

Description

This invention relates to improved chromatographic strips and methods of preparing them. The improved chromatographic strips of the invention are useful in analytical chromatography, particularly as immunochromatographic strips.

A number of materials are known for use as chromatographic strips. Generally, the material is "bibulous" or "porous," comprising a random or oriented pile of fibers such as found, for example, in cellulose, fiberglass, woven cloth, cotton, polyester, etc., and the like. The preferred material is paper, which is a random pile of cellulose fibers. The tortuous interstitial and interconnected capillaries of such a random pile of fibers create both a drive for and a resistance to a mobile phase, which, in a chromatographic system, traverses at least a portion of the strip. The mobile phase is generally a liquid medium, most usually solvent. The transfer of the mobile phase to channels within the random pile, which channels have ever smaller diameters, provides the free energy gradient to drive the mobile phase through the medium. Dead end pores trap the mobile phase and limit its traversal of the chromatographic strip.

The chromatographic strips are normally prepared from larger sheets from which they are cut by mechanical means. The most widely used form of mechanical cutting involves a blade or wire.

Mechanical cutting of the sheet into strips results in a deformation of the edge of the strip along the cutting line. This deformation takes the form of a compression of the edges of the strip. The fibers which form the strip, when cut mechanically, are pushed closer together at the cut edges when compared to the distance between the fibers in the body of the strip. This deformation of the edges of the strip frequently results in a faster rate of traversal for the liquid medium at the edges of the strip than through the body of the strip. The fronts of components traversing the strip become concave rather than flat.

In many situations employing a chromatographic strip it is important that the shape of the front of the traversing component be flat. In analytical and preparative chromatography, it is usually preferable to have a flat front. An example of such a situation is affinity chromatography. In such a test antibodies are attached to a porous insoluble support. During migration of an antigen-containing solution on the porous support, the migration of the antigen solute is specifically delayed in comparison to the migration of the solvent and other solutes. The relative delay decreases with increasing antigen concentration. Accurate quantitations of the concentration of analyte in a sample to be analyzed requires that the position of the analyte front relative to the solvent front be measured accurately. The position of a flat front can usually be measured with greater precision and accuracy than that of a

concave front, and a higher degree of accuracy is thereby obtained in a chromatographic assay. Moreover, in preparative chromatography a linear front permits more ready separation and isolation of the pure component.

U.S. Patent No. 4,168, 146 describes an immunoassay employing immunochromatography with antigens followed by contacting the immunochromatograph with an aqueous solution containing labelled antibodies. An enzyme chromatographic immunoassay is described in U.S. Serial No. 398,505, filed July 15, 1982.

EP-A-0157525 which is part of the state of the art by virtue of Art 54 (3) EPC discloses a chromatographic device in which a longitudinal edge of the material is provided with means such as indentations or a chemical substance for controlling the shape of the solvent front.

The present application discloses a device for use in a chromatographic system wherein a component of a mixture is partitioned between a liquid phase and an immobile phase. The device comprises at least one strip of a bibulous material. In the chromatographic system the component in a mobile phase, usually in a liquid medium, traverses at least a portion of the strip. The strip has a longitudinal edge that comes in contact with the traversing component during the chromatographic process and that lies in a direction substantially corresponding to the direction of traverse of the component. The longitudinal edge has the characteristic of substantially the same rate of traversal of the component along this edge when compared to the rate of traversal of the component along the body of the strip. The longitudinal edge has substantially the same degree of deformation as the body of the strip. Thus, the present device has the characteristic that the front of the traversing component remains substantially flat over the traversed portion of the strip. The device of the invention is prepared by a non-compressive or non-deformative cutting of a sheet of bibulous material into strips. Such non-compressive cutting may be achieved, for example, by cutting the sheet of bibulous material with a laser beam.

In the drawings:

Fig. 1 is a depiction of immunochromatographic strips prepared by mechanical cutting of the prior art, which strips have been utilized in an immunochromatography.

Fig. 2 is a depiction of immunochromatographic strips prepared in accordance with the present invention, which strips have been utilized in an immunochromatography.

