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[54] **PROCESS OF LIQUID CHROMATOGRAPHY FOR DOSED INTRODUCTION OF SMALL AMOUNTS OF LIQUID INTO A FLOW OF CARRIER LIQUID**
13 Claims, 2 Drawing Figs.

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[51] **Int. Cl.** **G01n 1/12**
[50] **Field of Search** ..... 73/422 GC

[56] **References Cited**
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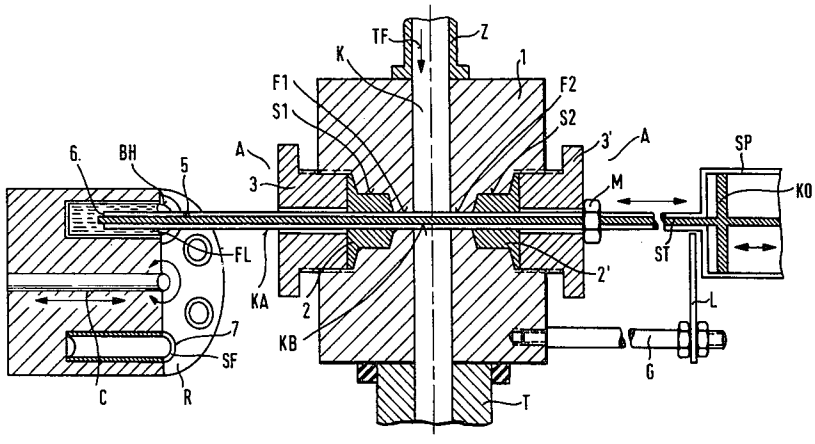
ABSTRACT: In the practice of liquid chromatography a tubule with at least one opening is arranged transversely in relation to the flow of the carrier liquid and is movable in an axial direction. In a first position the opening is situated outside of the flow of carrier liquid and the liquid to be dosed is charged into the interior of the tubule through the opening. Thereafter, the tubule is shifted into a second position so that the opening is then situated in the range of the flow of the carrier liquid. Thereupon, the liquid contained in the tubule is injected through the opening into the flow of the carrier liquid. The process prevents a pressure surge from being propagated in the flow of the carrier liquid.



