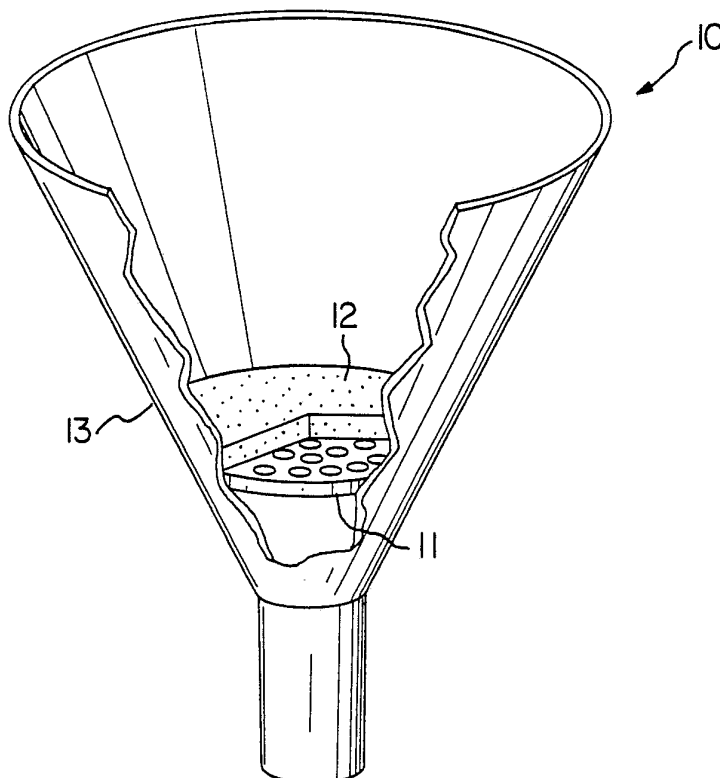




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US88/01740 (22) International Filing Date: 25 May 1988 (25.05.88) (31) Priority Application Number: 055,437 (32) Priority Date: 29 May 1987 (29.05.87) (33) Priority Country: US (71) Applicant: DRUG SCREENING SYSTEMS, INC. [US/US]; Plaza 47, Delsea Drive, Westville, NJ 08093 (US). (74) Agents: SPIVAK, Karl, L. et al.; Steele, Gould & Fried, Suite 3232, 1700 Market Street, Philadelphia, PA 19103 (US).		(81) Designated States: AT (European patent), AU, BE (European patent), BR, CH (European patent), DE (European patent), DK, FI, FR (European patent), GB (European patent), IT (European patent), JP, KR, LU (European patent), NL (European patent), NO, SE (European patent), SU. Published <i>With international search report.</i>
(54) Title: BASIC DRUG DETECTION SYSTEM (57) Abstract <p>A method for detecting basic narcotics or drugs in body fluids which comprises filtering body fluids through a cellulosic filtering means (12) treated with a binding agent for the narcotics or drugs and the filtering means. The binding agent is an acidic organic indicator or a polycarboxylic acid. The narcotics or drugs are then treated with a subsequent reagent, if required, to produce a color reaction. A device (10) for detecting basic narcotics or drugs is also disclosed which contains the filtering means (12) treated with the binding agent so as to concentrate the narcotic or drug prior to reaction with a suitable indicator.</p>		



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BASIC DRUG DETECTION SYSTEMField of the Invention

The present invention relates to testing devices used to ascertain the presence of certain types of basic narcotics or drugs in body fluids. More particularly, the invention is concerned with a means for concentrating such basic drugs that may be present in urine and detecting their presence colorimetrically by a suitable chemical reagent.

Background of the Invention

Due to the wide spread use of controlled substances or narcotics such as morphine, cocaine, amphetamines, tranquilizers, synthetic analgesics, and the like, it has become desirable to institute drug testing of athletes and others which are engaged in an occupation involving a public trust or in which an injury can occur if the party is not completely alert. Testing of athletic teams, bus drivers, etc. involve large group testing which must be conducted quickly, accurately and inexpensively. A highly sensitive, easily-read test for the detection of narcotics such as heroin in urine would be extremely helpful in a drug program. Narcotic screening has become extensive practice in industry, business, the Armed Forces, schools and in the courts and prison systems. Such screening is used both as a pre-employment procedure and as a monitoring tool. The present methods for the detection of these basic narcotics in urine are relatively costly and time consuming and must, in general, be performed by qualified personnel in well-equipped laboratories. It would be highly desirable and useful to be able to carry out a quick test of the presence of such narcotics in urine by a person who is untrained in chemical laboratory manipulations and who does not have at his disposal the instrumentation and laboratory equipment required in the present methods. The validity, such a test method must have a sensitivity to morphine in urine of approximately 1 microgram per milliliter of solution and must not require more than 23 to 50 milliliters of urine.

