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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61K 9/00, 9/08, B01D 61/00

A1

(11) International Publication Number: WO 93/24108

(43) International Publication Date: 9 December 1993 (09.12.93)

(21) International Application Number: PCT/US93/04351

(22) International Filing Date: 6 May 1993 (06.05.93)

(30) Priority data:
07/892,564 3 June 1992 (03.06.92) US

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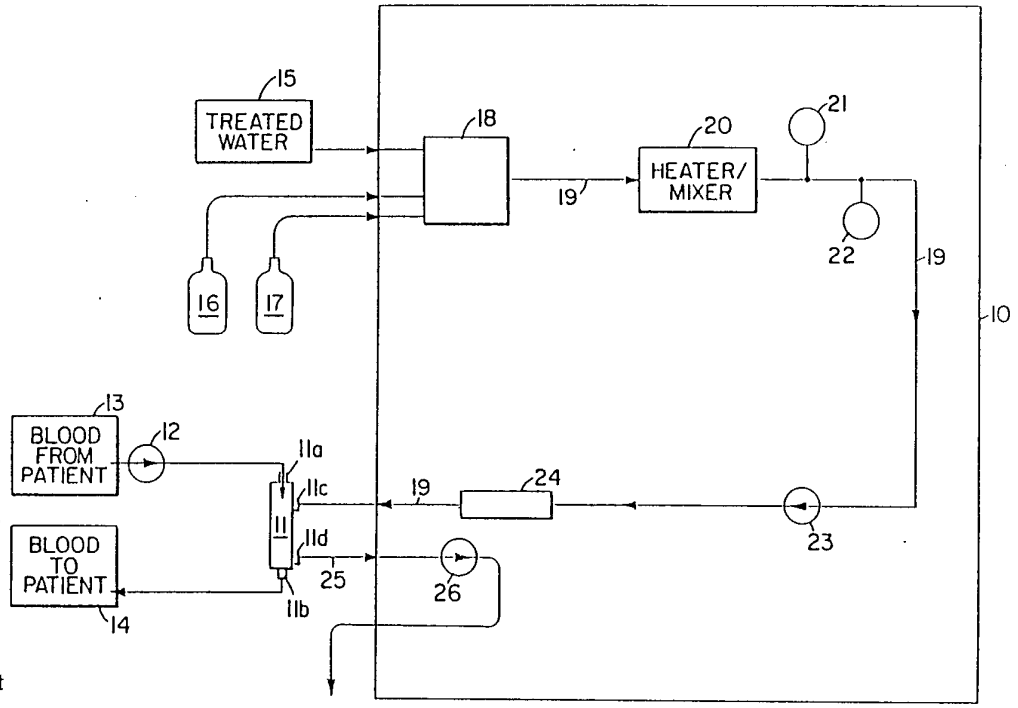
(81) Designated States: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: METHOD OF HEMODIALYSIS AND HEMODIALYSIS LIQUIDS INCLUDING HYDROCHLORIC ACID



(57) Abstract

Blood comes from the patient (13) through a blood pump (12) through an artificial kidney or membrane cartridge (11) and returns to the patient (14). The dialysate fluid is blended in a proportioning pump (18) by combining treated diluent water (15), acid concentrate (16), and bicarbonate (alkalizer/buffer) concentrate (17). These materials are blended at a machine set dilution ate (36.83X or 45X) to produce a final dialysate stream (19). Final dialysate fluid has at least 1 millimole of added acid. The dialysate fluid stream (19) passes into the cartridge (11) wherein the fluid contacts the exterior of the hollow dialysis membrane containing the blood. The contaminated dialysate (25) leaves the cartridge via pump (26) and directed to a drain.

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Method of hemodialysis and hemodialysis liquids including hydrochloric acid

Field of the Invention

The invention relates to the composition of an aqueous dialysate fluid used in the machine hemodialysis of human blood, most commonly, in the treatment of patients having end-stage renal failure. More particularly, the invention resides in a dialysate fluid system that can be used in available hemodialysis units at typical blending ratios or reagent proportions. The dialysate system can be used without the drawbacks of anions in the dialysate that can cause fatigue (weakness), nausea, vomiting and other debilitating symptoms.

