May 7, 1963 J. ISREELI 3,088,714

VARIABLE GRADIENT DEVICE

Filed Oct. 3, 1960 2 Sheets-Sheet 1

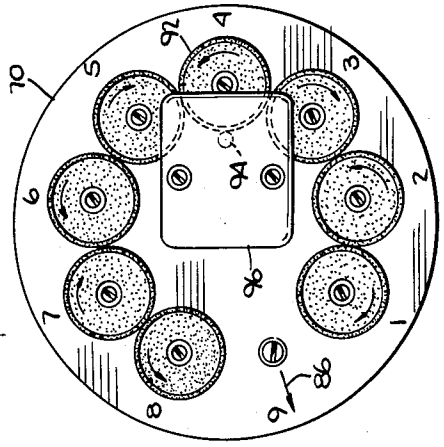


Fig. 2.

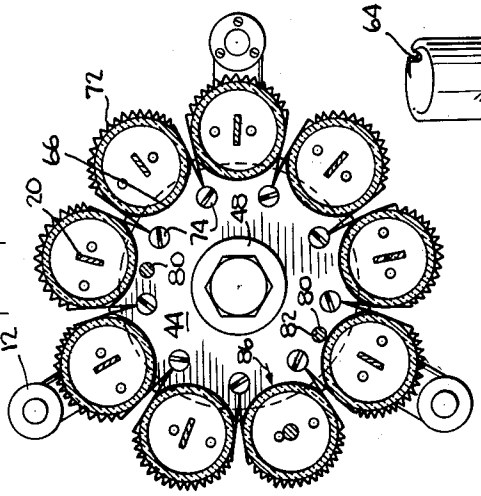


Fig. 3.

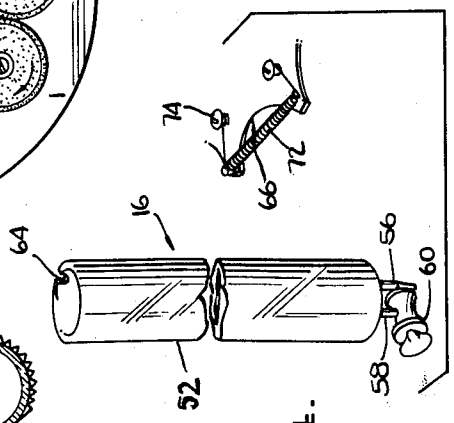


Fig. 4.

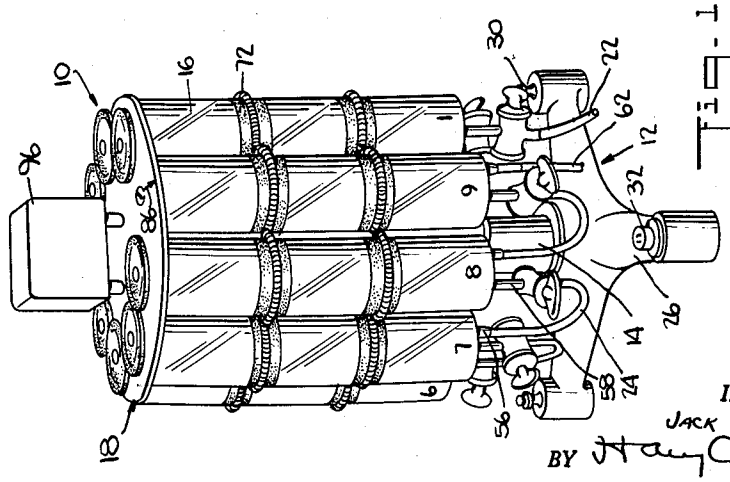


Fig. 1.

