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(54) Title: INTEGRATED COLLECTION AND ASSAY DEVICE FOR SALIVA AND BLOOD (57) Abstract Devices are described herein which combine an integrated diagnostic strip and an attachment for the collection of saliva or the collection of blood. In the preferred embodiment for collection and testing of saliva, the integrated collection and assay device includes a collapsible funnel shaped saliva collector, a saliva processing pad and one or more diagnostic assay strips. The collector, pad, and assay strips are in fluid communication with each other, thereby permitting capillary flow of saliva from the funnel to the assay strips. The device can be used for collection of blood in the same manner as the saliva. In the embodiment of the device for the collection and analysis of a blood sample, a needle and needle receptacle are attached to the strip to allow collection and direct application of blood to the strip, avoiding any contact by the party collecting the blood. Assay strips can be incorporated into the collection device, as well as an absorbant pad or filter to remove unwanted tissue or red blood cells from the sample.		

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INTEGRATED COLLECTION AND ASSAY DEVICE FOR SALIVA AND BLOOD

Cross Reference to Related Application

This application claims priority to provisional patent application
5 Serial No. 60/055,254 filed on August 4, 1997.

Field of the Invention

The present invention is in the field of diagnostic devices, and
more particularly in the area of a device for both collection and analysis
of a biological fluid such as saliva or blood.

10 Background of the Invention

Immunochromatographic assays using a membrane as a solid
support in a dipstick or flow through device are established for use in the
clinical laboratory as well as for "field" use, *i.e.* use outside of the clinic.
Assays using this type of format are available for abused drugs (cocaine,
15 cannabinoid, amphetamine, etc.), pregnancy and fertility testing (hCG and
hLH), and infectious diseases (chlamydia, streptococcus, infectious
mononucleosis). These existing chromatographic assays are typically
designed and used to analyze blood and urine.

It is preferable in some situations to conduct analysis on a saliva
20 sample rather than on blood or urine. When applicable, saliva testing of
certain small analytes has several advantages over blood or urine analysis.
Specimen collection is non-invasive and painless. A saliva specimen can
be taken at any convenient time, and can be obtained singly or
sequentially, if desired, to establish individualized analyte profiles or to
25 adjust drug dosages. Moreover, saliva sampling may be done at any
location and can be easily observed, if required. Saliva, unlike plasma or
serum, contains few binding proteins and permits measurement of the free
or biologically active analytes.

However, saliva also has several attendant problems. To many
30 individuals, saliva is visually repugnant and its handling is undesirable.
Saliva may be viscous or foamy; hence it is frequently difficult to

dispense or transfer saliva to a receptacle during sampling, particularly with any degree of accuracy. For example, it is difficult to control sample sicking of fresh samples onto a chromatographic membrane. Saliva contains numerous microorganisms and enzymes that can rapidly
5 putrefy the specimen unless stabilized or inhibited with effective preservatives to permit shipment or mailing in existing saliva collection devices. It is difficult and timely to collect more than 0.5 ml of saliva. Saliva generally is processed before use in an immunoassay to remove particulate and soluble mucopolysaccharide constituents. It is difficult to
10 pipette or measure before processing by filtration or centrifugation and a large amount of the specimen may be lost in handling. Specimen processing is obviously costly and time consuming.

Urine is frequently not an acceptable alternative. The urine levels of many analytes do not correlate with blood levels and are subject to
15 variable urine dilution due to patient hydration status and/or tampering, requiring referencing to another analyte, e.g. urinary creatinine. Urine has the additional problem that the sample is usually only collected in private, raising security and handling issues. Blood collection for analysis also presents disadvantages, such as the pain involved in needle
20 sticks and the inherent dangers associated with any use of needles.

Existing devices for collecting and testing of saliva do not fully solve the problems outlined above. There is a need for a device for collection of sample that also serves as the diagnostic device. This is especially a need as diagnostic testing moves from the laboratory to the
25 field where testing will be done by persons not experienced or trained in diagnostic test or sample collection procedures.

Summary of the Invention

Devices are described herein which combine an integrated diagnostic strip and an attachment for the collection of saliva or the
30 collection of blood. In the preferred embodiment for collection and testing of saliva, the integrated collection and assay device includes a collapsible funnel shaped saliva collector, a saliva processing pad and one

or more diagnostic assay strips. The collector, pad, and assay strips are in fluid communication with each other, thereby permitting capillary flow of saliva from the funnel to the assay strips. The device can be used for collection of blood in the same manner as the saliva.

