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(54) Title: MAGNETIC PARTICLE SCAVENGING DEVICE AND METHOD

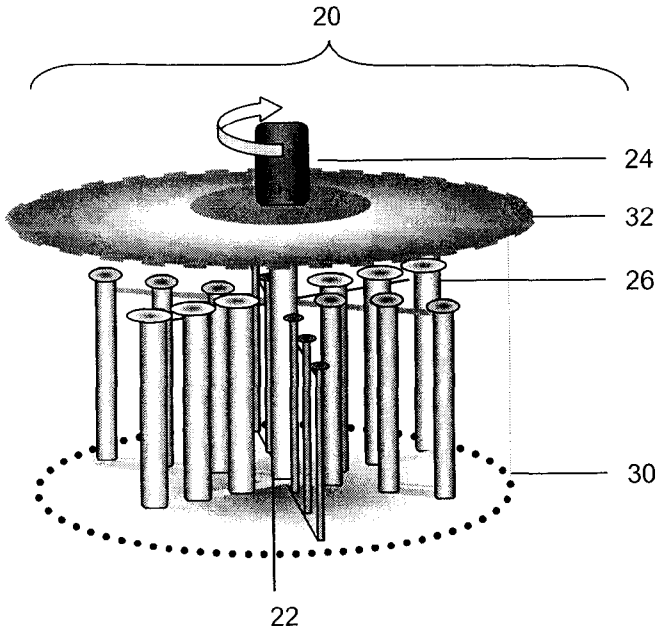

Figure 1

(57) Abstract: The present invention is directed to a device for removing magnetic particles from a liquid, the device comprising at least one container for holding a liquid containing magnetic particles; and at least one magnetic column for placing into the at least one container, wherein when the liquid comes into contact with the at least one magnetic column, the magnetic particles are attracted towards, and bind to, the at least one magnetic column such that when the liquid is separated from the at least one magnetic column, the magnetic particles are removed from the liquid.

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Magnetic Particle Scavenging Device and Method

Field of the Invention

[0001] This invention relates to liquids containing magnetic particles. More specifically, this invention is directed to a novel device and method for removing magnetic particles from a liquid.

Background of the Invention

[0002] Throughout this application, various references are cited to describe more fully the state of the art to which this invention pertains. The disclosures of these references are hereby incorporated by reference into the present disclosure in their entirety.

[0003] Devices and methods for removing magnetic particles are known from U.S. 2,029,078; U.S. 3,567,026; U.S. 3,676,337 U.S. 3,902,994; U.S. 4,141,687; U.S. 4,554,088; U.S. 4,663,029; U.S. 5,108,933; U.S. 5,200,084; U.S. 5,466,574; U.S. 5,622,831; U.S. 6,451,207; U.S. 6,468,810; U.S. 6,695,004; and U.S. 2006/0286137. Many of these devices and methods use external magnets that are not separated from the liquid into which they are inserted. Additionally, many of these devices and methods are only suitable for small volumes in experimental assays and are not suitable for larger scale volumes.

[0004] While the aforementioned devices are generally useful, it is desirable to provide a device and method that overcomes at least one deficiency of the prior art and further provides other advantages to the device itself.

Summary of the Invention

[0005] The present invention is a novel device and method for scavenging or removing magnetic particles from a liquid medium. The magnetic particles can be of any size, shape and configuration. For example, the magnetic particles can be, but are not limited to, filings, chippings, shavings etc. The devices and methods described herein find use in treating blood-borne diseases such as leukemia, diabetes, or viral infections. The devices and methods described herein are also useful in removing pollutants or contaminants from liquids other than blood or blood products such as, for example, bone marrow, cerebral spinal fluid (CSF), cell culture medium, a food, a milk, a beverage, reagents, oils, such as, for example, engine oil, lubricants such as, for example, machine lubricants, buffers, solvents, such as, for example, water, ethanol, formamide, phenol, chloroform, and other chemical liquids and chemical reagents. Other uses include removing DNA or RNA from solutions in experimental assays. The proteins can be enzymes, antibodies, receptors,

polypeptides, haptens etc. The polypeptides can be polypeptide hormones. The haptens can be low molecular compounds, such as lectins, hormones, drugs, pesticides, toxins etc.

[0006] According to an aspect of the present invention there is provided a device for removing magnetic particles from a liquid, the device comprising: a container for holding the liquid and a magnetic column. The container can be any container suitable for holding the liquid and would be known by persons skilled in the art. In one embodiment of the present invention, the container is a tube. In another embodiment of the present invention, the container is at least one well in a plate. In another embodiment of the present invention, the at least one well is a plurality of wells. In an embodiment of the present invention, the pate is a plastic plate. The container and the magnetic column are sufficient for removing magnetic particles in a small volume of liquid (see (26) of Figure 2). The magnetic column can be of any size, shape, and configuration. For example, the magnetic column can be, but is not limited to, a cake, a column, a needle, a bead, a nail, a scalpel, a spoon etc. Any size of magnetic column can be used individually to insert into a container to remove magnetic particles with or without mounting to a shaft. In one embodiment of the present invention, the container is non-magnetic.

[0007] According to an aspect of the present invention there is provided a device for removing magnetic particles from a liquid, the device comprising: a container for holding the liquid; a shaft; and at least one magnetic column mounted for movement about the shaft, wherein the magnetic column stirs the liquid and attracts the magnetic particles in the liquid. The movement about the shaft can be any movement as would be understood by persons skilled in the art. In one embodiment of the present invention, the movement about the shaft is multidirectional. In one embodiment of the present invention, the movement about the shaft is selected from the group consisting of stirring, rotation, vibration, swinging, circling, moving back and forth, up and down and combinations thereof.

[0008] In an aspect, the magnetic column is hollow and comprises an internal magnet. In an aspect, the magnet is removable from the magnetic column. In one embodiment of the present invention, the magnet is a permanent magnet. In another embodiment of the present invention, the magnet is an electromagnet. The magnetic column may further comprise a non-magnetic spacer and a removable cover. The outside of the magnetic column can be manufactured with some nail-like or network projections so that more substances can be held to it. In addition, the magnetic column can also be manufactured with hooks or other shapes (such as a knife or a spoon) in order to be more effective in holding substances.

[0009] In another aspect, a plurality of the magnetic columns is supported on the shaft in at least one array and each of the magnetic columns may be a different size and/or diameter. In an embodiment of the present invention, the at least one array is a single array supported on the shaft. In another embodiment of the present invention, the at least one array is a plurality of arrays supported on the shaft. In another embodiment of the present invention, the at least one array is any number of arrays as would be understood by persons skilled in the art. In another embodiment of the present invention, the at least one array is from 1 to about 20 arrays.

[0010] In another aspect, a plurality of arrays is supported on the shaft in an arrangement selected from the group consisting of substantially parallel (=), substantially crossed (X or +) and combinations thereof.

[0011] In another aspect, the movement of about the shaft is selected from the group consisting of manual, automated and combinations thereof.

[0012] In another aspect, the liquid is selected from blood, a blood product, bone marrow, cerebral spinal fluid (CSF), cell culture medium, a food, a milk, a beverage, an oil, such as, for example, engine oil, lubricants such as, for example, that taken from a machine, buffers, solvents including, but not limited to, water, ethanol, formamide, phenol, chloroform, and other chemical liquids and chemical reagents. In an aspect, the liquid is blood or a blood product.

[0013] In another aspect, the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids, or pollutants. When magnetic particles are used as solid supports, or the particles are larger than the targeted substances, the cells, bacteria, algae, viruses, proteins can be bound to the particles, instead of the particles being bound to the viruses, cells or proteins. However, once they are bound, there is no difference as they become complexes. When the particles are smaller than the targeted substances, the particles (nano-particles) are bound to the targeted substances. Whether the particles are bound to the targeted substances or the targeted substances are bound to the particles depends on the different situations. The magnet column then attracts the particle-cell/virus complexes to it.

[0014] The liquid could be a small or large volume as would be understood by persons skilled in the art. In an embodiment of the present invention, the volume is from about 10 µl to about 10^6 liters. For example, for research use, the volume could be as small volume as about 10 µl. In an embodiment of the present invention, the volume is about 0.1 ml. For industrial use, the volume could be as large as the volume of a swimming pool. In one embodiment where the magnet is expanded to a large size, the scavenger can be manufactured as a vacuum cleaner

and can be walked around the swimming pool so that the human hairs, algae, and other foreign (impurity) substances in the water can be removed. In one embodiment, the liquid is from about 300 ml to about 1000 ml. This volume may be used for clinical purposes.

[0015] According to another aspect of the present invention, there is provided a method of removing magnetic particles from a liquid, the method comprising: moving a magnetic column in the liquid to thereby attract the magnetic particles; and removing the magnetic column and attracted magnetic particles from the liquid. In an embodiment of the present invention, the moving is selected from the group consisting of stirring, rotation, vibration, swinging, circling, moving back and forth, up and down and combinations thereof. In an embodiment of the present invention, the moving is stirring.

[0016] In an aspect, the magnetic column is hollow and comprises an internal magnet and the magnet may be removable from the magnetic column. In another aspect, the magnetic column further comprises a non-magnetic spacer and a removable cover.