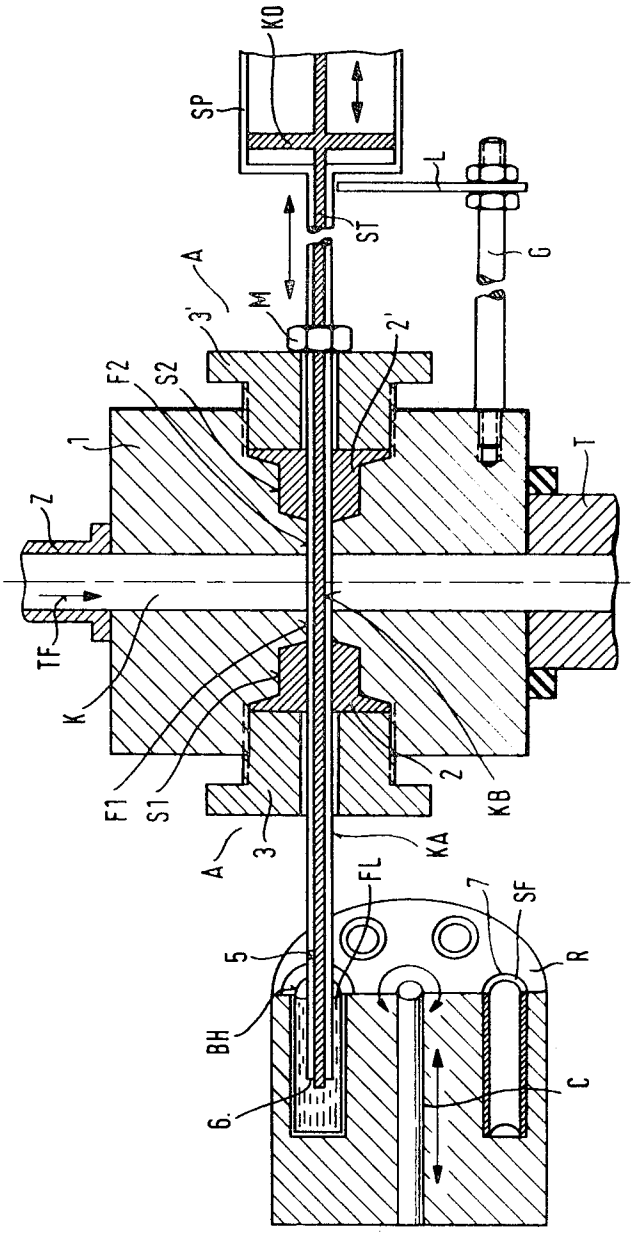


Fig. 1

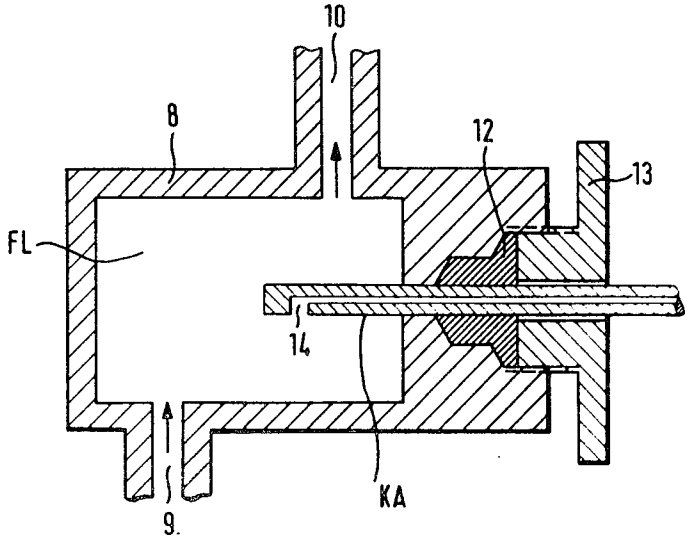


Fig. 2

PROCESS OF LIQUID CHROMATOGRAPHY FOR DOSED INTRODUCTION OF SMALL AMOUNTS OF LIQUID INTO A FLOW OF CARRIER LIQUID

BACKGROUND OF THE INVENTION

In liquid chromatography, very small amounts of liquid (e.g., 0.1–200 μl.) must be fed rapidly and in a precisely reproducible manner against a pressure e.g., 300 Kg./cm.²) which prevails in a carrier liquid associated with the separation column. When dispensing devices presently known in gas chromatography are employed, insuperable difficulties arise in connection with the seals for such devices. The perforation cap injection method, which is carried out by means of a piston injector, provides no guarantee of dosage reproducibility owing to the high internal pressure of the carrier liquid. Depending on the solvent, different materials must be employed as the perforation cap. Moreover, pressure surges, which may be propagated through the separation column to a detector and thus may significantly disturb the analytic procedure, appear with the introduction of the tubule of an injection device into the current of liquid, owing to the incompressibility of the carrier liquids employed. The process and the corresponding apparatus, wherein an injector, such as a syringe or the like, is introduced into the evaporator chamber or the chamber preceding the separation column, are completely valueless for use in liquid chromotography.

OBJECTS AND SUMMARY OF THE INVENTION

The purpose of the invention is to eliminate the above difficulties. Further, it provides for a process of liquid chromatography for dosed introduction of small quantities of liquid by means of an injection device into the flow of a carrier liquid so as to avoid a pressure surge propagated in the flow of the carrier liquid. The process of the invention is further characterized in that at least one lateral opening is provided in a tubule or a cannula of an injection member, with the member being movable transversely relative to the flow of the carrier liquid so as to be positioned outside of the flow of the carrier liquid at which time the lateral opening is brought into contact with the liquid to be dosed. At that time the liquid is introduced into the interior of the injector containing the tubule, and then the tubule is reciprocated back toward its initial position so that the lateral opening may be placed into the range of the flow of the carrier liquid. Finally, the liquid contained in the injector is then injected through the lateral opening into the flow of the carrier liquid, and, after the predetermined amount of liquid is introduced into the stream, the tubule may once again be returned into a position to be refilled.

