(1) Publication number:

**0 332 732** A2

(12)

## **EUROPEAN PATENT APPLICATION**

(21) Application number: 88109707.5

(5) Int. Cl.4: B01L 3/14 , G01N 21/78 , G01N 33/48

(22) Date of filling: 17.06.88

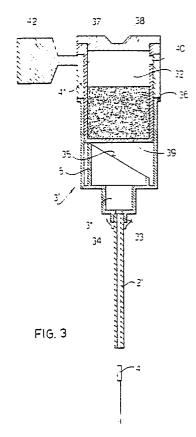
(30) Priority: 15.03.88 IT 19788

Date of publication of application:20.09.89 Bulletin 89/38

©4 Designated Contracting States: **DE ES FR GB IT** 

- 71) Applicant: FINBIOMEDICA S.r.I. Via Mestre, 19/D, I-20132 Milan(IT)
- Inventor: Vicario, Guido Piazza Giulio Cesare, 14 I-20145 Milan(IT)
- Representative: Dr. Ing. A. Racheli & C. Viale San Michele del Carso, 4 I-20144 Milano(IT)
- Device for carrying out photometric and spectrophotometric determinations and chemical microreactions and related prodedure.
- 57) The proposed device consists of a capillary tube (2, 2') with a microcell (3, 3') above it, integral with the tube and having parallel transparent surfaces. The capillary tube (2, 2) may be equipped with a micropiston (4) that can be inserted at its base, to push up the liquid contained in the capillary tube (2, 2') and introduce the desired amount into the microcell. The microcell (3") may be divided into a narrower lower chamber (31) and a wider upper chamber (32); a container (37), with a suitable chemical reagent, the bottom of which (39) can be pierced or cut, may be placed inside said lower chamber. It is also possible to identify the microcell with a label (42) that can be read by a scanner contained in the ◀analyzer and may also carry information on the analysis parameters.

The related sampling and analysis procedure is also described.



## DEVICE FOR CARRYING OUT PHOTOMETRIC AND SPECTROPHOTOMETRIC DETERMINATIONS AND CHEMICAL MICROREACTIONS AND RELATED PROCEDURE

15

25

35

The present invention refers to a device and the related procedure for photometric and spectrophotometric determinations on liquids of any type, such as, for example, sampling and measurement of blood levels of bilirubin in pediatrics, as well as chemical microreactions.

1

Measurement of bilirubin in the plasma of newborns is done essentially by photometric methods, i.e. by illuminating the plasma container, which must be transparent to the radiation used and is generally made of glass, with a photometric lamp.

Devices are already known that allow small amounts of blood to be drawn from the patient, based essentially on the use of a glass capillary tube the bottom end of which is brought into contact with a drop of blood from the newborn. The blood is drawn up into the tube, which has an internal diameter of approximately 1.6 mm., by capillarity. The bottom end of the tube filled with blood is then pressed down on a piece of a substance such as plasticine, about 10 mm thick, so that the plasticine that enters the opening forms a stopper for the capillary tube.

The plasma is subsequently separated from the corpuscular part of the blood by placing the stopped capillary, with its axis horizontal and the plasticine stopper facing outwards, in a centrifuge. In this manner, the corpuscular part of the blood collects near the plasticine stopper, while the plasma phase collects at the opposite end.

At this point the capillary, according to the known method, is disposed vertically, with the plasma in the upper part, and is placed directly on the optical axis of the bilirubinometer, thus acting as a phtometric cell.

This method has considerable drawbacks:

- a) the curve of the cylindrical wall of the capillary tube, together with the inevitable imperfections associated with glass drawing, causes such substantial inaccuracy in the results of the analysis as to be superimposable with biological variability;
- b) the excessive thickness of the liquid to be analyzed, which is five times the optimum thickness for the test (0,25 mm), also contributes to errors in the results;
- c) the considerable thickness mentioned under point b) means that the photometric lamps must have considerable light intensity, which can be obtained by increasing the voltage thus reducing the average lamp life to about 100 h.

A second known device also entails drawing the blood with a glass capillary tube, which is then stopped and centrifuged in a similar way to that indicated above. The capillary tube with the separated plasma and corpuscular part of the blood is then cut with an injection vial saw to divide the two sections, one containing the plasma and the other the corpuscular part. The plasma is then poured into an optical glass microcell with flat parallel sides 0,25 mm apart, so that an optically perfect layer is obtained and the bilirubin can be measured without photometric or methodological errors. The optical system does not require excessive light intensities and thus its life can be up to a hundred-fold that of the preceding system.

However this second device too holds some serious drawbacks:

- 1) it is not always easy to break the capillary and a certain ability and experience are necessary;
- 2) during this operation the operator could cut himself with glass splinters or the vial saw and thus possibly become infected by the newborn's blood:
- 3) horizontal balancing of the section of capillary tube containing the plasma and subsequent pouring into the microcell also require considerable manual ability.

