ABSTRACT

A disposable hemoperfusion assembly adapted for use in the detoxification of blood includes a housing having an inlet opening and an outlet opening which is adapted to be connected to a source of blood to be detoxified is disclosed. Blood detoxification means is disposed in the housing which includes an elongated base sheet material having adhesive means disposed on at least one side thereof, a layer or coating of chemically or physically reactive or adsorbent particles bonded to the adhesive side of the base sheet whereby substantially no fragmentation of the particles occurs when blood is passed through the detoxification means.
1 DISPOSABLE HEMOPERFUSION ASSEMBLY FOR DETOXIFICATION OF BLOOD AND METHOD THEREFOR

BACKGROUND OF THE INVENTION

There have been attempts to provide hemoperfusion devices for the detoxification of blood particularly where the blood may have lethal quantities of drugs or poisons and it is necessary to remove the toxic elements from the blood quickly, efficiently and safely.

Some of the conventional methods which may be used to reduce toxic levels of drugs after ingestion include gastric lavage and the use of emetics such as syrup of ipecac and apomorphine. These procedures, however, must be instituted before a potential lethal quantity of the drug has gained entrance into the blood by way of gastrointestinal adsorption. Other methods used are hemodialysis and peritoneal dialysis to reduce adsorbed drugs to a non-lethal level in the blood and tissue. These methods may be satisfactory except where the drug penetrates the semipermeable membrane slowly or not at all thereby preventing efficient dialysis. Investigators have since embarked on the hemoperfusion of blood to detoxify it by using an activated adsorbent type of material such as activated charcoal or ion exchange resins.

Animal experiments have affirmed problems which can exist when using these devices such as fragmentation of the adsorbent material, compacting of the particle bed and loss of some formed blood elements such as leucocytes and platelets. The fragmentation of the adsorbent is considered the most serious effect since there is a tendency to produce "adsorbent embolisation." Thus, the term "charcoal embolisation" emerges since most of the adsorbents used are activated carbons. Excess red blood cell destruction could lead to anemia, hemoglobinemia or hemoglobinuria. The problems which could arise due to loss of leucocytes and platelets are impairment to the mechanisms for preventing infection and clotting. Many devices employing these adsorbents have been used in the form of a cartridge having loosely packed activated carbons or ion exchange resins. However, fragmentation as noted above, occurs and there is a substantial platelet loss. To overcome the charcoal embolisation problem some experimenters have embedded the charcoal in a collapsible membrane. However, coating of the charcoal retards rapid removal of the toxic drug from the blood. Other experimenters have suggested and tried the use of bonding the charcoal particles into a solid mass by using a thermoplastic resin such as polyethylene powder and have used the bonded charcoal mass to filter gases.

SUMMARY OF THE INVENTION

An object of the present invention is to provide a disposable hemoperfusion assembly for the detoxification of blood which overcomes many of the difficulties and disadvantages heretofore encountered when employing chemically or physically reactive particles or activated adsorbent materials.

It is also an object of the invention to provide a disposable hemoperfusion assembly employing such materials bonded to the surface of a base sheet in fixed position wherein substantially all of the surface area of the activated material is exposed and is capable of contacting the blood as it passes thereover to remove the toxic materials therefrom while preventing compaction and fragmentation and minimizing the pressure drop across the assembly. It is also a further object of the invention to provide an inexpensive assembly which is readily coupled to a blood source for the detoxification of blood in mammals in which the assembly may be included in existing hemodialysis or peritoneal dialysis equipment to remove toxins therefrom.

My invention generally contemplates the provision of a disposable hemoperfusion assembly for the detoxification of blood which includes a housing having an inlet opening and an outlet opening and being adapted to be connected to a source of blood to be detoxified. Blood detoxification means is disposed in the housing which includes an elongated base sheet material having adhesive means disposed on at least one side thereof, a layer or coating of chemically or physically reactive or adsorbent particles bonded to the adhesive side of the base sheet whereby substantially no fragmentation of the particles occurs when blood is passed through the detoxification means.

The assembly may also include filter means positioned within the path of the outlet opening and having a porosity of at least the size of the formed elements of the blood so that fragments of the bonded particles which may break loose from the base sheet are prevented from entering the detoxified blood as it passes through the disposable assembly.

