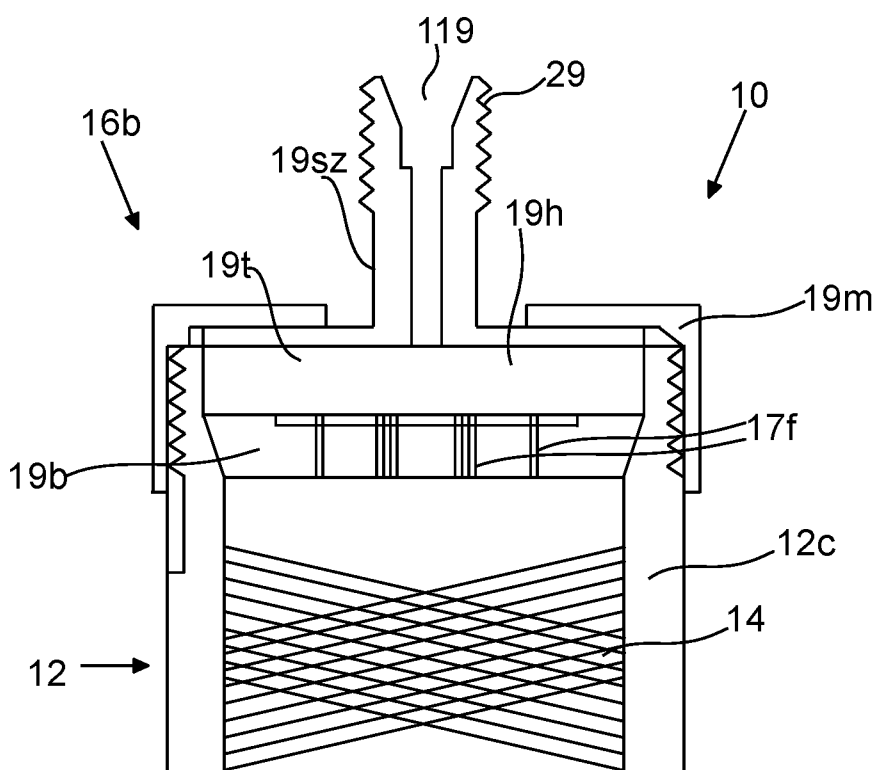


Fig. 6a

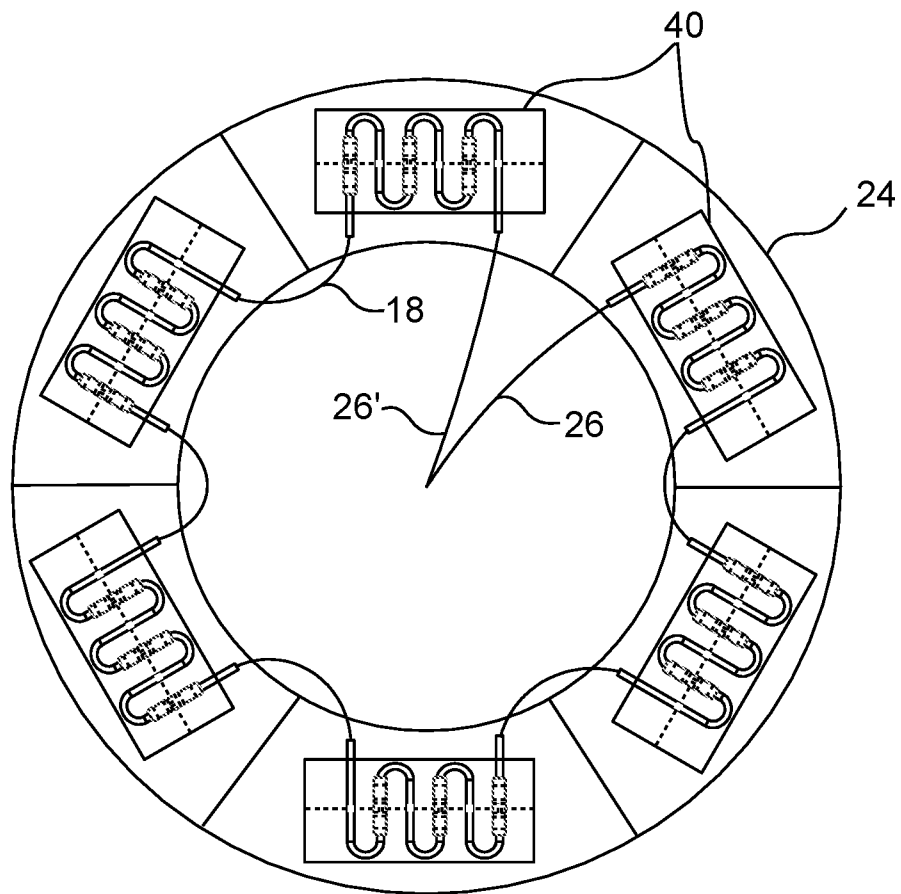


Fig. 9

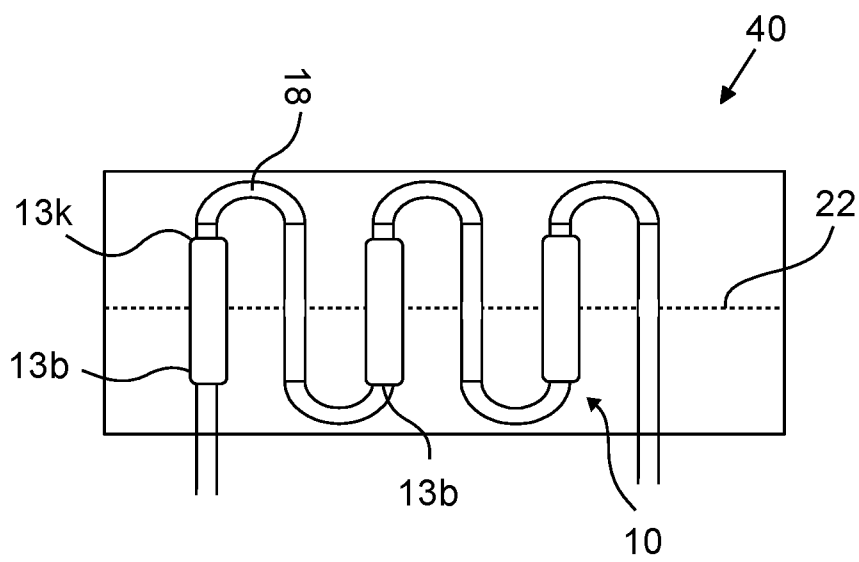


Fig. 8

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/HU2016/050042

A. CLASSIFICATION OF SUBJECT MATTER  
INV. G01N30/42 B01D15/18  
ADD.

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)  
G01N B01D

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)

EPO-Internal, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/173534 A1 (MARGRAFF RODOLPHE [FR] ET AL) 9 September 2004 (2004-09-09) cited in the application	1-4, 6-10, 12-20
Y	figures 1, 2, 5a, 5b paragraphs [0025], [0052] paragraph [0038] - paragraph [0049] -----	11
Y	US 4 422 941 A (VAUGHAN JR MAURICE H [US] ET AL) 27 December 1983 (1983-12-27)	11
A	column 10, line 5 - line 14; figures 17,26 ----- -/--	10



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

27 January 2017

Date of mailing of the international search report

07/02/2017

Name and mailing address of the ISA/

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/HU2016/050042

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>RODOLPHE MARGRAFFA ET AL: "Partitron 25, a Multi-Purpose Industrial Centrifugal Partition Chromatograph: Rotor Design and Preliminary Results on Efficiency and Stationary Phase Retention", JOURNAL OF LIQUID CHROMATOGRAPHY AND RELATED TECHNOLOGIES, MONTICELLO, NY, US, vol. 28, no. 12-13, 31 August 2004 (2004-08-31), pages 1893-1902, XP009168822, ISSN: 1082-6076, DOI: 10.1081/JLC-200063539 the whole document</p> <p>-----</p>	1-10, 12-18,21