[0017] In another aspect, a plurality of the magnetic columns is supported on the shaft in at least one array and each of the magnetic columns is a different size/length and/or diameter. In an embodiment of the present invention, the at least one array is a single array supported on the shaft. In another embodiment of the present invention, the at least one array is a plurality of arrays supported on the shaft. In another embodiment of the present invention, the at least one array is any number of arrays as would be understood by persons skilled in the art. In another embodiment of the present invention, the at least one array is from 1 to about 20 arrays.

[0018] In another aspect, a plurality of arrays is supported on the shaft in an arrangement selected from the group consisting of substantially parallel (=), substantially crossed (X or +) and combinations thereof.

[0019] In another aspect, the movement of about the shaft is selected from the group consisting of manual, automated and combinations thereof.

[0020]

[0021] In an aspect, the liquid is selected from the group consisting of blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, an oil, such as, for example, an engine oil, lubricants such as, for example, that taken from a machine, buffers, solvents including, but not limited to, water, ethanol, formamide, phenol, chloroform, other chemical liquids, other chemical reagents and combinations thereof. In an aspect, the liquid is selected from the group consisting of blood, a blood product and combinations thereof.

[0022] In another aspect, the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids, pollutants or combinations thereof.

[0023] In another aspect, the liquid is a large volume as would be understood by persons skilled in the art. In an embodiment of the present invention, the liquid is in a volume from about 300 ml to about 1000 ml.

[0024] According to another aspect of the present invention, there is provided a device for removing magnetic particles from a liquid, the device comprising: a chamber comprising an inflow conduit and an outflow conduit; and a magnet supported within the chamber between the inflow conduit and the outflow conduit, wherein the magnet attracts the magnetic particles in the liquid when the liquid flows from the inflow conduit to the outflow conduit.

[0025] In an aspect, the magnet is stationary.

[0026] In an aspect, the magnet can be in any shape or size as would be understood by persons skilled in the art.

[0027] In an aspect, the magnet can be installed on the inside and/or outside of the wall of the chamber.

[0028] In another aspect, the device further comprises a plurality of holding portions for supporting the magnet within the chamber.

[0029] In another aspect, the magnet comprises a protective coating.

[0030] In another aspect, the device comprises two portions that engage one another to form the chamber, one portion comprising the inflow conduit and another portion comprising the outflow conduit and the magnet.

[0031] In an aspect, the magnet is removable from the chamber and the two portions engage one another by screwing together.

[0032] In another aspect, the outer diameter of the magnet is smaller than the inner diameter of the chamber. In another aspect, the magnet comprises an aperture through which the liquid flows. In another aspect, the magnet is concave on one or both sides.

[0033] In an aspect, the liquid is selected from the group consisting of blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, an oil, such as, for example, an engine oil, lubricants such as, for example, that taken from a machine, buffers, solvents including, but not limited to, water, ethanol, formamide, phenol, chloroform, other chemical liquids, other chemical reagents, and combinations thereof. In an aspect, the liquid is selected from the group consisting of blood, a blood product and combinations thereof.

[0034] In an aspect, the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids, or pollutants.

[0035] In another aspect, the liquid is a large volume as would be understood by persons skilled in the art. In an embodiment of the present invention, the liquid is in a volume from about 300 ml to about 1000 ml.

[0036] According to another aspect of the present invention, there is provided a method of removing magnetic particles from a liquid, the method comprising: passing the liquid into a drip chamber comprising an internal magnet such that the liquid contacts and flows past the magnet, the magnet attracting the magnetic particles in the liquid; and passing the liquid out of the drip chamber.

[0037] In an aspect, the drip chamber comprises a plurality of holding portions for supporting the magnet within the chamber.

[0038] In another aspect, the magnet comprises a protective coating.

[0039] In another aspect, the drip chamber comprises two portions that engage one another to form the drip chamber, one portion comprising an inflow conduit and another portion comprising an outflow conduit and the magnet. In an aspect, the magnet is removable from the drip chamber and the two portions engage one another by screwing together.

[0040] In an aspect, the outer diameter of the magnet is smaller than the inner diameter of the drip chamber. In another aspect, the magnet comprises an aperture through which the liquid flows. In another aspect, the magnet is concave on one or both sides.

[0041] In another aspect, the liquid is selected from blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, an oil, such as, for example, an engine oil, lubricants such as, for example, that taken from a machine, buffers, solvents including, but not limited to, water, ethanol, formamide, phenol, chloroform, and other chemical liquids and chemical reagents. In an aspect, the liquid is blood or a blood product.

[0042] In another aspect, the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids, or pollutants.

[0043] In another aspect, the liquid is a large volume, such as from about 300 ml to about 1000 ml.

[0044] According to another aspect of the present invention, there is provided a method of treating a blood-borne disease or disorder in a subject, the method comprising: treating blood of the subject with magnetic particles targeted to bind to the disease- or disorder-causing moiety; and removing the magnetic particles and disease- or disorder-causing moiety from the blood by using the device described herein.

[0045] In an aspect, the blood-borne disease or disorder is selected from a cancer, a virus, and an autoimmune disease. In an aspect, the cancer is leukemia;

the virus is HIV, HBV, or HCV; rotavirus and the autoimmune disease is diabetes, systemic lupus erythematosus, or rheumatoid arthritis.

[0046] In another aspect, the disease- or disorder-causing moiety is selected from a cell, a viral particle, an autoimmune protein complex, a toxic agent, a protein complex, and a cholesterol complex.

[0047] In another aspect, the blood is removed from the subject for treatment and returned to the subject after treatment.

[0048] According to another aspect of the present invention, there is provided a use of the device described herein for treating a blood-borne disease or disorder in a subject, wherein magnetic particles targeted to bind to the disease- or disorder-causing moiety are present in the blood of the subject.

[0049] In an aspect, the blood-borne disease or disorder is selected from a cancer, a virus, and an autoimmune disease. In an aspect, the cancer is leukemia; the virus is HIV, HBV, or HCV; and the autoimmune disease is diabetes, systemic lupus erythematosus, or rheumatoid arthritis.

[0050] In another aspect, the disease- or disorder-causing moiety is selected from a cell, a viral particle, an autoimmune protein complex, a toxic agent, a protein complex, and a cholesterol complex.

[0051] Other features and advantages of the present invention will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples while indicating embodiments of the invention are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from the detailed description.

Brief Description of the Drawings

[0052] Embodiments will now be described, by way of example only, with reference to the attached figures, wherein:

[0053] Figure 1 is perspective view of a device of the present invention;

[0054] Figure 2 is a perspective view of the columns of the device of Figure 1;

[0055] Figure 3 is top plan view and side elevation view of the arrays of the device of Figure 1;

[0056] Figure 4 is a perspective view of the device of Figure 1 showing its assembly;

[0057] Figure 5a is a side elevation view of another device of the present invention;

[0058] Figure 5b is a side cross-section view of the device of Figure 5a;

[0059] Figure 5c is a side cross-section view of the device of Figure 5a in use;

[0060] Figure 6a is a side elevation view of the device of Figure 5a when disassembled;

[0061] Figure 6b is a cross-section view of the device of Figure 6a;

[0062] Figure 6c is a top cross-section view of the device of Figure 5a;

[0063] Figure 7a is an illustration of a method of use of a device of the present invention;

[0064] Figure 7b is an illustration of a method of use of a device of the present invention;

[0065] Figure 8 is an illustration of the binding of targeted particles to magnetic particles to form a complex and the binding of the complex to a magnet in accordance with an aspect of the present invention;

[0066] Figure 9 is a perspective view of a device of the present invention.

Detailed Description of the Invention

[0067] The present invention is directed to novel devices and methods for removing or scavenging magnetic particles from a liquid medium. These devices and methods find use in removing magnetic particles from biological liquids such as from blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, an oil, such as, for example, an engine oil, lubricants such as, for example, that taken from a machine, buffers, solvents including, but not limited to, water, ethanol, formamide, phenol, chloroform, and other chemical liquids and chemical reagents. The magnetic particles may themselves be contaminants or pollutants in the liquid or they may be bound to a contaminant or disease-causing moiety in the liquid. Alternatively, the magnetic particles may be a desirable component of the liquid that must be removed from the liquid for purification.

[0068] The invention is now herein described with reference to Figure 1, which shows one aspect of the device of the present invention. This device 20 comprises a shaft 22 that is connected to a knob 24. The shaft 22 and the knob 24 are connected to one another such that movement of the knob 24, in this embodiment rotation, causes a corresponding movement, in this embodiment, rotation of the shaft 22. In this way, the device 20 can be operated manually and/or automatically through movement, in this embodiment rotation, of the knob 24.

[0069] Mounted to the shaft 22 is a plurality of columns 26. The columns 26 are hollow, house magnets 28 (see Figure 2), and are rotational about the shaft 22.

The columns 26 are supported about the shaft in arrays of six columns each in the illustrated embodiment. Six columns and three arrays is merely an example. The columns and the arrays may be more or fewer according to the diameter of the device 20 as would be understood by persons skilled in the art. The length of the columns 26 may be shorter or longer according to the deepness or shallowness of the liquid volume inside the container 30 as would be understood by persons skilled in the art. Each of the arrays comprises different sized columns 26. The variation in sizes allows a corresponding variation in strength of the magnetic field, which permits customization of the device 20 by the end user as desired. The shaft 22 and columns 26 are insertable into a container 30 for holding liquid and the container may be closed using a cover 32.

[0070] It will be understood that the device 20 is multi-functional in that it may act as a stirrer when magnets 28 are not housed in the columns 26, whereas it can additionally act to attract magnetic particles in a liquid when magnets 28 are housed in the columns 26.