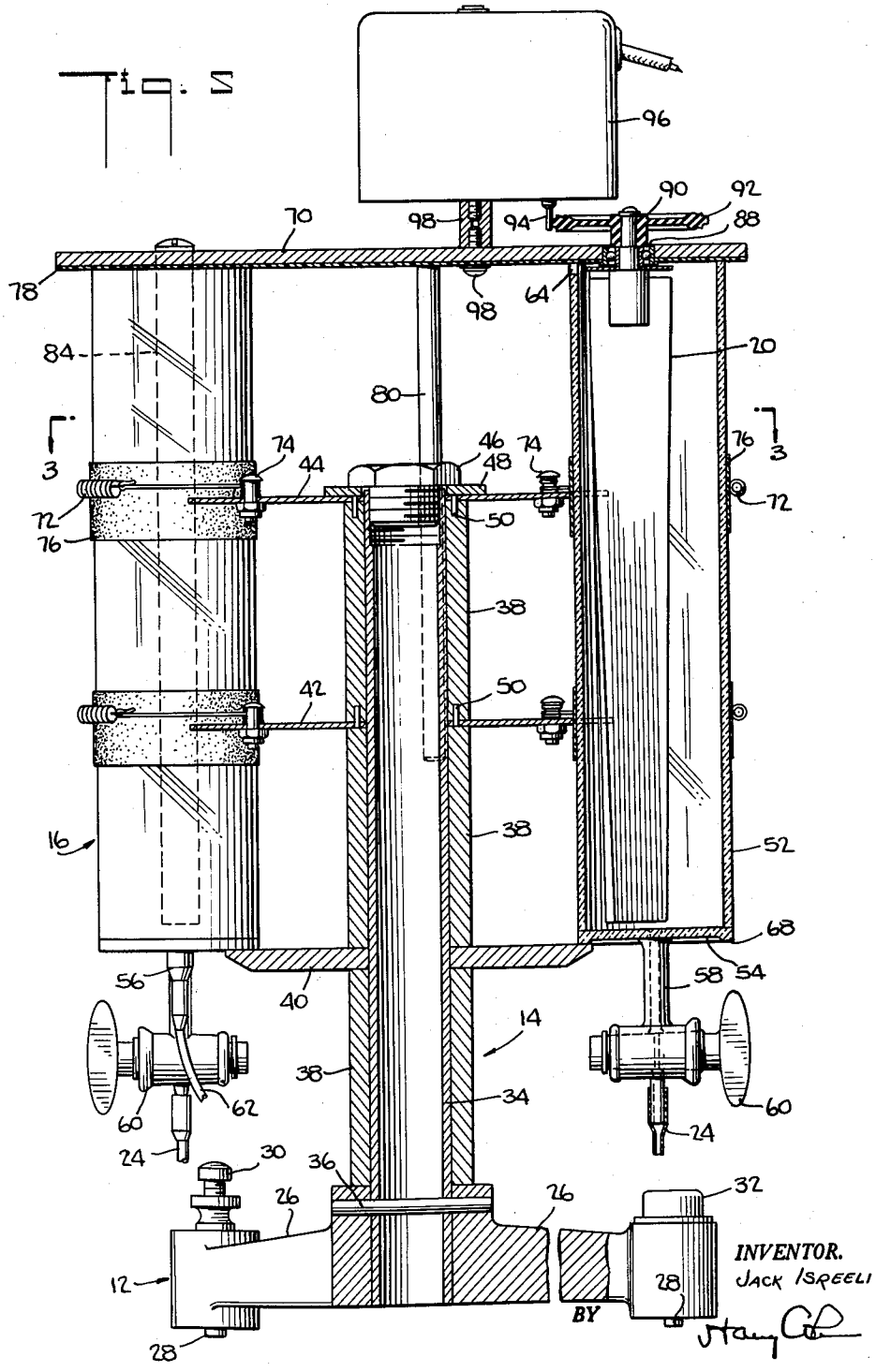
INVENTOR.
JACK ISREELI
BY Harry Cohn
ATTORNEY

May 7, 1963 J. ISREELI 3,088,714

VARIABLE GRADIENT DEVICE

Filed Oct. 3, 1960 2 Sheets-Sheet 2

Fig. 2



INVENTOR.
JACK ISREELI

BY

ATTORNEY

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VARIABLE GRADIENT DEVICE

Jack Isreeli, Tuckahoe, N.Y., assignor to Technicon Chromatography Corporation, Chauncey, N.Y., a corporation of New York

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This invention relates to variable gradient devices which are especially useful in chromatographic analysis.