X	<p>CH 655 577 A5 (TALAMONA A. F.) 30 April 1986 (1986-04-30)  the whole document</p> <p>-----</p>	1,3,8, 10,12, 14-17
X	<p>US 3 853 765 A (TANIMURA T ET AL) 10 December 1974 (1974-12-10) the whole document</p> <p>-----</p>	1,3,10, 14-17
X	<p>FR 2 883 770 A1 (KROMATON SARL SARL [FR]) 6 October 2006 (2006-10-06) figures 9-14,17</p> <p>-----</p>	1-4,10, 14,15
A	<p>MARCHAL L ET AL: "Mass transport and flow regimes in centrifugal partition chromatography", AI CH E JOURNAL, JOHN WILEY &amp; SONS, INC, US, vol. 48, no. 8, 1 August 2002 (2002-08-01), pages 1692-1704, XP002469489, ISSN: 0001-1541, DOI: 10.1002/AIC.690480811 the whole document</p> <p>-----</p>	18-21
A	<p>CN 202 631 489 U (ROESSELET ROBATEL; SHANGHAI CHEMICAL MACHINERY PLANT CO LTD) 26 December 2012 (2012-12-26) the whole document</p> <p>-----</p>	1-21

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/HU2016/050042

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004173534	A1	09-09-2004	AT 395591 T 15-05-2008
		CN 1756956 A	05-04-2006
		EP 1599724 A1	30-11-2005
		FR 2852104 A1	10-09-2004
		JP 2006519991 A	31-08-2006
		US 2004173534 A1	09-09-2004
		WO 2004079363 A1	16-09-2004
US 4422941	A	27-12-1983	NONE
CH 655577	A5	30-04-1986	NONE
US 3853765	A	10-12-1974	NONE
FR 2883770	A1	06-10-2006	NONE
CN 202631489	U	26-12-2012	NONE