[0071] Turning now to Figure 2, the columns 26 and magnets 28 are shown in isolation. The magnets 28 are shown in three different sizes 28a, 28b, and 28c. Additionally, non-magnetic spacers 34 are shown in three different sizes 34a, 34b, and 34c. The non-magnetic spacers may be made of any non-magnetic material, such as metal (aluminum, lead or copper, for example), porcelain, glass, ceramics, plastic, or wood. By combining these magnets 28 and spacers 34 in different permutations, the resulting magnetic field may be adjusted to meet the needs of the end user. For example, column 26a includes only magnets 28 and produces a strong magnetic field. Column 26b includes three magnets 28 separated by one spacer 34 each, creating an intermediate magnetic field at three different planes within the container 30. Finally, column 26c includes two magnets 28 separated by three spacers 34, creating a weaker magnetic field at two different and distant planes within the container 30. This combinatorial arrangement of magnets 28 and spacers 34 allows for a near limitless customization of the magnetic field by the end user.

[0072] This combinatorial arrangement is advantageous because any magnetic particles in the liquid may float for some time rather than settle to the bottom of the container 30 immediately due to their different specific gravities. By adjusting the plane of the magnetic field, the magnetic particles may be attracted to the magnetic columns 26 immediately rather than waiting for the particles to sink in the liquid. Additionally, the size of the magnets may be adjusted in order to create a stronger or weaker magnetic field, depending upon the concentration or size of the magnetic particles in the liquid.

[0073] From Figure 2 it will be evident that the columns 26 are tubes having one closed end and one open end into which the magnets 28 and spacers 34 may be inserted. The open end may be protected by a lid 36, thereby preventing liquid in the container 30 from contaminating the magnets 28 and spacers 34. In this way, the magnets 28 and spacers 34 are reusable without necessarily requiring cleaning between each use.

[0074] Figure 3 illustrates the arrangement of the columns 26 into arrays 38. As is shown in Figures 1 and 2, three arrays 38 containing six columns each, for example, may be assembled about the shaft 22. Alternatively, a single array 38 or any number of arrays may be assembled about the shaft 22. The arrays 38 may be assembled about the shaft 22 in any arrangement as would be understood by persons skilled in the art. In an embodiment of the present invention, the arrays 38 are assembled about the shaft 22 in an arrangement selected from the group consisting of substantially parallel (=), substantially crossed (X or +) and combinations thereof. Figure 3 illustrates the assembling of the arrays 38 about the shaft 22 in a substantially crossed arrangement. The arrays 38 may contain columns 26 of different sizes or diameters, creating large 38a, medium 38b, and small 38c arrays. These arrays 38a, 38b, and 38c may be assembled about the shaft in any combination and each of the arrays 38 need not contain only one type of column 26 as is shown in the Figures. It is contemplated that different columns 26 may be combined together in a single array 38. Thus, the end used is provided with even more customizability with respect to the magnetic field that is created.

[0075] Turning now to Figure 4, assembly of the device 20 is shown. The knob 24 and shaft 22 are inserted through a hole in the cover 32 and the shaft is attached to the arrays 38 containing magnets 28 and optionally spacers 34 in the desired configuration. The shaft 22 is hollow and can thus be placed on top of a post 40 that extends upwardly from the container 30. Alternatively, the shaft 22 can be placed or fixed on any spot where the various motions or movements can be accomplished as would be understood by persons skilled in the art. The shaft 22 is rotatable on the post 40 by using the knob 24. At this point, the device 20 may be operated manually by simply turning the knob 24, thereby causing the arrays 38 to spin within the container 30. Alternatively, the device 20 may be inserted into an automated housing 42 that may control the speed of rotation and other desired parameters, such as time, UV sterilization, temperature, and light source.

[0076] In Figure 4, housing 42 is an example device for the medical use purpose. In use, the device 20 is assembled as described in a desired configuration using the magnets 28, spacers 34, and arrays 38. A liquid containing magnetic particles is placed into the container 30 and the knob 24 is turned. This causes

stirring of the liquid and movement of the magnetic field throughout the liquid, thereby increasing the likelihood that the magnetic particles in the liquid will be found within the magnetic field and thus be attracted to the magnets 28. After a period of time, the liquid may be removed from the container 30 and/or the arrays 38 may be removed from the liquid, depending upon whether the purified liquid is the desired end product or whether the magnetic particles are the desired end product. The magnetic particles will be attracted to the columns and this attraction will not cease until the columns are demagnetized, for example, by removal of the magnets therein.

[0077] Turning now to Figures 5 and 6, another aspect of the device of the present invention is illustrated. Here, the device takes the form of a hollow drip chamber 44 having an inflow conduit 46 and an outflow conduit 48 through which liquid 58 may flow. A magnet 28 is supported within the drip chamber 44 on holding portions 50. The outside diameter of the magnet 28 is smaller than the inside diameter of the drip chamber 44 so that the liquid 58 may flow past the magnet 28 through spaces 60 between the holding portions 50 and out through the outflow conduit 48. Alternatively, the magnet 28 may have the same diameter as the inside diameter of the drip chamber 44, however, in this case, there should be at least one aperture in the magnet 28 to allow the liquid 58 to flow therethrough. It will be understood that the magnet 28 in this aspect of the device is stationary and does not move with the liquid 58. Alternatively, the magnet 28 may be mounted to the wall, inside and/or outside of the chamber 44. The chamber 44 also can be modified to let the inflow conduit 46 and the outflow conduit 48 be connected to a vein or artery of a patient by implanting the device in the patient's body to capture disease causing moieties.

[0078] The drip chamber 44 is made from two portions that engage one another to form the drip chamber 44. One portion 62 comprises the inflow conduit 46, while the other portion 64 comprises the outflow conduit 48 and the magnet 28. As is shown in Figure 6, the two portions 62, 64 screw together to form the drip chamber 44. It will be understood that the two portions could engage one another by methods other than screwing, such as by a friction fit or by snapping together, for example. Alternatively, the drip chamber 44 could be provided as a unitary device that does not come apart, having the magnet 28 manufactured therein. The drip chamber 44 may be transparent so that the dripping speed can be monitored. The material of drip chamber may be the same as the material of the syringe or the coating 52 materials.

[0079] In the illustrated embodiment, the magnet 28 has a protective coating 52. The material of the protective coating 52 may be consistent with that of

the syringe or other medical use consumables. It should be a non-toxic, and regulatory approved grade material, such as, for example polyethylene or polythene. The thickness of the protective coating may be from about 0.2 to about 1.0 mm. The coating 52 does not interfere with the magnetic field produced by the magnet 28 and is present to prevent any adverse reaction from occurring between the magnet 28 and the liquid 58 with which it is in contact. For example, if the liquid 58 is blood, the coating 52 may be biocompatible and inert. Additionally, the coating 52 may be shaped so as to form concave wells 54 on either or both sides of the magnet 28. The wells 54 are formed on both sides of the magnet 28 so that the orientation in which that magnet 28 is placed in the drip chamber 44 does not matter. The wells 54 function to increase the contact time of the liquid with the magnetic field in order to help ensure that any magnetic particles 56 in the liquid 58 are attracted and held in place by the magnet 28 while the liquid 58 continues to flow past.

[0080] If the liquid 58 is blood or a blood product, the drip chamber 44 may be suspended below a medical liquid container 66 such as that shown in Figure 7. In this embodiment, the blood or blood product flows from the medical liquid container 66 into the drip chamber 44 and eventually into the subject. In this way, the blood or blood product can be cleaned of magnetic particles 56 prior to its entry into the subject. The blood or blood product may be the subject's own blood or blood product that had been earlier removed. In one aspect, targeted magnetic particles 56 were bound to malignant cells, for example, found within the subject's blood. By passing this blood through the drip chamber 44, the malignant cells will be removed from the blood along with the magnetic particles 56 prior to returning the blood to the subject's system.

[0081] In use, a liquid 58, containing magnetic particles 56, is allowed to flow into the drip chamber 44 via the inflow conduit 46. The liquid 58 contacts the magnet 28 and any magnetic particles 56 found in the liquid are attracted to and held in place by the magnet 28 while the liquid 58 continues to flow past the magnet 28 and out through the outflow conduit 48. Upon exiting the drip chamber 44, the liquid 58 will be substantially free of magnetic particles 56.

[0082] The invention is now herein described with reference to Figures 7a and 7b, which show another aspect of the device of the present invention. In particular, Figure 7a shows the device comprising a medical liquid container 66 and a magnetic column 72. In this particular embodiment, blood 58 is taken from a patient suffering from leukemia and collected in the medical liquid container 66. The leukemia cells in the collected blood 58 are bound by magnetic particles 56. The magnetic column 72 is submersed in the collected blood 58 in the medical liquid

container 66 and swirled or stirred. The leukemia cells that are bound to the magnetic particles 56 in the blood 58 magnetically bind to the magnetic column 72 and are removed from the blood with the magnetic column when the magnetic column is removed from the medical liquid container 66. The leukemia cell-free blood can then be transfused back into the patient. Referring now to Figure 7b, the medical liquid container 66 is a blood bottle with a drip-chamber 44. There is an opening 76 in the shoulder of the blood bottle through which the magnetic column 72 can be inserted. Once again, blood 58 is taken from a patient suffering from leukemia and collected in the blood bottle. The leukemia cells in the collected blood 58 are bound by magnetic particles 56. The magnetic column 72 is inserted through the opening 76 in the shoulder of the blood bottle and submersed in the collected blood 58 and swirled or stirred. The leukemia cells that are bound to the magnetic particles 56 in the blood 58 magnetically bind to the magnetic column 72 and are removed from the blood with the magnetic column when the magnetic column is removed from the blood bottle. The captured leukemia cells can then be placed into a separate container for analysis.