The technique of gradient elution in chromatography requires that the eluent, which is introduced into the chromatography column at the top thereof and flows downwardly through the column for eluting the various zones of the chromatogram, be of varying concentration in order to improve resolution in certain zones. A variable gradient device for providing continuous varying concentrations of eluent to a chromatography column is described in an article by E. A. Peterson and H. A. Sober entitled "Variable Gradient Device for Chromatography" which appeared in the May 1959 issue of Analytical Chemistry. Essentially, the device consists of a series of identical mixing chambers which contain eluent of varying composition in hydrostatic equilibrium. The chambers are in fluid flow communication with each other and the eluent is removed from a chamber at one end of the series of chambers causing the liquids in each of the other chambers to flow into the succeeding chamber, in a continuous fashion, so that the concentration of each liquid in each of the chambers is continuously changing and the concentration of the effluent which is being removed from a chamber at one end of the series is also varying in a continuous manner. The shape of the gradient curve of concentration of the effluent supplied to the chromatography column may be varied over a wide range by varying the concentrations of the liquids in the mixing chambers in the manner described in the aforementioned article.

The primary purpose of the present invention is to provide an improved variable gradient device which is especially well adapted to provide variable gradients of concentrations of liquid, in a continuous manner, to a chromatography column and which is simple in construction and inexpensive to manufacture, and yet provides extremely accurate results.

Another object is to provide improved means for supporting a plurality of chambers for the eluent in a manner which permits the use of non-precision made chambers for the eluent and minimizes the effects of irregularities of such chambers in the accurate positioning of the chambers in the device and which assures that the open ends of the chambers are flat and parallel and lie in the same horizontal plane, whereby the open ends of the chambers may be closed by a single cover.

A further object is to provide a variable gradient device with a separate mixer which may be removably mounted on the chambers and which has provision for predetermining the position of the stirring means of the mixer with respect to the corresponding chambers.

Another object is to provide a variable gradient device which permits positioning of the chambers in such a manner so as to provide easy access to the inlets and outlets of the chambers.

The above and other objects, features and advantages of this invention will be fully understood from the following description considered in connection with the accompanying illustrative drawings of the presently preferred embodiment of this invention.

In the drawings:

FIG. 1 is a perspective view of a variable gradient device according to the present invention;

FIG. 2 is a top plan view of the device;

FIG. 3 is a horizontal sectional view, on a smaller scale, taken on line 3—3 of FIG. 5;

FIG. 4 is a perspective view of a liquid mixing chamber and part of the device, in disassembled relation; and

FIG. 5 is a vertical sectional view of the device, on a larger scale than FIG. 1.

Referring now to the drawings in detail, the variable gradient device 10 comprises a supporting base or stand 12 having an upstanding central tube or column 14 which is surrounded by a series of mixing chambers 16 arranged in a circular row. A mixer 18 is supported on the upper ends of the mixing chambers and has stirring paddles 20 which extend into the chambers through their open tops for stirring and mixing the liquids in the chambers. As here shown, there are nine chambers but it will be understood that the number of chambers may vary and may consist of any number from two or more. For ease of reference in this description of the invention, each of the chambers and chamber positions have been numbered from 1 to 9, the number 9 indicating the last chamber or position in the series of chambers and the number 1 indicating the first chamber or position. The liquid outlet 22 of chamber 1 is adapted to be connected to the top of a chromatography column. Except for adjacent chambers 1 and 9, each chamber is in fluid flow communication with its adjacent chamber through the connecting conduit 24 at each of the lower ends of each chamber. During the operation of the device, liquid flows in succession from chamber 9 through each of the other chambers 1 where it is discharged to the chromatography column so that during such liquid flow, the concentration of the liquid in each of chambers 1 through 8 is being varied continuously and an effluent of continually varying concentration is being transmitted to the chromatography column. Variable gradients of concentration of eluent may be obtained, as indicated above, by varying the concentration of the liquid which is placed into any one or more of the chambers when said chambers are filled with liquid before the operation of the device is commenced.