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Clarke, "Isolation and Identification of Drugs", The Pharmaceutical Press, London, 1969, pp 431-432, which is herein incorporated by reference discloses chemical reagents which can be utilized in the detection of common narcotic substances.

OBJECTS AND SUMMARY OF THE INVENTION

It is an object of this invention to provide a device for the detection of a basic narcotic substance including tranquilizers and other CNS affecting drugs present in minute amounts in body fluids.

It is another object of the present invention to provide a device which is broadly adaptable to a wide variety of colorimetric reactions and which will increase the sensitivity of the color reaction in drug testing by several fold over the corresponding solution reaction.

It is a further object of this invention to provide a device capable of rapidly and colorimetrically detecting, in the hands of untrained people, extremely minute amounts of a basic narcotic substance in urine.

It is a still a further object of the invention to detect the presence of a multiplicity of narcotic substances or CNS affecting compounds in body fluids of mammals.

These and other objects of the invention can be achieved by providing a cellulosic filtering means which is treated with a binding agent and a suitable chemical detecting reagent. The filtering means serves to collect, and therefore to concentrate any basic drug or narcotic which may be present in the body fluids and which may be too dilute to be detected by conventional techniques. It is particularly advantageous in detecting narcotic or drug use where the drug user has abstained from drug use for a few days in anticipation of the test.

The filtering means of the present invention in essence filters the narcotic or drug from urine that is passed through the filtering means by binding these narcotics or drugs through a binding agent for the filtering means and the narcotic or drug. The chemical reagent for the particular narcotic being detected is then poured onto the

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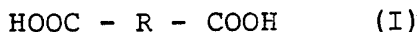
filtering means, and a characteristic color appears which indicates that the narcotic or drug is present.

Advantageously, the filtering means is used in connection with a funneling means so as to facilitate collection and concentration at the disk. The body fluid or urine sample is first poured onto a disk impregnated with a suitable binding agent, and then a suitable chemical reagent is poured over the disk. A characteristic color appears on the disk indicating whether or not a narcotic or drug is present.

According to a further embodiment of the invention, the chemical reagent may be bound through a binding agent to a filter disk. The color change will then appear on the disks when the specimen tested is added. The disk can comprise more than one layer of filter material with each layer being impregnated with a different binding agent or reagent that may be more reactive with a particular narcotic or drug.

Among the various basic narcotics or drugs which may be detected there are included cocaine, morphine, heroin, amphetamines phencyclidine, PCP, chlordiazepoxide, propoxphene, synthetic analgesics, alkaloids, catecholamines, etc.

The binding agent which is utilizable in the present invention is a polycarboxylic acid compound wherein at least one of the carboxylic acid groups binds with the free hydroxyl groups of the cellulosic material comprising. The filtering means and another carboxylic acid group binds with a basic group of a narcotic being tested. Preferably, the polycarboxylic acid compounds are compounds of the formula:



wherein R is selected from the group consisting of a cycloalkyl of 4 to 6 carbon atoms, alkyl of 2 to 12 carbon atoms, alkylene of 2 to 12 carbon atoms, heterocyclic of five or six carbon atoms and phenyl.

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The suitable acids which may be used as the binding agent include maleic acid, fumaric acid, adipic acid, succinic acid, phthalic acid, etc.

Reagents which interact with the basic narcotic or drug to produce a color reaction include cobaltous thiocyanate and tetrabromophenolphthalein ethyl ester.

Other objects and a fuller understanding of the invention will be had by referring to the following description and claims of a preferred embodiment, taken in conjunction with the accompanying drawings, wherein like reference characters refer to similar parts throughout the several views.

Brief Description of the Drawings

Fig. 1 is a perspective view of the testing device of the invention;

Fig. 2 is a schematic presentation of a specific embodiment of a multi-layered disk of the invention, and;

Fig. 3 is a side sectional view of a disposable test funnel having a reagent impregnated portion.

Description of the Preferred Embodiment of the Invention

Although specific terms are used in the following description for the sake of clarity, these terms are intended to refer only to the particular structure of the invention selected for illustration in the drawings, and are not intended to define or limit the scope of the invention.

