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(54) **FLASH CHROMATOGRAPHY CARTRIDGE**

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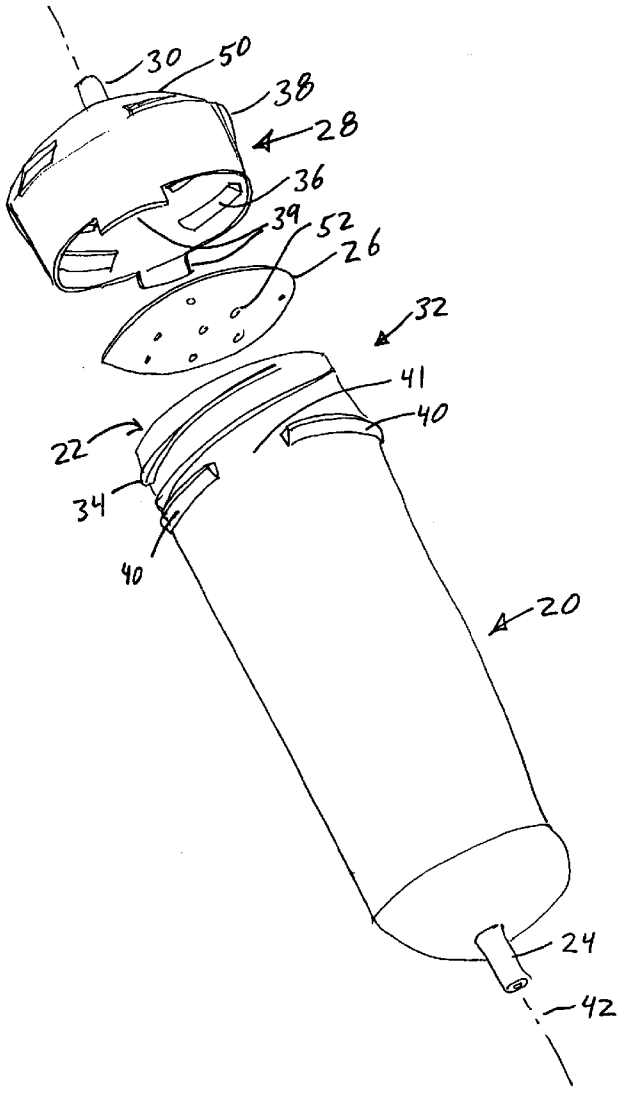
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(57) **ABSTRACT**

A low pressure liquid chromatographic cartridge has a tubular polymer container that receives a chromatographic packing material. The container has an outlet port located at its downstream end and container threads formed on its upstream end. A polymer cap, with an inlet port on an upstream end, screws onto the container threads. A flange depending from the cap mates with the lip of the container to form a fluid tight seal between the polymer cap and container suitable for use in low pressure liquid chromatography.