The purpose of the present invention is to provide a sampling device for photometric and spectrophotometric analysis on any type of liquid, such as, for example, analysis of blood bilirubin, capable of overcoming the above problems, i.e. that permits simple, safe drawing of the liquid for analysis, separation of the phases making up the liquid if necessary and accurate analysis.

A further purpose is to provide a device that also permits other analyses on the liquid, involving chemical microreactions, using suitable reagents.

A further purpose is to be able to identify the sampling and analysis device with a suitable code that can be read by a scanner attached to the analyzer, containing, as well as identification of the sample to be analyzed, any information on characteristic analysis parmeters so that this code serves to control all the working parameters of the analyzer (wave length of the light radiation, conversion factors, temperature, duration and intensity of shaking, incubation, times etc.). This means that clinical analyses can easily be carried out not only by specialized analysts, but also by doctors and medical workers who are not experts in laboratory practice.

The main purpose has been achieved by providing a device for sampling liquids, particularly blood, for photometric and spectrophotometric ana-

15

lysis and a related sampling and analysis process as stated in the attached claims 1 and 8.

Further advantageous arrangements, suitable for clinical analyses including chemical microreactions, have been described in claims 2 to 7, 9 and 10

The present invention will now be better described with reference to the accompanying drawings, in which:

fig. 1 is a vertical cross section along line 1-1 in fig. 2 showing a first embodiment;

fig. 2 is a horizontal cross section along line 2-2 in fig. 1;

fig. 3 is a vertical cross section of a second embodiment of the invention in the first working stage;

fig. 4 is a view of the device according to fig. 3 in a later working stage;

fig. 5 is an exploded perspective view of the embodiment in figs. 3 and 4.

With reference to figures 1 and 2, they show the device 1 consisting of a capillary tube 2 and a microcell 3 set above said capillary and integral with it. The microcell 3 has flat parallel surfaces, preferably set 0,25 mm apart. In the bottom part of the capillary tube 2 a micropiston 4 is shown, which can be pushed up inside the capillary tube to the desired height.

The device is operated as follows: the base of the capillary tube 2 is brought into contact with a drop of blood from the patient, which is sucked up by capillarity and reaches a certain height inside the capillary tube. The capillary tube 2 is then pressed down on a 10 mm thick piece of plasticine so that the plasticine enters the bottom opening forming a stopper. The device is then placed with its axis horizontal, with the plasticine stopper facing towards the outside of the centrifuge rotor, and centrifuged, so that the corpuscular part of the blood is separated from the plasma phase. If centrifuging is not necessary, the next step can be performed immediately.

Once separation has been achieved, the device 1 is placed with its axis vertical again, then the liquid contained in the capillary tube 2 is pushed upward by pressing the capillary down repeatedly on a piece of plasticine, which forms successive stoppers that gradually reach up higher into the capillary 2, or by inserting at the base of the capillary tube a micropiston 4 of plastic material connected to an electronically controlled motor, said piston being inserted to the desired height.

The plasma, stratified in the top part of the capillary tube 2 and pushed by the micropiston 4, thus enters the microcell 3, which can be subjected to photometric analysis with low intensity lamps, giving highly accurate results thanks to the reduced

thickness and perfect flatness of the walls 3a and 3b of the microcell 3.

Figure 3 shows a similar device to the one in the preceding figures, in which analogous components to those already described have been designated by primed numbers, with the sole difference that a piercing element 5 is inserted in the microcell 3', preferably positioned centrally with respect to the hole in the base of the microcell, which connects the microcell to the capillary tube 2'. The capillary tube 2', the bottom end of which can be inserted into a container 30 of any shape containing the liquid to be drawn, is connected at its top end to the microcell 3'.

This consists of two superimposed communicating cubic areas. The lower one 31, smaller in volume, will have thin transparent walls, parallel and facing each other, allowing optical measurements to be made perferctly. The upper area 32, larger in section, demarcates an upper chamber 32, symmetrical with the lower chamber 31. The lower chamber 31 ends in a cylindrical narrowing forming a neck 33 into which the capillary tube 2' is inserted. The connection and seal between the neck and the capillary tube are guaranteed by an elastic sheath 34, having a clindrical shape and variable diameter, the top of wich encloses the neck 33 and the bottom the capillary tube 2. This elastic sheath 34 serves as the connection for the arm of a mechanical shaker designed to shake the liquids inside.

At the bottom of the upper chamber 32 is set a piercing element 5 consisting, for example, of a cylindrical element 11 the top edge of which is cut slantwise 35.