Background of the Invention

Individuals requiring renal system support, or who have end-stage renal disease or renal failure, have kidneys temporarily or permanently incapable of removing products of metabolism and other substances from the blood for excretion in urine. Products of metabolism or metabolites typically include such components as urea, natural biochemical metabolites, drug metabolites, excess electrolytes, etc. Individuals with end-stage renal disease have the option of either undergoing the replacement of a diseased kidney through the transplant of a healthy kidney, or undergoing periodic hemodialysis (daily or weekly treatments) to reduce the concentration of harmful materials in the blood stream. Other individuals need hemodialysis for brief periods of renal support.

Hemodialysis is a process in which solute molecules, which constitute undesirable waste products in human blood, can be transported (i.e., removed from the blood stream) across a membrane into a dialysis fluid. The driving force of such transport is (1) the difference in pressure across the membrane and (2) the difference in chemical potential of each individual solute molecule across the membrane. Dialysis requires that membranes separating blood from dialysis fluid permit diffusional transfer of at least some of the molecular species present in blood into the fluid while effectively preventing any return contamination of blood or commingling of the blood and the dialysis fluid. Dialysis is a passive separation process with low operating costs using no external thermal or chemical energy sources. The basic hemodialysis separation obtained is

between large cells and molecules, such as RBC, WBC and proteins, and small molecules such as urea, electrolytes, and other small molecule metabolites. To obtain reasonable separation rates, machines are designed with large areas of membranes and are used at relatively small flow rates. Modern hemodialysis machines utilize small diameter hollow-fiber dialysis membranes bathed in dialysate fluids. Such membranes are in the form of a cylindrical cartridge having a large number of hollow-fiber membranes in fluid connection with a blood inlet and outlet. The blood flows through the hollow interior membrane space. The hollow-fiber membrane exterior is bathed in dialysate fluid. Hollow-fiber membranes are typically manufactured from cellulose derivatives such as cellulose ester and other polymeric materials such as, polysulfone, polyacrylonitrile, polymethylmethacrylate, polyamide, polyimidazole, hollow-fiber glass, etc.

Dialysis fluids are prepared with a pH and composition compatible with blood. As the composition of the solutes result in a pH which is significantly different from that of blood, a buffer is added to adjust the pH of the fluid to an acceptable value for blood compatibility. This buffer may be sodium acetate, sodium bicarbonate, or other similar material capable of adjusting the pH and maintaining blood compatability. Use of sodium acetate has been linked to patient symptoms of hypotension and fatigue, as well as other debilitating physical effects. The use of bicarbonate in dialysis minimizes the formation of sodium acetate during pH adjustment. Accordingly, a need exists for development of an acetate-free dialysis fluid for use in hemodialysis.

Brief Discussion of the Invention

We have found that the tendency of dialysate fluids to cause debilitating symptoms can be substantially reduced by using an acid concentrate having a source of acid consisting essentially of hydrochloric acid. The dialysate fluids of the invention are typically prepared in a three-stream dilution by combining an alkalizer/buffer concentrate stream and an acid concentrate stream with a stream comprising an aqueous, non-

pyrogenic, stable, bacteria-free diluent. Such a three-stream system, when operated at appropriate ratios of alkalizer/buffer to diluent and acid to alkalizer/buffer, produces the useful dialysate composition of the invention.

Brief Discussion of the Drawings

Figure 1 is a block diagram of typical hemodialysis equipment containing machine elements for the preparation of the dialysate fluid and elements to direct fluid to the membrane within the artificial kidney to remove contaminants from patient's blood.

Detailed Description of the Invention

In the preparation of a dialysate fluid used in common hemodialysis equipment, an alkalizer/buffer concentrate and an acid concentrate are added to an aqueous diluent stream at appropriate mixing ratios to produce the useful dialysate fluid which is directed to the dialysis membrane. The acid concentrate has a pH less than about 3.0, while the alkalizer/buffer has a pH greater than about 7.4. When diluted at a current machine ratio, the alkalinity of the alkalizer/buffer and the acid of the acid concentrate neutralize to a pH of 6.8-7.4. The source of bicarbonate ion typically comprises alkali metal bicarbonate salts. Such materials in aqueous solution typically yield bicarbonate ion and, depending upon pH, some free carbonate (CO_3^{-2}) ion. The relative proportions of carbonate and bicarbonate ions typically depend on the pH of the alkalizer/buffer solution and the amount of bicarbonate salt initially added to form the alkalizer/buffer solution. The alkalizer/ buffer solution must contain, at a minimum, a source of bicarbonate (HCO_3^-) ion. The alkalizer/buffer material can contain other ionized and non-ionized solutes that are compatible in aqueous solution with the dialysis product and the source of carbonate and bicarbonate ion. However, preferably, the alkalizer/buffer concentrate consists essentially of a source of bicarbonate as a source of alkalinity. The alkalizer/buffer solution contains little or no