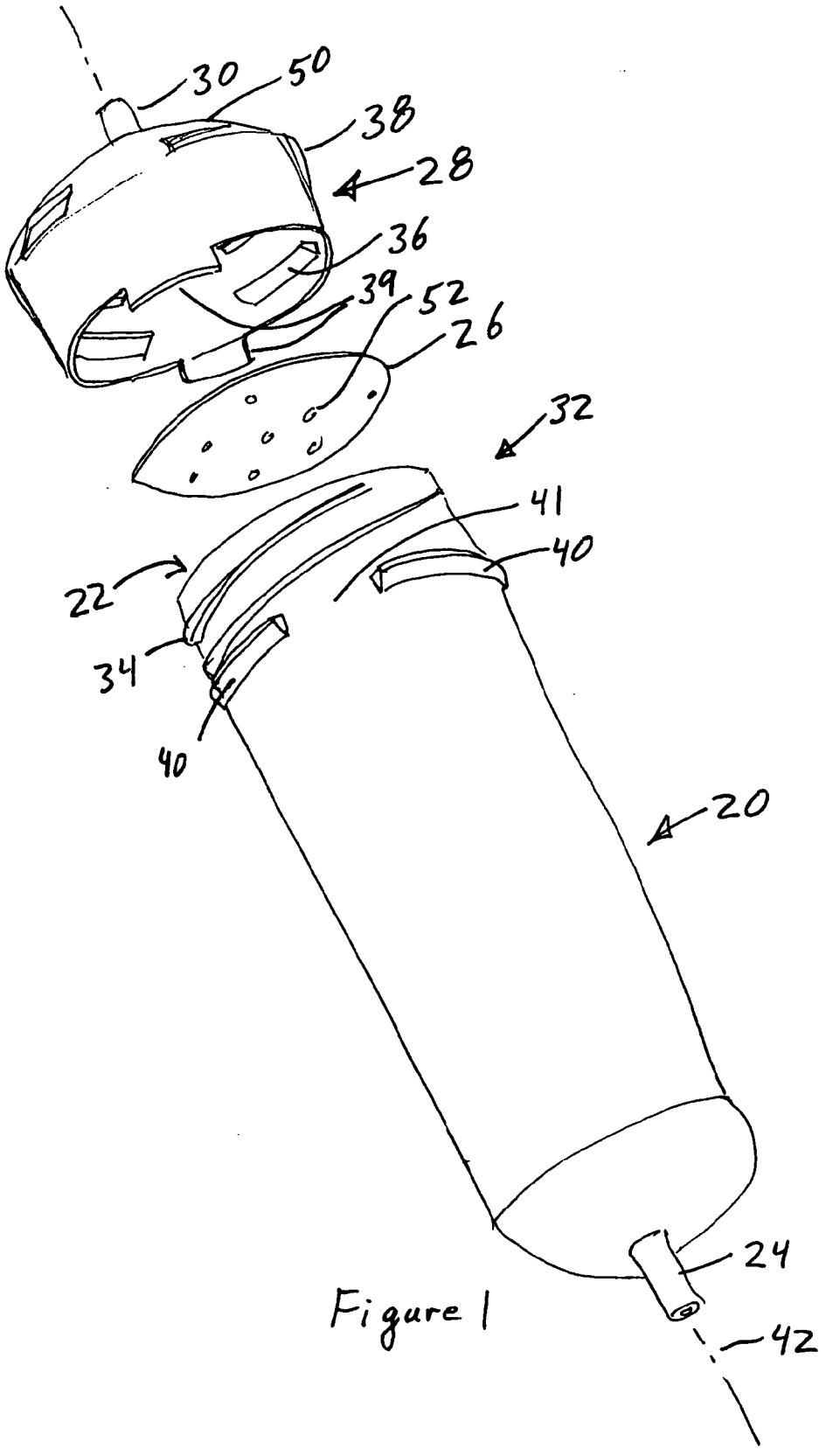


Figure 1

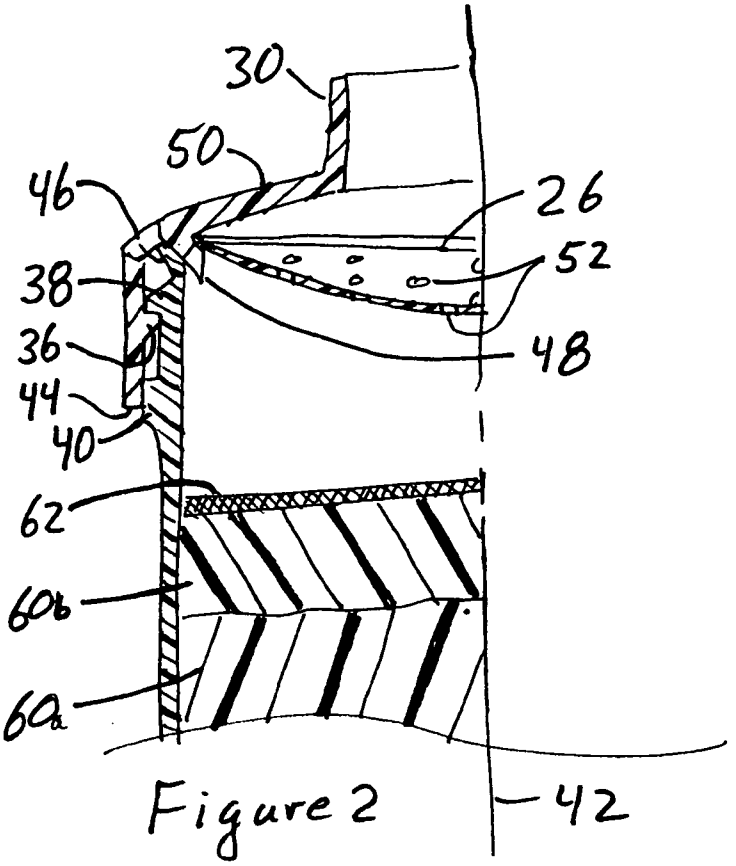


Figure 2

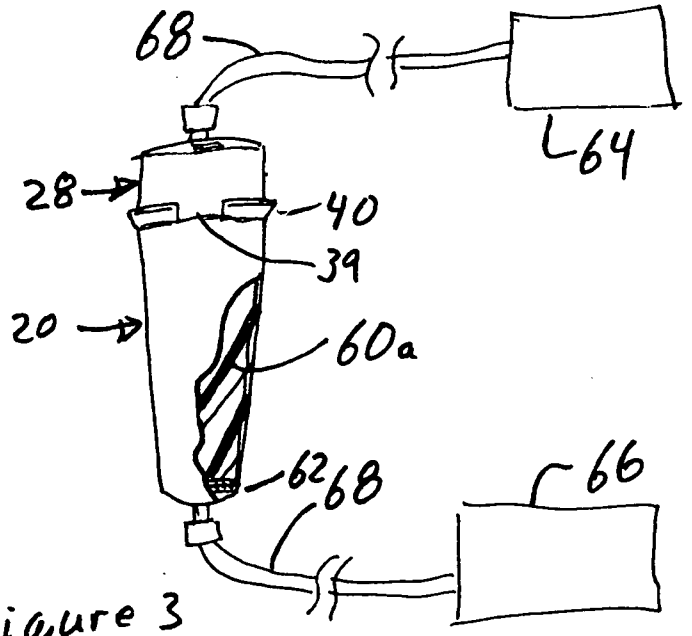


Figure 3

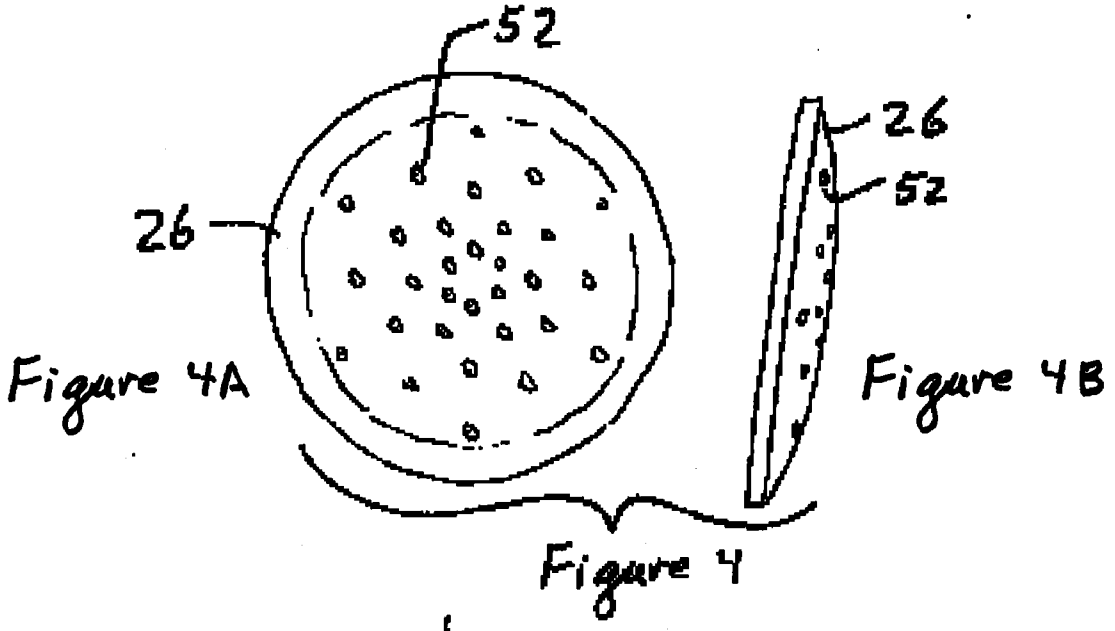


Figure 4A

Figure 4B

Figure 4

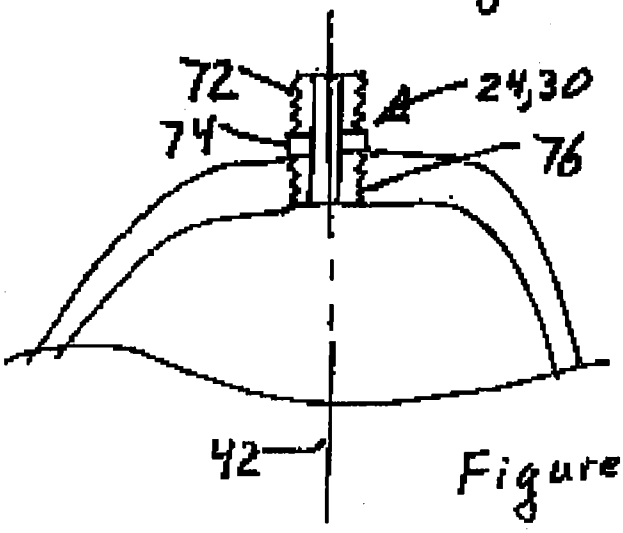


Figure 5

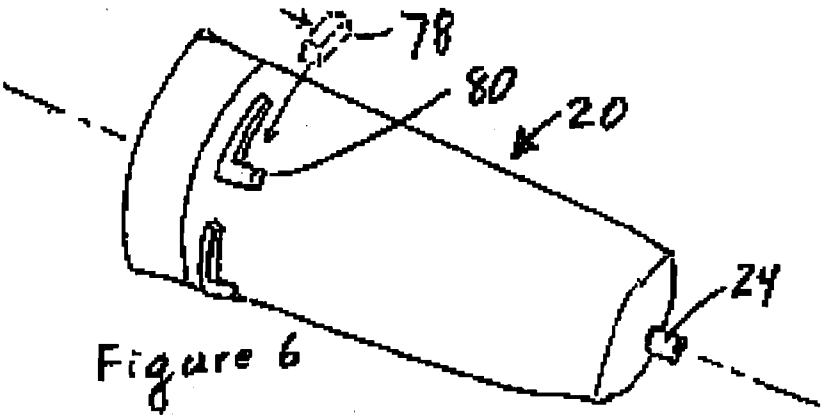


Figure 6

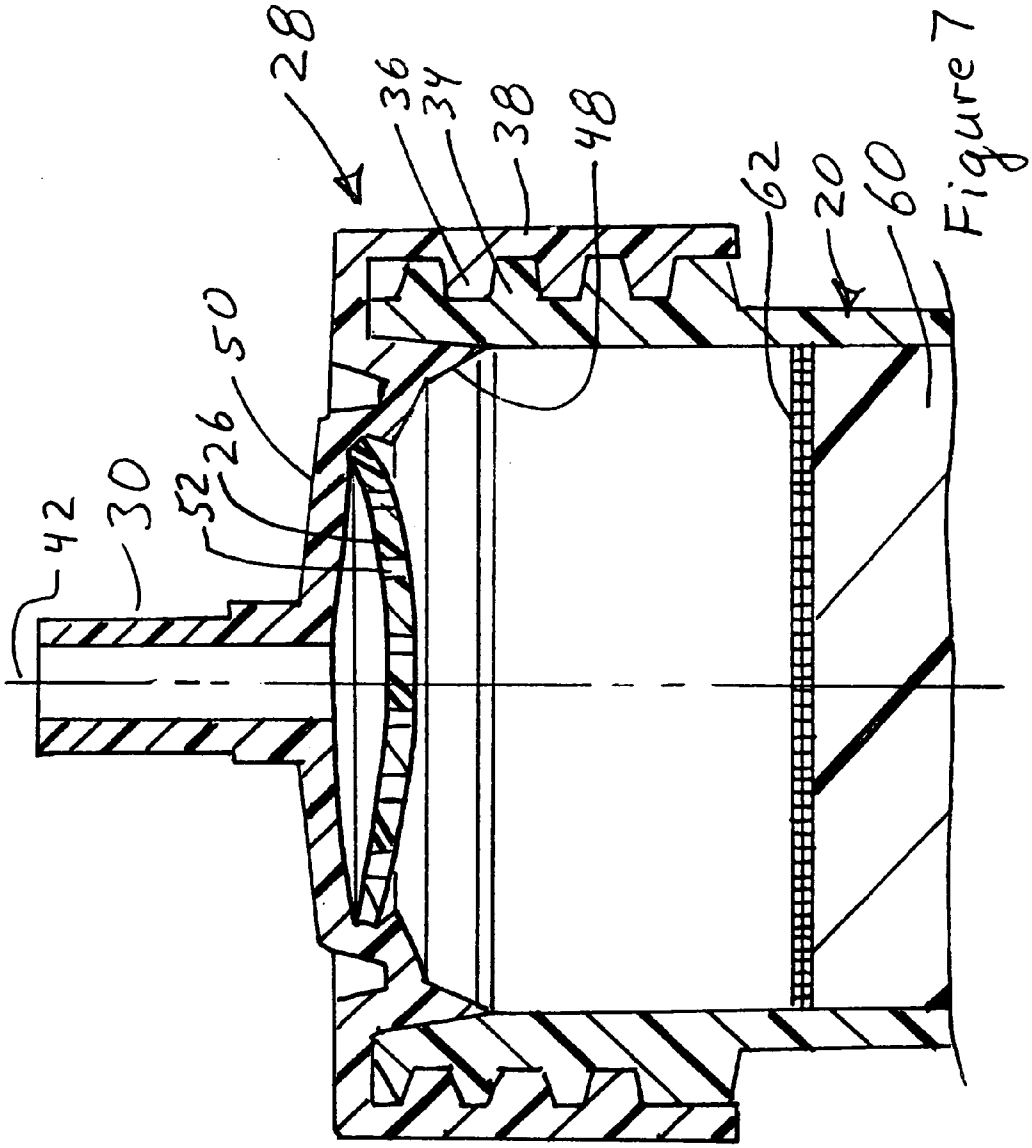


Figure 7

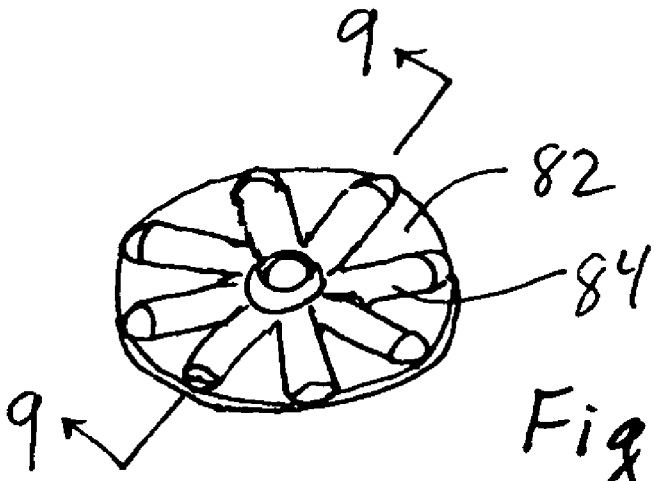


Figure 8

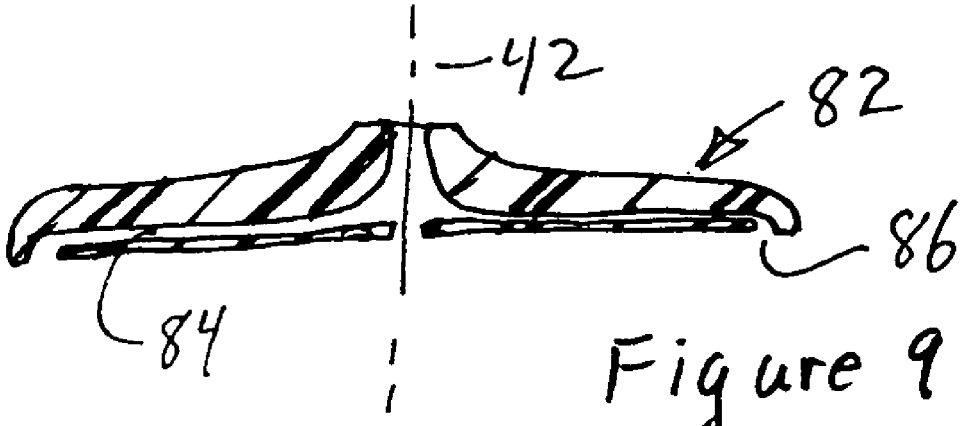


Figure 9

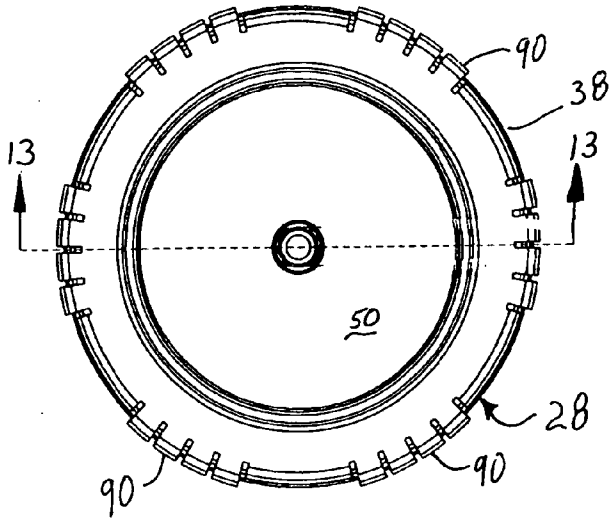


Fig. 12

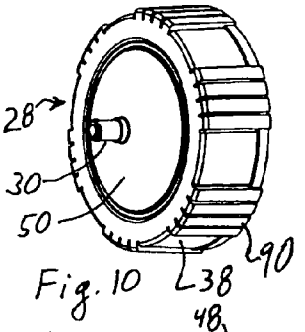


Fig. 10

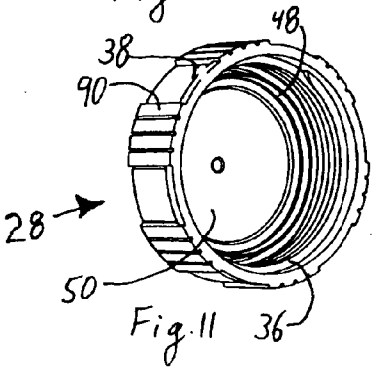


Fig. 11

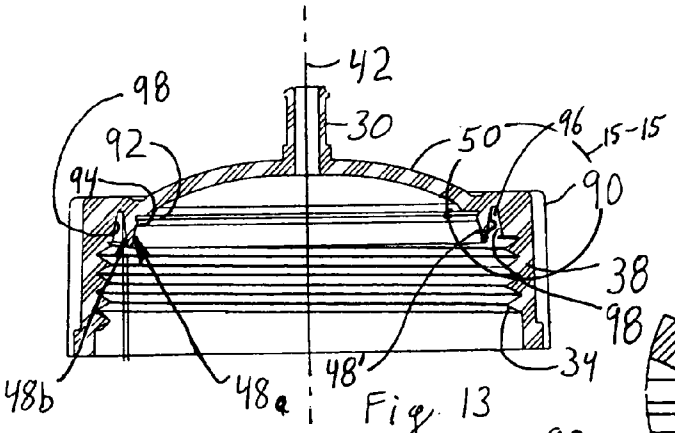


Fig. 13

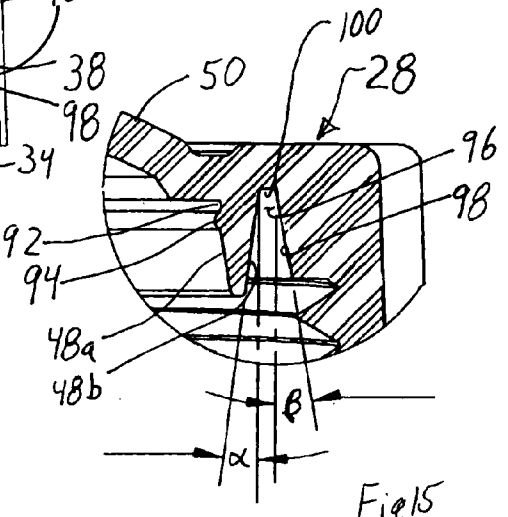


Fig15

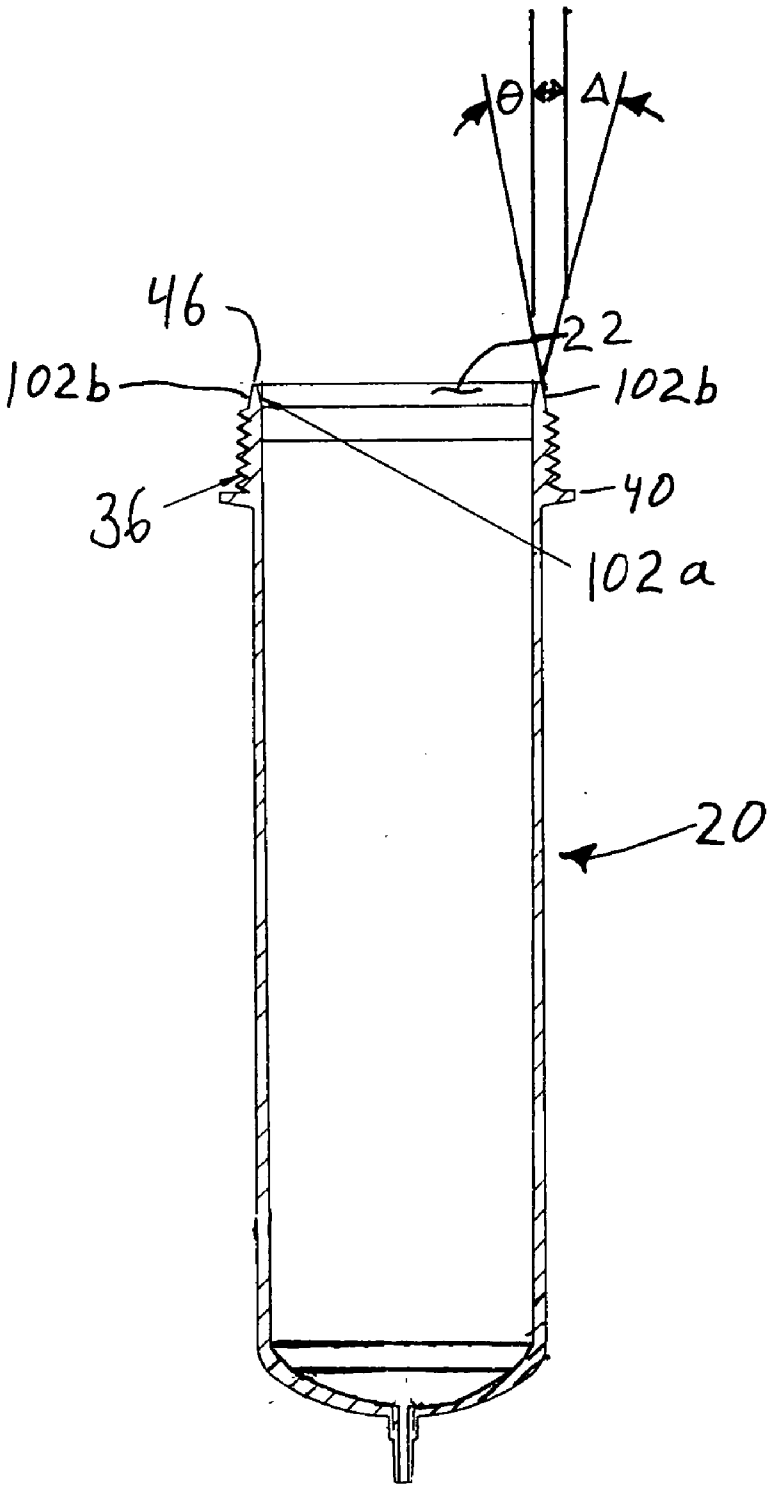


Fig. 14

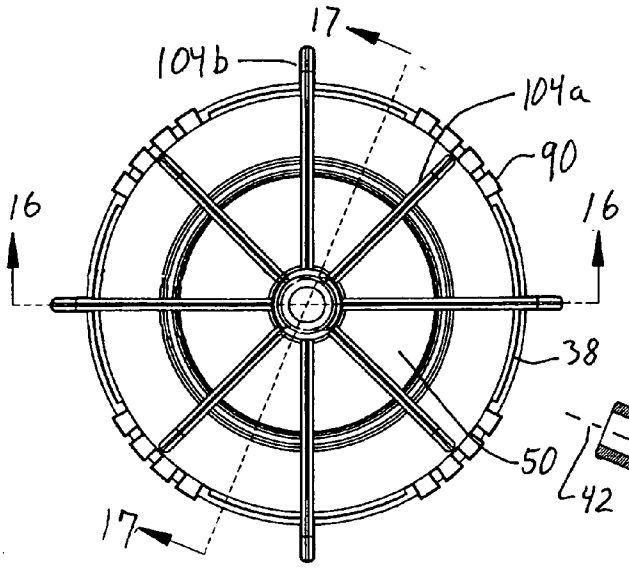


Fig. 19

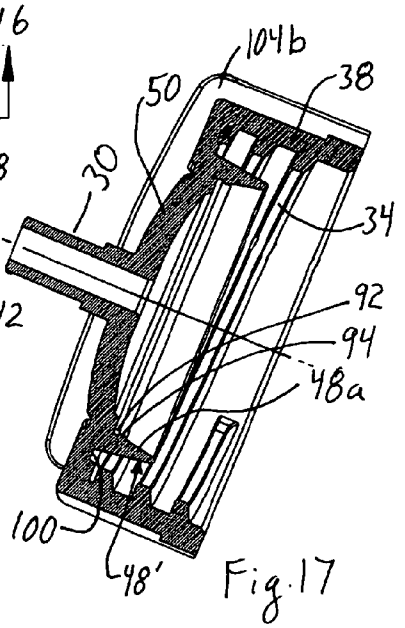


Fig. 17

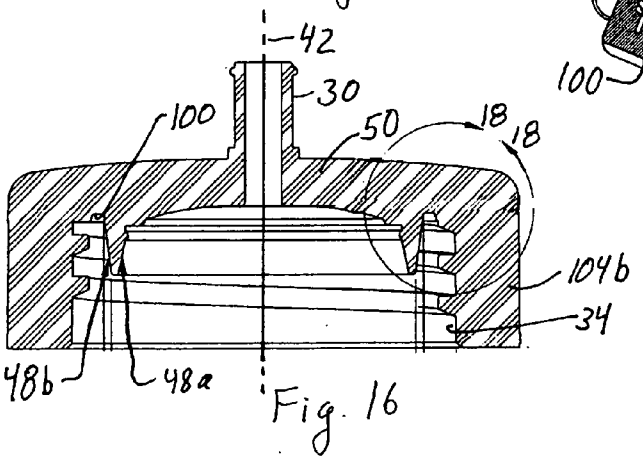


Fig. 16

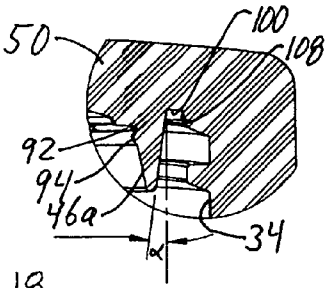


Fig. 18

FLASH CHROMATOGRAPHY CARTRIDGE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 10/842,288 filed May 10, 2004, the entire contents of which are hereby incorporated by reference.

BACKGROUND OF THE INVENTION

[0002] This invention relates to method and apparatus involving cartridges for use in flash chromatography and low pressure liquid chromatography equipment.

[0003] Chromatographic analysis passes fluids through columns containing specially treated sorbent which allows the chemicals in the fluid to be eluted at different times and thus form separated peaks on a chromatogram. In order to prepare or clean up the fluid being analyzed the fluid is often passed