The base or stand 12 of the device includes three arms 26 arranged symmetrically with respect to each other and each arm is provided with a supporting pin 28 for supporting the device on a horizontal surface. Two of the pin supports are adjustable and may be moved into and out of its respective arm, by operation of screw 30, to level the device and for this purpose the third arm includes a level 32. In this manner it is made certain that column 14 is always vertical during gravity-feed operation of the device.

The lower end of a vertically extending hollow tube 34 of column 14 is inserted into a centrally located hole in the base 12 and a pin 36 secures the tube to the base. The accuracy of these parts and the connection between them is such as to assure that the tube 34 is substantially perpendicular to the base 12. A series of vertically spaced sleeves 38 is provided on tube 34 and a horizontal circular support plate 40 is clamped by the lower and intermediate sleeves in the space therebetween. A horizontal circular plate 42 is spaced vertically from plate 40 and is clamped by intermediate and upper sleeves 38 in the space therebetween. A similar circular plate 44, spaced vertically from plate 42 and parallel thereto, is mounted on the upper end of upper sleeve 38 and is clamped in position by bolt 46 which screws into the upper end of tube 34. A washer 48 is clamped between the head of bolt 46 and the upper surface of plate 44. Pins 50 join plates 42 and 44 to the lower and upper ends, respectively, of upper sleeve 38 and bolt 46 secures the assembly of sleeves and plates in position on tube 34.

Each of the chambers 16 comprises a hollow open top cylindrical tube 52, preferably made of glass, which has a closed lower end 54 provided with a tubular liquid inlet

member 56 and a tubular liquid outlet member 58. The outlet member is provided with a stop cock 60 and the inlet and outlet of the chamber extends below lower end 54. As best seen in FIG. 1, the outlet 58 of one chamber is connected to the inlet 56 of the adjacent lower numbered chamber by the connecting conduit 24, so that liquid may flow from one chamber to the next lower numbered chamber as previously described. The stop cock 60 is closed during filling of the chambers and, of course, is open during the operation of the device and it will be noted that the stop cocks and inlets 56 and outlets 58 extend downwardly from lower end 54 below lower plate 40 to permit easy access to the stop cocks and the inlets and outlets. Inlet 56 of the last chamber, chamber number 9, is suitably sealed off by any convenient means, such as closed tube 62 and the outlet 58 of the first chamber, chamber number 1, is provided with the previously mentioned tube 22 which is adapted to be connected to the inlet of a pump for pumping the liquid to one or more chromatography columns or which may be connected to the chromatography column directly for transmitting the liquid by gravity to the column. The upper end of each of the open top mixing chambers 16 is provided with a cut-out portion 64 which vents the interior of the chamber to the atmosphere to assure hydrostatic equilibrium between the chambers and free flow of liquid from and between the chambers. In addition, the cut-out 64 helps orient the chamber for correct positioning on the device and in this regard it will be observed that the cut-out portions face inwardly toward the central column 14.

Plates 42 and 44 are identical and each plate, as best seen in FIGS. 3 and 4, includes a series of circular cut-out portions 66 along the outer circumference of the plate and the cut-out portions of one plate are in vertical alignment with corresponding cut-out portions of the other plate. Each cut-out portion is adapted to be contacted by a chamber 16 along a portion of the outer surface of the side wall of said chamber to provide a short arcuate line of contact between the plate and the chamber for support of the chamber when mounted on the device. A relatively small portion only of the rim 68 of the lower end 54 of each chamber rests on the upper surface of plate 40. Accordingly, each chamber is engaged at two vertical spaced portions of the outer surface of its side wall by vertical spaced members, namely the plates 42 and 44, and is also engaged at a portion only of its lower end by plate 40, whereby a three point stable support is provided for each chamber.

In order to make certain that the flat cover 70 will properly engage the upper edges of the chambers completely therearound except for the vent opening 64, the chambers are cut from lengths of hollow tubing in a manner which assures that the upper ends of the chambers are flat, and lie in the same horizontal plane when mounted on the device 10. This is accomplished by cutting the hollow tubing by a saw whose cutting edge lies in a plane parallel to the upper surface of supporting plate 40 with the tubing held in a fixture in the same manner as the three point support provided by device 10 for the chamber. Because of the line contact of the vertically spaced plates 42 and 44 with the vertically spaced portions, respectively, of the outer surfaces of the side walls of the chambers and because of proper indexing of the chambers assured by cut-outs 64, variations in such outer surfaces do not affect the correct mounting of the chambers on the device, whereby it is assured that the tops of the chambers always lie in the same horizontal plane.

