(10)

PATENT SPECIFICATION (11) 1 557 984

1 557 984

(21) Application No. 38013/76 (22) Filed 14 Sept. 1976
(31) Convention Application No. 7 510 863 (32) Filed 29 Sept. 1975 in
(33) Sweden (SE)
(44) Complete Specification published 19 Dec. 1979
(51) INT. CL.² G01N 21/00
(52) Index at acceptance
G2J 35
G1B CB



(54) CAPILLARY SAMPLING OPTICAL CUVETTE

(71) We, JAN EVERT LILJA AND SVEN ERIK LENNART NILSSON, both subjects of the King of Sweden, of Frodes väg 17, 291 65 Kristianstad, Sweden, and Hasselvägen 17, 2nd Floor, 291 60 Kristianstad, Sweden, respectively, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a cuvette sampling a liquid and which permits mixing the sample with a reagent in the cuvette and making a direct optical analysis of the sample.

In making wet-chemical analyses a sample is normally measured with a 'single-use' pipette and the reagent is measured into a vessel with a pipette or dispenser. The reagent usually has a relatively large volume, which results in a relatively small error on measuring the volume, whereas the volume of the sample normally is small, which implies a high dilution after mixing of reagent and sample. To attain a high precision the sample volume must therefore be measured with great exactitude. The sample and reagent mixture is transferred after the reaction time, if any, to an optical measuring cuvette for measurement.

The present invention provides a cuvette for sampling a liquid and permitting mixing the sample with a reagent contained within the cuvette and making a direct optical analysis of the sample, which cuvette comprises a body having a chamber containing a reagent and having a capillary sampling inlet for transporting a sample by capillary action from the exterior of the cuvette to the chamber, there being a light path through the chamber defined by a pair of generally opposed, planar, transparent surfaces.

The cuvette may be such that the said transparent surfaces are contained in or constitute a pair of flexible walls which in use may be pressed together to provide a predetermined optical path length through the chamber.

In such a case the chamber may contain a spacer to define the optical path length upon compression of the walls.

Such a spacer element may also serve as a carrier of the reagent and may be of ferromagnetic material so as to cause mixing of the sample and the reagent when the cuvette is placed in a varying magnetic field.

Alternatively, the cuvette may be made of a substantially rigid material.

The reagent may be in the form of a solid material deposited in the chamber by evaporation, freeze-drying, spraying or screen printing or in the form of a gel.

For some analyses it is preferable that the cuvette be one in which the body contains a plurality of chambers, each having a capilliary opening, there being a light path through each chamber, each path being defined by a pair of generally opposed, planar, transparent, surfaces.

In such a case, it may be that a plurality of communicating chambers are arranged in parallel or in series.

The invention includes a method of analysis which comprises contacting the capilliary opening of a chamber of a cuvette of the invention with a body of sample liquid to fill the cavity, and passing light through the optical path of the chamber to perform an optical analysis of the sample liquid.

The invention therefore permits sampling a liquid, mixing and chemically reacting the sample with a suitable reagent, for instance to develop a colour, in the sampling cuvette vessel. The invention

thus simplifies the sampling procedure, reduces the number of items of apparatus used and in most cases, depending upon the type of analysis, considerably improves the exactitude of the analysis by making the analysing procedure less dependent on the operating technique of the operator. Compared with the conventional manual procedures, the gain of time can also be considerable.

The cuvette chamber may contain an exactly determined amount of reagent, preferably in solid form. The remaining volume of the cuvette chamber is in use filled with sample liquid. This gives a predetermined relationship between the amounts of sample liquid and reagent. The sample liquid will usually dissolve the reagent, which implies that two earlier manual measuring procedures are replaced by one in which the manufacturing exactitude will be determinative of the measuring exactitude.

The reagent may be so formulated that the dissolution of the reagent takes place at a desired speed e.g. not too rapidly. An increased dissolution rate can be obtained by means of vibratory mixing. The dissolution rate can be reduced by coating the reagent, e.g. with a slower dissolving substance, which in turn provides the possibility of carrying out chemical reactions in several steps and of separating sensitive reagents from one another.

Mixing suitably takes place by vibration since the liquid layer is so thin that the conventional mixing procedures are ineffective. Mixing is most simply carried out in situ in a photometer but can also be carried out in a separate vibrator. The optimum vibration frequency and amplitude are to a certain extent dependent upon the physical configuration and location of the measuring cuvette. If use is made of a separate vibrator a standard photometer can be utilized on making optical analyses.