through a sorbent under pressure. Further, for low pressure liquid chromatography (LPLC) or flash chromatography the fluid may be passed through a sorbent at a pressure of 20-100 psi. This operating pressure is sufficiently high that these cartridges, which have relative large diameter bodies leak at the seams. Threaded connections are thus not used to form the body when the body is made of polymers. Thus, these cartridges are traditionally made of plastic and have sonically welded ends. But even that welded construction will leak if there are defects in the welds. That welded construction and the accompanying manufacturing and material costs cause in undesirably high costs, especially as the cartridges must be either discarded, or must under go extensive and thorough cleaning after a single use, or at most after a few uses with similar fluids. There is thus a need for a low cost, disposable cartridge.

[0004] Further, the welded construction requires the chromatographic packing material be placed in the cartridge before it is welded, or it requires careful packing of the column under pressure, both of which limit the usefulness of the cartridge and increase its cost.

[0005] Recently one company has introduced a disposable cartridge made of molded polypropylene having an end fitting that uses openings in a number of cantilever members to engage detent members which fit into the openings to create an interference fit to snap-lock the end fitting onto the cartridge. This is described in U.S. Pat. No. 6,565,745. But this interference fit is created at the factory and again creates a cartridge that does not allow the user to easily vary the contents of the cartridge. There is thus a need for a cartridge that allows a user to easily vary the contents.

[0006] Secondary cartridges are sometimes tied into the system for use, but these secondary cartridges are limited in size to 70 ml (or between 20-25 g of material). These secondary cartridges lie with tubing 1 to 2 feet away from the sample. The use of secondary cartridges increases the amount of run time and expensive solvent, due to elution of the sample. It causes dilution of sample because the cartridge is 1 to 2 feet away from the sample. The tubing and secondary cartridge also allows the addition of air which may or may not affect the chemical composition or performance. Also secondary cartridges have a capacity limit of 20-25 g which does need meet the needs of all users since at times up to 60 g is needed to be loaded. This forces an end user to separate the chemicals into several separate cartridges. The secondary cartridge is also an additional expense, and requires additional time for loading.

[0007] There is thus a need for a cartridge that can be sealed to function under LPLC pressures but which allows the user to access the inside of the cartridge before it is sealed.

[0008] Moreover, welded cartridges are limited by being pressure rated to only about 45 psi, due to leaking and instability at higher pressures. This pressure limits the end user, because high pressures are desirable for separating chemical compositions that are thick and viscous. Without these higher pressures these thick, viscous chemicals can not be distinguished. There is thus also a need for a larger capacity cartridge that can be used at higher pressures, especially for viscous fluids.