As illustrated in Fig. 1, the test device of the invention may comprise a means 10 for collecting and concentrating body fluids, for example, urine, for testing for the presence of basic narcotics and drugs. The means 10 may, for example, comprise a funnel 13 having a perforated support 11 on which there is placed a cellulosic disk 12. A binding agent is placed into solution and poured through the funnel 13 so as to bind on the disk 12. The test fluid which is suspected of containing a narcotic or drug is then passed through the funnel 13 whereby the narcotic or drug interacts with the binding agent and remains on the disk. A suitable test reagent for the narcotic or drug is poured

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through the funnel and the development of a specific color on the disk indicates the presence of a narcotic or drug.

The disk 12 can consist of cellulosic filter paper or regularly woven cellulosic filaments in the form of a fabric with weft and warp threads or can be in the form of an unwoven fabric. It is also possible to use thin felt- or fleece-like meshwork in which the fibre structure is not uniform, provided that they have the necessary neutral color and stability. It is preferred to use natural cellulosic material or anionic synthetic resin fabric of monofile or spun filaments which can consist of cellulose materials, for example cotton, cellulose, carboxymethyl cellulose, flax or sisal. Within the given limits, the meshwork can be varied, depending upon the color reaction of the indicator layer. Normally, there are used a meshwork to impregnate the meshwork with reagents which only penetrate into the indicator layer upon wetting. This separate impregnation is of colorless material. However, with colored meshwork, there are obtained mixed colors with the colors of the indicator layer, which can sometimes increase the contrast. In addition, it is also possible recommended when there is a possibility that two or more binding agents, detection reagents and/or adjuvants might react together during storage.

As shown in Fig. 2, the disk used in concentrating the narcotic or drug may comprise a multi-layered disk 20. In the first layer 21 a chemical reagent capable of detecting a narcotic or drug may be bound directly to the disk layer or through a binding agent. The second layer 23 may be associated with the first layer 21 through a neutral boundary layer 22 which prevents interaction between the different chemical reagents.

The second layer 23 may contain a binding agent and acidic organic color indicator for cannabinoids, for example, fast Blue BB.

Layer 21 may contain tetrabromophenophthalein which changes color indicating the presence of amphetamines. The multilayered disk is advantageous for use when the testing

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of the narcotic in the body fluids includes tests for cannabinoids or tranquilizers and other basic drugs such as heroin. In such a case, one layer can test for the cannabinoids or tranquilizers and the other layer can test for other narcotics.

Fig. 3 illustrates a filter 30 which is impregnated in part 31 with a binding agent. The filter 30 is intended for use with a conventional funnel. After urine is passed through the funnel an indicator is added and the color is observed to indicate the presence of a narcotic or drug.

The indicators which may be utilized in the invention are known and commercially available. These indicators include the following:

<u>Indicator</u>	<u>Chemical Composition</u>	<u>Drug or Narcotic Tested</u>
Marquis Reagen	Formaldehyde in H_2SO_4	Opiates, amphetamines, diazepam, phenothiazines, propoxphenes
Mecke Reagent	Selenious acid in H_2SO_4	Opiates, mescaline, amphetamines
Froehde Reagent	Molybdic acid in H_2SO_4	Opiates, mescaline, amphetamines
Iodoplatinate Reagent	Platinic chloride and potassium iodide	Opiates, PCP, cocaine, amphetamines, propoxphenes, benzodiazepines

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<u>Indicator</u>	<u>Chemical Composition</u>	<u>Drug or Narcotic</u> <u>Tested</u>
Mandelin Reagent	Ammonium vandate in H_2SO_4	Opiates, amphetamines, mescaline, phenothiazines

From the foregoing it is believed that those familiar with the art will readily recognize and appreciate the novel concepts and features of the present invention. Numerous variations, changes and substitutions of equivalents will present themselves from persons skilled in the art and may be made without necessarily departing from the scope and principles of this invention. As a result, the embodiment described herein is subject to various modifications, changes and the like, with the scope of this invention being determined solely by reference to the claims appended hereto.

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What Is Claimed Is:

1. A method for detecting basic narcotics or drugs in body fluids which comprises filtering said body fluids through a cellulosic filtering means treated with a binding agent for basic narcotics or drugs and for said filtering means, said binding agent being a compound of the formula



wherein R is selected from the group consisting of a cycloalkyl of 4 to 6 carbon atoms, alkyl of 2 to 12 carbon atoms, alkylene of 2 to 12 carbon atoms, heterocyclic of five or six carbon atoms and phenyl, and then

contacting said filtering means with a color indicator for the narcotic or drug on the filtering means.