The invention will be illustrated with reference to the accompanying drawings which schematically and on a large scale illustrate several embodiments. In the drawings:

Fig. 1 shows a measuring cuvette according to the invention;

Fig. 2 shows a section on the line II-II in Fig. 1;

Fig. 3 shows a modified embodiment of the cuvette;

Fig. 4 shows a section on the line IV-IV in Fig. 3;

Fig. 5 shows another embodiment of the measuring cuvette according to the invention;

Fig. 6 shows a section on the line VI-VI in Fig. 5;

Fig. 7 shows an embodiment in which the cuvette has parallel-connected cavities;

Fig. 8 shows an embodiment in which the cuvette has series-connected cavities;

Fig. 9 shows a cuvette with somewhat outwardly bulging walls;

Fig. 10 shows the cuvette according to Fig. 9 from one end;

Fig. 11 shows a cuvette having an inlet channel;

Fig. 12 shows this cuvette in section on the line XIII-XIII;

Fig. 13 shows a cuvette having a spacing element; and

Fig. 14 shows a section on the line XV-XV in Fig. 13.

The cuvette illustrated in the drawings comprises a body 10 of glass or plastics which is transparent to permit making optical analyses. According to Figs. 1 and 2 the body 10 has a chamber or cavity 11 which is intended to accommodate a liquid sample and the dimension of which is such that it can be filled by capillary force. The dimensions of the cavity are exactly determined, in particular the distance between the walls defining the cavity.

The cavity 11 of the cuvette is supplied with a reagent (that is, an agent to react with the sample drawn into said cavity) by evaporation, freeze-drying, spraying, screen printing or in another suitable manner depending on the manner in which the cuvette is manufactured. The amount of reagent may be predetermined and is chosen having regard to size of the cavity. By coating the reagent the dissolution rate thereof in the sample can be controlled; for instance for the dissolution of reagents in a definite sequence, which is suitable in making analyses in several reaction steps, or for the isolation of sensitive reagents. After a reagent has been deposited in the cavity the cuvette is ready for use. When the cuvette illustrated in Fig. 1 is to be used the outwardly open side of the cavity is brought in contact with the liquid sample to be examined, whereby said sample penetrates into the cavity 11 and there mixes with the reagent either spontaneously or with the aid of, for instance, a vibrator which may be a separate unit or part of the analysing apparatus, for instance a photometer, in which the sample is to be analysed. The sample is then placed in the analysing apparatus, and the analysis is carried out.

As will appear from Figs. 1 and 2 an annular bead 30 is disposed on the outer side of the upper wall defining the chamber or cavity (see Fig. 2). This bead 30 has for its object to protect the enclosed portion of the wall against being scratched or otherwise damaged when the cuvette

is handled before making the analysis.

Figs. 3 and 4 show a modified embodiment of the cuvette 10 which has a cavity or chamber 12 and two channels 13 which extend from opposite sides of the cuvette and open into the cavity 12. Thus a sample can here be drawn straight through the cuvette, which may be advantageous in certain cases. A recess 31 having a planar bottom is arranged in each of the opposite walls of the cuvette above the cavity 12. Said recesses are situated opposite one another and serve the same purpose as the annular bead 30 in the foregoing embodiment.

The cuvette according to Figs. 5 and 6 has a cavity or chamber 14 of varying depth, which has been realized by stepping one of the surfaces of the cavity to form levels 15 spaced different distances from the opposite surface. The number of such levels can be varied and the height difference between the levels will be determinative for the measuring exactitude. The outermost cavity can serve as a receiving cavity which is devoid of reagent and from which the sample can be drawn at a suitable rate into the other cavities. Of course, a bead 30 or recess 31 according to the two preceding embodiments may be disposed above one or more levels.

The cuvette as shown in Fig. 7 has four parallel-connected cavities or chambers 23, 23′, which are linked to a common channel 25 by branch channels 24 which continue on the opposite side of the cavities and open into the atmosphere to prevent air inclusions in the cavities when samples are drawn thereinto. The cavities 23, 23′ can contain reagents of the same or different kinds for making control analyses and various kinds of analyses, respectively. In a preferred embodiment the cavities 23′ instead of containing a solid reagent deposited on the walls thereof, may contain a gel, for instance, one gel of a given type in the upper cavity of the figure and another gel in the lower cavity thereof. This will provide the advantage that a sample can be caused to react with two different reagents in the cavities 23 while particles of a size determined by the choice of gel diffuses into the gel in the respective cavity 23′ to react with a specific reagent contained in the gel.