The benefits of the present invention may be achieved by cutting a sheet of bibulous material into chromatographic strips employing means that do not compress (non-compressive) or deform (non-deformative) the longitudinal side edge of said strip. By the term "non-compressive" or "non-deformative" is meant that the cutting does not substantially distort the cut edges of the strip when compared to the body of the strip or when compared to edges cut by

compressive cutting means. That is, the relationship of the pores within the bibulous material is substantially the same near the cut edge as it is in the body of the strip. The pores are not compressed near the cut edge as the pores are near the edge cut by compressive cutting means.

The preferred means for achieving non-deformative or non-compressive cutting of sheet of a bibulous material to produce chromatographic strips in accordance with the present invention is a laser beam. Laser cutting devices are well known in the art and are discussed in, for example, "Laser in Elektroniktechnologie und Materialbearbeitung" by M. Nowicki (1982) pp 125-138.

The parameters for cutting the sheets, such as intensity of the laser beam, the speed of cutting, and the like will be interdependent and will also depend on the nature of the bibulous material, the thickness of the bibulous material, the ultimate use of the chromatographic strips, and so forth. In general, the cutting parameters will be sufficient to cut the sheet of bibulous material but insufficient to produce significant deformation or compression of the cut edges which would result in accelerated traversal of the liquid medium along the side edge of the strip when compared to the rate of traversal of the liquid medium along the body of the strip or when compared to the rate of traversal along an edge cut by compressive means.

The following are parameters for cutting paper having a thickness from about 0.05 to 2 mm, which parameters are provided by way of example and not limitation.

The energy of the laser beam will be from about 5 to 350 watts CW (continuous wave), preferably from about 50 to 100 watts CW. The cutting speed will depend upon the intensity of the laser beam and should be adjusted, where appropriate, to minimize discoloration of the bibulous material. The cutting speed is adjusted to maintain optimal cut edge quality. At an intensity of the laser beam of about 50 watts CW the cutting speed generally will be from about 5-50 centimeters per second, preferably from about 20-25 centimeters per second. The particular energy and cutting speed to be employed in a specific situation may be easily determined by those skilled in the art keeping in mind the above teaching.

Where discoloration of the chromatographic material might occur during the laser cutting operations an air pressure stream may be focused on the area of the sheet being cut. In general, the pressure of the air stream should be sufficient to reduce any discoloration of the chromatographic material and should not interfere with the cutting operation. The pressure may vary from about 20 to 100 psig, preferably from about 50 to 70 psig.

The non-deformative cutting method of the present invention may be applied to all types of bibulous materials which find use in chromatographic systems. Chromatographic material means a material susceptible to traversal by a mobile

material, either a solvent or a solute (traversing component) in response to capillary force, gravitational force, electrostatic force, positive pressure, or the like. Such materials include inorganic powders such as silica, magnesium sulfate, and alumina; natural polymeric materials, particularly cellulosic materials, such as fiber containing papers, e.g., filter, paper, chromatographic paper, etc.; synthetic or modified naturally occurring polymers, such as nitrocellulose, cellulose acetate, poly (vinyl chloride), polyacrylamide, cross linked dextran, agarose, polyacrylate, etc.; either used by themselves or in conjunction with other materials; ion exchange resins; ceramic materials; and the like.

The chromatographic strips are generally prepared from sheets of uniform thickness of the bibulous material. The strips may have a variety of thicknesses, usually from 0.05 to 2 mm, preferably 0.1 to 0.5 mm, and may vary in shape usually being rectangular, square, oval, or circular, preferably rectangular. The particular dimensions and shape will be determined by the chromatographic method in which the strips will be employed, normally having a maximum width, perpendicular to the flow, of less than 30 cm and a maximum length, parallel to the flow, less than 40 cm; more frequently a maximum width of 2 cm and a maximum length of 15 cm, preferably a maximum width of 1 cm and a maximum length of 10 cm. All that is required in the present invention is that the strip have at least one longitudinal edge generally corresponding to the direction of flow of the traversing component. Longitudinal edge intends a border of the chromatographic material and is the boundary where the material begins or ends. The structure of the bibulous material may be varied widely and includes fine, medium fine, medium, medium coarse and coarse. The surface may be varied widely with varying combinations of smoothness and roughness combined with hardness and softness. The chromatographic strip may be used independently or it may be supported by a variety of inert supports. Exemplary of such supports are Mylar®, polystyrene, polyethylene, or the like.