[0009] In LPLC the fluid sample is sometimes prepared by passing it through one or more cartridges of different material, each of which has a different sorbent to clean the fluid of particular undesirable materials or chemicals. Because the fluid sample can vary, a wide variety of cartridges with different sorbents sealed in the cartridges must be maintained. Further, the removal and reconnection of these various cartridges is cumbersome and time consuming, and the cost of each cartridge is expensive. There is thus a need for a way to reduce the complexity and cost of using different sorbents.

[0010] Sometimes a Y fitting is used to inject one or more fluids into the LPLC cartridge. The connection and use of these Y fittings is cumbersome. Further, the fitting must be either discarded or cleaned after each use. There is thus a need for a better and less expensive way to introduce fluid or materials into the cartridge.

SUMMARY

[0011] A low pressure liquid chromatographic cartridge is provided having a tubular polymer container adapted to receive a chromatographic packing material. The container has an outlet port located at a downstream end of the container and configured for connecting to chromatographic equipment during use of the cartridge. Container threads are formed on an upstream end of the container. A polymer cap has cap threads located on the cap to threadingly engage the container threads. The cap also has an inlet port located on an upstream end of the container. The port is configured for connecting to chromatographic equipment during use of the cartridge. A resilient fluid tight seal is interposed between the cap and container suitable for use in low pressure liquid chromatography. A locking tab is provided on a skirt of the cap and is located and configured to engage a recess on the container when the seal engages the cap and container. The locking tab locks the cap in position relative to the container.

[0012] In further variations the seal comprises a resilient ring extending from a top of the cap with the seal being located and sized to engage a lip of the container. Preferably a fluid dispenser is interposed between the container and the cap. The dispenser has a plurality of fluid outlets located across a substantial portion of a cross-section of the container to dispense fluid from the inlet of the cap over the cross-section. The fluid dispenser preferably takes the form of a dish having a plurality of holes extending through the dish, so as to place the inlet and the outlet in fluid communication. Moreover, the dish preferably, but optionally has a rim placed between the cap and the container. In further embodiments the locking tab extends parallel to a longitudinal axis of the container and extends from a distal end of a skirt of the cap. Further, the inlet can take the form of a tube threadingly

engaging one of the cap or container, with the tube having a threaded exterior distal end located on an exterior of the engaged one of the cap or container. Advantageously the seal and lip abut at an inclined angle with the seal extending inward toward a longitudinal axis of the container and cap. Moreover, the seal preferably joins the top of the cap at a corner which encircles a longitudinal axis of the container. Still further, the fluid dispenser has a periphery located in that corner. Preferably chromatographic packing material is placed in the cartridge by the user before the cap is locked onto the container. Preferably, but optionally, the material to be analyzed is also placed in the cartridge by the user before the cap is locked onto the container. This allows the user to custom select and place any of a plurality of different chromatographic packing materials in the container.

[0013] In a further embodiment there is provided a low pressure liquid chromatography cartridge having a tubular container adapted to receive a chromatographic packing material. The container has an outlet port located at a downstream end of the container and configured for use with chromatographic equipment during use of the cartridge. The container also has container threads formed on an upstream end of the container. A cap is provided with an inlet port located on an upstream end of the cap, with port being configured for use with chromatographic equipment during use of the cartridge. The cap also has cap threads located on the cap to threadingly engage the container threads. Locking means on the container and cap prevent manual removal of the cap. Resilient sealing means are provided for sealing the cap to the container when a user places the cap on the container and engages the locking means.

[0014] In still further variations, the cartridge has means for distributing fluid from the inlet port over a cross-section area of the container during use of the cartridge. Moreover, chromatographic packing material and materials to be analyzed can be placed in the container by the user of the cartridge before the locking means are locked.

[0015] There is also provided a method for a user to perform low pressure liquid chromatography. The method includes placing at least one chromatographic packing material in a tubular container which has an outlet port located at a downstream end of the container. The outlet is again configured for use with chromatographic equipment. Container threads are formed on an upstream end of the container. The method includes threadingly engaging threads on a cap with the container threads. The cap is also provided with an inlet port on an upstream end of the cap. The method further includes sealing the cap to the container by tightening the threads and engaging a seal between the cap and the container. The seal provides a fluid tight seal below about 100 psi suitable for LPLC use.

[0016] In further variations the method includes locking the cap to the container. A still further variation includes connecting the inlet to a source of fluid for chromatographic analysis; and distributing the fluid from the inlet over a cross-section area of the container. Moreover, distributing step preferably, but optionally includes collecting the fluid in a fluid dispenser having a wall with a plurality of holes spread across the cross-section and passing the fluid through those holes. Inclining the surface with the holes toward a central longitudinal axis of the fluid dispenser which also passes through the fluid dispenser is also a preferred variation. In a still further variation the distributing step is performed by a fluid dispenser with a periphery that is interposed between the cap and the container.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] These and other features and advantages of the invention will be better understood by reference to the following drawings in which like numbers refer to like parts throughout, and in which:

[0018] FIG. **1** is a perspective view of a first embodiment of a cartridge with a screw cap;

[0019] FIG. **2** is a partial sectional view of the juncture of the cap and cartridge of FIG. **1**;

[0020] FIG. **3** is a schematic view of the cartridge of FIG. **1** connected to chromatographic equipment;

[0021] FIGS. **4***a-b* are top and side views, respectively, of the fluid dispenser shown in FIG. **1**;

[0022] FIG. **5** is a partial sectional view of a further embodiment of inlet and outlet fittings for use with the cartridge of FIG. **1**;

[0023] FIG. **6** is a plan view showing a further embodiment of a container and locking mechanism;

[0024] FIG. **7** is a partial sectional view of a further embodiment of the connection of the cap and the container of FIG. **1**;

[0025] FIG. **8** is a further embodiment of a fluid dispenser;

[0026] FIG. **9** is a section of the fluid dispenser of FIG. **8** taken along section **9-9** of FIG. **8**;

[0027] FIG. **10** is a front perspective view of a further embodiment of a cap;

[0028] FIG. **11** is a rear perspective view of the cap of FIG. **10**;

[0029] FIG. **12** is a top plan view of the cap of FIG. **10**;

[0030] FIG. **13** is a sectional view taken along section **13-13** of FIG. **12**;

[0031] FIG. **14** is a cross-sectional view of a further embodiment of a container for use with the cap of FIG. **10**;

[0032] FIG. **15** is a partial sectional view taken along circular section **15-15** of FIG. **14**;

[0033] FIG. **16** is a sectional view of a further embodiment of a cap taken along section **16-16** of FIG. **19**;

[0034] FIG. **17** is a sectional view of the cap of FIG. **16**, taken along section **17-17** of FIG. **19**;

[0035] FIG. **18** is a circular sectional view taken along section **18-18** of FIG. **16**; and

[0036] FIG. **19** is a top plan view of the further embodiment of the cap of FIG. **16**.

DETAILED DESCRIPTION

[0037] Referring to FIGS. **1-2** and **7**, a cartridge is provided comprising tubular container **20** suitable for flash chromatography. The container has a cap **28** with inlet and outlet ports **24**, and **30**, respectively. The container **20** has an open end **22** at and upstream or proximal end, and an outlet port **24** at a downstream or distal end. A fluid dispenser **26** is placed in or upstream of the open end **22** and a cap **28** is fastened over the open end **22** and fluid dispenser. An inlet port **30** is provided on the cap **28**. A locking mechanism **32** is placed on one or both of the container **20** and cap **28** to hold the cap to the container. A seal **48** between the cap **28** and container **20** is held in fluid tight compression by mating threads **32**, **34** and the locking mechanism **32**.

[0038] In use, the inlet **30** is placed in fluid communication with a source of fluid to be processed in a low pressure liquid

chromatography (LPLC) or flash chromatography process. Processing or filtering media is placed in the container **20**. The sample fluid to be tested is passed through the media in the container, and the resulting fluid is removed from the outlet port **24** for further processing or other treatment or analysis. Preferably, but optionally, the outlet port **24** is placed in fluid communication with the LPLC equipment or other chromatographic equipment for the processing or treatment. Advantageously the downstream or distal end of the container **20** is slightly curved or domed or inclined so the fluid being processed is funneled toward the outlet **24**.

[0039] In more detail, the locking mechanism **32** can advantageously, but optionally take the form of mating threads on the container **20** and the cap **28**. FIG. **1** shows external threads **34** on the container mating with internal threads **36** on a skirt **38** of the cap **28**. But the container threads **24** could be internal threads and the cap threads **36** could be external threads. The threads can **34**, **36** be single lead, or multiple lead. The threads **34**, **36** can be continuous or segmented.