Also, in accordance with the invention, a further process of liquid chromatography for dosed introduction of small amounts of liquid by means of traversing an injection device into a flow of carrier liquid so as to avoid a pressure surge being propagated in the current of liquid with the ultimate cleaning of a tubule associated with the injection device is characterized in that in addition to the first lateral opening there may be at least one further terminal or end side opening in the dosage device. At least one lateral opening of the tubule which is movable transversely in relation to the flow of the carrier liquid is situated outside of the flow of liquid in a first of several possible positions of the tubule, and at least one opening thereof is brought in contact with the liquid to be dosed. Then the interior of an injector containing the tubule is filled with the liquid in this first position. After the filling, the end side opening and the lateral openings with the exception of one opening or in the case where there is no end side opening, the lateral openings with the exception of one opening are closed. The tubule is then shifted into a second position in such a manner that the open lateral opening is placed in the range of the flow of the carrier liquid, whereupon the liquid contained in the injector is then injected through the lateral opening into the flow of carrier liquid. The remaining openings are released after the introduction of the liquid and after the analysis and the tubule bore is rinsed with the carrier liquid penetrating from the flow of carrier liquid through a lateral opening and the tubule is then returned into its first position.

Another object of the invention is to provide apparatus for the realization of the process disclosed herein. Such apparatus includes a separation column head provided with intersecting bores, one bore being arranged for travel of the carrier liquid and the other arranged to receive the cannula which, when projected beyond one side of the head per se, is adapted to be filled through appropriate perforations therein any may then be retracted into the head to deposit a predetermined dosage into the carrier liquid.

BRIEF DESCRIPTION OF THE DRAWING

The invention will be better understood, and further objects and advantages will become more apparent, from a reading of the following detailed specification taken in conjunction with the drawings, in which:

FIG. 1 is a view of the apparatus partially in cross section and partially in elevation; and

FIG. 2 is a cross-sectional view of a further embodiment of the dosage device.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Turning now to FIG. 1, the column head is identified as 1 and is shown as having a bore K extending therethrough, one end of the head being provided with feed pipe Z and the other end with a separation column T.

As shown, the head 1 is provided with diametrically opposed bores F1 and F2 which are arranged to receive the hollow needle KA for reciprocation therein. The tubule KA is of smaller diameter than the passageway K so that flow therethrough is not impeded. The tubule KA is arranged to project beyond each side of the column head 1 and the bores S1 and S2, through which it passes, are provided with perforated Teflon packing members 2 and 2', each of which is sealed against leakage by means of gland members 3 and 3'. It is advantageous to position the tubule KA in channels F1 and F2 with a snug fit to substantially prevent the carrier liquid flowing in passageway K from contacting (and thus chemically attacking) the packing members 2, 2'.

A piston rod ST is surrounded by the cannula KA and is adapted to be sealed against leakage with the rod being reciprocable, either manually or automatically, by the piston KO. Note double arrow at piston KO. In one end position the terminal or end of the piston rod ST is scarcely protruding beyond the end wall of the tubule opening 6, whereas the other end position is determined by the required volume that should be rendered free in tubule bore KB for the liquid FL to be dosed. The stroke of piston rod ST is piston KO.

Piston rod ST is not absolutely necessary for sucking the liquid FL into the interior of the tubule KA or for injecting the liquid from the openings arranged in tubule KA that are to be described later in more detail. It is sufficient if the tubule KA is formed as a part of an injector SP (as customary in medicine), wherein only the piston KO must be displaced for filling of the liquid FL or emptying from tubule KA and parts of injector SP surrounding piston KO.

Furthermore, a lateral opening 5 is arranged in the tubule wall, the opening being situated in the external space denoted A in the position illustrated. There may also be several other laterally disposed openings 5, possibly situated under the Teflon packings 2 and 2' as well as beyond the gland members 3 and 3' (i.e., in front of or behind the column head), as will be better understood as the description progresses.

The tubule KA proper is likewise reciprocable by hand or automatically in the direction indicated by the double arrows. As illustrated in FIG. 1, the tubule is situated in a first position by means of a nut M which abuts the gland member 3'. The second position (not shown) is determined by nut M abutting against side bar L which is attached to the column head 1 by means of a rod G. The stroke of this translatory movement is

to be dimensioned so that lateral opening 5 is situated outside gland member 3 in one end position of travel and inside head bore K of column head 1 in another end position of travel. The length of tubule KA, furthermore, is to be selected so that when the tubule is in its second end position, the opening 6 provided at the end thereof is situated outside or at least still inside Teflon packing 2. Furthermore, piston rod ST must have a sufficient length so that, as shown in the drawing, its tip projects from opening 6 or can be led at least up to the opening 6.