Chromatographic strips prepared in accordance with the teaching contained herein find particular use in affinity chromatography, for example, immunochromatography. Immunochromatographic methods comprise any number of different specific embodiments. The general characteristics of an immunochromatographic method are that an antigen or antibody is immobilized on the chromatographic material and the complementary binding partner, antibody or antigen, in a liquid medium traverses a portion of a strip of the bibulous material.

Exemplary of an immunochromatographic method is the immunoassay disclosed in U.S. Patent No. 4,168,146 (herein incorporated by reference in its entirety). The disclosed method is based on utilizing strips of a porous carrier material having antibodies bound to it. In the method a portion of each of the strips is contacted

with an aqueous sample containing the antigen to be quantified. Capillary migration is allowed to take place. The antigen-containing area of the strip is detected by wetting it with antibodies in an aqueous vehicle. The antibodies are normally bound to a signal producing system such as, for example, a water soluble fluorescent color indicating compound or to an enzyme that catalyzes a color-developing reaction.

Another immunochromatographic method is disclosed in European Patent Application No. 83304094.2 filed July 14, 1983 (EP 0100619).

The disclosed method allows detection of an analyte in a sample where a quantitative determination may be readily made without special equipment. The sample is immunochromatographed on a bibulous carrier to which is conjugated a specific binding partner for the analyte. The immunochromatography may be conducted in the presence or absence of a labelled conjugate. The label is a member of an enzymatic signal producing system, which includes one or more enzymes. After chromatographing the samples, if the labelled conjugate was not included in the sample, the chromatograph is contacted with a labelled specific binding pair member which binds to the chromatograph in relation to the distance travelled by the analyte in the sample. By providing appropriate reagents to produce a detectable signal, e.g., two enzymes where the substrate of one enzyme is the product of another enzyme, a final product is produced which provides for a detectable signal. In such a case the distance travelled by the analyte may be defined, which distance is related to the amount of analyte in the sample.

The present invention, therefore, comprises a diagnostic device for use in immunoassays. The diagnostic device comprises a bibulous material providing liquid travel through capillarity and at least one non-diffusively bound member of a specific binding pair ("mip"). The device may also include one or more members of a signal producing system. Generally, the analyte to be measured is a mip selected from the group consisting of ligand and receptor. The ligand and receptor are related in that the receptor specifically binds to a polar and spacial organization of the ligand, being able to distinguish the ligand from other compounds having similar characteristics. The signal producing system member, for example, may be an enzyme or a fluorescent compound. Generally, the immunochromatographic strip contains a plurality of mips attached thereto. The thickness of the immunochromatographic strip will generally vary from about 0.05 mm to about 2 mm, more usually being about 0.1 mm to 0.5 mm, preferably from about 0.2 mm to about 0.4 mm. Usually, the strip will have a width of from about 2 to 12 mm, preferably from about 3 to 8 mm, and will have a length of from about 20 to 250 mm, preferably from about 30 to 150 mm.

Methods for binding a wide variety of materials to a bibulous support are found in the literature. See for example, U.S. Patent No. 4,168,146. The

amount of a mip which is bound to the bibulous material will vary depending upon the size of the immunochromatographic strip and the amount required to bind the homologous mip. Generally, the amount of mip will range from about 10^{-5} to 10^{-15} moles per square centimeter, more usually from about 10^{-7} to 10^{-12} moles per square centimeter. The number of moles per unit area will be varied in order to insure that there is sufficient modification of the distance traversed by the traversing component along the affinity chromatographic strip within the concentration range of interest.

Also included within the scope of the present invention are diagnostic kits which comprise (1) at least one chromatographic strip prepared in accordance with the present invention to which is attached a member of a specific binding pair, (2) a member of the specific binding pair conjugated to a member of a signal producing system, and (3) any other members of the signal producing system as well as any buffers or the like for conducting an affinity chromatographic assay.

The following examples, although not within the scope of the claims, are illustrative of the way in which the present invention may be carried out.