It will be understood that the chambers 16 are formed of tubing of the same internal diameter and that even though precision tubing is unnecessary the tubing is nevertheless selected so that variation in internal diameter of the tubing is slight and non-critical. Accordingly, it will be understood that at the start of the operation and with all valves closed, the level of the liquid will be the same in each chamber, and that when the valves are opened the liquid level will drop uniformly in all chambers to provide an accurate variable gradient.

The plates 42 and 44 are provided with the springs 72 which grip a portion of the outer surface of the chamber and resiliently hold the chamber in contact with the cut-out portions 66 of the plates. The ends of the springs are held by the screws 74 which are secured to the plates. A protective layer 76 of suitable material may be provided on the outer surface of the chamber to prevent the marring of those portions of the surface which are contacted by the springs 72.

The cover 70 of the mixer 18 is adapted to rest on the upper ends of the chambers 16 to provide a good seal and prevent excessive evaporation of the liquid, and the cover may be provided with a protective layer 78 of suitable material which contacts the upper edges of the chambers. A pair of pins 80 extend downwardly from the cover and each of the plates 42 and 44 has a pair of holes 82 through which the pins extend so that when the mixer is placed in operative position on the chambers, the stirring paddles 20 are properly oriented with respect to the chambers and, in addition, the interfitting pins and holes prevent shifting of the mixer in its operative mounted position. It will be noted that a stirring paddle is provided for each of chambers 1 through 8 and a rod 84 is provided for chamber 9, it being understood that chamber 9 does not receive any liquid for mixing. The volume of rod 84 is the same as the volume of each of the stirring paddles 20. A decal 86 may be provided on cover 70 and a similar decal may be provided on plate 44 to permit quick positioning of rod 84 with chamber 9. It will be understood that in lieu of rod 84 another stirring paddle 20 may be provided, if so desired.

The upper end of each paddle is mounted in a bearing 88 provided in cover 70 and has a shaft portion 90 on which is mounted a friction wheel 92. The edges of the friction wheels are in driving contact with each other and one of the friction wheels is driven by a shaft 94 which is operated by a motor 96. The motor is mounted on cover 70 by the securing elements 98. Operation of the motor drives one of the friction wheels which in turn causes the rotation of the other friction wheels and the rotation of the stirring paddles for mixing the liquids in each of the chambers.

While I have shown and described the preferred embodiment of the invention, it will be understood that the invention may be embodied otherwise than as herein specifically illustrated or described, and that certain changes in the form and arrangement of parts and in the specific manner of practicing the invention may be made without departing from the underlying ideas or principles of this invention within the scope of the appended claims.

What is claimed is:

1. A variable gradient device, comprising a supporting base having means for adjusting said base into a horizontal position, a column extending vertically upwardly from said base, and means connected to said column for supporting a plurality of vertical cylindrical chambers arranged laterally of each other in a circular row around said column and connected in fluid flow communication with each other, said chamber supporting means comprising three horizontal circular plates spaced vertically from each other, the lowest plate of said horizontal plates having a flat horizontal upper surface for engaging a portion only of the lower end of each of said chambers, said other plates each having circular cut-out portions along the circumference, thereof, for engaging vertically spaced portions, respectively, of the side wall of each of said chambers, whereby each of said chambers is supported by engagement of three vertically spaced portions thereof by said supporting means.

2. A variable gradient device, comprising a supporting

base having means for adjusting said base into a horizontal position, a column extending vertically upwardly from said base, and means connected to said column for supporting a plurality of vertical cylindrical chambers arranged laterally of each other in a circular row around said column and connected in fluid flow communication with each other, said chamber supporting means comprising three horizontal circular plates spaced vertically from each other, the lowest plate of said horizontal plates having a flat horizontal upper surface for engaging a portion only of the lower end of each of said chambers, said other plates each having circular cut-out portions along the circumference, thereof, for engaging vertically spaced portions, respectively, of the side wall of each of said chambers, whereby each of said chambers is supported by engagement of three vertically spaced portions thereof by said supporting means, and spring means at each of said cut-out portions for biasing each of said chambers into engagement with the corresponding cut-out portions.