[0083] In an embodiment of the present invention, targeted substances can be made to bind to magnetic support material. The targeted substances can be members of any specific binding pair, such as, for example, a pair of bio-specific ligands and receptors, antigen and antibodies, or anything having specific binding affinities. The determination of any member of a bio-specific binding pair is dependent upon its selective interaction with the other member of the pair. For example, in forming an immune-complex, a "sandwich" is formed in which the "layers" are magnetic-particle/antigen/antibody or magnetic-particle/antibody/antigen. The sandwich can also be magnetic-particle/receptor/viruses or magnetic-particle/receptor/cells. Referring now to Figure 8, magnetically responsive particles provide a solid support. In this particular embodiment, the magnetic particles are composed of an iron core, such as an iron oxide core, and a silica/polymer shell. The size range of the magnetic particles may be from about 10 nm to about 500 μm. The bio-affinity components are attached to the particle by covalent binding or by biotin/streptavidin coupling. The bio-affinity components are needed for the cells, viruses and other targeted substances to be attached to the particles, such as antigen-antibody, ligand-receptor, etc. In this particular embodiment, the particle is coated with silica or polymer so that it can provide a high surface area to present for example, more than one receptor and be surrounded by a few targeted substances, e.g. it can form flower-like complexes. For the same reason, if one cell has more than one receptor in the cell's membrane, more than one particle can be adhered to one cell according to the design. In this

particular embodiment, the magnetic responsive particle itself is not magnetized. It plays the role of a carrier and behaves as a true colloid. It becomes magnetic only when it is subjected to a magnetic field. In addition, the coating materials can protect the, for example iron, of the particle from direct contact with the liquid in order to avoid certain chemical reactions between the, for example iron, of the particle with the liquid components. This can be a very important safety issue when the particles are used for clinical purposes.

[0084] The invention is now herein described with reference to Figure 9, which shows another aspect of the device of the present invention. In this particular embodiment, the device 20 is a scavenger used in industry, such as, for example, in the swimming pool industry. In this embodiment, where the magnet is expanded to a large size, the device 20 is a scavenger and is manufactured in the form of something like a vacuum cleaner to remove human hairs and other impurity substances from water in a swimming pool wherein the liquid container is the pool and the shaft 22, the knob 24, the columns 26, and the post 40, make up the device 20. The device 20 could be motorized or moved manually by pushing the handle 78 such that the device 20 moves through the water in a swimming pool, in this embodiment, over the interior surface of the swimming pool on wheels 80 supported by post 40, so that the human hairs, algae, and other foreign (impurity) substances in the water can be removed. This embodiment is more effective and economical than filter cleaning.

[0085] The devices described herein find use in methods of removing magnetic particles from a liquid. The type of liquid is non-limiting and some examples include blood, blood products, bone marrow, CSF, cell culture medium, foods, milk, beverages, an oil, such as, for example, an engine oil, lubricants, buffers, solvents including, but not limited to, water, ethanol, formamide, phenol, chloroform, and other chemical liquids and chemical reagents. The magnetic particles themselves may be desirable to remove from the liquid, or the magnetic particles may be bound to a component in the liquid that is desirable to remove. For example, the magnetic particles may be targeted to bind to cells, bacteria, algae, viruses, proteins, nucleic acids, or pollutants found in the liquid. In this way, the devices described herein may be used to clean polluted or contaminated water or to remove bits of metal scrapings found in engine oil and lubricants. Alternatively, the devices may be used to treat diseases or disorders such as cancer, including leukemia, viruses, including HIV, HBV, or HCV, or autoimmune diseases, including diabetes, systemic lupus erythematosus, or rheumatoid arthritis. These listed diseases and disorders are considered non-limiting, as any liquid disease or disorder (any disease or disorder that involves circulating cells, viruses, proteins,

auto-antibodies in a bodily fluid, such as blood, bone marrow, CSF) may be treated using the presently claimed devices. The devices described herein also find use in experimental assays, such as in isolating proteins, bacteria, viruses, DNA or RNA from liquid solutions.

[0086] In treating such diseases or disorders, the magnetic particles are targeted to bind to the disease-causing moiety. For example, in the case of leukemia, the magnetic particles would be targeted to the malignant cells. In the case of a viral infection, the magnetic particles would be targeted to a viral particle. In the case of an autoimmune disorder, the magnetic particles would be targeted to an autoimmune protein complex. Other protein complexes or cholesterol complexes may be targeted in order to treat other diseases or disorders.

[0087] The description as set forth is not intended to be exhaustive or to limit the scope of the invention. Many modifications and variations are possible in light of the above teaching without departing from the spirit and scope of the following claims. It is contemplated that the use of the present invention can involve components having different characteristics. It is intended that the scope of the present invention be defined by the claims appended hereto, giving full cognizance to equivalents in all respects.

Claims

1. A device for removing magnetic particles from a liquid, the device comprising:

- at least one container for holding a liquid containing magnetic particles; and

- at least one magnetic column for placing into the at least one container, wherein when the liquid comes in contact with the at least one magnetic column, the magnetic particles are attracted towards, and bind to, the at least one magnetic column such that when the liquid is separated from the at least one magnetic column, the magnetic particles are removed from the liquid.

2. The device of claim 1, further comprising a shaft upon which the at least one magnetic column is supported on the shaft for movement about the shaft.

3. The device of claim 2, wherein the movement about the shaft is in any direction.

4. The device of claim 2 or 3, wherein the movement about the shaft is multi-directional.

5. The device of any one of claims 2 to 4, wherein the movement about the shaft is selected from the group consisting of rotation, vibration, swinging, circling, back and forth, up and down and combinations thereof

6. The device of any one of claims 1 to 5, wherein the at least one magnetic column is hollow and comprises an internal magnet.

7. The device of claim 6, wherein the internal magnet is selected from the group consisting of a permanent magnet and an electromagnet.

8. The device of claim 6 or 7, wherein the internal magnet is removable from the at least one magnetic column.

9. The device according to any one of claims 1 to 8, wherein the at least one magnetic column further comprises a non-magnetic spacer.

10. The device according to any one of claims 1 to 9, wherein the at least one magnetic column comprises a removable cover.

11. The device according to any one of claims 2 to 10, wherein the at least one magnetic column is a plurality of magnetic columns.

12. The device of claim 11, wherein at least two of the magnetic columns of the plurality of magnetic columns have different dimensions.

13. The device of claim 11 or 12, wherein the plurality of magnetic columns is supported on the shaft in at least one array.

14. The device of claim 13, wherein the at least one array is a plurality of arrays supported on the shaft.

15. The device of claim 14, wherein the plurality of arrays are supported on the shaft in an arrangement selected from the group consisting of substantially parallel, substantially crossed and combinations thereof.

16. The device according to any one of claims 2 to 15, wherein the movement is manual.

17. The device according to any one of claims 2 to 15, wherein the movement is automated.

18. The device according to any one of claims 1 to 17, wherein the liquid is selected from the group consisting of blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, oils, lubricants, buffers, solvents selected from the group consisting of water, ethanol, formamide, phenol, chloroform, reagents, and combinations thereof.

19. The device of claim 18, wherein the liquid is blood or a blood product.

20. The device according to any one of claims 1 to 19, wherein the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids or pollutants.

21. The device according to any one of claims 1 to 20, wherein the liquid has a volume of from about 10 µl to about 10^6 liters.

22. The device of claim 21, wherein the volume is from about 300 ml to about 1000 ml.

23. A method of removing magnetic particles from a liquid, the method comprising:

- contacting a liquid containing magnetic particles with at least one magnetic column in the liquid to thereby attract and bind the magnetic particles to the at least one magnetic column; and
- separating the liquid from the at least one magnetic column and bound magnetic particles to remove the magnetic particles from the liquid.

24. The method of claim 23, wherein the at least one magnetic column is supported on a shaft for movement about the shaft.

25. The method of claim 24, wherein the movement about the shaft is in any direction.

26. The method of claim 24 or 25, wherein the movement about the shaft is multi-directional.

27. The method of any one of claims 24 to 26, wherein the movement about the shaft is selected from the group consisting of rotation, vibration, swinging, circling, back and forth, up and down and combinations thereof

28. The method of any one of claims 24 to 27, wherein the at least one magnetic column is hollow and comprises an internal magnet.

29. The method of claim 28, wherein the internal magnet is removable from the at least one magnetic column.

30. The method of claim 28 or 29, wherein the at least one magnetic column further comprises a non-magnetic spacer.

31. The method according to any one of claims 28 to 30, wherein the at least one magnetic column comprises a removable cover.

32. The method according to any one of claims 28 to 31, wherein the at least one magnetic column is a plurality of magnetic columns.

33. The method of claim 32, wherein at least two magnetic columns of the plurality of magnetic columns have different dimensions.

34. The method of claim 32 or 33, wherein the plurality of magnetic columns is supported on the shaft in at least one array.