The following abbreviations are used hereafter: HRP — horse radish peroxidase; NHS — N-hydroxy succinimide; EDAC — ethyl dimethylaminopropyl carbodiimide; DMF — dimethyl formamide; BSA — bovine serum albumin. Temperatures not otherwise indicated are Celsius, while parts are by weight except for mixtures of liquids which are by volume.

EXAMPLE 1

Preparation of Immunochromatographic Sheets

A sheet of Whatman 31 ET[®] chromatography grade scientific paper of about 550 cm² was immersed in 1.8 l. CH₂Cl₂, 0.2 M in carbonyldiimidazole, and the mixture gently stirred for one hour at room temperature. Additional sheets were activated in the same activating solution. Each sheet was then washed with 300 ml CH₂Cl₂ and air dried with an air gun over about 20 sec. The sheet was then immersed in a solution of 500 µl of a 49 mg/ml solution of antitheophylline and 200 ml of buffer 0.1 M sodium phosphate, pH 7.0, 0.2M NaCl; and the mixture was mildly shaken for 4 hours at room temperature. After washing with the phosphate buffer, the solution was then immersed in 4% aqueous Dextran T10 solution to serve as a preservative, followed by blotting the sheet, freezing and lyophilizing.

EXAMPLE 2

Preparation of Immunochromatographic Strips

A Coherent Model 42, CO₂ laser at 50 watts CW (from Coherent, Inc., Palo Alto, California) and Anomatic II CNC[®] X-Y table (by which the laser beam is oriented on the X-Y axis to cut the immunochromatographic strips) were employed. A Coherent Model 303 coaxial gas jet was used at an air pressure of 60 psig. A standard cutting box was used.

The cutting box was placed on the X-Y table and a sheet of plexiglass was placed on the cutting box. A narrow slot was cut in the plexiglass using the laser beam. An immunochromatographic sheet prepared in Example 1 was placed over the plexiglass. The sheet was cut into strips which were 4.5 mm wide and 90 mm in length. Cutting speeds of 19 and 26 centimeters per second were employed. The performance of the immunochromatographic strips cut at the two different speeds was substantially identical.

EXAMPLE 3

Preparation of HRP-Oxyamine

To 5 ml of 10 mg/ml horse radish peroxidase in 5 mM sodium acetate, pH 4.5 buffer, was added 50 μ l 0.2 M sodium periodate and the mixture stirred for 30 min, followed by chromatography on a G-50 Sephadex[®] column, eluting with 2mM sodium acetate buffer, pH 4.5. The protein fractions were pooled to 29 ml, the mixture cooled to 4°C and 2.9 ml of 0.2 M 2,2'-oxy-bis-ethylamine in 0.5 M carbonate buffer, pH 9.5, at 4°C added. The pH of the mixture was adjusted to 9.5 with 1 N sodium hydroxide, stirred for 2 hrs and 3.52 ml of a 4 mg/ml sodium borohydride-water solution added and the mixture allowed to react for 3 hr, followed by chromatography through a Sephadex G-50 column.

The above procedure was repeated using 400 mg of HRP and 3.5 g of 2,2'-oxy-bis-ethylamine. No significant change in enzyme activity was observed between the native amine and the modified amine, which has about four additional amino groups.

EXAMPLE 4

Conjugation of Theophylline and HRP

Into a reaction flask was introduced 8.1 mg of 1-methyl-3-(3'-carboxypropyl)xanthine, 3.8 mg of NHS, 6.7 mg EDAC and 125 μ l DMF and the mixture allowed to stand overnight at room temperature.

To four 1.3 ml samples of HRP-oxyamine (1 mg) from Example 3 in 0.1 M sodium carbonate, pH 9.0 was added varying amounts of the ester prepared above to provide for preparations having mole ratios of theophylline to HRP of 400; 200, and two of 100 each. Into the first reaction mixture (400 mole ratio) was added 0.217 ml of DMF and 66 μ l of the above ester in 8.25 μ l increments over a period of about 2 hrs. Into the second reaction mixture (200 mole ratio), 0.238 ml of DMF was added and 33 μ l of the ester added incrementally in 8.25 μ l increments. Into the third reaction mixture (100 mole ratio), 0.24 ml of DMF was added and 16.5 μ l of the ester added in 8.2 μ l increments, while in the final reaction mixture (100 mole ratio), no DMF was added, and 8.25 μ l of the ester was added in 2.1 μ l increments. During the addition, the temperature was maintained at 4°C, and the mixture then allowed to stand overnight at 4°C.