The end opening 6 is absolutely necessary for an accurate operation of the device of the invention. It can be replaced by a lateral opening arranged at the terminal end, e.g., in the manner of opening 5, or be completely omitted. However, if the opening at the end is eliminated, a cleaning of the tubule interior with the carrier liquid TF flowing through head bore K, as it will be carried out in a step still to be described, is more difficult. In such a case, tubule KA must be cleaned in a position wherein lateral opening 5 is no longer situated in the range of the carrier liquid.

In one embodiment of the invention, a revolving drum R, rotatable about a shaft C and displaceable along shaft C in parallel with the axis of the tubule, is situated in front of opening 6 of tubule KA at a distance determined by the distance from the end opening 6 and the lateral opening 5. Revolving drum R contains a plurality of containers BH for the liquid FL to be dosed and a stopper plug SF provided with a protective sack means in bore 7. Revolving drum R is rotatable about shaft C so that either container BH or stopper SF may be situated at the level of the tubule tip. Furthermore, it is displaceable along shaft C so that the tip of tubule KA is immersed into liquid FL contained in container BH or the tip is introduced into the protective pocket provided in bore 7 in a sealed manner. Of course, container BH or stopper SF may also be manually placed over or on the tip of tubule KA without any need for the revolving drum R.

In still another embodiment of the invention, the container BH may include a housing 8, as shown in FIG. 2, the housing being filled by a liquid FL which is to be dosed. Housing 8 is provided with an inlet feed line 9 and a discharge outlet line 10. In the position illustrated in this view, a part of tubule KA, sealed in relation to the atmosphere and housing 8 by a further Teflon seal 12 and gland-packing member 13, is situated inside housing 8 for the purpose of drawing out liquid FL. A lateral opening 14 is thus situated in the range of liquid FL (the lateral opening may be replaced by an end opening 6 as shown in FIG. 1 or by further lateral openings). Through a displacement of injector piston KO (see FIG. 1) to the right, liquid FL may be drawn by suction through opening 14, while all other openings that may be arranged on tubule KA and not situated inside housing 8 must be sealed. When the interior of the tubule or injector member is filled with liquid FL, tubule KA may be withdrawn from housing 8, whereafter opening 14 must be sealed with a stopper SF and the perforation in the gland member 13 must be tightly closed. However, it is also possible to move tubule KA only to such an extent that the lateral opening 14 therein is closed by the packing 12. But, in this event, the stroke of such movement must be selected so that lateral opening 5 (see FIG. 1), which permits introduction of liquid FL into the flow of carrier liquid TF, is placed in the range of the bore K for the purpose of injection.

OPERATION OF THE EMBODIMENTS

The introduction of liquid FL contained in container BH into the flow of carrier liquid TF is performed in the following steps. Assume at the outset that tubule KA is in the abutment position on gland member 3' and the tip of piston rod ST projects from opening 6. Container BH is moved into position over the tip and thus over openings 5 and 6. Then piston rod ST is pulled back by means of piston KO over a length extending behind opening 5. Since piston rod ST is guided in a tight manner inside tubule bore KB, it sucks the liquid FL into tubule bore KB. Subsequently, container BH is removed from the tip of tubule KA (i.e., the revolving head R is displaced along shaft C away from the tip of tubule KA and turned about shaft C until stopper SF reaches alignment with the tip and is then again displaced toward the tip) and the stopper SF is placed on the tip. (If end opening 6 is completely omitted, stopped SF need not be placed on the tip.) This procedure is followed by reciprocating tubule KA back toward the column head 1 until nut M abuts against side bar L and the lateral opening 5 is situated inside bore K, the revolving drum R also participating in this stroke so that opening of tubule KA remains covered. The displacement of tubule KA transversely through bore K produces no pressure surge in the carrier liquid TF, since the volume displaced by tubule KA inside head bore K remains the same at all times. Thereafter, piston rod ST is shifted toward opening 5 and it displaces liquid FL present in tubule bore KB through opening 5 and into the flow of carrier liquid TF. Liquid FL is carried along by carrier liquid TF into the separation column T and separated therein.