35. The method of claim 34, wherein the at least one array is a plurality of arrays supported on the shaft.

36. The device of claim 35, wherein the plurality of arrays are supported on the shaft in an arrangement selected from the group consisting of substantially parallel, substantially crossed and combinations thereof.

37. The method according to any one of claims 24 to 36, wherein the movement is manual.

38. The method according to any one of claims 24 to 36, wherein the movement is automated.

39. The method according to any one of claims 24 to 38, wherein the liquid is selected from the group consisting of blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, oils, lubricants, buffers, solvents selected from the group consisting of water, ethanol, formamide, phenol, chloroform and combinations thereof, reagents and combinations thereof.

40. The method of claim 39, wherein the liquid is selected from the group consisting of blood, a blood product and combinations thereof.

41. The method according to any one of claims 24 to 40, wherein the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids or pollutants.

42. The method according to any one of claims 24 to 41, wherein the liquid has a volume of from about 10 µl to about 10^6 liters.

43. The method of claim 42, wherein the volume is from about 300 ml to about 1000 ml.

44. A device for removing magnetic particles from a liquid, the device comprising:

- a chamber comprising an inflow conduit and an outflow conduit; and
- a magnet supported within the chamber between the inflow conduit and the outflow conduit,

wherein the magnet attracts and binds the magnetic particles in the liquid when the liquid flows from the inflow conduit to the outflow conduit.

45. The device of claim 44, wherein the magnet is stationary.

46. The device of claim 44 or 45, further comprising a plurality of holding portions for supporting the magnet within the chamber.

47. The device according to any one of claims 45 to 46, wherein the magnet comprises a protective coating.

48. The device according to any one of claims 45 to 47, comprising two portions that engage one another to form the chamber, one portion comprising the inflow conduit and another portion comprising the outflow conduit and the magnet.

49. The device of any one of claims 45 to 48, wherein the magnet is removable from the chamber.

50. The device of claim 48, wherein the two portions engage one another by screwing together.

51. The device of any one of claims 45 to 50, wherein the magnet is mounted to the wall of the chamber.

52. The device according to any one of claims 45 to 51, wherein the outer diameter of the magnet is smaller than the inner diameter of the chamber.

53. The device according to any one of claims 45 to 52, wherein the magnet comprises an aperture through which the liquid flows.

54. The device according to any one of claims 45 to 53, wherein the magnet is concave on one or both sides.

55. The device according to any one of claims 45 to 54, wherein the liquid is selected from the group consisting of blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, oils, lubricants, buffers, solvents selected from the group consisting of water, ethanol, formamide, phenol, chloroform and combinations thereof, reagents and combinations thereof.

56. The device of claim 55, wherein the liquid is selected from the group consisting of blood, a blood product and combinations thereof.

57. The device according to any one of claims 45 to 56, wherein the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids or pollutants.

58. The device according to any one of claims 45 to 57, wherein the liquid has a volume of from about 10 µl to about 10^6 liters.

59. The device of any one of claims 45 to 58, wherein the volume is from about 300 ml to about 1000 ml.

60. The device of any one of claims 45 to 59, wherein the inflow conduit and the outflow conduit are configured to be connected to a vein or artery of a patient directly or indirectly.

61. The device of any one of claims 45 to 59, wherein the inflow conduit and the outflow conduit are configured to be connected to a vein or artery indirectly via tubing.

62. The device of any one of claims 45 to 59, for use *in vivo* or in *vitro*.

63. A method of removing magnetic particles from a liquid, the method comprising:

- passing the liquid into a drip chamber comprising an internal magnet such that the liquid contacts and flows past the magnet, the magnet attracting and binding the magnetic particles in the liquid;

- passing the liquid out of the drip chamber.

64. The method of claim 63, wherein the drip chamber comprises a plurality of holding portions for supporting the magnet within the chamber.

65. The method of claim 63 or 64, wherein the magnet comprises a protective coating.

66. The method according to any one of claims 63 to 65, wherein the drip chamber comprises two portions that engage one another to form the drip chamber, one portion comprising an inflow conduit and another portion comprising an outflow conduit and the magnet.

67. The method of claim 66, wherein the magnet is removable from the drip chamber.

68. The method of claim 66 or 67, wherein the two portions engage one another by screwing together.

69. The method of any one of claims 63 to 68, wherein the magnet is mounted to the wall of the chamber.

70. The method according to any one of claims 63 to 69, wherein the outer diameter of the magnet is smaller than the inner diameter of the drip chamber.

71. The method according to any one of claims 63 to 70, wherein the magnet comprises an aperture through which the liquid flows.

72. The method according to any one of claims 63 to 71, wherein the magnet is concave on one or both sides.

73. The method according to any one of claims 63 to 72, wherein the liquid is selected from the group consisting of blood, a blood product, bone marrow, CSF, cell culture medium, a food, a milk, a beverage, oils, lubricants, buffers, solvents

selected from the group consisting of water, ethanol, formamide, phenol, chloroform, reagents and combinations thereof.

74. The method of claim 73, wherein the liquid is selected from the group consisting of blood, a blood product and combinations thereof.

75. The method according to any one of claims 63 to 74, wherein the magnetic particles are bound to cells, bacteria, algae, viruses, proteins, nucleic acids or pollutants.

76. The method according to any one of claims 63 to 75, wherein the liquid has a volume of from about 10 µl to about 10^6 liters.

77. The method of any one of claims 63 to 76, wherein the liquid has a volume of from about 300 ml to about 1000 ml.

78. The method of any one of claims 63 to 77, for being conducted *in vivo* or in *vitro*.

79. A method of treating a blood-borne disease or disorder in a subject, the method comprising:

- treating blood of the subject with magnetic particles targeted to bind to a moiety causing the disease or disorder; and
- removing the magnetic particles and disease- or disorder-causing moiety from the blood by using the device of any one of claims 1 to 22 and 44 to 62.

80. The method of claim 79, wherein the blood-borne disease or disorder is selected from the group consisting of a cancer, a virus and an autoimmune disease.

81. The method of claim 80, wherein the cancer is leukemia.

82. The method of claim 80, wherein the virus is HIV, HBV or HCV.

83. The method of claim 80, wherein the autoimmune disease is diabetes, systemic lupus erythematosus or rheumatoid arthritis.

84. The method according to any one of claims 79 to 83, wherein the disease- or disorder-causing moiety is selected from the group consisting of a cell, a viral particle, an autoimmune protein complex, a toxic agent, a protein complex, cholesterol complex and combinations thereof.

85. The method according to any one of claims 79 to 84 wherein the blood or bone marrow is removed from the subject for treatment and returned to the subject after treatment.

86. Use of the device of any one of claims 1 to 22 and 44 to 62 for treating a blood-borne disease or disorder in a subject, wherein magnetic particles targeted to bind to the disease- or disorder-causing moiety are present in the blood of the subject.

87. The use of claim 86, wherein the blood-borne disease or disorder is selected from the group consisting of a cancer, a virus and an autoimmune disease.

88. The use of claim 87, wherein the cancer is leukemia.

89. The use of claim 87, wherein the virus is HIV, HBV or HCV.

90. The use of claim 87, wherein the autoimmune disease is diabetes, systemic lupus erythematosus or rheumatoid arthritis.

91. The use according to any one of claims 86 to 90, wherein the disease- or disorder-causing moiety is selected from the group consisting of a cell, bacteria, algae, viral particle, an autoimmune protein complex, a toxic agent, a protein complex, a cholesterol complex and combinations thereof.