[0040] Preferably, but optionally, a lip or flange **40** extends outward around the outer circumference of the container **20** adjacent the trailing end of the threads. Preferably, one or more gaps or spaces or recesses **41** are formed in the flange **40**. As used herein, the leading end of the threads refers to the ends that first engage the mating threads, and the trailing end refers to the last to engage end of the threads. The outward direction means away from the longitudinal axis **42** of the container **20**.

[0041] Referring to FIG. **2**, the polymer cap **28** is sealed to the polymer container **20** sufficiently to allow flash chromatography up to about 100 psi. A lip **44** is formed on the distal edge of the skirt **38** of the cap **28** so the lip **38** abuts the flange **40** on the container to limit the tightening of the cap on the container **20**, and to help seal the cap to the container. A locking tab **39** extends from the skirt **28** along the direction of axis **42**. The locking tab **39** is sized and shaped to fit into one of the recesses **41** on the flange **40**. Thus, when the cap **28** is threaded onto the container **20** by threads **34**, **36**, the tabs **39** advance axially along axis **42** and fit into the recesses **41** to lock the cap from further rotation, and to lock the cap from unscrewing and the accompanying leaking. The tabs could be located on the container and the recesses on the cap.

[0042] Advantageously the locking tabs **39** are configured so the shape matches that of the flange **40**, making it difficult to manually grab the tabs **39** and manipulate them to unscrew the cap **28**. Advantageously, but optionally, the distal or downstream edge of the locking tab **39** tapers toward the axis **42** and that helps remove defined edges of sufficient size that the edge can be manually grabbed, and that helps avoid unlocking the cap. The locking tabs **39** thus provide means for preventing manual removal of the cap.

[0043] A shaped lip **46** is also preferably, but optionally placed around the opening **22** on the proximal or upstream end of the container **20**. The shaped lip **46** is shown as inclined outward at an angle of about 30° from a line parallel to axis **42**. The container lip **46** abuts a sealing surface **48** on the cap **28** to provide a fluid tight seal. Different angles and lip shapes could be used, especially if different types of seals are used.

[0044] The cap sealing surface **48** is shown as comprising an annular seal depending from the inside of the cap **28**. The sealing surface **48** is shown as connected to a top wall **50** adjacent the juncture of the top wall **50** with the side walls or skirt **38** of the cap **28**. The top wall **50** is preferably, but optionally slightly domed or slightly curved outward. The sealing surface **46** is advantageously a thin walled ring, and preferably, but optionally has a slight conical shape narrowing toward the downstream end of the cap **28** and inward toward the axis **42**. The cap sealing surface **48** thus preferably has a larger diameter at the upstream or proximal end where it fastens to the cap **28**, and has a smaller diameter, open end located downstream and inward of the upper end to form a cone with the smaller end facing downstream.

[0045] Preferably, but optionally, the cap sealing surface **48** is integrally molded with the cap **28**, although a two part assembly is also believed suitable. Referring to FIGS. **1-2**, a series of rectangular openings appear near the juncture of the skirt **38** and the top of the cap **28** and these openings allow mold slides to pass through the cap to integrally mold the seal **48** with the cap. Referring to FIG. **2**, at the periphery where the cap sealing surface **48** extends downstream and inward toward axis **42**, a corner is formed and the outer edge of the fluid dispenser **26** is placed in this corner.

[0046] As the cap **28** is threaded onto the container **20** using threads **34**, **36**, the downstream side of the cap sealing surface **48** abuts the upstream side of the cap lip **44** to form a fluid tight seal. The cap lip **44** on the distal or downstream edge of the cap **28** abuts the flange **40** on the container to prevent over-tightening and preferably, but optionally also form a redundant seal. As the cap **28** is threadingly tightened on the container **28** the conical cap sealing surface **48** is resiliently urged toward the container lip **46**, squeezing and further sealing the periphery of the fluid dispenser **26** between the seal **48** and the cap **28**. The fluid dispenser is thus held between the container and the cap, and distributes fluid along axis **42** across at least a substantial portion of a cross section of the container.

[0047] Referring to FIGS. **1**, **2** and **4**, the fluid dispenser **26** has a containing volume within which the fluid being processed collects and spreads over the cross-section of the container **20** in order to more evenly distribute the fluid over the material in the container. A plurality of holes **52** in the downstream surface of the fluid dispersing device allow the fluid to exit the fluid dispenser **26**. Various shaped fluid dispensers **26** could be used, including a container with a flat bottom, or inclined bottoms. As used herein, inclined surfaces include curved surfaces. As the container **20** is preferably, but optionally cylindrical in shape, these shapes result in a cylinder with a flat bottom, or a shallow conical surface or a downwardly curved surface. A flat surface on the dispensing device risks some fluid collecting in the device, and is thus not preferred. Various shaped and sized holes and hole patterns could also be used, with the holes **52** being preferably arranged to distribute the fluid being processed evenly over the cross-sectional area of the container **20**. If a curved fluid dispenser **26** is used then the holes **52** may advantageously be larger in diameter as the holes get further from the longitudinal axis.

[0048] Still referring to FIGS. **1-2** and **4** the fluid dispenser **26** comprises a circular, domed dish having a plurality of holes **52** extending through the dish. The dish shaped fluid dispenser **26** is preferably, but optionally curved toward the downstream direction so that fluid entering the cap **28** through the inlet port **30** collects in the dish and passes through the holes **52**. One hole is preferably located at the lowermost or most downstream portion of the surface to avoid fluid collecting in the fluid dispenser **26**. Preferably the lowest opening **52** is on the longitudinal axis **42**. A lip or rim of the dispenser is held between the container **20** and the cap **28**, and in the

preferred embodiment is held by the lip of the container resiliently urging the seal **48** against the rim of the dispensing device **26** against the top **50** of the cap.

[0049] The fluid entering the cap **28** through inlet port **30** enters at pressures of about 20-100 psi, and preferably about 50 psi, and at a flow rate of about 10-100 ml/min, although the pressure and flow rate can vary. The pressure and flow rate of the fluid entering the cap **28** and collecting on the fluid dispenser **26** is sufficient that the fluid spreads across the upstream surface of the dish shaped fluid dispenser **26** and squirts through the holes **52** like a showerhead to more evenly distribute the fluid over the cross-section of the container.

[0050] Referring to FIGS. **1-3**, the container **20** is at lest partially filled with a chromatographic packing material **60** selected to suit the fluids being analyzed and the operating pressures and conditions. This is advantageously done by the user just before the cap **28** is locked onto the container **20**. Various silica based sorbents are commonly used, and various sorbents **60***a*, **60***b* (FIG. **2**) or other chromatographically useful materials can be layered by the user to achieve different effects on the fluid being processed. The level of the chromatographic packing material **60** can be varied by the user to leave a predetermined volume inside the container **20**, with fluids or other materials being added to fill that predetermined volume.

[0051] The dish shaped dispensing device **26** is preferably thin, with a thickness of about 1/16 inch (16 mm) is believed suitable when the dish is made of polypropylene. The thickness and material will vary with the operating pressures and fluids being used. A radius of curvature of about 1-2 inches for the dish shaped dispensing device is believed suitable, and 1.5 inch curvature is used in one embodiment, but other curvatures could be used. The holes **52** are preferably, but optionally all the same diameter and are equally spaced. A diameter of about 0.03 to 0.04 inches (about 7-10 mm) for the holes **52** is believed suitable. The spacing and size of the holes **52** can vary to suit the fluids and pressures being used, and are preferably varied to ensure uniform flow through the dispensing device **26** across the entire cross-section of the container. The dispensing device **26** can be made of materials suitable for the processing of the desired fluid. The fluid dispenser **26** is preferably made of a polymer, such as polyethylene or polypropylene, and preferably of high density polypropylene. Other polymers can be used, although are preferably used that are low cost and suitable for injection molding to form disposable containers and caps. But metal dispensing devices are also believed suitable, such as stainless steel.

[0052] Referring to FIGS. **1** and **3**, in use a desired amount of filtering media or chromatographic packing material **60**, such as a silica sorbent, is placed in the downstream end of the container **20** by the user. Removing a partially secured, and unlocked screw cap **28** allows easy access to place the chromatographic packing material **60** in the container, to adjust the amount of material in the container, to add a different material or sorbent to the container or to adjust the amount of free volume in the container to receive the sample fluid or material or sorbent. A frit **62** can optionally be placed on the upstream and/or downstream end of the chromatographic packing material **60** as desired. The cap **28** and fluid dispenser **26** are then fastened to the container **20** to seal the media **60** inside the container **20**. The inlet port **24** can then be connected to a chromatographic fluid source or fluid pressurizing source **64** and the outlet **26** connected to chromatographic processing equipment **66** using tubing **68** which tubing is typically flexible. The cap **28** is preferably not removable from the container **20** once it is installed by the end user and the locks **29** engage the recesses **41**. Thus, any adjustment of the chromatographic packing material **60** or other contents of the container **20** is done before the cap **28** is sealingly fastened to the container **28**. The fluid to be processed is then passed through the inlet **30**, through the fluid dispersing device **26**, through the contents of the container **20** (e.g., through chromatographic packing material **60**) and out the outlet **24**. After use the container **20** and cap **28** can be discarded.