5 In the embodiment of the device for the collection and analysis of a blood sample, a needle and needle receptacle are attached to the strip to allow collection and direct application of blood to the strip, avoiding any contact by the party collecting the blood. Assay strips can be incorporated into the collection device, as well as an absorbant pad or
10 filter to remove unwanted tissue or red blood cells from the sample.

Brief Description of the Drawings

Figures 1a and 1b illustrate a first embodiment of the device for the collection and analysis of a saliva sample. Figure 1a is an elevational view and Figure 1b is a top plan view of the device.

15 Figures 2a and 2b illustrates a second embodiment of the device for the collection and analysis of a blood sample.

Detailed Description of the Invention

There is a need for convenient, efficient and cost effective assay devices for the measurement of analytes present in either blood and
20 saliva. The use of such combination devices with saliva would overcome public aversion and fear of drawing blood as well as problems due to undesirable matrix and nonspecific binding effects commonly encountered in the analysis of small hydrophobic analytes in blood, plasma or serum. The devices disclosed herein overcome the inherent problems with
25 collection of saliva specimens. It is furthermore suitable for both on site interpretation by the patient in the case of simply visual assay systems or for mailing of the completed test to a testing lab for instrumental quantitation and interpretation in the case of more complex assays or test panels requiring evaluation of individualized patient profiles. The same
30 device can therefore be used for a universal home, office, or lab test.

Saliva Collection Device

Briefly, the integrated collection and assay devices include a fluid collector, a processing and metering pad and/or filter, and one or more assay strips. The fluid collector can be adapted for collection of saliva or blood. The assay strips can be any type presently used. Nitrocellulose is a preferred material. Preferably, the assay strips are laminated dipsticks such as described in U.S. Patent No. 5,500,375, the disclosure of which is incorporated herein by reference.

A preferred embodiment of the device is illustrated in detail in Figures 1a and 1b. The device 10 includes holder 12 having a stem portion 14 and a funnel portion 16. In one embodiment, the holder 12 can be a double sheet of plastic that is laminated together at the stem portion, as described further below. For example, the holder can be made of polyethylene or another clear, flexible plastic. The funnel portion 16 is sealed on the edges to form lateral seals, 18 and 20, that extend down the stem portion 14. Thus, an open top collection "funnel" is formed in the funnel portion 16, which is in fluid communication with the stem portion 14, as shown from the top view in Figure 1b.

At the neck 22 of the device 10, or the juncture of the funnel portion 16 and stem portion 14, is the processing and metering pad 24. Pad 24 is preferably an absorbent pad or sponge which serves to filter oral debris and mucopolysaccharides from the sample. It can be formed of any suitable material, preferably of a fibrous nature, most preferably a material such as a cellulose or cellulose derivative. In some embodiments, the material may be charged or contain substances which effect separations or passage through the filter. For example, the pad may also contain buffers and reagents such as dissociating or mucolytic agents and surfactants which may be required. The pad further serves to meter the amount of sample which is transferred to the assay strip. This is accomplished by selection of the size, shape, porosity and composition of the pad, which can be adjusted as necessary to optimize separation and metering of sample volume.

The device includes one or more assay strips. These may be of the same or different materials, providing for measurement of multiple analytes in the sample. As shown in Figure 1a, assay strip 26 extends from the pad 24 into stem portion 14. Assay strip 26 includes carrier 28 which supports thereon membrane 30, which is in liquid communication with pad 24. Assay strip 26 can be any chromatographic assay strip but is preferably designed as described in U.S. Patent Nos. 5,500,375 and 5,710,009, the disclosures of which are incorporated herein by reference. In the preferred embodiment, membrane 30 is a nitrocellulose strip which includes sample application region 32, adjacent to the processing or metering pad 24. The membrane 30 further includes a mobilization zone 34, having immobilized thereupon mobilizable labelled reagent, for example. The membrane also includes one or more trap zones. Three are shown in Figure 1a as 36, 38, 40, which contain various reagents for capturing unreacted analyte or labelled analyte, for example, depending upon the design of the assay. In this preferred embodiment, the membrane further includes one or more detection zones which may be the same as one or more of the trap zones. The section of holder 12 overlying the detection zones is preferably clear so that the results of the assay can be read.

A major advantage of this device is the capability of holding more than one test strip, thus permitting correction for saliva dilution by referencing to another saliva constituent, *e.g.* creatinine, or to another relevant analyte, *e.g.* HDL/LDL ratio. For example, in one embodiment, device 10 includes more than one assay strips in the form of dipsticks, for example, up to about six, where there are three on each side mounted back-to-back.