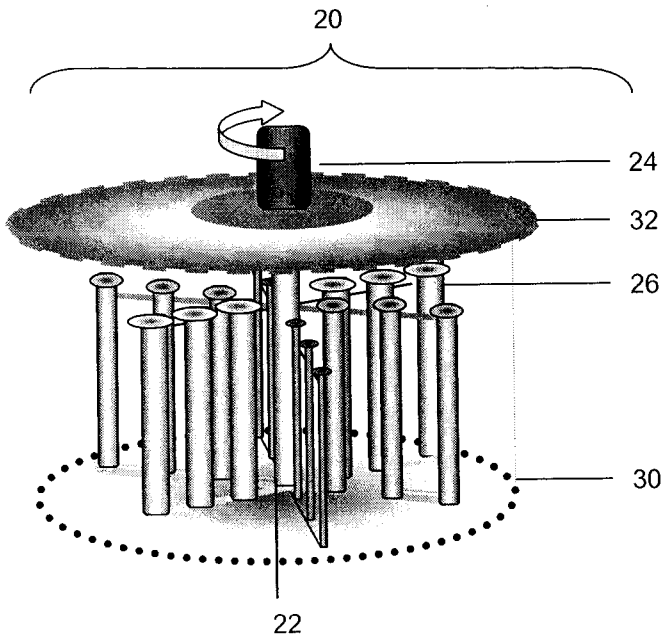


Figure 1

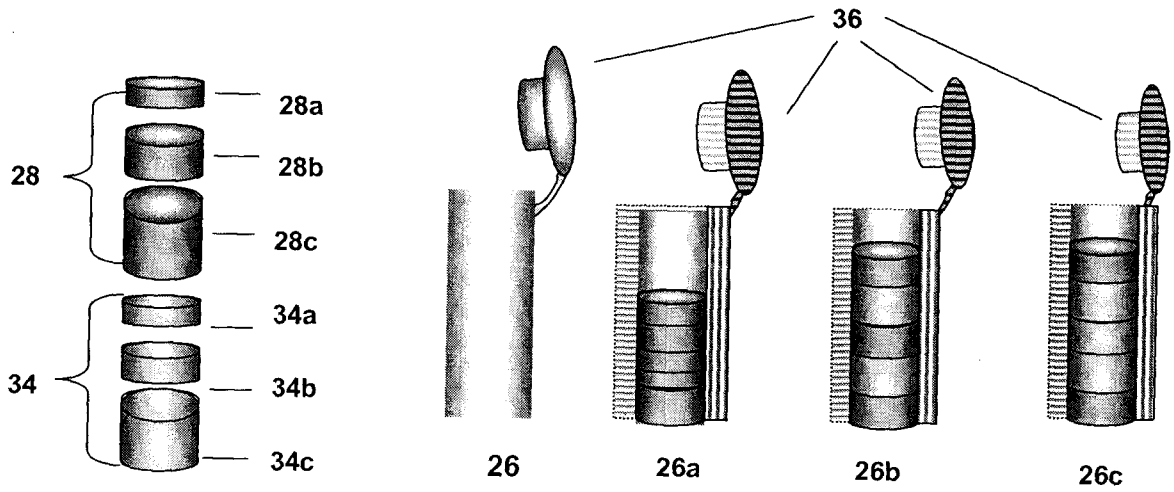


Figure 2

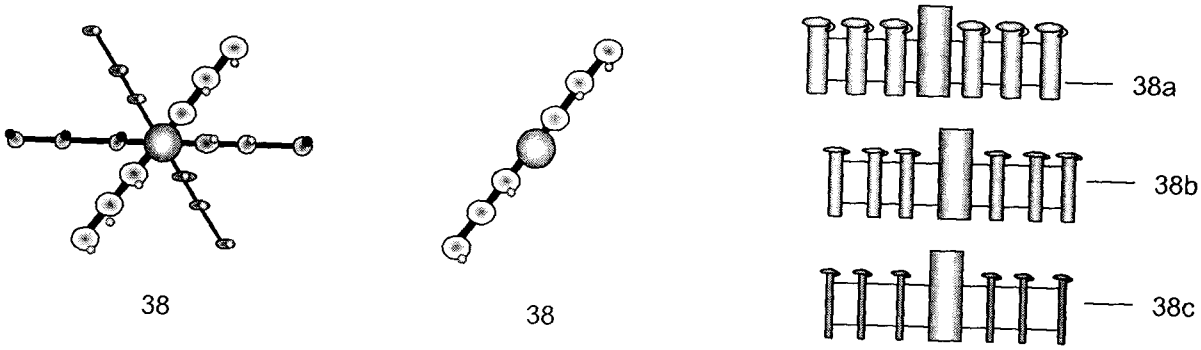


Figure 3

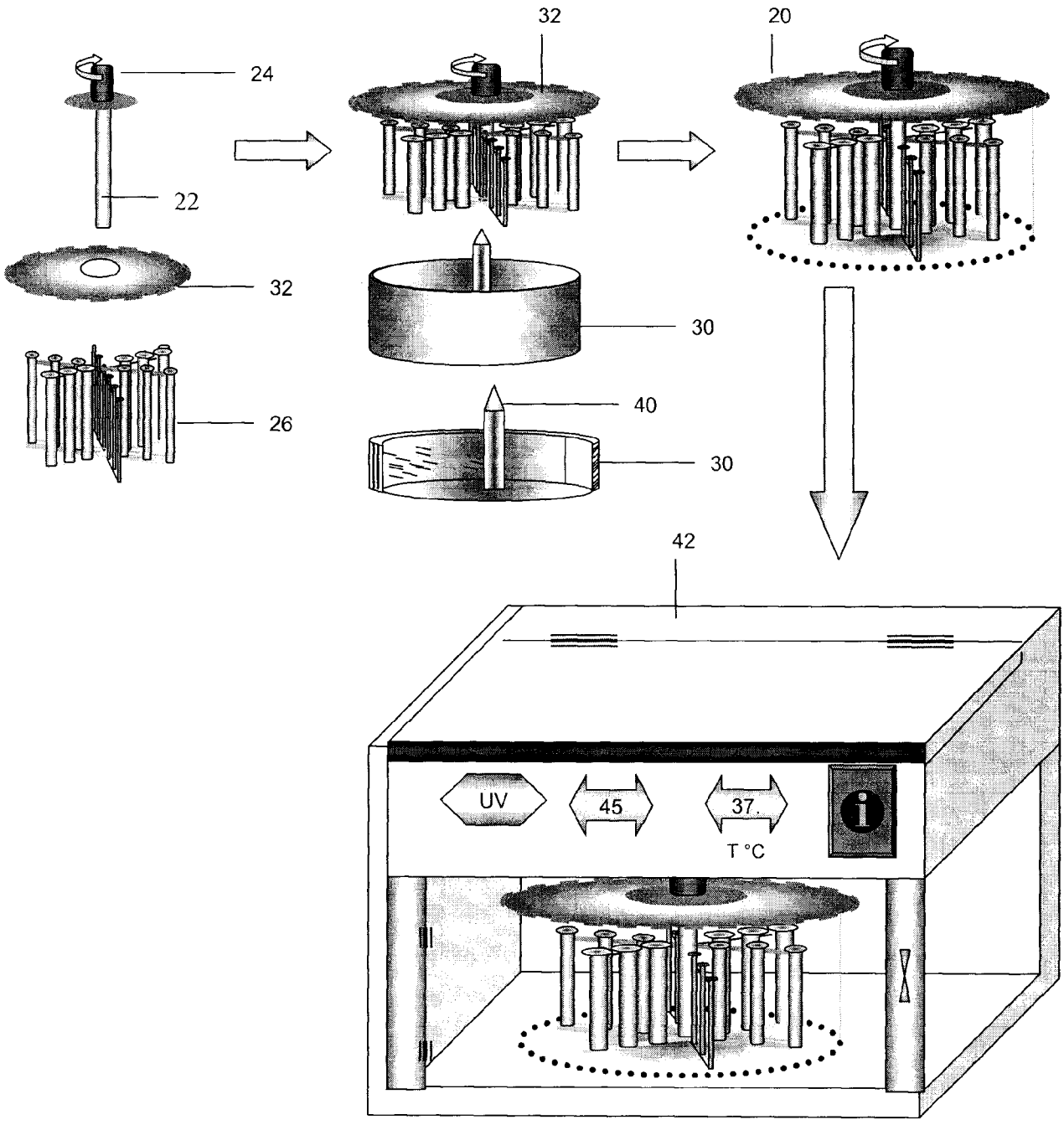


Figure 4

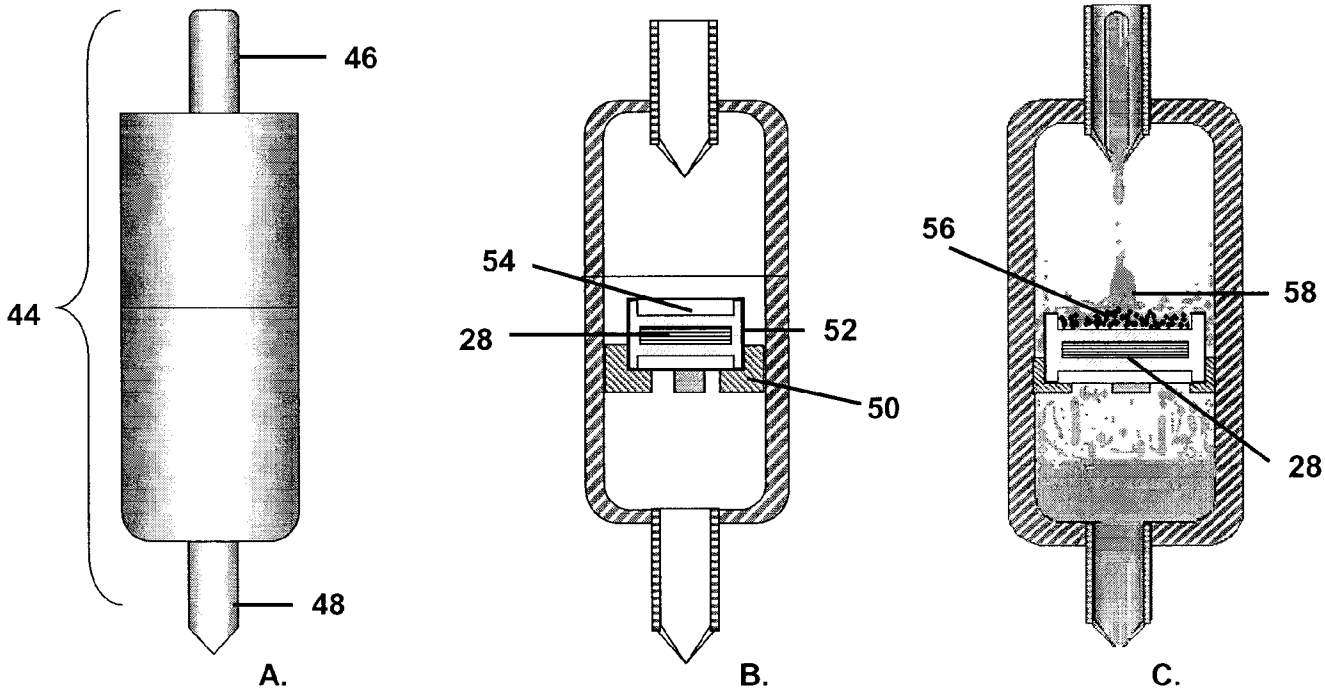


Figure 5

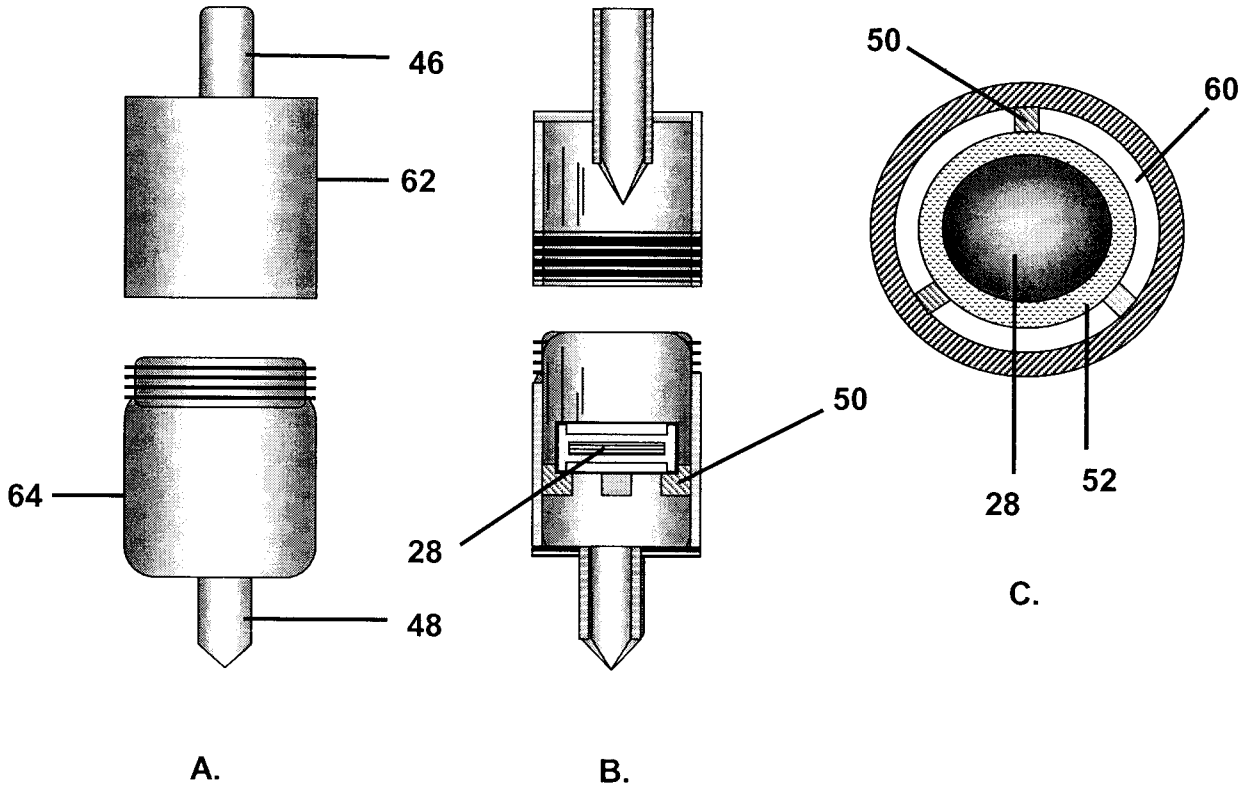
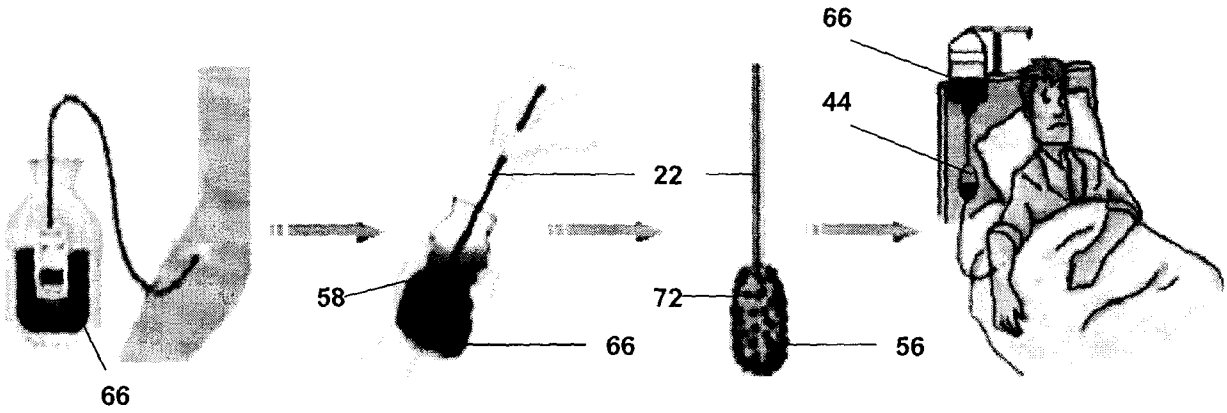