2. The method of claim 1 wherein said polycarboxylic acid is maleic acid.

3. The method of claim 1 wherein said polycarboxylic acid is adipic acid.

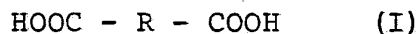
4. The method of claim 1 wherein said body fluid is urine.

5. The method of claim 1 wherein said filtering means is a filtering disk.

6. The method of claim 5 wherein said disk comprises a plurality of layers, at least one of said layers being a cellulosic layer treated with said binding agent for said layer and a narcotic or drug.

7. The method of claim 1 wherein said color indicator is selected from the group consisting of cobaltous thiocyanate and tetrabromophenolphthalein ethyl ester.

8. A method for detecting basic narcotics or drugs in body fluid which comprises filtering said body fluid through a filtering means comprising a first layer impregnated with a binding agent comprising a compound of the formula:



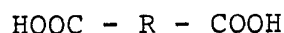
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wherein R is selected from the group consisting of a cycloalkyl of 4 to 6 carbon atoms, alkyl of 2 to 12 carbon atoms, alkylene of 2 to 12 carbon atoms, heterocyclic of five or six carbon atoms and phenyl, and a second cellulosic layer impregnated with an acidic organic indicator for cannabinoids which is bound to said second layer, said organic indicator being capable of coupling with a cannabinoid, observing a color change of said second layer when a cannabinoid is present, and then adding an indicator for said basic narcotic drug.

9. The method of claim 8 wherein said acidic organic indicator is fast Blue BB.

10. A device for concentrating basic narcotics or drugs in body fluids comprising a cellulosic filtering means having a binding agent bound to said filtering means, said binding agent being capable of further binding to a basic narcotics or drugs, said binding agent being a compound of the formula



wherein R is selected from the group consisting of a cycloalkyl of 4 to 6 carbon atoms, alkyl of 2 to 12 carbon atoms, alkylene or 2 to 12 carbon atoms, heterocyclic of five or six carbon atoms and phenyl.

11. The device of claim 8 wherein said binding agent is a maleic acid.

12. The device for claim 11 wherein said binding agent is adipic acid.

13. The device of claim 10 wherein said filtering means comprises a disk.

14. The device of claim 13 wherein said disk is multilayered.

15. The device of claim 13 wherein said filtering means is supported in a funnel.

16. The device of claim 13 wherein at least one layer is bound with a binding agent which is an indicator for cannabinoids.

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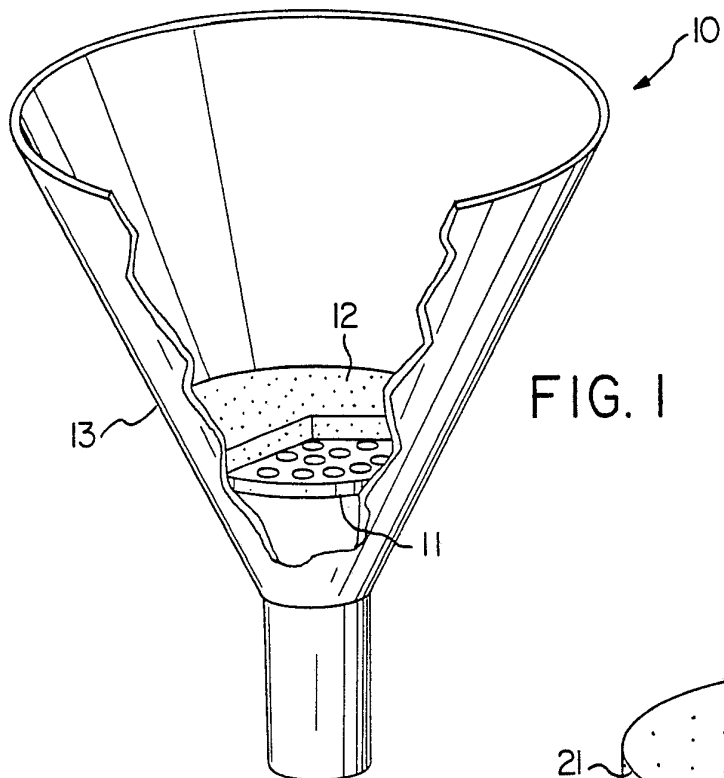


