

- [54] **APPARATUS FOR REMOVING LIPIDS
FROM THE HUMAN BLOODSTREAM**
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[57] **ABSTRACT**

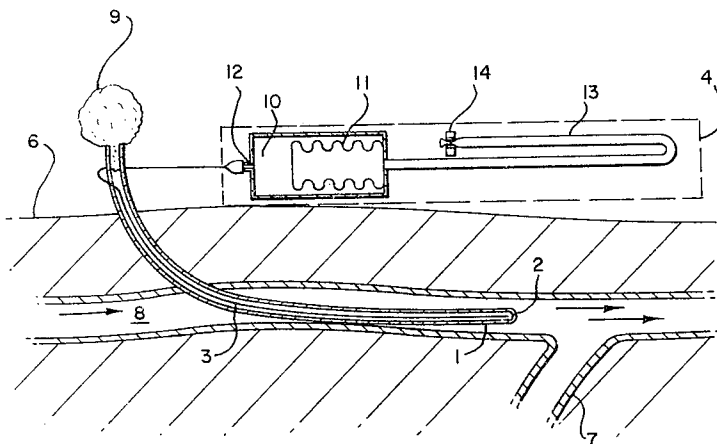
A catheter for monitoring the concentration of lipids in the bloodstream made from a material that selectively absorbs lipids. The catheter is inserted in the bloodstream while the interior wall of the catheter is washed continuously or periodically with a nontoxic solvent delivered through a lipid-impermeable fiber to dissolve the absorbed lipids. The lipid-rich solvent is contacted with an absorbent located at the open end of the catheter and outside the epidermis to evaporate the solvent. The absorbent is analyzed periodically for lipids.

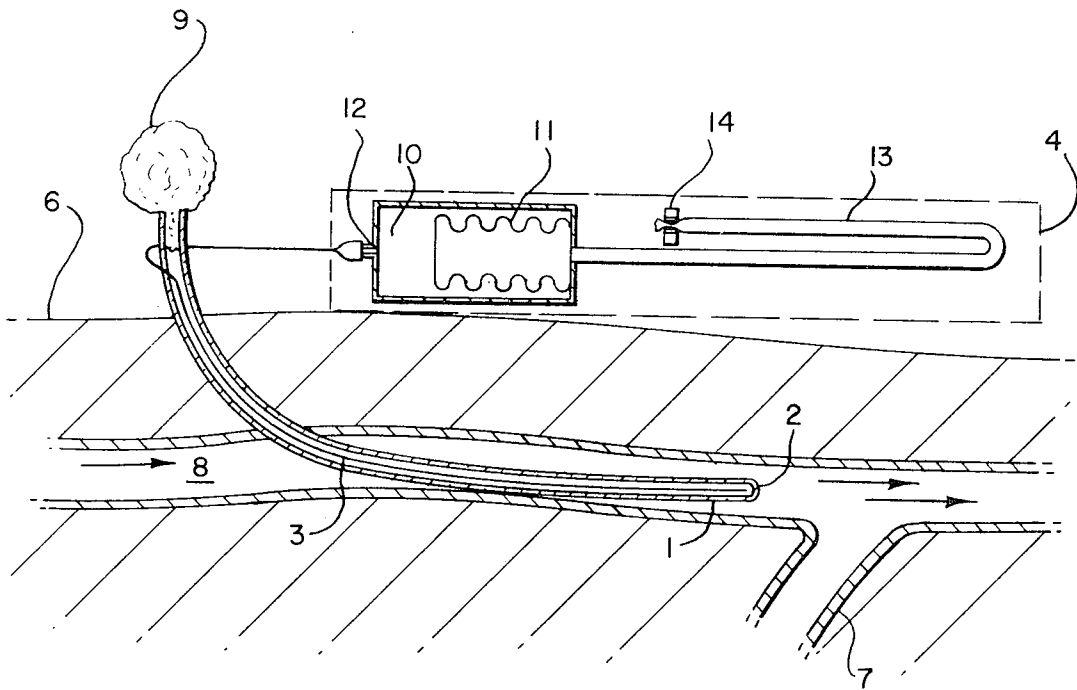
6 Claims, 1 Drawing Figure

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APPARATUS FOR REMOVING LIPIDS FROM THE HUMAN BLOODSTREAM

This invention relates to an apparatus for selectively removing lipid materials from the bloodstream of an animal.

The human bloodstream contains a wide variety of lipid and semilipid materials in trace amounts that are either accidentally ingested such as the pesticide DDT and the carcinogenic hydrocarbon 3, 4-benz [a] pyrene or are produced by the body such as regulatory hormones. These materials as a class are nearly insoluble in water, and are carried primarily in association with proteins of the blood plasma and in micelles in blood plasma. In many instances the concentrations of certain lipids may become excessive and cannot be removed by usual elimination processes. On the other hand, a hormone imbalance condition may exist wherein it may be desirable to administer one or more hormones to reestablish the desired balance.