The holder 12 surrounding the assay strip 26 is preferably laminated to seal the assay strip within the holder in an air tight and substantially liquid tight manner. The collapsible funnel shaped saliva collector, processing pad and one or more laminated dipsticks are all in communication with each other, thereby permitting capillary flow of

saliva from the funnel to the detection sites on the dipsticks followed by visual or instrumental detection or quantitation of one or more analytes. An advantage of this device is that the strip can remain funnel up or lying down during and following sample collection. In the latter case, the

5 laminated strip allows the wicking of saliva in the downward position, *i.e.* with the force of gravity. The assay times in these positions are decreased by as much as one half of the time required when the strip is in a vertical position. The strip is also protected in the horizontal

10 (downward) position from flooding because it is laminated or has some other form of seal which controls flow along the surface of the membrane rather than transversely through the pores of the membrane.

In another embodiment of the device, not shown in the Figures, a capillary tube serves as the collection means rather than the funnel of the first embodiment. This allows placement of the collection means directly

15 into the mouth so that saliva can be funneled into the absorbent filtering pad and from thence to the chromatographic assay strip of the device. This embodiment can be constructed shaped either like a conventional thermometer type device or in an inverted "J" shape such that the short end of the "J" is inserted into the mouth and the long arm hangs out of

20 the mouth in an upside down configuration. In this configuration, the assay can be conducted faster because the fluid is moving down hill with the aid of gravity.

Integral to performance of the unitary saliva test device, if it is run in the upside down position, is the ability to limit access of the fluid to

25 the chromatographic region by using the filtering and metering pad.

Method for Saliva Collection

The device is held vertically to collect a saliva specimen, and the saliva specimen is directly deposited into the funnel. The saliva sample contacts the pad which filters the sample and meters its application to the

30 membrane. More than one dipstick can be accommodated, either side by side or back to back. The flow of saliva into and on the dipstick membrane, and thus the assay time, can be controlled by the porosities of

the pad and the dipstick membrane. Lamination of the dipstick membrane further controls the fluid flow and restricts channeling at the sides and above the surfaces of the dipstick membrane.

- 5 The assay commences during saliva collection and continues until the test is done. This may require five to ten minutes. The volume of the specimen which will be deposited will typically be between about 0.1 to one ml, depending on the number of dipsticks. After completion of the test, the results may be read visually and interpreted by the user, and the entire device disposed of, without any direct handling of the specimen.
- 10 Alternatively, for quantitative evaluation or more complex interpretations, the unit may be placed in a sealed container and sent to a testing lab for further analysis, for example, for reading in a reflectometer when in the diagnostic strips include stable reagents such as chromatophors.

Blood Collection Device

- 15 In another embodiment of a collection device, the device includes handling means that facilitate collection of a blood sample. Using this device, the sample can be collected in a relatively painless manner from a region such as the ear lobe. As shown in Figures 2a and 2b, the device includes a flexible strip 52 having stirrups 54, 56 for a thumb (54) and
- 20 a finger (56) at opposing ends. The strip is preferably made of a flexible plastic such as polyethylene, or a fibrous material. This can be used with any standard assay collection device, or the funnel device described above, where tissue, hair or even red cells can be filtered out in the pad
- 24.

- 25 A very short needle or sharp point 58 for breaking the skin, hereafter called the "sharp" is supported upon the strip 52, shown at the "thumb" end 54 in Figure 2b. A variety of different materials can be used to form the sharp, including metal, glass, plastics, and organic materials. In a preferred embodiment the "sharp" is a hard crystal such
- 30 as a sugar so that it cannot cause a problem should it somehow be released into the body of either the tester or testee.

On the opposing end of the strip, on the "finger" end as shown in Figure 2b, is an impervious surface 60 that protects the thumb and finger from the needle. This surface 60 is cup shaped so that the male end or "sharp" of the snap is guided to the center. This receptacle may accept
5 the sharp and snap it off so that the strip becomes unable to break skin after one use. The impervious material is formed of a rigid plastic or metal surface.

The snap pieces, the sharp and the impervious surface, can be attached to the strip using standard techniques, such as an adhesive, or in
10 the same way that a snap is attached to a piece of cloth, *i.e.* they can consist of two pieces of metal or plastic, one on either side of the strip but having interdigitating pieces such that each piece stabilizes the other. Alternatively, the strip can consist of a material such as a plastic which is formed by a combination of extrusion molding and/or die cutting.