The reaction mixtures were then worked up by chromatography on G-25 Sephadex with stan-

dard buffer. Folin and UV spectroscopic analysis indicated theophylline/HRP ratios of 6.9, 4.0, 1.6 and 2.1, respectively.

EXAMPLE 5

Immunochromatographic Assay

In carrying out the assay, the strips prepared in Example 2 were employed. Samples containing 0, 2.5, 5.0, 10, 20 and 40 μ g/ml (10 μ l) were mixed with 0.5 ml of a solution containing 0.1 M NaH_2PO_4 , 0.2 M NaCl, pH 7.0, 1 mg/ml BSA, 0.05% Triton QS-15, 100 μ g/ml glucose oxidase (Sigma, E.C. 1.1.3.4), and 0.2 μ g/ml HRP-theophylline conjugate. The end of a strip was dipped into this mixture. After the solution had reached the top of the strip by capillary migration (6-12 min), the strip was removed from the enzyme solution and totally immersed in a development solution comprising 15 ml of 50 mM glucose and 200 μ g/ml of 4-chloro-1-naphthol and allowed to stand for 20 min. The results are depicted in Fig. 2.

For purposes of comparison assays were also conducted employing immunochromatographic strips prepared from the sheet of Example 2 by cutting the sheets on a slitter. Referring to Fig. 1 it can be seen that the slitter cut strips exhibit extensive concavity of the front resulting from accelerated traversal of the liquid sample along the longitudinal edges of the strip when compared to the rate of traversal of the liquid sample along the body of the strip.

Fig. 2 demonstrates that the accelerated traversal of the liquid sample along the longitudinal edges of the strips cut in accordance with the invention has been minimized when compared to the rate of traversal of the liquid sample along longitudinal edges of strips cut using a slitter.

Claims

1. A device for use in a chromatographic system wherein a component of a mixture is partitioned between a liquid phase and an immobile phase, said device comprising at least one chromatographic strip consisting essentially of a bibulous material, wherein in said system said liquid phase forms a front traversing at least a portion of said strip, said strip having a body and at least one longitudinal edge lying in a direction substantially corresponding to the direction of traverse of said liquid phase characterised in that the longitudinal edge of said strip has the characteristic that the relationship of the pores within the bibulous material is substantially the same near the cut edge as the relationship of the pores in the body of said strip and wherein said strip has straight edges that have not been treated with a chemical that can control the shape of the traversing front; and is not a strip that is 4.5 mm wide by 90 mm long, made of chromatography grade filter paper, containing antitheophylline coupled thereto with carbonyldiimidazole and a 49 mg/ml solution of antitheophylline, and having its longitudinal edge cut with a laser.

2. The device of Claim 1 wherein said strip is cut



The cutting box was placed on the X-Y table and a sheet of plexiglass was placed on the cutting box. A narrow slot was cut in the plexiglass using the laser beam. An immunochromatographic sheet prepared in Example 1 was placed over the plexiglass. The sheet was cut into strips which were 4.5 mm wide and 90 mm in length. Cutting speeds of 19 and 26 centimeters per second were employed. The performance of the immunochromatographic strips cut at the two different speeds was substantially identical.

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The reaction mixtures were then worked up by chromatography on G-25 Sephadex with stan-

dard buffer. Folin and UV spectroscopic analysis indicated theophylline/HRP ratios of 6.9, 4.0, 1.6 and 2.1, respectively.

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Claims

1. A device for use in a chromatographic system wherein a component of a mixture is partitioned between a liquid phase and an immobile phase, said device comprising at least one chromatographic strip consisting essentially of a bibulous material, wherein in said system said liquid phase forms a front traversing at least a portion of said strip, said strip having a body and at least one longitudinal edge lying in a direction substantially corresponding to the direction of traverse of said liquid phase characterised in that the longitudinal edge of said strip has the characteristic that the relationship of the pores within the bibulous material is substantially the same near the cut edge as the relationship of the pores in the body of said strip and wherein said strip has straight edges that have not been treated with a chemical that can control the shape of the traversing front; and is not a strip that is 4.5 mm wide by 90 mm long, made of chromatography grade filter paper, containing antitheophylline coupled thereto with carbonyldiimidazole and a 49 mg/ml solution of antitheophylline, and having its longitudinal edge cut with a laser.