other materials that significantly contribute to the alkaline pH of the alkalizer/buffer material. The amount of bicarbonate in the concentrate depends primarily on the blending ratio of concentrate to diluent stream used in the production of a pH of 6.8 to 7.4 in the hemodialysis dialysate fluid. Each type of hemodialysis machine has a characteristic dilution ratio. The concentrates are formulated for the dilution ratio of the machine.

We have found that the use of hydrochloric acid (HCl) as a sole source of acid in the acid concentrate reduces the tendency of the fluids to produce debilitating symptoms in dialysis patients. The acid concentrate material used in preparing the dialysate fluid is typically prepared in aqueous solution with HCl in combination with other solutes. The amount of acid used in the acid concentrate also depends on the hemodialysis machine used and the blending ratio characteristic of the machine. The acid concentrate material of the invention can contain a physiologically compatible acid in sufficient amount to result in a minimum of at least 1 millimolar acid for the dialysate fluid in a 45X machine or a 36.83X machine, or higher, depending on the operating concentration selected. By physiologically campatible acid, we mean acid that, in the concentrations used in the dialysate fluid, produces little or no adverse physiological impact on the blood present in the hemodialysis machine or on the patient undergoing dialysis. Further, by physiologically compatible acid, we mean an acid having an acid cation which is identical to or significantly related to cations present in normal human metabolism.

The concentration of acid in the concentrates diluted to form the dialysate fluids of the invention can be increased to increase resistance to precipitate, typically carbonate fractions in the dialysis fluid during use. The concentrates can be used to provide HCl at a concentration sufficiently high to result in adding at least one millimole, into the final dialysis fluid concentration which can effectively prevent the

production of harmful precipitates at a dialysate fluid pH between 6.8 and 7.4, preferably 6.8 to 7.2.

The dialysate fluid of the invention can also contain a variety of other physiological solutes and other solutes useful in treating the dialysis patient. Solutes common in humans include sodium, potassium, chloride, calcium, magnesium, phosphate, dextrose, sulfate, iron, copper, and others. The amount of such materials in the dialysate fluid is adjusted for the requirements of the individual dialysis patient. For example, the amount of dextrose used must be tailored for the diabetic patient. The amounts of Ca++, Na+, and K+ must be tailored for the cardiac patient. The dialysate fluids can contain, in each liter, from about 75 to 150 milliequivalents of sodium ion, 0 to 4 milliequivalents of potassium ion, 0 to 4 milliequivalents of calcium ion, 0 to 1.5 milliequivalents of magnesium ion, 70 to 115 milliequivalents of chloride ion, 20 to 40 milliequivalents of bicarbonate ion, etc. The fluid can also contain 0 to 250 milligrams of dextrose per 100 ml of dialysate fluid. Other solutes present in the dialysate solution can be tailored to the specific patient.

Other materials can be placed in the dialysate solution to treat the blood of the dialysis patient. For example, the dialysate solution can contain hormones, antibiotics, anticoagulants, and other nutrients. Useful hormones include materials such as insulin, steroids, prostaglandins, etc.; antibiotics include penicillin, cephlo-sporins, etc.; anticoagulants such as heparin, coumarin anticoagulants, indan-1,3-dione coagulants; and nutrients such as amino acids, dextrose, vitamins, etc.

Machines used in hemodialysis contain sensors, pumps, and control units that control the flow rate, flow direction, fluid pressure, fluid temperature, dilution ratios of the buffer alkalizer concentrate and the acid concentrate into the diluent water stream.