In the diagnosis of pregnant women or diseased humans, it is highly desirable or even essential to obtain an accurate analysis of the hormones present in trace amounts and their relative proportions. The regulatory hormones in general are found in trace concentrations of the order of parts per million. Conventional analysis for regulatory hormones requires successively taking several units of blood and extracting the hormones therefrom followed by reinfusion of the blood. This procedure is time consuming, expensive, and attended, as are all transfusions and infusions, with some hazard.

This invention provides a novel and practical apparatus for removing lipid substances such as hormones, pesticides, and carcinogens of the lipid class from circulating human blood whereby the lipid material is absorbed from the blood into the permeable wall of a lipid-absorbing catheter inserted in the bloodstream, is eluted from the wall by a continuous or pulse of solvent contained inside the catheter and is carried out of the catheter to the exterior of the body where it accumulates on surfaces from which the solvent is released by evaporation. The evaporating surfaces may be removed periodically for analysis and replaced by a fresh surface without surgical intervention.

Reference is made to the attached drawing showing one embodiment of this invention.

A catheter 1 made of a lipid-absorbing elastomer and sealed at one end 2 contains a hollow fiber 3 to inserted that the lower end of fiber 3 comes close to the end 2 of the silicone catheter 1. The outer end of fiber 3 is drawn through the wall of catheter 1 and is connected to a system 4 for supplying solvent to the fiber 3 continuously. Other systems providing for pulsed, or periodic injection of solvent may be used.

Catheter 1 with its contained hollow fiber 3 is inserted through the epidermis 6 into the vein 7 of a human subject by the conventional surgical procedure of venopuncture with a hollow needle of sufficient diameter to contain the catheter 1. The catheter 1 and its contained hollow fiber 3 is inserted into the vein for a sufficient length, of about several centimeters, to provide contact with the flowing blood 8. After insertion, the end 7 of catheter 1 remains outside the epidermis 6. A porous evaporator 9 is inserted as a plug into the catheter 1. The evaporator 9 may take any one of several forms including a porous ceramic plug, a cellulosic wad, a suitably rolled filter paper, or any other of a variety of configurations from which solvent may be evaporated into ambient air.

The exterior end of the hollow fiber 3 is connected to a device 4 which is a preferred embodiment of this invention is an atmospheric micropump. The pump 4 provides, over a period of several hours or days a carefully regulated and very small stream of solvent into the farthest interior end 2 of the catheter 1 so that the solvent issuing from the interior end of hollow fiber 3 will flow backward gradually over the interior wall of the catheter 1 dissolving therefrom lipid materials and carrying them out onto evaporator 9. At evaporator 9, circulating ambient air is sufficient to cause evaporation of the solvent which is in the catheter 1. Suitable nontoxic solvents include ethanol, diethyl ether, and anesthetics halothane, or methoxyflurane and mixtures thereof.

Lipids circulating in the bloodstream though in very small concentrations, upon contact with the exterior surface of the lipid-permeable catheter dissolve in it since it has a high affinity for lipids as compared to the bloodstream. However, they would accumulate in the catheter with an ever increasing concentration were it not for the elution of the lipids from the interior catheter wall by the solvent. Evaporation of the solvent at the evaporator 9 leaves the lipids there in ever increasing concentration. A particular advantage of this apparatus is that the evaporator 9 may be removed at any time and replaced by a fresh evaporator in order that presence or absence of a particular hormone, of the ratio of hormones may be confirmed as the experiment continues. State otherwise, this device provides means for continuously monitoring the types of lipids being removed without disturbing the catheter and thereby causing pain to the subject. Therefore, it is possible to analyze accumulatively or otherwise the lipids received to evaporators 9 to enable a decision to be made as to how long the catheter should be implanted.

With respect to lipid pesticides such as DDT or the lipid carcinogens such as 3,4-benzpyrene, it is likely that long periods of exposure of the blood to the catheter would be required to reduce effectively their concentrations in the body, although analysis to determine concentration levels in the blood can be accomplished in a relatively short time.

Solvent is delivered at a predetermined and essentially constant rate from the chamber 10 under the force exerted by the expansion of bellows 11. The chamber is filled by replacing the gas therein with the liquid so while the bellows is contracted from its equilibrium position. This is accomplished conveniently by evacuating the chamber 10 and the bellows 11 to substantially zero pressure. The chamber is then filled with solvent by inserting the hollow fiber 3 into a solvent bath at atmospheric pressure. The solvent then proceeds through the fiber 3, and orifice 12 into chamber 10. When the chamber is filled, the fiber is inserted into catheter 1. The bellows is then expanded by diffusing gas from the atmosphere through tube 13 formed from an elastomeric wall and clamped at end 14. Under the force exerted by the diffused gas, the bellows expands at a substantially constant rate. The bellows is formed so that it exerts a substantially constant resistive force over a relatively wide subatmospheric pressure range.

By employing the bellows exerting a substantially constant resistive force during expansion, a slight pressure change on its inside surface effects a large change in the volume of chamber 10. In addition, the rate of volume change as a function of pressure change is substantially constant. By regulating the gas pressure to increase at very slow rates, liquid delivery can be effected for long periods at a substantially constant rate. Any structure and composition can be employed to replace the bellows 11 so long as it exerts a substantially constant resistive force when expanded within its defined mechanical limits and within a pressure range between zero and atmospheric pressure. The rate of gas pressure increase on the expanded wall is regulated by diffusing gas through a porous barrier open to the atmosphere. The diffusion rate and consequent rate of pressure increase is regulated by the structure and composition of the diffusion barrier.