Also disclosed is a method for making and using the disposable hemoperfusion assembly of the invention herein. The assembly comprises providing detoxification means including an elongated base sheet material having adhesive means on at least one side thereof; forming a layer or coating of chemically or physically reactive or adsorbent particles and bonding the particles to the side of the base sheet having the adhesive means thereon; positioning the coated base sheet material into the housing in such a manner so as to provide a path for blood to pass therethrough in which the blood contacts substantially the entire free surface of the bonded particles on the base sheet material. In applying the layer of the particles care should be taken so that the major portion of the particles is free from bonding material to insure adequate adsorption.

Also, as the blood passes through the detoxification means the blood may be further filtered by positioning a filter having a porosity of at least the size of the formed elements of the blood in the blood path so that fragments of the bonded particles which may break loose are prevented from entering the detoxified blood as it passes through the disposable assembly.

DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of the use of the invention herein in which a mammal, such as a dog, is being detoxified by passing blood upwardly through the disposable hemoperfusion assembly of the invention herein by means of a suitable pump.

FIG. 2 is a partial sectional elevational view of the disposable hemoperfusion assembly as illustrated in FIG. 1.

FIG. 3 is a partial sectional view taken along the lines 3-3 of FIG. 2.

FIG. 4 is a fragmentary elevational view of the base sheet material illustrated as being coated on both sides thereof.
FIG. 5 is a partial sectional view of a disposable hemoperfusion device employing the base sheet material of FIG. 4.

FIG. 6 is a fragmentary elevational view of an alternate form of base sheet material and is illustrated as being an open web material having a coating of adsorbent materials on both sides thereof.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

For a better understanding of the invention herein reference is had to FIGS. 2 and 3 which illustrate the disposable hemoperfusion assembly. Disposable hemoperfusion assembly 10 includes a housing or tubular member 12 preferably made of a high impact moldable plastics material such as polycarbonate, polystyrene, or any other type of material which is inert to and is non-toxic to blood. Closure members 14 and 16 are mounted over the open ends of housing 12 and are generally configured in the shape of a funnel to provide inlet opening 15 and outlet opening 17, not shown. Closure members 14 and 16 are preferably made of the same material as housing 12 and are identical in configuration and structure so that a description of closure member 14 will serve to describe the corresponding configuration and structure of the closure member 16.

As illustrated in FIG. 2, end closure 14 is generally cylindrical in shape having a flat base 18 and a wall 20 formed around the periphery of base 18 so as to provide a recess. The diameter of the closure member 14 is substantially equal to the external diameter of housing 12 so that the open end closure of the housing will nest in the recess formed in member 14. Closure member 14 when mounted over the open end of housing 12 can be sealed by any appropriate means, for example, by swage fitting, by employing a suitable adhesive by threaded engagement or any other suitable means. Formed in the base of closure member 14 is spout 26 which provides a passageway for inlet opening 15. A suitable cap 30 is mounted over the open end of spout 26. As depicted in FIG. 2, spout 26 is formed centrally of base 18 so that inlet opening 15 is in axial alignment with the central axis of housing 12. Base sheet material 34 may be in the form of a film as illustrated in FIGS. 2 and 4 or may be in the form of an opened web as illustrated in FIG. 6. Base sheet 34 is coated with a suitable adhesive which is capable of adhering to the base sheet and also capable of bonding adsorbent particles 40 in fixed position thereto. It should be understood that the base sheet material 34, adhesive 36 and the particles 40 should not interact in such a manner as to cause toxicity in mammals. Also, all of the component parts of hemoperfusion assembly 10 must be compatible with and nontoxic to blood.

The chemically or physically reactive or adsorbent particles 40 may include activated carbon, ion exchange resins, dextran gels such as Sephadex which is a dry insoluble powder of macroscopic beads which are synthetic organic compounds derived from polysaccharide dextrins and is sold by Pharmacia Fine Chemicals Inc. Also, any combination of the particles 40 may be employed either in admixture or in separate compartments.

It has been found that the size of particles 40 may be up to about 5,000 microns and may be in the range of from 100 to 2,000 microns. Preferably, particles 40 may range in size from 297 to 1,000 microns. Still more preferably, they may range in size from about 297 to 840 microns and most advantageously from about 500 to 600 microns.