Detailed Description of the Drawing

Figure 1 shows a block diagram of a typical dialysis machine. The artificial kidney or membrane cartridge 11 is shown having an inlet 11a and an outlet 11b to permit the flow of blood through the cartridge. Blood comes from the patient 13 through a blood pump 12 through the cartridge 11 and returns to the patient 14. The dialysate fluid is blended in a proportioning pump 18 by combining treated diluent water 15, acid concentrate 16, and bicarbonate (alkalizer/buffer) concentrate 17. These materials are blended at a machine set dilution rate (36.83X or 45X) to produce a final dialysate stream 19. The dialysate stream 19 passes through a heater/mixer 20 which ensures uniformity and physiological temperature. The proper operation of the dialysis machine is monitored by a conductivity monitor 21, thermometer 22, and pressure regulator 23. The dialysate fluid stream 19 passes into the cartridge 11 through inlet 11c, wherein the fluid contacts the exterior of the hollow dialysis membrane containing the blood in the internal membrane passage. The dialysate receives material by diffusion from the blood across the membrane. The contaminated dialysate 25 leaves the cartridge at outlet 11d due to the influence of pump 26 and is directed to a drain. In the operation of the hemodialysis unit, the alkalizer/buffer material is blended within a three-stream dilution unit at a ratio of 1.6 to 2 parts by volume of the alkalizer/buffer concentrate per each part by volume of the acid concentrate. Perferably, about 1.7 to about 1.9 parts of alkalizer/buffer material is used with each part by volume of the acid concentrate material in the three-stream hemodialysis equipment dilution system. Further, for each part of the acid concentrate, about 30 to 50 parts of purified water (pyrogen-free, bacteria-free, USP or equivalent) is used. In 45X hemodialysis systems, for each part of the acid concentrate, 1.72 parts of the alkalizer/buffer about 42.28 parts (vol.) of purified water is used. In 36.83X systems, for each part of acid concentrate, 1.83 parts alakalizer/buffer in 35 parts (vol.) of purified water are used. The dialysate fluid is blended by combining the three streams in a blending unit and is

directly introduced into the housing or cartridge holding the membrane (artificial kidney). The fluid obtains the impurities from the blood held in the interior of the membrane by diffusion through the membrane's surface to the exterior dialysate fluid. The contaminated fluid is directed out of the housing to a drain.

The blending equipment of the hemodialysis unit is operated at a rate such that about 250 to 1000 ml of dialysate fluid are delivered to the exterior surface of the membrane (artificial kidney) unit per minute having the constituents proportioned as described above. The preferred rate of dilution of the concentrates and purified water results in a stream of about 400 to 600 ml of dialysate fluid per minute.

Proper proportioning of the dialysate constituents during dilution and subsequent hemodialysis can readily be monitored by a conductivity sensor because the relative conductivities of the aqueous diluent (low conductivity) and the concentrates (high conductivity) are significantly different from the conductivity of the diluted fluid. Should the dilution system fail and deliver diluent or concentrate to the dialysis unit, conductivity sensors can monitor and terminate flow at that time. The conductivity of the fluid should preferably be maintained at about 13.0 to 14.5 milliSiemens.

An illustrative dialysate fluid (HCl-based) prepared from the acid concentrate that is at least 1 millimolar in acid.

Ion	Concentration
Na+	90-135/L
HCO_3-	25-45 mEq/L
Cl- (salt) and Hydrochloric acid anion (Cl-)	105-120 mEq/L
Ca++	0-6 mEq/L (preferably, 0.1-5 mEq/L)
Mg++	0-6 mEq/L (preferably, 0.1-2.5 mEq/L)

These illustrative dialysate fluids are prepared from an acid concentrate and an alkalizer/buffer. The preferred alkalizer/buffer material used in the invention contains about 50 to 95 grams of sodium bicarbonate per liter of material or can contain about 10 to 30 grams of sodium chloride and 40 to 90 grams sodium bicarbonate. Perferably, the alkalizer/buffer material contains about 80 to 85 grams of sodium bicarbonate per liter.

Typical aqueous acid concentrates suitable for combination with the alkalizer/buffer material set forth above are prepared as illustrated hereafter:

Preparation 1 (36.83X Dilution)

Ingredient	Concentration
NaCl	172.2 gm/L
HCl (12.1 N)	18.2 gm/L
KCl	5.49 gm/L
dextrose	73.66 gm/L
water	q.s.
(pH 0 to 2.0)	

Expressed in different terms:

H+	184.15 mEq/L
Cl-	3204.25 mEq/L
Na+	2946.4 mEq/L
K+	73.7 mEq/L
dextrose	7366 mgm/dL

Preparation 2 (36.83X Dilution)