15 An assay strip 64 such as one described above for the first embodiment can be supported upon either the top or bottom surface of and laminated to the strip 52. Assay strip 64 is not limited to particular embodiments but preferably is a laminated strip such as those described above with respect to the first embodiment. An inherent advantage of the
20 use of a laminated strip in the device is that lamination of an approximately five micron pore membrane retards the migration of red blood cells sufficiently to eliminate the need for red blood cell separation. Red blood cells can be prevented from lysing by the presence of detergent and various pressures.

25 An absorbent pad 66 adjacent the sharp 58 is in fluid communication from the sharp 58 to the assay strip 64 can be used to filter the sample similarly to the way the pad 24 performs in the first embodiment.

Method for Collection of Blood

30 The flexible strip is held between the thumb and forefinger similarly to how one holds forceps to collect blood. When the thumb and forefinger are brought together with the tissue from which the sample is

to be obtained, for example, a fold of skin, or a thin section of an ear such as the earlobe, the needle on one end of the strip breaks the skin and blood is pressed onto the adjacent absorbent material. The absorbent pad may be on the same end as the sharp or on the other end. In any case it
5 is sufficiently in contact with the sharp to absorb the amount of blood required for testing.

It may be equally efficacious to insert the strip with a sharp (sugar crystal) into the jaws of a toothless staple like device that can be closed with sufficient pressure to cause the sharp to break the skin and release
10 sufficient fluid onto the strip for the diagnostic test.

This blood collection device is particularly useful for quantitative testing, since quantitative testing depends very much on controlling the sample (blood) volume being tested.

The teachings of the references cited herein are specifically
15 incorporated herein. Modifications and variations of the present invention will be obvious to those skilled in the art from the foregoing detailed description and are intended to be encompassed by the following claims.

What is claimed is:

1. A saliva collection device comprising
a collapsible funnel shaped saliva collector,
a saliva processing pad, and
one or more diagnostic assay strips,
wherein the collector, pad, and assay strips are in fluid
communication with each other, thereby permitting capillary flow of
saliva from the funnel to the assay strips.
2. The device of claim 1 wherein the device is formed of an
integral flexible plastic material.
3. The device of claim 1 wherein the device include diagnostic
assay strips for detection or measurement of multiple analytes.
4. The device of claim 1 packaged in a sealed container for
transport or disposal.
5. A collection device comprising
unitary means having positioned thereon a needle and needle
receptacle,
wherein the needle and needle receptacle are opposably positioned
to allow contact of the needle with the needle receptacle through a portion
of tissue or skin to obtain a sample of a body fluid such as blood, and
means for holding the needle and needle receptacles in opposition
to provide contact of the needle through the portion of tissue or skin with
the needle receptacle.
6. The device of claim 5 wherein the device further comprises
diagnostic assay strips for detection or measurement of analyte in the
sample of body fluid.
7. The device of claim 6 further comprising filter or
absorbent means to separate materials in the sample of body fluid prior to
contact with the diagnostic assay strips.

8. The device of claim 6 further comprising a funnel shaped collection device to direct the sample of body fluid to the diagnostic assay strips.

9. A method for collection and analysis of saliva comprising providing for an individual to spit into a saliva collection device comprising

a collapsible funnel shaped saliva collector,
a saliva processing pad, and
one or more diagnostic assay strips,
wherein the collector, pad, and assay strips are in fluid communication with each other, thereby permitting capillary flow of saliva from the funnel to the assay strips.

10. A method for collection of a body fluid such as blood comprising providing a collection device comprising

unitary means having positioned thereon a needle and needle receptacle,

wherein the needle and needle receptacle are opposably positioned to allow contact of the needle with the needle receptacle through a portion of tissue or skin to obtain a sample of a body fluid, and

means for holding the needle and needle receptacles in opposition to provide contact of the needle through the portion of tissue or skin with the needle receptacle,

applying the needle and needle receptacle to opposite sides of a portion of tissue or skin, and

pressing the needle towards the needle receptacle until the needle contacts the needle receptacle.

11. The method of claim 10 wherein the body fluid is blood.

12. The method of claim 10 wherein the device further comprises a filter or absorbant pad to separate sample from tissue or other materials after collection and diagnostic assay strips, wherein the pad is in fluid connection with the assay strips.