After the piston rod ST moves beyond the lateral opening 5, liquid FL is no longer injected into carrier liquid TF. The dosing or injection procedure is completed and tubule KA may be returned into its first abutment position, whereafter stopper SF may be removed from the tip of tubule KA and fresh liquid FL may be introduced. The sequence of movements is then repeated.

However, tubule bore KB may also be cleaned immediately before a new analysis. For such a purpose, piston rod ST is stopped adjacent to the lateral opening 5, whereafter the stopper SF is removed, prior to the movement of the opening 5 into alignment with bore K. Carrier liquid TF, which is subjected to internal pressure, then penetrated through opening 5 into internal bore KB in tubule KA and displaces the residues of liquid FL. When the internal bore KB is rinsed sufficiently, piston rod ST may either be shifted so that lateral opening 5 is blocked, or tubule KA may then be brought into its second position of abutment so that lateral opening 5 is covered by the Teflon packing 2 (or other corresponding packing member). A further injection may then be carried out.

That which is claimed is:

1. In a liquid chromatography injection device for introducing into a first, or carrier liquid metered quantities of a second liquid, the improvement comprising

a. a separation column head,

b. a first channel extending through said separation column head and containing said carrier liquid,

c. a second channel extending through said separation column head and intersecting said first channel,

d. a hollow tubule contained in said second channel and traversing said first channel; said hollow tubule being movable in said second channel into and between first and second positions; said hollow tubule extending fully across said first channel in said first and second positions and in any other position therebetween,

e. means for moving said tubule into and between said first and second positions,

f. dosage-dispensing means containing said second liquid and positioned externally of the location of intersection between said first and second channels, said dosage-dispensing means communicating with said tubule at least in the first position thereof,

g. a lateral opening provided in said tubule; said opening communicating with said first channel in the second position of said tubule.

h. means for introducing a quantity of said second liquid from said dosage-dispensing means into said tubule in the first position thereof and injecting the last-named quantity of said second liquid from said tubule into said carrier liquid in the second position of said tubule and

i. packing members sealingly surrounding said tubule at opposite sides of said first channel in all said positions of said tubule.

2. A device according to claim 1, wherein the means defined in (H) include an elongated rod disposed within said tubule and a reciprocable piston connected with said rod to cause movement of the latter.

3. A device according to claim 1, wherein said dosage-dispensing means includes

A. a housing having an inlet and an outlet; said second liquid traverses said housing by flowing through said inlet and said outlet and

B. sealing means provided in said housing; said tubule is surrounded by the last-named sealing means and extends into said housing at least in the first position of said tubule.

4. A device as defined in claim 1, wherein said tubule is disposed in said second channel in a snug fit at least between said first channel and the respective packing members on either side of said first channel.

5. A device according to claim 1, wherein the dosage-dispensing means is rotatable about its axis relative to the column head and in a plane perpendicular to the first channel.

6. A device according to claim 1, wherein the axis of rotation of the dispensing means is in a plane parallel to the tubule.

7. A device according to claim 5, wherein the rotatable dispensing means is provided with a plurality of dosage devices and at least one stopper means.

8. A device according to claim 5, wherein the dispensing means is reciprocable relative to the column head.

9. A device according to claim 2, wherein the tubule is connected to an injection body movable therewith as a unit; said piston is positioned in said injection body.

10. A device according to claim 9, wherein the injection body and the piston are each reciprocable independently of the other.

11. A device according to claim 1, wherein the tubule is provided with abutment means arranged to cooperate with the separation column head.

12. A device according to claim 1, wherein the separation column head supports stop means offstanding therefrom and arranged to cooperate with abutment means carried by said tubule.

13. A method of injecting metered quantities of liquid by means of a hollow tubule into a carrier liquid flowing through a channel, comprising the steps of

A. positioning said tubule to pass entirely through said channel in an intersecting relationship therewith,

B. moving said tubule into a first position in which the inside of the tubule communicates with a means containing the liquid to be injected and in which communication is interrupted between said channel and the inside of said tubule; in said first position said tubule passes entirely through said channel in said intersecting relationship therewith,

C. introducing a quantity of the last-named liquid from said means into said tubule in the first position thereof,

D. moving said tubule into a second position in which the inside of the tubule communicates with said channel and in which said tubule passes entirely through said channel in said intersecting relationship therewith and

E. injecting said quantity of liquid from the inside of said tubule into said channel containing said carrier liquid.

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