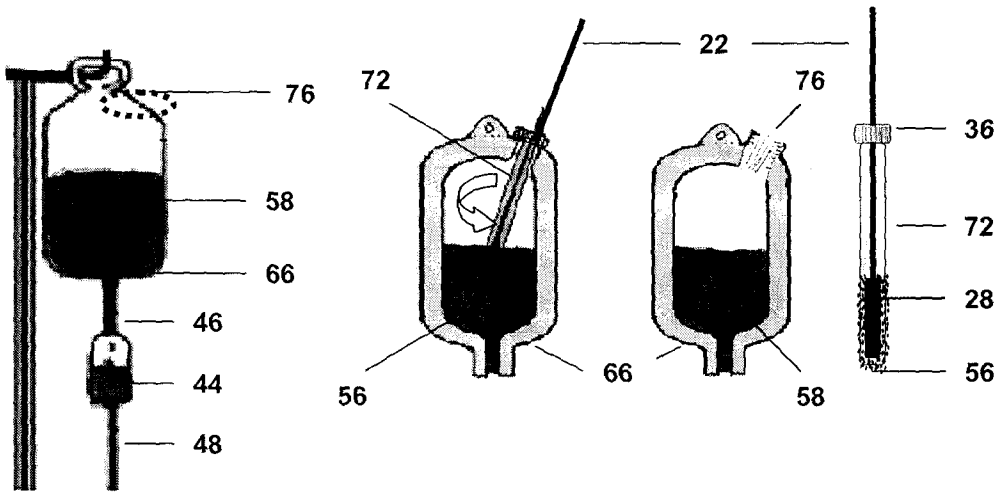


Figure 6

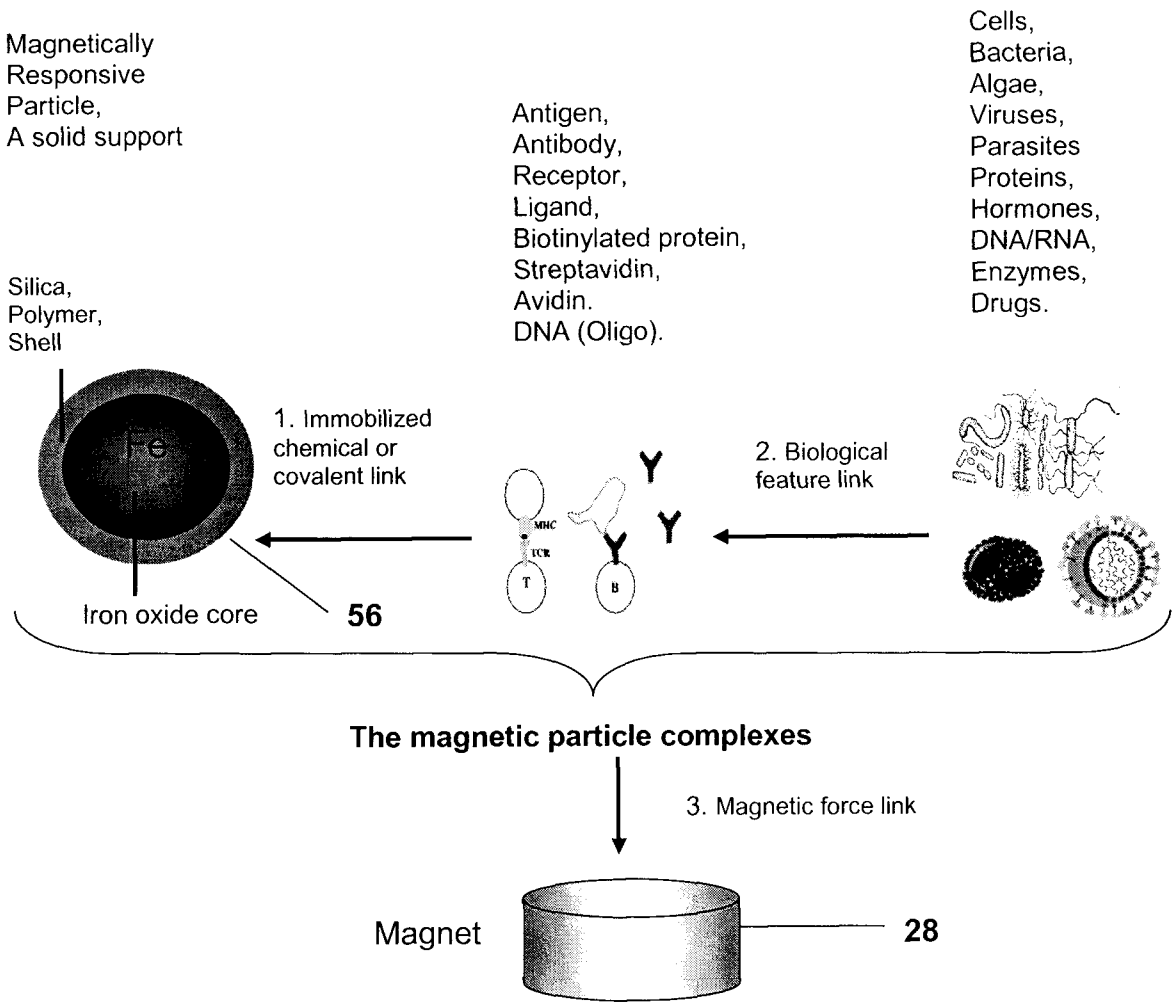


A



B

Figure 7



1. Antibodies attach to the shell of a magnetic bead or particle chemically.
2. Viruses or cancer cells adheres to the beads by biological features.
3. The magnetic particle-viruses **complexes** attracted by a magnetic force.