2. The device of Claim 1 wherein said strip is cut



from a sheet of said bibulous material by non-compressive cutting means.

3. The device of Claim 1 or Claim 2 wherein a member of a specific binding pair is non-diffusively bound to said strip.

4. The device of Claim 3 wherein the member of the specific binding pair is an antigen or an antibody.

5. The immunochromatographic device of Claim 3 or Claim 4 wherein the device is further bound to a member of a signal producing system.

6. A method for preparing the chromatographic strip of Claim 1 from a sheet of bibulous material, characterised in that it comprises cutting the longitudinal edges of said strips from said sheet by non-compressive cutting means.

7. A method of Claim 6 wherein said non-compressive cutting means is a laser beam.

8. A paper chromatographic strip characterised in that said strip has a substantially non-compressed longitudinal edge and wherein the strip has straight edges that have not been treated with a chemical that can control the shape of the traversing front; and

is not a strip that is 4.5 mm wide by 90 mm long, made of chromatography grade filter paper, containing antitheophylline coupled thereto with carbonyldiimidazole and a 49 mg/ml solution of antitheophylline, and having its longitudinal edge cut with a laser.

9. A diagnostic kit, which comprises-

(a) the device of Claim 3 or Claim 4,

(b) a member of said specific binding pair bound to a member of a signal producing system, and

(c) any other members of said signal producing system.

Patentansprüche

1. Vorrichtung zur Verwendung in einem chromatographischen System, worin eine Komponente einer Mischung zwischen einer flüssigen Phase und einer unbeweglichen Phase verteilt wird, wobei die Vorrichtung wenigstens einen chromatographischen Streifen umfaßt, der im wesentlichen aus einem saugfähigen Material besteht, worin in dem System die flüssige Phase eine Front bildet, die mindestens einen Teil des Streifens durchwandert, wobei dieser Streifen einen Körper und wenigstens einen Längsrand aufweist, der in einer Richtung liegt, die im wesentlichen der Richtung der Durchwanderung der flüssigen Phase entspricht, dadurch gekennzeichnet, daß der Längsrand des Streifens die Charakteristik aufweist, daß das Verhältnis der Poren innerhalb des Saugfähigen Materials in der Nähe des geschnittenen Randes im wesentlichen das gleiche ist wie das Verhältnis der Poren im Körper des Streifens, und worin der Streifen gerade Ränder hat, die nicht mit einer Chemikalie behandelt worden sind, die die Form der durchwandernden Front beeinflussen kann; und

das er nicht ein Streifen ist, der 4,5 mm breit auf 90 mm lang ist, hergestellt aus Filterpapier chromatographischer Güte, das Antitheophyllin, mit

Carbonyldiimidazol und einer 49 mg/ml Lösung von Antitheophyllin daran gekuppelt, enthält, und dessen Längsrand mit einem Laser geschnitten wurde.

2. Vorrichtung nach Anspruch 1, worin der Streifen mit nicht-zusammenpressenden Schneidmitteln aus einem Bogen des saugfähigen Materials geschnitten wird.

3. Vorrichtung nach Anspruch 1 oder Anspruch 2, worin ein Mitglied eines spezifischen Bindungspaares nicht-diffundierbar an den Streifen gebunden ist.

4. Vorrichtung nach Anspruch 3, worin das Mitglied des spezifischen Bindungspaares ein Antigen oder ein Antikörper ist.

5. Immunochromatographische Vorrichtung nach Anspruch 3 oder Anspruch 4, worin die Vorrichtung weiter an ein Mitglied eines Signal-erzeugenden Systems gebunden ist.

6. Verfahren zur Herstellung des chromatographischen Streifens nach Anspruch 1 aus einem Bogen saugfähigen Materials, dadurch gekennzeichnet, daß es das Schneiden der Längsränder der Streifen aus dem Bogen durch nichtzusammenpressende Schneidmittel umfaßt.