FIG. 1

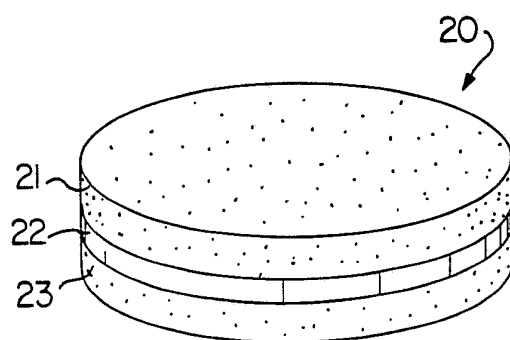


FIG. 2

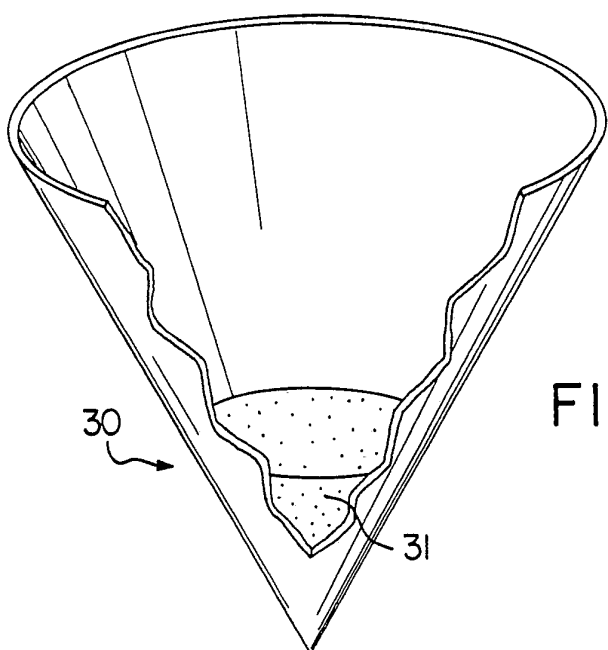


FIG. 3

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INTERNATIONAL SEARCH REPORT

International Application No PCT/US88/01740

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ³		
According to International Patent Classification (IPC) or to both National Classification and IPC IPC(4): G01N 21/78, 33/94 US. CL.: 210/502.1, 508; 422/56 US. CL.: 422/58; 428/65, 411.1; 436/92, 98, 170, 178, 901, 169		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁴		
Classification System	Classification Symbols	
U.S.	162/160, 162; 210/502.1, 508; 422/56, 57, 58, 61; 428/65, 411.1; 436/92, 93, 96, 98, 131, 164, 169, 170, 178, 901; 527/311; 536/63	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁵		
APS: Key Words-Maleic acid, Adipic acid, Paper, Filter###, Cellulos##		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ¹⁴		
Category *	Citation of Document, ¹⁶ with indication, where appropriate, of the relevant passages ¹⁷	Relevant to Claim No. ¹⁸
X Y	US, A, 3,915,649 (FORGIONE) 28 October 1975, see the entire document, especially column 3, lines 2-4.	10-11 13-15
Y	US, A, 3,547,780 (FINNERTY et al) 15 December 1970, see the entire document.	10, 12-15
Y,P	US, A, 4,673,639 (SLIFKIN) 16 June 1987, see claims 4 and 12.	10, 12-15
Y	US, A, 3,992,158 (PRZYBYLOWICZ et al) 16 November 1976, see the entire document.	14
Y	US, A, 2,671,715 (BECKLEY) 09 March 1954, see the entire document.	15
A	US, A, 3,275,416 (ZAAR et al) 27 September 1966, see the entire document.	
A	US, A, 3,625,652 (FUJIMOTO et al) 07 December 1971, see the entire document.	
A	US, A, 3,915,639 (FRIEDENBERG) 28 October 1975, see the entire document.	
<p>* Special categories of cited documents: ¹⁵</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search ²		Date of Mailing of this International Search Report ²
19 August 1988		1 2 SEP 1988
International Searching Authority ¹		Signature of Authorized Officer ²⁰
ISA/US		Robert J. Hill, Jr.

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category*	Citation of Document, ¹⁶ with indication, where appropriate, of the relevant passages ¹⁷	Relevant to Claim No ¹⁸
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A	US, A, 3,966,410 (JAHNSEN) 29 June 1976, see the entire document.	
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A	GB, A, 1,426,177 (DE FAUBERT MAUNDER et al) 25 February 1976, see the entire document.	
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