Ingredient	Concentration
NaCl	172.2 gm/L
HCl (12.1 N)	20.0 gm/L
KCl	5.49 gm/L
$MgCl_2.6H_2O$	3.74 gm/L
dextrose	73.66 gm/L
$CaCl_2.2H_2O$	9.48 gm/L
water	q.s.
(pH 0 to 2.0)	

Expressed in different terms:

H+	202.6	mEq/L
Cl-	3388.4	mEq/L
Mg++	36.8	mEq/L
Na+	2946.4	mEq/L
Ca++	128.9	mEq/L
K+	73.7	mEq/L
dextrose	7366	mgm/dL

Preparation 3 (36.83X Dilution)

Ingredient	Concentration	
NaCl	172.2	gm/L
HCl (12.1 N)	23.6	gm/L
KCl	5.49	gm/L
$CaCl_2.2H_2O$	9.48	gm/L
dextrose	73.66	gm/L
$MgCl_2.6H_2O$	3.74	gm/L
water (pH 0 to 2.0)	q.s.	

Expressed in different terms:

H+	239.4	mEq/L
Cl-	3425.2	mEq/L
Mg++	36.8	mEq/L
Na+	2946.4	mEq/L
Ca++	128.9	mEq/L
K+	73.7	mEq/L
dextrose	7366	mgm/dL

Preparation 4 (45X Dilution)

Ingredient	Concentration
NaCl	263.0 gm/L
HCl (12.1 N)	13.3 gm/L
KCl	6.7 gm/L
$CaCl_2.2H_2O$	9.9 gm/L
dextrose	90.0 gm/L
$MgCl_2.6H_2O$	3.4 gm/L
water	q.s.
(pH 0 to 3.0)	

Expressed in different terms:

H+	135.0 mEq/L
Cl-	4893.8 mEq/L
Mg++	33.8 mEq/L
Na+	4500.0 mEq/L
Ca++	135.0 mEq/L
K+	90.0 mEq/L
dextrose	mgm/dL

Preparation 5 (45X Dilution)

Ingredient	Concentration
NaCl	263.0 gm/L
HCl (12.1 N)	17.7 gm/L
KCl	6.7 gm/L
$CaCl_2.2H_2O$	9.9 gm/L
dextrose	9000 mgm/L
$MgCl_2.6H_2O$	3.4 gm/L
water	q.s.
(pH 0 to 3.0)	

Expressed in different terms:

H+	179.6 mEq/L
Cl-	4938.4 mEq/L
Mg++	33.8 mEq/L
Na+	4500.0 mEq/L
Ca++	135.0 mEq/L
K+	90.0 mEq/L
dextrose	9000 mgm/dL

Preparation 6 (36.83X Dilution)

Ingredient	Concentration
NaCl	172.2 gm/L
HCl (12.1 N)	8.16 gm/L
KCl	5.49 gm/L
$CaCl_2.2H_2O$	9.48 gm/L
dextrose	73.66 mgm/L
$MgCl_2.6H_2O$	3.74 gm/L
water	q.s.
(pH 0 to 2.0)	

Expressed in different terms:

H+	82.8 mEq/L
Cl-	3268.6 mEq/L
Mg++	36.8 mEq/L
Na+	2946.4 mEq/L
Ca++	128.9 mEq/L
K+	73.7 mEq/L
dextrose	7366 mgm/dL

Preparation 7 (36.83X Dilution)

Ingredient	Concentration
NaCl	172.2 gm/L
HCl (12.1 N)	10.16 gm/L
KCl	5.49 gm/L
$CaCl_2.2H_2O$	9.48 gm/L
dextrose	73.66 mgm/L
$MgCl_2.6H_2O$	3.74 gm/L
water	q.s.
(pH 0 to 2.0)	

Expressed in different terms:

H+	103.1	mEq/L
Cl-	3288.9	mEq/L
Mg++	36.8	mEq/L
Na+	2946.4	mEq/L
Ca++	128.9	mEq/L
K+	73.7	mEq/L
dextrose	7366	mgm/dL

Preparation 8 (36.83X Dilution)

Ingredient	Concentration	
NaCl	172.2	gm/L
HCl (12.1 N)	23.6	gm/L
KCl	5.49	gm/L
dextrose	73.66	mgm/L
water	q.s.	
(pH 0 to 2.0)		

Expressed in different terms:

H+	239.4	mEq/L
Cl-	3425.2	mEq/L
Na+	2946.4	mEq/L
K+	73.7	mEq/L
dextrose	7366	mgm/dL