Fig. 8 shows two series-connected cuvette cavities or chambers 26 into which a sample is drawn through a channel 27. Said cavities may contain reagents of the same kind for making control analyses or of different kinds for making different analyses. As in the previous embodiment one cavity may contain a solid reagent and the other cavity — the inner one — a gel.

The cuvette shown in Figs. 9 and 10 is made of a more elastic plastics material than the cuvettes previously illustrated and has a cavity or chamber 16 which — as will appear from the end view in Fig. 10 is defined by outwardly bulging walls which by a mechanical device are compresed to take a predetermined distance from each other in the subsequent analysis. The cuvette according to Figs. 11 and 12 likewise consists of elastic plastics material and has a cavity or chamber 18 with an inlet channel 19. In this case also the walls defining the cavity are compressed in the subsequent analysis. The thickness tolerance of the cuvette material will be decisive of the measuring exactitude both in the former and the latter apparatus, as will the stability of the device by means of which the walls are compressed.

The cuvette shown in Figs. 13 and 14 is also made of elastic material and formed with a cavity or chamber 20 and inlet channel 21 in the same way as the cuvette shown in Fig. 11. But the cuvette in Figs. 13 and 14 has an internal spacing element 22 which can serve to determine the spacing to which the surfaces defining the cavity 20 can be compressed, and to support the reagent. Furthermore, the spacing element 22 may have a mixing function if it is made of ferromagnetic material and mixing is realized by placing the cuvette in a varying magnetic field.

In case the sample drawn into the cuvette is not immediately analysed, or in case the analysis takes a long time, means may be provided to close the outwardly facing open end of the cavity and inlet channel, respectively. Such means may be a plastics head which is pulled over the opening, or a material of suitable consistency into which the cuvette is dipped and which immediately seals the opening.

If desired, the cuvette can readily be provided with means such as projections and recesses which operate measuring equipment in the subsequent analysis.

Measuring cuvettes as described are useful for making analyses of the most varied kinds. It has, however, been found to be of special advantage in the determination of haemoglobin, where it has proved possible to reduce the error margin. If the cuvette has a receiving cavity from which the sample is supplied, by capillary force, to a plurality of chambers containing different solid and/or gel reagents, a large number of analyses can be rapidly made particularly if the cuvette is fed into an automatic measuring apparatus which is controlled by specially designed cuvette parts.

As will appear from the foregoing, the cuvette according to the invention in an extremely simple way permits making analyses which without exception have hitherto been difficult and time-consuming and necessitated great skill of the operator to avoid errors.

WHAT WE CLAIM IS:—

1. A cuvette for sampling a liquid and permitting mixing the sample with a reagent contained within the cuvette and making a direct optical analysis of the sample, which cuvette comprises a body having a chamber containing a reagent and having a capillary sampling inlet for transporting a sample by capillary action from the exterior of the cuvette to the chamber, there being a light path through the chamber defined by a pair of generally opposed, planar, transparent surfaces.

2. A cuvette as claimed in claim 1 wherein the said transparent surfaces are contained in or constitute a pair of flexible walls which in use may be pressed together to provide a predetermined optical path length through the chamber.

3. A cuvette as claimed in claim 2 wherein the chamber contains a spacer to define the optical path length upon compression of the walls.

4. A cuvette as claimed in claim 3, wherein the spacing element also serves as a carrier of the reagent.

5. A cuvette as claimed in claim 3 or claim 4, wherein the spacing element is of ferromagnetic material so as to cause mixing of the sample and the reagent when the cuvette is places in a varying magnetic field.

6. A cuvette as claimed in claim 1 made of a substantially rigid material.

7. A cuvette as claimed in any preceding claim, wherein the reagent is in the form of a solid material deposited in the chamber by evaporation, freeze-drying, spraying or screen printing.

8. A cuvette as claimed in any one of claims 1 to 6 wherein the reagent is in the form of a gel.

9. A cuvette as claimed in any preceding claim wherein the body contains a plurality of chambers, each having a capillary opening, there being a light path through each chamber, each path being defined by a pair of generally opposed, planar, transparent, surfaces.