To prevent coagulation of the blood of the subject upon contact with the surface of the catheter, a number of well-known expedients may be used to the simplest of which is to incorporate into the wall of the catheter by previous admixture, anticoagulants such as heparin, capable of slow release into the adjacent blood. Alternatively, the solvent supplied through the hollow fiber may be presaturated with heparin so that the heparin gradually diffuses through the catheter wall, at a rate necessarily very slow because of the lipid-absorbing power of this catheter wall and therefore its relative impermeability to compounds like heparin.

It is necessary to employ nontoxic solvents since any solvent that will dissolve lipid will absorb, to some extent, in a catheter wall which is capable of dissolving lipid, and therefore will enter the bloodstream at a rate determined by the surface area of the catheter, the concentration of solvent in the catheter wall and the blood flow rate next to the catheter.

For this reason powerful solvents for certain lipids like benzene, carbon disulfide, and carbon tetrachloride cannot be used at all because of their toxicity.

The anesthesia liquids, for example diethyl ether, methoxyflurane, and halothane, are excellent solvents for hormones such as the androgens and testosterone, and are good solvents for chlorinated lipids like DDT and polynuclear aromatic hydrocarbons like 3,4 benz [α] pyrene. They are useful in this invention, singly or in combination, provided that their rate of diffusion into the bloodstream is less than that required to produce anesthesia, but as a class they powerfully swell certain elastomers such as silicone rubber, out of which the catheter might be made, and may necessitate use of very short catheter of low surface area.

Anhydrous ethanol or ethanol at its minimum boiling azeotrope (95 percent) composition is preferred because all lipids of interest are slightly soluble in it, because it does not very rapidly diffuse through elastomers of interest into blood, and because the small quantity that does diffuse into the blood is harmless.

Combination of ethanol with one or more anesthesia liquids give improved extraction power while not causing the degree of swelling of the catheter characteristic of the undiluted anesthesia nor the rate of diffusion into the bloodstream.

Suitable materials from which the catheter can be formed include silicone rubbers, polyisobutylene, butadiene rubbers, butadiene-styrene copolymers or the like. In a preferred embodiment of this invention the catheter is made of polydimethyl siloxane gum stock by extrusion and subsequent cross-linking. The extruded tube having an outside diameter of approximately 1 millimeter (1,000 microns) and an inside diameter of about 750 microns the end being sealed by compression of the raw extrudate prior to the cross-linking step. A preferred hollow fiber is made of nylon and has a diameter of approximately 500 microns outside and a diameter of approximately 200 microns inside. Nylon fibers are preferred because of their relative impermeability to ethanol, diethyl ether, and lipid materials. Thus, unwanted reextraction of the lipid into the solvent contained in the hollow fiber from the exterior solvent inside the catheter is prevented.

It will be understood that a constant rate of input of solvent is not essential. This device will function equally well if solvent is caused to flow through it by reason of simple capillary at-

traction into the evaporator 6 through the hollow fiber the other exterior end of which projects into a simple reservoir, at a rate determined by the rate of removal from the evaporation, and that periodic or pulsed injections of solvent will also effect removal of lipid. Pulsed injections of anesthesia liquids are useful in that the catheter wall is subject to periodic pulsing of its burden of lipid, while on the other hand the wall never swells with the anesthesia solvent to the same extent that it would if the perfusion were continuous.

I claim:

1. Apparatus for absorbing lipid materials comprising a lipid-permeable tube closed at one end and open at the opposite end, a hollow lipid-impermeable fiber in the tube for supplying a solvent for lipids to the closed end of the tube and an absorbent inserted in the open end of the tube permitting solvent evaporation while retaining lipids.

2. The apparatus of claim 1 wherein the tube comprises a silicone rubber.

3. The apparatus of claim 1 wherein the tube comprises a lipid-permeable elastomer containing a particulate heparin blood-anticoagulant.

4. An apparatus for absorbing lipid materials comprising a lipid-permeable tube closed at one end and open at the opposite end, a hollow lipid-impermeable fiber in the tube for supplying a solvent for lipids to the closed end of the tube, an absorbent inserted in the open end of the tube permitting solvent evaporation while retaining lipids, and a pump attached to said hollow fiber for delivering solvents, continuously or periodically.

5. The apparatus of claim 1 wherein the fiber is a polyamide.

6. The process for monitoring the concentration of lipids in the bloodstream of a live animal, which comprises inserting into the bloodstream the closed end of a lipid-permeable tube closed at one end and open at the opposite end, said tube having a hollow lipid-impermeable fiber for supplying a solvent for lipids to the closed end of the tube and having an absorbent inserted in the open end of the tube permitting solvent evaporation while retaining lipids while permitting the open end of the tube to extend through the epidermis, periodically or continuously passing a solvent for lipids through the fiber into the tube and to the absorbent and periodically determining the lipid concentration on said absorbent.

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