Figure 8

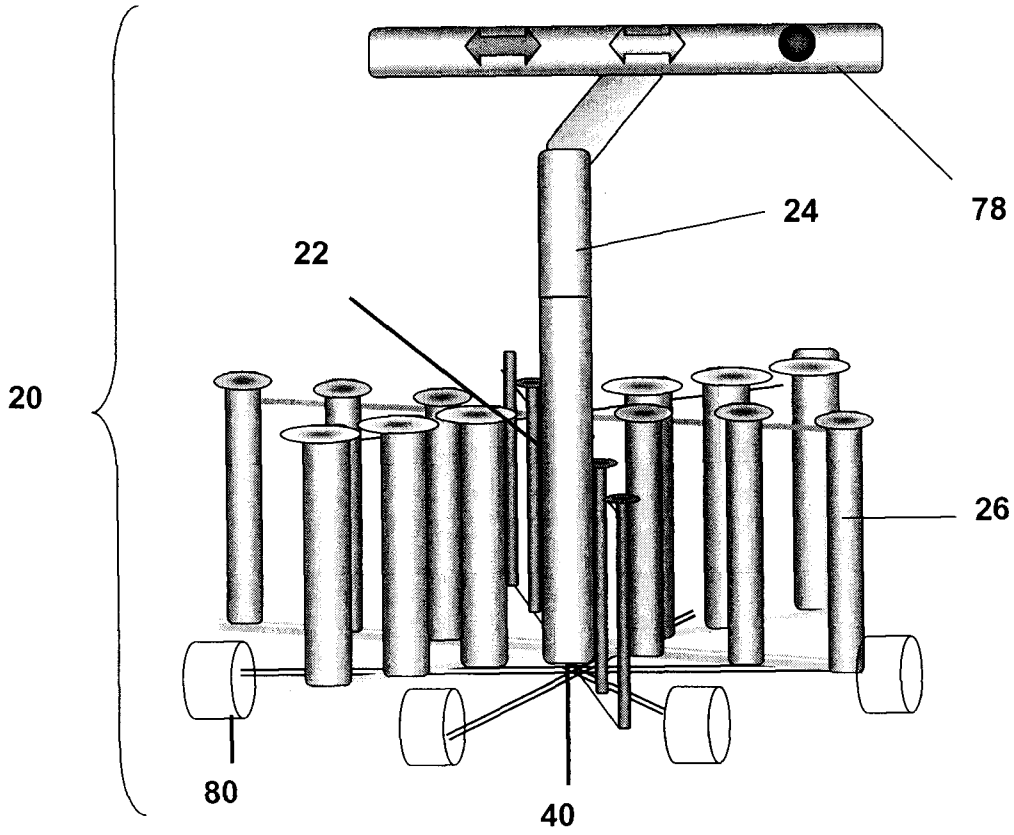


Figure 9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2012/000198

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***B03C 1/02*** (2006.01) , ***A23L 1/48*** (2006.01) , ***A61M 1/38*** (2006.01) , ***B01D 43/00*** (2006.01) , ***B03C 1/10*** (2006.01) , ***B03C 1/28*** (2006.01) (more IPCs on the last page)
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)
IPC: B03C 1/02 (2006.01), A23L 1/48 (2006.01), A61M 1/38 (2006.01), B01D 43/00 (2006.01), B03C 1/10 (2006.01), B03C 1/28 (2006.01), B03C 1/30 (2006.01), A61K 35/14 (2006.01), C07K 1/22 (2006.01), C12M 1/00 (2006.01), C12N 1/00 (2006.01), C12N 15/10 (2006.01)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
None

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
EPOQUE (X-Full and Internal (EPODOC)) Canadian Patent Database Google Scholar
IEEE Online Database ESPACENET
key words used: internal, interior, magnet+, column, 'magnetic column', array, field, particle+, bind+, adher+, attach+, collect+, separat+,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US20100288705 A1 **GRIEBEL** (18 November 2010) (18-11-2010) (see paragraphs [0003], [0005], [0019] to [0026], [0051] and [0065] to [0078], along with figs. 4 to 9)	1, 6 to 9, 18, 20 to 23 and 86
X	US20090220979 A1 **DAVIS ET AL.** (03 September 2009) (03-09-2009) (see paragraphs [0008], [0010], [0025], [0113], [0136], [0142] to [0144] and [0167], along with figs. 1A to 1D, 3A to 3F and 8C to 8F)	1, 6 to 8, 18 to 23 and 86 to 91
X Y	US7604748 B2 **NEWMAN ET AL.** (20 October 2009) (20-10-2009) (see col. 1, lines 21 to 23, col. 5, line 62 to col. 6, line 39 and col. 6, lines 51 to 64, along with figs. 1 to 8, 14 and 15)	44, 45, 47 to 55, 58 and 59 60 to 63 and 65 to 77
X	US5498550 **FUJIWARA ET AL.** (12 March 1996) (12-03-1996) (see col. 1, lines 21 to 44, col. 2, line 66 to col. 3, line 5, col. 18, lines 50 to 57, col. 20, lines 35 to 47, col. 22, line 30 to col. 23, line 58 and col. 24, lines 24 to 64, along with figs. 3, 7a, 7b, 9, 10a to 10e and 11)	1, 10, 19, 44, 45 and 55 to 57

[X] Further documents are listed in the continuation of Box C. [X] 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
"E" earlier application or patent but published on or after the international filing date
"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)
"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
"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
"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
"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
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 May 2012 (24-05-2012)	01 June 2012 (01-06-2012)

Name and mailing address of the ISA/CA	Authorized officer
Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Daniel Weslake (819) 997-2999

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 20030120202 A1 **GORDON** (26 June 2003) (26-06-2003) (see paragraphs [0061], [0065] to [0067] and [0071]], along with figs. 2 and 8)	60 to 63 and 65 to 77
A	WO8705536 **SCHRÖDER** (24 September 1987) (24-09-1987) (see pg. 2, line 12 to pg. 4, line 15, along with fig. 1)	1 and 23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2012/000198

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [X] Claim Nos. : 78 to 85

because they relate to subject matter not required to be searched by this Authority, namely :

a method of medical treatment consisting of treating as blood-borne disease or disorder in a subject. It should also be noted that, although not excluded for the purposes of this report, **claims 39** to **41** and **60** to **62** appear to also include subject matter that falls within the realm of a method of medical treatment.

2. [ ] Claim Nos. :

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. [ ] Claim Nos. :

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

The claims are directed to a plurality of inventive concepts as follows:

Group A - Claims 1 to **43** are directed to a method of and device for removing magnetic particles from a liquid, wherein the device is provided with at least one magnetic column that is supported on a shaft, with the support being provided in a manner that enables the at least one magnetic column to 'move about' the shaft, thereby enabling the magnetic particles to be more readily collected on the at least one magnetic column (this alleged invention includes the feature recited in dependent

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

B03C 1/30 (2006.01), ***A61K 35/14*** (2006.01), ***C07K 1/22*** (2006.01), ***C12M 1/00*** (2006.01), ***C12N 1/00*** (2006.01), ***C12N 15/10*** (2006.01)

...continuation of Box III - continued from pg. 2

and **24** because, as will be explained in greater detail in the written opinion, both **D1** and **D2** disclose all the features taught in independent **claims 1** and **23**, but not those taught in independent **claims 44** and **63**, thus leading to a lack of unity a posteriori deficiency).

Group B - Claims 44 to **78** are directed to a method of and device for removing magnetic particles from a liquid, wherein the liquid containing the magnetic particles flows through a chamber containing a magnet, thereby enabling the magnetic particles to separate from the flowing liquid and collect on the at least one magnetic column. (the inventive concept of this alleged invention is patentably distinct from the inventive concept of the **Group A** claims, thus leading to the lack of unity deficiency).

Group C - Claims 79 to **91** are considered to be 'linking' claims in that, due to their dependencies, these claims cannot stand as a group by themselves. Consequently, these claims can be included as either part of claim **Group A** or as part of claim **Group B** but NOT both.

The claims must be limited to one inventive concept as set out in Rule 13 of the PCT.

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