10. A cuvette as claimed in claim 9, wherein a plurality of the chambers communicate with a receiving space by capillary passages.

11. A cuvette as claimed in claim 10, wherein a plurality of communicating chambers are arranged in parallel or in series.

12. A cuvette as claimed in any one of the preceding claims, wherein the or a reagent is coated to regulate the dissolution rate thereof.

13. A cuvette as claimed in any one of the preceding claims made from transparent plastics material or glass.

14. A cuvette substantially as hereinbefore described with reference to Figs. 1 of the accompanying drawings.

15. A method of analysis which comprises contacting the capillary opening of a chamber of a cuvette as claimed in any preceding claim with a body of sample liquid to fill the cavity, and passing light through the optical path of the chamber to perform an optical analysis of the sample liquid.

16. A method as claimed in claim 15 wherein mixing of the sample and reagent in the chamber is promoted from out-side the cuvette.

17. A method as claimed in claim 15 or claim 16 wherein the analysis is a haemoglobin assay.

Jan Evert Lilja and Sven Erik Lennart Nilsson
Per BOULT WADE & TENNANT,
34 Cursitor Street, London EC4A 1PQ
Chartered Patent Agents.

Printed for Her Majesty's Stationery Office by The Tweeddale Press Ltd., Berwick-upon-Tweed, 1979.
Published at the Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.

As will appear from the foregoing, the cuvette according to the invention in an extremely simple way permits making analyses which without exception have hitherto been difficult and time-consuming and necessitated great skill of the operator to avoid errors.

WHAT WE CLAIM IS:—

1. A cuvette for sampling a liquid and permitting mixing the sample with a reagent contained within the cuvette and making a direct optical analysis of the sample, which cuvette comprises a body having a chamber containing a reagent and having a capillary sampling inlet for transporting a sample by capillary action from the exterior of the cuvette to the chamber, there being a light path through the chamber defined by a pair of generally opposed, planar, transparent surfaces.

2. A cuvette as claimed in claim 1 wherein the said transparent surfaces are contained in or constitute a pair of flexible walls which in use may be pressed together to provide a predetermined optical path length through the chamber.

3. A cuvette as claimed in claim 2 wherein the chamber contains a spacer to define the optical path length upon compression of the walls.

4. A cuvette as claimed in claim 3, wherein the spacing element also serves as a carrier of the reagent.

5. A cuvette as claimed in claim 3 or claim 4, wherein the spacing element is of ferromagnetic material so as to cause mixing of the sample and the reagent when the cuvette is places in a varying magnetic field.

6. A cuvette as claimed in claim 1 made of a substantially rigid material.

7. A cuvette as claimed in any preceding claim, wherein the reagent is in the form of a solid material deposited in the chamber by evaporation, freeze-drying, spraying or screen printing.

8. A cuvette as claimed in any one of claims 1 to 6 wherein the reagent is in the form of a gel.

9. A cuvette as claimed in any preceding claim wherein the body contains a plurality of chambers, each having a capillary opening, there being a light path through each chamber, each path being defined by a pair of generally opposed, planar, transparent, surfaces.

10. A cuvette as claimed in claim 9, wherein a plurality of the chambers communicate with a receiving space by capillary passages.

11. A cuvette as claimed in claim 10, wherein a plurality of communicating chambers are arranged in parallel or in series.

12. A cuvette as claimed in any one of the preceding claims, wherein the or a reagent is coated to regulate the dissolution rate thereof.

13. A cuvette as claimed in any one of the preceding claims made from transparent plastics material or glass.

14. A cuvette substantially as hereinbefore described with reference to Figs. 1 of the accompanying drawings.

15. A method of analysis which comprises contacting the capillary opening of a chamber of a cuvette as claimed in any preceding claim with a body of sample liquid to fill the cavity, and passing light through the optical path of the chamber to perform an optical analysis of the sample liquid.

16. A method as claimed in claim 15 wherein mixing of the sample and reagent in the chamber is promoted from out-side the cuvette.

17. A method as claimed in claim 15 or claim 16 wherein the analysis is a haemoglobin assay.

Jan Evert Lilja and Sven Erik Lennart Nilsson
Per BOULT WADE & TENNANT,
34 Cursitor Street, London EC4A 1PQ
Chartered Patent Agents.

Printed for Her Majesty's Stationery Office by The Tweeddale Press Ltd., Berwick-upon-Tweed, 1979.
Published at the Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.