The surface area of particles 40 may vary widely. However, it has been found that where particles 40 are type PCB activated carbon made by the Pittsburgh Activated Carbon Company, the surface area of particles 40 may range from about 1,150 to 1,250 square meters per gram.

Spout 26 is formed having a tubular tip 27 projecting from base 18 of end closure 14. Tip 27 has a conical or tapered exterior having a bore 15 to provide the outlet passageway for hemoperfusion assembly 10. A retaining collar 28 projects forwardly from base 18 of end closure 14 in concentric relationship with conical tip portion 27. Retaining collar 28 is spaced from tip 27 a distance sufficient to accommodate coupling means disposed on the end of the flexible tubular members, not shown, connecting disposable hemoperfusion assembly 10 to a blood source as seen in FIG. 1. The interior surface of retaining collar 28 is formed having thread means 29 such as is commonly referred to as a female Luer connector and coupling means disposed on the ends of the flexible tubings of FIG. 1 are commonly referred to as the male Luer coupling means or male adapters for a Luer connector. Spout 26 is constructed similarly to the structure disclosed in U.S. Pat. No. 3,402,713.

As noted above, closure member 16 comprises identical structure as that described in closure member 14 and like parts are similarly numbered employing the primes of the corresponding portions.

Disposed in hemoperfusion assembly 10 is detoxification means 32 which comprises an elongated base sheet material 34 preferably in the form of a plastic film such as is sold by DuPont Company under the tradename MYLAR. Adhesive material 36 is coated on one or both sides of base sheet 34 and is preferably pressure sensitive so as to readily bond particles 40 thereto. It is preferable to have about 2 grams per sq. inch of adsorbent material bonded to the base sheet material 40. Particles 40 are uniformly coated on base sheet 34 to form a unilayer of bonded particles 40 as illustrated in FIGS. 2 and 3.

Detoxification means 32 is wound about a central core 42 preferably by employing adhesive material 36 to bond one end of elongated base sheet material 34 thereto. Thereafter, base sheet material 34 is wound about core 42 so as to form a coil of substantially uniformly spaced concentric layers of adsorbent particles 40 spaced from each layer by base sheet material 34 as illustrated in FIGS. 2 and 3. A suitable adhesive material may be any one of the chloro sulfonated polyethylene synthetic rubbers such as is sold under the tradename HYPALON 20. It should be understood that any adhesive material may be employed which is non-toxic and inert to blood and the other components forming hemoperfusion assembly 10. Also, the adhesive material 36 should effect a substantially permanent bond between base sheet material 34 and adsorbent particles 40. In this connection, particles 40 should be bonded to base sheet material 34 and have a bond strength sufficient to resist washings of the adsorbent material prior to use so that they do not become loose and pass into.
the detoxified blood when used. Since particles 40 are bonded the disadvantage of clogging of assembly 10 by compaction is prevented. Also, the particles 40 should have a hardness sufficient to withstand the mechanical pressures of manufacture and handling and subsequent use.

As noted above, various types of particles 40 have been found useful for practicing the invention herein. Particles 40 which are preferred are formed of activated charcoal of the type having a hardness sufficient to withstand mechanical pressures of manufacture, handling and subsequent use. Such activated carbons are made from coconuaut shell charcoal such as is sold under the tradename PCB by the Pittsburgh Activated Carbon Company. Also, resins which have been found to be suitable are those such as are sold under the tradename Amberlite XAD-2 made by the Rohm & Haas Company and are insoluble cross linked polymers in the form of beads. These ion exchange resins may be admixed with activated carbon or may form separate elements of the detoxification means 32.

When detoxification means 32 is wound about coil 42 it is sealed in tubular sleeve 46 which fits tightly about detoxification means 32 so as to prevent channeling or bypassing of blood therethrough without first contacting particles 40. Tubular sleeve 46 is preferably made of a plastic material such as polyeter. Detoxification means 32, after being fitted with tubular sleeve 46, is positioned in housing 12 and sealed therein by suitable potting material 47 such as an epoxy resin which immobilizes or fixes detoxification means 32 in place as illustrated in FIGS. 2 and 3.