3. A variable gradient device, comprising a supporting base, a member extending vertically from said base, a plurality of vertical chambers, and means connected to said member for supporting said chambers arranged laterally of each other and connected in fluid flow communication with each other, said chamber supporting means including a horizontal member having a flat upper surface for engaging a portion only of the lower end of each of said chambers, said lower ends of each of said chambers having liquid inlets and liquid outlets extending downwardly therefrom below said horizontal member.

4. A variable gradient device, comprising a supporting base, a member extending vertically from said base, a plurality of vertical chambers, and means connected to said member for supporting said chambers arranged laterally of each other and connected in fluid flow communication with each other, said chamber supporting means comprising three horizontal members spaced vertically from each other, the lowest member of said horizontal members having a flat horizontal upper surface for engaging a portion only of the lower end of each of said chambers, and said other members having parts thereof for engaging vertically spaced portions, respectively, of the side wall of each of said chambers, whereby each of said chambers is supported by engagement of three vertically spaced portions thereof by said supporting means, said lower ends of each of said chambers having liquid inlets and liquid outlets extending downwardly therefrom below said lowest member.

5. A variable gradient device, comprising a supporting base, a member extending from said base, means connected to said extending member for supporting a plurality of open ended chambers arranged adjacent to each other and connected in fluid flow communication with each other, mixer means removably mounted on said open ended chambers for stirring the liquids therein, said mixer means having stirring members for extending through said open ends into said chambers in said mounted condition of said mixer means, and cooperating means on said mixer means and said chamber supporting means for predetermining the position of said mixer means on said chambers.

6. A variable gradient device, comprising a supporting base, a member extending from said base, means connected to said extending member for supporting a plurality of open ended chambers arranged adjacent to each other and connected in fluid flow communication with each other, mixer means removably mounted on said open ended chambers for stirring the liquids therein, said mixer means having stirring members for extending through said open ends into said chambers in said mounted condition of said mixer means, and cooperating means on said mixer means and said chamber supporting means for predetermining the position of said mixer means in said chambers comprising a plurality of pins extending from said mixer means and a plurality of corresponding holes for said pins provided in said chamber supporting means.

7. A variable gradient device, comprising a supporting base, a member extending from said base, means connected to said extending member for supporting a plurality of open ended chambers arranged adjacent to each other and connected in fluid flow communication with each other, mixer means removably mounted on said open ended chambers for stirring the liquid therein, said mixer means comprising a cover for mounting on said open ended chambers in covering relation therewith and a plurality of stirring members for extending through said open ends into said chambers in said mounted condition of said mixer means, and cooperating means on said mixer means and said chamber supporting means for predetermining the position of said mixer means on said chambers comprising a plurality of pins extending from said cover and a plurality of corresponding holes for said pins provided in said chamber supporting means.

8. A variable gradient device, comprising a supporting base, a member extending from said base, means connected to said extending member for supporting a plurality of open ended chambers arranged adjacent to each other and connected in fluid flow communication with each other, said chamber supporting means comprising a plurality of plates spaced from each other, one of said plates having a flat surface for engaging a portion only of one end of each of said chambers, and another plate of said plurality of plates having parts thereof for engaging the outer surface of said chambers, respectively, whereby each of said chambers is supported by engagement of portions thereof with said supporting means, mixer means removably mounted on said open ended chambers for stirring the liquids therein, said mixer means having stirring members for extending through said open ends into said chambers in said mounted condition of said mixer means, and cooperating means on said mixer means and said chamber supporting means for predetermining the position of said mixer means on said chambers.