A container 37 can be inserted into the upper chamber 32 from above, the base 39 of said container already being prepared for cutting and piercing; the outside diameter of the container 37 is slightly smaller than the inside diameter of the upper chamber 32. The desired chemical reagent in the desired physical state (liquid, solid) can be placed inside the container 37. The container 37 is provided with a stopper 38 and a vent-hole 40, initially closed by a tear-off seal 41. The circumference of this seal extends beyond the vent-hole 40 and rests on a ledge formed by a further projection 36 of the upper chamber 32. The tear-off seal 41 also has a tab 42 bearing codes that can be read by a scanner belonging to the analyzer and contain identification of the specimen for analysis, as well as all information concerning the parameters that the scanner must read for the analysis to be performed correctly.

Once the liquid to be analyzed has been pushed up inside the capillary tube 2 to the desired height, by one of the methods described earlier, and the chemical reaction is to be started, the tear-

55

10

35

45

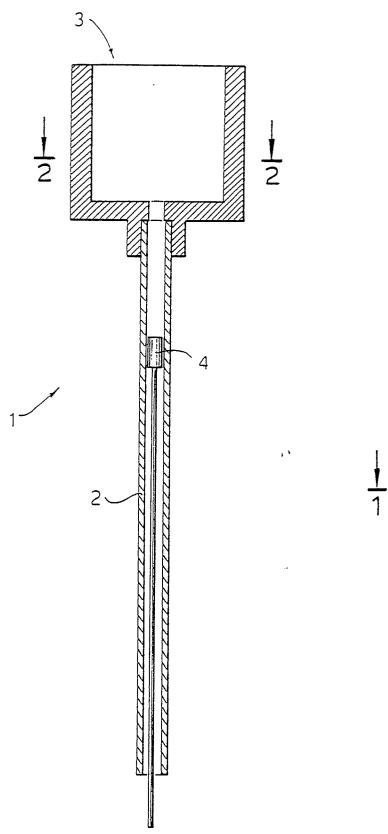
off seal 41 is removed, upon which air can enter the container 37. This container can be pushed downward, manually or automatically, until its base 39 is pierced by the cutting edge 35 and the walls of the container 37 descend to occupy space 36. The chemical reagent is thus mixed with the liquid to be analyzed contained in the cell 3 and reacts. By resting on the top edge of the upper chamber 32, the tear-off seal 41 prevents the container from being accidentally inserted into the microcell during transport or handling and its base 39 thus being cut. The arm of a shaker sets the elastic neck 34 in vibration to mix the reagent and the specimen, so that after the time required for the reaction, measurement can be carried out in the cell 31.

phases, is pushed upwards in the capillary tube until a sufficient amount of liquid or phase of the liquid has entered said microcell (3, 3).

- 9. A procedure according to claim 8, characterized in that the chemical reagent is put into a container (37) set inside the microcell (3', 3") and that this reagent is brought into contact with the liquid to be analyzed by breaking the container (37).
- 10. A procedure according to claim 8 or 9, characterized in that the specimen to be analyzed is identified by a code that can be read by a scanner attached to the analyzer, it being possible for said code to carry information regarding the analysis parameters.

## Claims

- 1. A device for carrying out photometric and spectrophotometric determinations as well as chemical microreactions in liquids of any type, comprising a capillary tube (2, 2') for drawing the liquid to be analyzed, characterized in that one end (2a) of said capillary tube is sealed to a microcell (3, 3') having at least two flat transparent parallel surfaces (3a, 3b).
- 2. A device according to claim 1, characterized in that the capillary tube (2, 2') is equipped with a micropiston (4) of plastic material that can be inserted into said capillary tube to the desired height.
- 3. A device according to any of the preceding claims, characterized in that a breakable container (37) containing a suitable chemical reagent is inserted into the microcell (3, 3').
- 4. A device according to any of claims 1, 2 and 3, characterized in that the microcell (3') is divided into two chambers, an upper chamber and a lower chamber.
- 5. A device according to claim 3 or 4, characterized in that the microcell (3') is equipped with means (35) for breaking said container (37).
- 6. A device according to any of the preceding claims, characterized in that a tab (42) is connected to the microcell (3, 3'), bearing a code that can be read by a scanner attached to the analyzer that identifies the microcell and can contain information regarding the analysis parameters.
- 7. A device according to claim 6, characterized in that the tab (42) is connected to the microcell by means of a breakable tear-off system.
- 8. A sampling procedure for liquid, in particular blood, for photometric and spectrophotmetric analyses, that provides for the liquid to be drawn by capillarity into a capillary tube (2, 2') which is then stopped and, if necessary, centrifuged, characterized in that the capillary tube is made fast with a microcell, that the liquid, possibly separated into



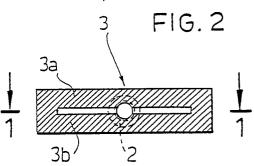


FIG. 1