[0053] This user access and easy modification of the contents of the cartridge was not previously possible as the containers were welded shut at the factory to ensure they didn't leak under the operating pressures. There is thus advantageously provided a low cost, disposable cartridge made of a polymer which has a threaded, sealed cap on the container. The locking tabs **39** and mating recesses **41** provide locking means on the container and cap for preventing manual removal of the cap. The locking tab **39** forms a member resiliently urged into a recess, and various arrangements of such resiliently engaging parts, such as various forms of spring loaded detents and spring loaded mating members can be devised to form the locking means, especially given the disclosures herein. The seal **48** and lip **46** provide resilient sealing means for sealing the cap to the container when a user places the cap on the container. The sealing means includes numerous other seal types, including one or more O ring seals interposed between abutting portions of the cap **28** and container. **20**

[0054] There is also provided a method in which a chromatographic packing material **60** is placed in a container either by the manufacturer, or the user, but with the cap not being locked to the container, as by partially threading the cap onto the container but not engaging the locking tabs **39** with the recesses **41**. Alternatively, the cap is not placed on the container. The user removes the cap **28** and either alters the prior amount of chromatographic packing material **60**, or adds chromatographic packing materials of a different type, or adds further materials or chemicals to affect the fluid being processed by the user in the cartridge, or even adds analyte or fluid to be analyzed. The user then places the cap **28** on the container and seals and locks the cap to the container **20**. The desired processing is then performed using the cartridge and modified sorbent contained in the cartridge. Given the ability to remove the cap **28** and access the inside of the container **20** immediately before fluid is passed through the container, a variety of process variations can be devised.

[0055] The inlet and outlet ports **30**, **24**, respectively preferably comprise fittings adapted for use in chromatographic applications, and Luer fittings are commonly used. Advantageously the desired fittings at ports **24**, **30** are integrally molded with the container **20** and cap **28** to form a unitary construction.

[0056] Referring to FIG. **5**, in a further embodiment the fittings can comprise metal or plastic tubes **72** having external engaging threads **74** adapted for use with chromatographic equipment. A 1/4-28 threaded fitting is believed suitable for the engaging threads **74**. The tubes **72** can have an opposing end with sealing threads **76** configured to sealingly engage mating threads formed at the location of one or more of the ports **24**, **30**. The threaded portion of the cap **28** and container **20** may need to be thickened to provide sufficient threaded engagement. The sealing threads **76** preferably form a seal suitable for use up to about 100 psi or higher. Using slightly

different thread dimensions or lead angles on the mating threads of the fitting **72** and container or cap can help achieve the desired leak proof seal.

[0057] Referring to FIG. **7** a slightly different cap and container are shown in which there are continuous threads **34**, **36**. There is no flange **40** on the container **20**, and the lip on the container is only slightly inclined away from the longitudinal axis **42**. The fluid dispenser **26** is held in a corner formed by a slight inward projection of the cap which projection extends toward the axis **42**. The fluid dispenser **26** can be snapped into position in the cap **28**, and tightening the cap onto the container preferably, but optionally helps further squeeze the periphery of the dispenser **26** between abutting portions of the cap. FIG. **7** shows the top **59** with an annular recess **51** which allows the thickness of the top **50** to remain fairly constant which helps molding of the cap **28**. Further, the recess **51** adds flexibility to the sealing surface **48** on the cap **50** and that is believed to enhance the performance of the fluid tight seal which must maintain the seal under flash chromatography and LPLC conditions.

[0058] Referring to FIGS. **8-9**, a further embodiment of the fluid dispenser **26** is shown which has a generally a disk shaped support for a plurality of radially extending flow channels **84** having openings **86** in fluid communication with inlet **88**. Fluid to be analyzed enters through central inlet **88** that is advantageously located on the longitudinal axis **42**, and flows across the cross-section of container **20** (FIG. **1**) through channels **86** and then out openings **86** onto the packing material. The openings **86** are preferably at the distal end of each channel **86**, but could be located at one or more locations along the length of channel **86**. This configuration is more difficult to mold than the fluid dispenser of FIG. **1**. This embodiment of the fluid dispenser **26** is held between the cap **28** and container **34** as is the prior embodiment of the fluid dispenser. Various ways of holding the fluid dispenser **26** in the desired position will be apparent to one skilled in the art given the disclosures herein, including various clamps, ledges, snap-fits. The various forms of the fluid dispenser **26** comprise means for distributing the fluid to be analyzed over the packing material and over the cross-section of the container **20**.

[0059] The threads **24**, **36** provide means for fastening the cap **28** to the container **20**. But the threads represent one specific form of inclined mating surfaces, and other means for fastening the cap to the container include the broader use of inclined mating surfaces. Thus, a lug **78** on one of the cap **28** or container **20** can mate with a bayonet mount **80** on the other of the cap or container to fasten the cap to the container. Placing the recess **41** on a trailing end of an inclined surface on the bayonet could allow the bayonet to also lock the lug into position so as to combine the locking means and the fastening means.

[0060] A further embodiment is shown in FIGS. **10-14**. The cap **28** has a continuous skirt **38** that is preferably, but optionally, stiffened with increased thickness areas, such as by using ribs **90**. The ribs **90** are preferably, but optionally aligned parallel to axis **42**. Several groups with 3-5 ribs in each group are believed suitable. The ribs and any spaces between the ribs provide for an improved manual griping surface to tighten the cap **28**. The spacing between groups of ribs is thus advantageously equal.

[0061] The inside of the skirt **38** has threads **34** which mate with threads **36** (FIG. **14**) on the upstream end of the container **20**. The threads are preferably continuous rather than intermittent or segmented threads. For containers having diameters over about 1 inch (about 2.5 cm) the continuous threads provide a more uniform gripping and holding force better suited to resist pressure variations occurring in the container **20** during use in flash chromatography. For containers having threads **36** about 2 inches (about 5 cm) in diameter or greater the threads are preferably pipe threads to provide better holding and sealing.

[0062] The sealing surface is modified in this alternative embodiment. The sealing surface is located on an annular sealing flange **48'** having a base on its upstream end that is wider than the downstream, distal end. The sealing flange **48'** has a conical shape, preferably with a flat distal downstream end. The sealing flange **48'** has two inclined surfaces, one inner surface **48***a* faces radially inward toward axis **42**, and the other outer face **48***b* faces away from axis **42**. Inner face **48***a* abuts a mating face on the container to form a fluid seal as described in more detail later.

[0063] The inner face **48***a* is inclined at an angle α of about 7.5° relative to an axis parallel to axis **42**. The opposing surface **48***b* has a similar angle of inclination, but in the opposing direction, and the angle of surface **48***b* can vary.

[0064] The base of the sealing flange **48'** has a groove **92** encircling the upstream inner periphery of the flange. A slightly raised boss **94** is located on the downstream edge of the groove **92**. The top wall **50** of the cap **28** joins the upstream side of the groove **92** to provide a generally flat wall joining the upstream wall of groove **92**. The juncture with the top wall could be offset a desired distance, but the tangential connection is preferred.

[0065] The groove **92** is sized to receive the peripheral edge of the fluid dispensing device **26**. The dispensing device is preferably a thin, curved surface with holes **52** (FIG. **7**). The diameter of groove **92** is sized to receive the periphery of the dispensing device **26**, and is preferably slightly smaller to slightly compress the dispensing device **26**. The boss **96** narrows the opening into which the dispensing device **26** is placed, so the circular periphery of the dispensing device **26** forms a snap-fit with the groove **92**. The flat portion where the upper wall **50** joins the groove **90** helps guide the peripheral edge of the fluid dispensing device **26** into the groove **90**. The inclined inner face **48***a* also helps guide the fluid dispensing device toward the groove **90**. The tight fit between the circular dispensing device **26** and the circular groove **92** allows the dispensing device to resist deformation of the cap **28** by abutting the walls of groove **92** to maintain those walls in a circular configuration.

[0066] The annular sealing flange **48'** is offset radially inward from the skirt **38** of the cap **28**. A shaped annular groove **96** separates the flange **48** from the upstream end of the skirt **38**. The groove **96** has a conical cross-section that is narrower at its upstream end and wider at its downstream end. The radially inward side of the groove **96** is formed by the sealing surface **48***b* and the radially outward side of the groove **96** is formed by inclined surface **98** formed as an inward facing surface on the inside of the skirt **38**, at the upstream end of the skirt. The inclined surface **98** is inclined relative to axis **42** at an angle β of about 10°. The groove **96** has an upstream end **100** which is shaped to conform to the lip of the container **20** defining the opening **22**. In the illustrated embodiment the end **100** is flat, located in a plane orthogonal to axis **42**.