Before mounting end closure 14 and 16 on housing 12 it is preferred to mount filters 50 at each end of tubular member 12. A suitable filter material which is compatible with blood and the other elements forming hemoperfusion assembly 10 is sold under the tradename Dafab 120 which are monofilament polyester screens having 40 micron openings formed therein. The porosity of the filters is sufficiently small but are large enough to permit the formed elements of the blood to pass therethrough without effecting cellular damage thereto. Also, filter elements 50 and detoxification means 32 are such that the pressure drop between the inlet opening 15 and the outlet opening 15 is less than 25 millimeters Hg gauge per three inches of length of detoxification unit 32 at a flow rate of 100 ml per min. It is necessary to maintain a minimal pressure drop since excessive pressure exerted against the formed elements of blood can cause cellular damage and possibly hemolysis of the red blood cells.

In FIGS. 4, 5 and 6 alternative embodiments of detoxification means 32 are illustrated. Detoxification means 32 is illustrated in FIGS. 4 and 5 as an elongated base sheet material 34 which has applied to each side thereof adhesive material 36 so that each side of base sheet material 34 is coated with a layer of particles 40. Detoxification means 32 is wound about a central core 42 in which a double layer of particles 40 are interposed between each coil of base sheet material 34. Detoxification means 32 is encased in thermoplastic sleeve 46 and is mounted in hemoperfusion assembly 10 by a suitable epoxy potting material 47. The hemoperfusion assembly 10 of FIG. 5 is constructed in accordance with the embodiment of FIGS. 1 and 2 described above.

FIG. 6 is similar to FIG. 4 except that elongated base sheet material 32 is made of an opened web material rather than a film as shown in FIG. 4. Adhesive material 36 is applied to both surfaces of elongated base sheet material 32 so that particles 40 are bonded to the web portions of elongated base sheet material 32 and is wound about central core 42 and fitted within hemoperfusion assembly 10.

In practicing the invention herein reference is had to FIG. 1 which illustrates the use of the apparatus and hemoperfusion assembly of the invention herein to detoxify a mammal such as a dog. The dog is suitably restrained on a table and is administered anesthesia through the mouth which is illustrated by tube T placed in its mouth. The dog blood is anticoagulated in a well known manner with a dose of a suitable anticoagulant as by intravenously administered heparin. A flexible conduit 60 is connected to pump P at one end with its other end coupled to the femoral artery of the dog. Tube 61 is connected to the inlet opening of hemoperfusion assembly 10 and pump P. Toxic blood is pumped from the femoral artery of the dog into pump P and through flexible conduit 61 where the toxic blood passes through hemoperfusion assembly 10 through conduit 62 and then through bubble trap B which removes any gases which may be trapped in the system. The detoxified blood is conducted downward through a third flexible tube 64 which is coupled to the outlet opening of bubble trap B at one end and to the femoral vein at its other end. Thus, a complete circuit is provided in which toxic blood is pumped through hemoperfusion assembly 10 in an upward direction and allowed to flow downwardly through bubble trap B to remove any gases therefrom before the detoxified blood is conducted back into the dog. It has been found that many toxic substances which are adsorbed into the blood such as barbituates, sodium salicylate, amphetamine, morphine sulphate, meprobamate, glutethimide, etc., can be efficiently and rapidly removed from the blood.

By way of example, hemoperfusion assembly 10 will be described using activated carbon type PCB made by the Pittsburgh Activated Carbon Company as the adsorbent material of detoxification means 32. Detoxification means 32 is bonded to a base sheet about 73 grams of adsorbent particles 40 which range in size of from 297 to 840 microns, a mean pore diameter of 13 to 21 A, a hardness of 92 and a surface area of from 1,150 to 1,250 square meters per gram. Hemoperfusion assembly 10 is washed with normal saline until less than 0.2 micrograms of activated carbon per liter of saline is collected on a 0.2 micron millipore filter. The washing procedure performs a second function of removing substantially all entrapped air in detoxification means 32. Then, caps 30 and 30’ are mounted in place to seal the inlet and outlet openings of hemoperfusion assembly 10. When the hemoperfusion assembly 10 is connected into the circuit as illustrated in FIG. 1, all of the saline solution contained in hemoperfusion assembly 10 is removed by blood and thereafter the detoxified blood is allowed to circulate through the animal to be detoxified.