9. A variable gradient device, comprising a supporting base having means for adjusting said base into a horizontal position, a column extending vertically upwardly from said base, means connected to said column for supporting a plurality of vertical open top chambers arranged laterally of each other and connected in fluid flow communication with each other, said chamber supporting means comprising three horizontal members spaced vertically from each other, the lowest member of said horizontal members having a flat horizontal upper surface for engaging a portion only of the lower end of each of said chambers, and said other members having parts thereof for engaging vertically spaced portions, respectively, of the side wall of each of said chambers, whereby each of said chambers is supported by engagement of three vertically spaced portions thereof by said supporting means, mixer means removably mounted on said open ended chambers for stirring the liquids therein, said mixer means having stirring members for extending through said open tops into said chambers in said mounted condition of said mixer means, and cooperating means on said mixer means and said chamber supporting means for predetermining the position of said mixer means on said chambers comprising a plurality of pins extending from said mixer means and a plurality of corresponding holes for said pins provided in said other members.

10. A variable gradient device, comprising a supporting base, a column comprising a series of clamping members spaced from each other and extending vertically upwardly from said base, and means connected to said column for supporting a plurality of chambers arranged laterally of each other and connected in fluid flow communication with each other, said chamber supporting means comprising a series of members spaced vertically from each other, said members being held in position in said spaces, respectively, between said clamping mem-

bers, the lowest member of said plurality of members having a flat horizontal upper surface for engaging a portion of the lower end of each of said chambers, and the other members of said plurality of members each having parts thereof for engaging the outer surface of the side wall of each of said chambers.

11. A variable gradient device, comprising a series of individual liquid containers for the valve-controlled flow of liquid from the bottom of each of the containers into another container of the series, in succession, a support having a horizontal surface, each of said containers having a bottom with a portion only of said bottom in engagement with said horizontal surface for the support of said containers on said support, and means for holding the containers in said engagement with said support, each bottom of each of said containers being provided with a valve controlled passage separate from the support and connected in liquid flow communication with the other containers of the series for the aforementioned flow of the liquid in series from one container to another.

12. A variable gradient device, comprising a series of individual liquid containers for the valve-controlled flow of liquid from the bottom of each of the containers into another container of the series, in succession, a support having a horizontal surface, each of said containers having a bottom with a portion only of said bottom in engagement with said horizontal surface for the support of said containers on said support, and releasable means engaging the sides of the containers for holding the containers in said engagement with said support, each bottom of each of said containers being provided with a valve controlled passage separate from the support and connected in liquid flow communication with the other containers of the series for the aforementioned flow of the liquid in series from one container to another.

13. A variable gradient device, comprising a series of individual liquid containers for the valve-controlled flow of liquid from the bottom of each of the containers into another container of the series, in succession, a support having a horizontal surface, each of said containers having a bottom with a portion only of said bottom in

engagement with said horizontal surface for the support of said containers on said support, and means for holding the containers in said engagement with said support, each bottom of each of said containers being provided with a valve controlled passage separate from the support and positioned outwardly thereof and connected in liquid flow communication with the other containers of the series for the aforementioned flow of the liquid in series from one container to another.

14. A variable gradient device, comprising a series of individual liquid containers for the valve-controlled flow of liquid from the bottom of each of the containers into another container of the series, in succession, a support having a horizontal surface, each of said containers having a bottom with a portion only of said bottom in engagement with said horizontal surface for the support of said containers on said support, and means for holding the containers in said engagement with said support comprising vertically spaced parts in engagement with the sides of the containers, said vertically spaced parts having recessed edges which engage circumferential portions of the sides of the containers for positioning the containers laterally of each other on said support, each bottom of each of said containers being provided with a valve controlled passage separate from the support and connected in liquid flow communication with the other containers of the series for the aforementioned flow of the liquid in series from one container to another.

References Cited in the file of this patent

UNITED STATES PATENTS

351,208	Searles	Oct. 19, 1886
2,475,191	Marvin et al.	July 5, 1949
2,516,965	Dresser	Aug. 1, 1950
2,755,018	Grela et al.	July 17, 1956
2,954,028	Smith	Sept. 27, 1960

OTHER REFERENCES

"Variable Gradient Device for Chromatography," by Peterson and Sober, pub. in "Analytical Chemistry," vol. 31, No. 5, May 1959.