Preparation 9 (45X Dilution)

Ingredient	Concentration	
NaCl	263.6	gm/L
HCl (12.1 N)	6.18	gm/L
KCl	6.7	gm/L
$MgCl_2.6H_2O$	3.4	gm/L
dextrose	90.0	gm/L
$CaCl_2.2H_2O$	9.9	gm/L
water	q.s.	
(pH 0 to 3.0)		

Expressed in different terms:

H+	62.7	mEq/L
Cl-	4821.5	mEq/L
Na+	4500.0	mEq/L
K+	90.0	mEq/L
Mg++	33.8	mEq/L
Ca++	135.0	mEq/L
dextrose	9000	mgm/dL

Preparation 10 (45X Dilution)

Ingredient	Concentration	
NaCl	263.0	gm/L
HCl (12.1 N)	17.7	gm/L
KCl	6.7	gm/L
$MgCl_2.6H_2O$	3.4	gm/L
dextrose	90.0	gm/L
$CaCl_2.2H_2O$	9.9	gm/L
water	q.s.	
(pH 0 to 3.0)		

Expressed in different terms:

H+	179.6	mEq/L
Cl-	4938.4	mEq/L
Na+	4500.0	mEq/L
K+	90.0	mEq/L
Mg++	33.8	mEq/L
Ca++	135.0	mEq/L
dextrose	9000	mgm/dL

We have found that these preparations provide the efficient, non-contaminating, operation of a hemodialysis machine providing effective removal of solutes from blood without the debilitating symptoms caused by other fluids. We have found that the solutions are typically stable and are not likely to promote the growth of microorganisms over typical manufacturer transportation storage and use periods. We have also tested the solutions of the invention and have found that the solutions are non-precipitating and can be used in common

hemodialysis machines without a substantial reduction in the operating efficiency of semipermeable hollow-fiber membrane units.

The above discussion, preparations and figures describe the invention with respect to the current and preferred embodiments developed to date. However, those skilled in the art will understand that a variety of modifications and variations of the invention may be derived without departing from the essence or spirit and scope of the invention. Therefore, the invention resides in the claims hereinafter appended.

WHAT IS CLAIMED IS:

1. A dialysis fluid for use in a 36.83X hemodialysis machine, which fluid comprises an aqueous dilution product formed by combining (i) an alkalizer/buffer containing a source of alkalinity comprising aqueous bicarbonate; and (ii) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution.

2. The fluid of claim 1 wherein the dilution product is formed by combining an aqueous diluent with the acid concentrate and the alkalizer/buffer concentrate.

3. The fluid of claim 2 wherein the aqueous diluent is combined with the acid concentrate prior to combination with the alkalizer/buffer concentrate.

4. The fluid of claim 2 wherein about 1 part of the acid concentrate and about 35 parts of aqueous diluent are combined with about 1.8 parts of alkalizer/buffer concentrate.

5. A dialysis fluid for use in a 36.83X hemodialysis machine, which fluid comprises:

(i) about 90-155 mEq/L sodium ion;

(ii) 25-45 mEq/L bicarbonate ion; and

(iii) about 105-120 mEq/L of Cl- anion, which is formed by combining:

(a) an alkalizer/buffer containing a source of alkalinity comprising aqueous sodium bicarbonate; and

(b) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution.

6. The fluid of claim 5 wherein the dilution product is formed by combining an aqueous diluent with the acid concentrate and the alkalizer/buffer concentrate.

7. The fluid of claim 6 wherein the aqueous diluent is combined with the acid concentrate prior to combination with the alkalizer/buffer concentrate.

8. The fluid of claim 6 wherein about 1 part of the acid concentrate and about 35 parts of aqueous diluent are combined with about 1.8 parts of alkalizer/buffer concentrate.

9. A dialysis fluid for use in a 36.83X machine, which fluid comprises an aqueous dilution product comprising about 90-155 mEq/L sodium ion, 25-45 mEq/L bicarbonate ion, 105-120 mEq/L chloride ion, and a physiologically acceptable concentration of potassium ion, calcium ion, magnesium ion, dextrose or mixtures thereof, which dilution product is formed by combining:

(i) an alkalizer/buffer concentrate containing a source of alkalinity comprising about 50-90 grams of sodium bicarbonate per liter of alkalizer/buffer concentrate; and

(ii) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution.