[0067] Referring to FIG. **14**, the container lip **46** is shown as flat, and joins two inclined sealing surfaces comprising

inward facing sealing surface **102***a* and outward facing sealing surface **102***b*. The sealing surfaces **102***a*, **102***b* are inclined toward each other in an upstream direction to form a generally conical cross section having a top surface comprising lip **46**.

[0068] The sealing surfaces are about 0.2 inches (0.5 cm) long measured along axis **42**. Inward facing sealing surface **102***a* is inclined at an angle Δ of about 15° relative to axis **42**, and sealing surface **102***b* is inclined at an angle θ of about 10° relative to axis **42**. Threads **36** extend from the downstream end of the surfaces **102***a*, **102***b* to the outwardly extending flange **40**. Shaped groove **96** is formed to receive the lip **46**, with the surface **98** having a length about the same as or slightly longer than abutting surface **102***b*. The threads **36** in the cap **28** preferably stop before inclined sealing surface **98**, but could be formed in the inclined surface **98**.

[0069] The lip **46** defines the upstream opening **22** to the container **20**. The container has a downstream end that is domed to better withstand increased operating pressures and to accommodate larger diameter containers **20**.

[0070] Referring to FIGS. **13-15**, the seal between the cap **28** and container **20** is described. The shaped groove **96** is configured to receive and seals both sides of the container adjacent the lip **46**. The inward facing surface **98** on the skirt **38** of the cap abuts and seals against outward facing surface **102***b* of the container lip. The outward facing surface **48***b* of the annular seal **48'** abuts and seals against the inward facing surface **102***a* of the container's lip. The surfaces **102***a*, **102***b* are inclined at 15° and 10°, respectively, and they abut surfaces **48***b* and **98** respectively, which are inclined at angles of about 7.5° and 10°, respectively. The abutting surfaces **102***a*, **48***b* are inclined so there is an angle of about 7.5° of interference. The abutting surfaces **102***b*, **98** are inclined so there is little or no interference. The interference fit, abutting surfaces **48***b*, **102***a* are radially inward of abutting surfaces **98**, **102***b*. The skirt **38** and mating surfaces **102***b*, **98** thus form a relatively rigid support to prevent radially outward movement of inclined surface **48***b*, so that surface **102***a* is tightly forced against mating surface **48***b* to form a seal.

[0071] Advantageously the lip **46** is advanced into shaped groove **96** until the lip **46** abuts the end **100** to form a further sealing surface. Outwardly extending flange **40** abuts the lip **44** on the cap to prevent over-tightening and stripping of the threads **34**, **36**.

[0072] Viewed in cross-section, the lip **46** of the container **20** forms a trapezoidal surface and the shaped channel has a similar shaped trapezoidal cross-sectional shape in which the outward located inclined walls are inclined at about the same angle, while the inward located walls are inclined for an interference, sealing fit. During use the pressure in low pressure liquid chromatography container **20** can reach 100 psi or more. The radially outward pressure on inner surface **48***a* urges the flange **48'** against the container interposed between the flange **48'** and skirt **38** to provide further sealing pressure between the abutting surfaces **48***b* and **102***a*, and between abutting surfaces **102***b* and **98**.

[0073] Further, the circular groove **92** is located downstream of the end **100** of the shaped groove **96**, and on opposing sides of the annular flange **48'**. The circular groove **92** forms a narrower cross-section at the base of the flange **48'** so that the flange tends to flex locally at or by the location of the groove. That localized bending allows a greater contact surface between abutting surfaces **48***b* and **102***a*. The localized bending at circular groove **92** also causes the walls forming the groove **92** to more tightly grip the periphery of the fluid dispensing device **26** located in the groove, and that provides greater resistance to deformation of the circular shape of the groove that may be caused by increased pressure in the low pressure liquid chromatographic container **20**.

[0074] The angles α and Δ can vary, but advantageously create an interference on the mating surfaces. Interference angles of 5-15° are believed suitable. The angle α can be from about 7° to 15°. Larger angles up to about 30° are believed possible, but are not as suitable. Angles of 6° or less are not desirable because they can leak at higher pressures and/or with larger diameters of the container **20**. The angles β and θ are preferably the same, and can vary from the 10° angle of the preferred embodiment. Angles from 7-15° are believed suitable for β and θ. Slight interference angles can be used, but are not preferred. The above angles and dimensions are believed suitable when the cap **28** and container **20** are made of polypropylene, such as PP9074 med polypropylene. The dimensions can vary with different materials and operating conditions for the low pressure liquid chromatographic container **20**.

[0075] Referring to FIGS. **16-19**, a further embodiment is disclosed that is particularly suited for larger diameter containers **20**, or higher operating pressures, or both. In this embodiment, the skirt **38** is thickened in the radial dimension, and the top wall **50** is also thickened. The continuous internal threads **34** comprise power threads having lower angles of inclination on the leading thread face and an even lower angle of inclination on the trailing face of the thread. A flat crest and an increased thickness is typically provided between the thread root and crest. A NPT Thread is preferred. These NPT Threads require more force to unscrew the threads and that prevents loosening of the cap under pressure variations that may occur during chromatographic use. The thickened threads also carry more force along the direction of axis **42** so as to accommodate larger forces on the cap **28**. The thickened flange provides radial stiffness and further ensures a sliding interference fit between surfaces **48***b* and **102***a* (FIG. **14**).

[0076] The threads **34** can stop at about the location on axis **42** of the distal end of flange **48'** and the beginning of the shaped recess **96**, or the threads can continue into the shaped recess **96** as is shown. When the threads **34** extend into the inclined surface **98**, the surface becomes intermittent and the seal is not as good. The container **20** will have correspondingly shaped external or male NPT Threads **36**, but those are not shown.

[0077] Preferably, but optionally, the cap **28** also has a number of external ribs **104** to strengthen the cap. Preferably, but optionally, some of ribs **104** extend only over the top wall **50**, while others continue along the exterior of the flange **38**. The depicted embodiment has two ribs **104***a* extending only over the top wall **50**, and two ribs extending over the top wall **50** and the flange **38**. In addition to strengthening the cap **50**, the rigs also provide a manual gripping surface.

[0078] In the embodiments of FIGS. **10-19**, it is believed possible to omit the inclined surfaces **98**, **102***b* and provide the seal between inclined surfaces **102***a* and **48***b*. The surfaces **48***b* and **102***a* are generally aligned, as are the inclined surfaces **98** and **102***a*. While the surfaces may be inclined to form an interference fit as they slide along each other as the cap is advanced along axis **42** as it is screwed onto the container, the surfaces are aligned sufficiently to abut and form a sealing surface.

[0079] In the embodiments of FIGS. **10-19**, the fluid inlet **30** is integrally molded with the cap **28**. But it could be an inserted fitting as described herein. Likewise the outlet is shown as integrally molded, but it could be an inserted fitting as described herein.

[0080] As required, detailed embodiments of the present invention are disclosed herein; however, it is to be understood that the disclosed embodiments are merely exemplary of the invention, which may be embodied in various forms. Therefore, specific structural and functional details disclosed herein are not to be interpreted as limiting, but merely as a basis for the claims and as a representative basis for teaching one skilled in the art to variously employ the present invention in virtually any appropriately detailed structure.

[0081] The above description is given by way of example, and not limitation. Given the above disclosure, one skilled in the art could devise variations that are within the scope and spirit of the invention, including various ways of sealing the cap to the container and various process steps that alter the material in the container through which the fluid being analyzed is passed. Further, the various features of this invention can be used alone, or in varying combinations with each other and are not intended to be limited to the specific combination described herein. Thus, the invention is not to be limited by the illustrated embodiments but is to be defined by the following claims when read in the broadest reasonable manner to preserve the validity of the claims.

1. A low pressure liquid chromatographic cartridge having a longitudinal axis, comprising:

a tubular polymer container adapted to receive a chromatographic packing material, the container having an outlet port located at a downstream end of the container and configured for connecting to chromatographic equipment during use of the cartridge, the container having container threads formed on an upstream end of the container and a lip defining an opening to the container with a inward facing inclined sealing surface adjacent the lip and facing the longitudinal axis;

a polymer cap having an inlet port located on an upstream end of the container, the port being configured for connecting to chromatographic equipment during use of the cartridge, the cap having cap threads located on a skirt of the cap to threadingly engage the container threads;

an annular sealing flange depending from the cap and located radially closer to the longitudinal axis than the skirt, the flange having an outward facing inclined sealing surface facing away from the axis with an upstream end of the flange being further from the axis than a downstream distal end of the flange; the outward facing inclined surface on the flange generally aligned with and located to abut the inward facing inclined surface on the container to form a resilient fluid tight seal between the cap and container suitable for use in low pressure liquid chromatography when the cap is screwed onto the container.

2.-**32**. (canceled)

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