7. Verfahren nach Anspruch 6, worin die nicht-zusammenpressenden Schneidmittel ein Laserstrahl sind.

8. Chromatographischer Papierstreifen, dadurch gekennzeichnet, daß der Streifen einen im wesentlichen nichtzusammengepreßten Längsrand aufweist, und worin der Streifen gerade Ränder hat, die nicht mit einer Chemikalie behandelt worden sind, die die Form der durchwandernden Front beeinflussen kann; und

daß er nicht ein Streifen ist, der 4,5 mm breit auf 90 mm lang ist, hergestellt aus Filterpapier chromatographischer Güte, das Antitheophyllin, mit Carbonyldiimidazol und einer 49 mg/ml Lösung von Antitheophyllin daran gekuppelt, enthält, und dessen Längsrand mit einem Laser geschnitten wurde.

9. Diagnostisches Kit, das umfaßt

(a) die Vorrichtung nach Anspruch 3 oder Anspruch 4,

(b) ein Mitglied des spezifischen Bindungspaares, gebunden an ein Mitglied eines Signal-erzeugenden Systems und

(c) irgendwelche andere Mitglieder des Signal-erzeugenden Systems.

Revendications

1. Dispositif destiné à être utilisé dans un système chromatographique, dans lequel un constituant d'un mélange est partagé entre une phase liquide et une phase immobile, ledit dispositif comprenant au moins une bande chromatographique consistant essentiellement en une matière absorbante, ladite phase liquide formant dans ledit système un front parcourant au moins une partie de ladite bande, ladite bande comprenant un corps et au moins un bord longitudinal s'étendant dans une direction correspondant pratiquement à la direction de parcours de ladite phase



liquide, caractérisé en ce que le bord longitudinal de ladite bande possède la particularité que la relation entre les pores à l'intérieur de la matière absorbante est pratiquement identique, près du bord de coupe, à la relation entre les pores dans le corps de ladite bande, ladite bande ayant des bords droits qui n'ont pas été traités avec une substance chimique pouvant réguler la forme du front de parcours; et

n'est pas une bande qui possède une largeur de 4,5 mm pour une longueur de 90 mm, constituée de papierfiltre de qualité pour chromatographie, contenant de l'antithéophylline couplée à du carbonyldiimidazole et une solution à 49 mg/ml d'antithéophylline, et ayant son bord longitudinal coupé au moyen d'un laser.

2. Dispositif suivant la revendication 1, dans lequel la bande est coupée dans une feuille de la matière absorbante par des moyens de coupe non compressifs.

3. Dispositif suivant la revendication 1 ou la revendication 2, dans lequel un élément d'une paire à liaison spécifique est lié, sans possibilité de diffusion, à la bande.

4. Dispositif suivant la revendication 3, dans lequel l'élément de la paire à liaison spécifique est un antigène ou un anticorps.

5. Dispositif immunochromatographique suivant la revendication 3 ou la revendication 4, qui est en outre relié à un élément d'un système engendrant un signal.

6. Procédé de préparation de la bande chromatographique suivant la revendication 1 à partir d'une feuille de matière absorbante, caractérisé en ce qu'il consiste à couper les bords longitudinaux desdites bandes dans ladite feuille par des moyens de coupe non compressifs.

7. Procédé suivant la revendication 6, dans lequel les moyens de coupe non compressifs consistent en un faisceau laser.

8. Bande chromatographique en papier, caractérisée en ce qu'elle possède un bord longitudinal pratiquement non comprimé et des bords droits qui n'ont pas été traités avec une substance chimique qui peut réguler la forme du front de parcours; et

n'est pas une bande qui possède une largeur de 4,5 mm pour une longueur de 90 mm, constituée de papierfiltre de qualité pour chromatographie, contenant de l'antithéophylline couplée à du carbonyldiimidazole et une solution à 49 mg/ml d'antithéophylline, et ayant son bord longitudinal coupé au moyen d'un laser.

9. Kit de diagnostic, qui comprend:

(a) le dispositif suivant la revendication 3 ou la revendication 4,

(b) un élément de la paire à liaison spécifique lié à un membre d'un système engendrant un signal, et

(c) n'importe quels autres membres dudit système engendrant un signal.

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