1/2

FIG. 1A

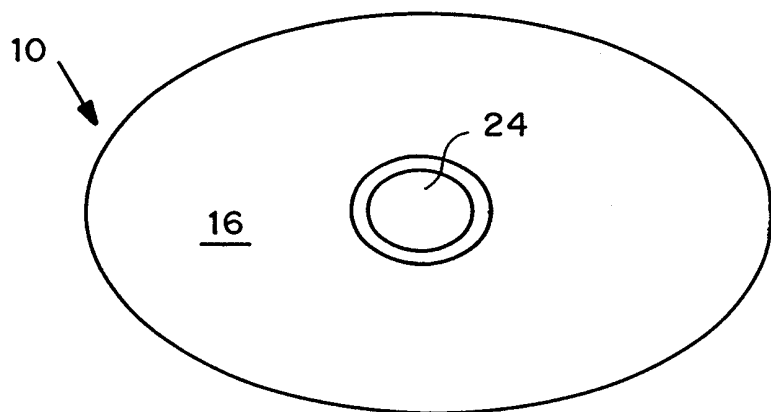
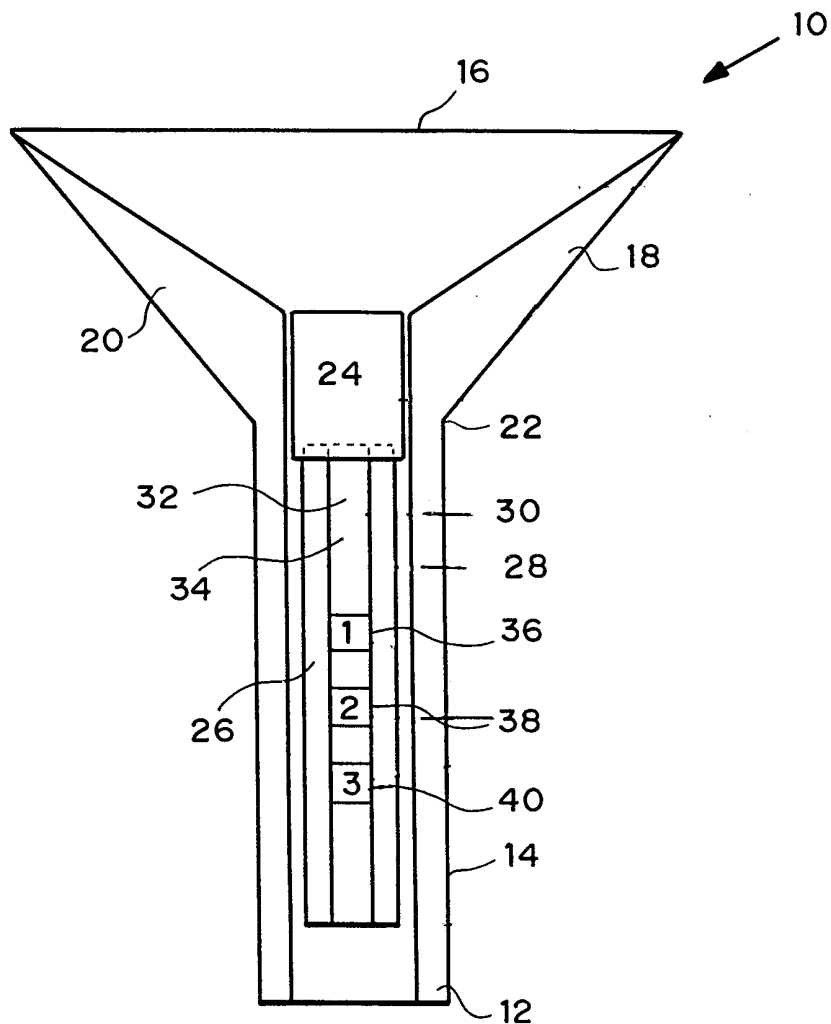
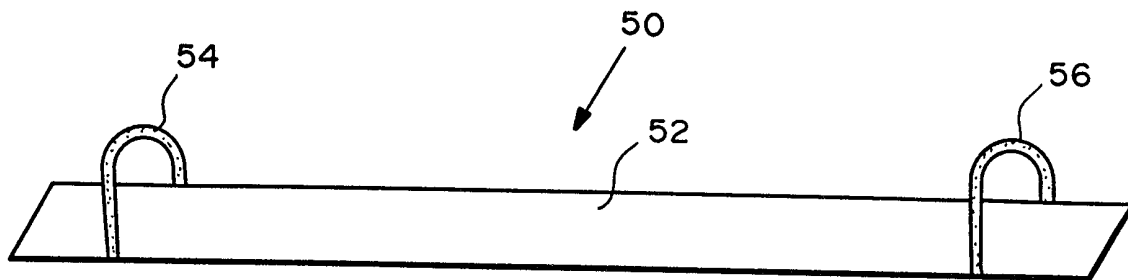


FIG. 1B

FIG. 2A*FIG. 2B*