The animal, a dog, to be detoxified was administered 175 milligrams per kilogram of body weight of sodium phenobarbital intravenously and allowed to remain in this condition for approximately 1 hour without further treatment. In previous experiments the dosage of phe-
3,888,250

nobarbital administered to the dog proved to be lethal. After about 1½ hours elapsed time, perfusion was started by pumping blood from the femoral artery through hemoperfusion assembly 10. Perfusion ceased after 5 hours. The hemoperfusion assembly was disconnected from the dog and within approximately 30 minutes the dog was able to rise on his front legs and subsequently went on to full recovery.

An analysis of the perfused blood from the dog indicated no significant hemolysis and no evidence of damage to the dog due to "charcoal embolism" and removal of the drug from the blood to a non lethal level.

From the foregoing description it is apparent that the disadvantages and difficulties heretofore encountered have been overcome. Further, the hemoperfusion assembly of the invention herein provides an assembly which is readily and easily constructed to achieve a uniform product design and performance.

What is claimed is:

1. A hemoperfusion apparatus useful in the detoxification of blood comprising:
a. a housing having spaced outlet and inlet openings, blood transfer means connected thereto adapted to be connected to a source of blood to be detoxified and having an interior passageway for the blood extending between the inlet and outlet openings; and,
b. a detoxification cartridge assembly disposed in the passageway in the housing, said cartridge assembly including a base supporting sheet having a coating of adhesive on at least one side thereof and a unilayer of individually spaced apart particles of adsorbent material between 100 and 5,000 microns in size bonded by the adhesive to the coated side of the sheet so that the major portion of the particles are free from bonding material whereby to prevent fragmentation of the adsorbent material said sheet being formed to provide a cartridge having alternate layers of base sheet material and adsorbent particles, said particles being in intimate contact with said layers;
c. said sheet material, adhesive, adsorbent particles and portions of the housing which the blood engages being inert to each other and being nontoxic and inert to blood.

2. The assembly of claim 1 wherein the particles of adsorbent material include chemically reactive material.

3. The assembly of claim 1 wherein the particles of adsorbent material include physically reactive material.

4. The assembly of claim 1 further includes a filter means having a porosity greater than the formed elements of blood is mounted in the path of said outlet opening so that any particles having a size greater than the formed elements of blood are removed from the detoxified blood.

5. The assembly of claim 1 wherein the base sheet material is a plastic film.

6. The assembly of claim 1 wherein the base sheet material is an open web.

7. The assembly of claim 1 wherein the adhesive means is a pressure sensitive adhesive.

8. The assembly of claim 1 wherein said particles are activated carbon.

9. The assembly of claim 1 wherein said particles have a particle size preferably of from 297 to 840 microns.

10. The assembly of claim 1 wherein said particles are macroscopic beads derived from polysaccharide dextran.

11. The assembly of claim 8 wherein the carbon particles have a mean pore diameter of 18–21 Å and a total surface area of 1,150 to 1,250 sq. meters per gram.

12. The assembly of claim 1 wherein said adsorbent particles are bonded to each side of said base sheet material.

13. The assembly of claim 1 wherein said detoxification means is formed into a coil and is encased in a tubular sleeve formed of a plastic film material.

14. The apparatus as set forth in claim 1 wherein said cartridge is free of internal bypass channels and said cartridge is disposed in the housing with its longitudinal axis extending in a direction between the inlet and outlet openings and having engagement with the wall portions of the housing surrounding the cartridge so as to prevent bypassing around the cartridge whereby blood introduced into the inlet opening passes between the layers of sheet material in the cartridge in engagement with the adsorbent particles to the outlet opening.

15. A method of detoxifying blood comprising the steps of:
a. providing a source of blood to be detoxified,
b. connecting a hemoperfusion apparatus to said blood source, said apparatus including a detoxification cartridge assembly having a base supporting sheet having a coating of adhesive on at least one side thereof and a unilayer of individual spaced apart particles of adsorbent material between 100 and 5,000 microns in size bonded by the adhesive to prevent fragmentation of the adsorbent material to the coated side of the sheet so that the major portion of the particles are free from bonding material, to said sheet being formed to provide a cartridge having alternate layers of base sheet material and adsorbent particles in intimate contact with said layers; and,
c. connecting said apparatus to the blood source; and,
d. pumping said blood between the layers of the sheet material in engagement with the adsorbent particles whereby to detoxify said blood.

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