10. The fluid of claim 9 wherein the dilution product is formed by combining an aqueous diluent with the acid concentrate and the alkalizer/buffer concentrate.

11. The fluid of claim 10 wherein the aqueous diluent is combined with the acid concentrate prior to combination with the alkalizer/buffer concentrate.

12. The fluid of claim 10 wherein about 1 part of the acid concentrate and about 35 parts of the aqueous diluent are combined with about 1.8 parts of the alkalizer/buffer concentrate.

13. A method of hemodialysis of human blood which comprises introducing human blood into the interior of a hollow fiber hemodialysis membrane in a 36.83X hemodialysis machine and contacting the exterior of the membrane with a fluid which comprises an aqueous dilution product formed by combining:

(i) an alkalizer/buffer containing a source of alkalinity comprising aqueous bicarbonate; and

(ii) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution; and withdrawing the dialysate from the membrane and returning the blood to a patient.

14. The method of claim 13 wherein the dilution product is formed by combining an aqueous diluent with an acid concentrate and the alkalizer/buffer concentrate.

15. The method of claim 13 wherein the dialysate fluid is maintained at a temperature of about 35-40°C.

16. A dialysis fluid for use in a 45X hemodialysis machine, which fluid comprised an aqueous dilution product formed by combining

(i) an alkalizer/buffer containing a source of alkalinity comprising aqueous bicarbonate; and

(ii) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution.

17. The fluid of claim 16 wherein the dilution product is formed by combining an aqueous diluent with the acid concentrate and the alkalizer/buffer concentrate.

18. The fluid of claim 17 wherein the aqueous diluent is combined with the acid concentrate prior to combination with the alkalizer/buffer concentrate.

19. The fluid of claim 17 wherein about 1 part of the acid concentrate and about 42.3 parts of aqueous diluent are combined with about 1.7 parts of alkalizer/buffer concentrate.

20. A dialysis fluid for use in a 45X hemodialysis machine, which fluid comprises:

(i) about 90-155 mEq/L sodium ion;

(ii) 25-45 mEq/L bicarbonate ion;

(iii) about 105-210 mEq/L of Cl- anion; which is formed by combining:

(a) an alkalizer/buffer concentrate containing a source of alkalinity comprised essentially of aqueous sodium bicarbonate; and

(b) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution.

21. The fluid of claim 20 wherein the dilution product is formed by combining an aqueous diluent with the acid concentrate and the alkalizer/buffer concentrate.

22. The fluid of claim 21 wherein the aqueous diluent is combined with the acid concentrate prior to combination with the alkalizer/buffer concentrate.

23. The fluid of claim 20 wherein about 1 part of the acid concentrate and about 42.3 parts of the aqueous diluent are combined with about 1.7 parts of the alkalizer/buffer concentrate.

24. A dialysis fluid for use in a 45X machine, which fluid comprises an aqueous dilution product comprising about 90-155 mEq/L sodium ion, 25-45 mEq/L bicarbonate ion, 105-120 mEq/L chloride ion, and a physiologically acceptable concentration of potassium ion, calcium ion, magnesium ion, dextrose or mixtures thereof, which dilution product is formed by combining:

(i) an alkalizer/buffer concentrate containing a source of alkalinity comprising about 50-90 grams of sodium bicarbonate per liter of alkalizer/buffer concentrate; and

(ii) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution.

25. The fluid of claim 24 wherein the dilution product is formed by combining an aqueous diluent with the acid concentrate and the alkalizer/buffer concentrate.

26. The fluid of claim 25 wherein the aqueous diluent is combined with the acid concentrate prior to combination with the alkalizer/buffer concentrate.

27. The fluid of claim 25 wherein about 1 part of the acid concentrate and about 42.3 parts of aqueous diluent are combined with about 1.7 parts of alkalizer/buffer concentrate.

28. A method of hemodialysis of human blood which comprises introducing human blood into the interior of a hollow fiber hemodialysis membrane in a 45X hemodialysis machine and contacting the exterior of the membrane with a dialysis fluid which comprises an aqueous dilution product formed by combining:

(i) an alkalizer/buffer containing a source of alkalinity comprising aqueous bicarbonate; and

(ii) an acid concentrate comprising hydrochloric acid in sufficient amount to result in the addition of at least 1 millimole of the acid to a use solution; and

withdrawing the dialysate from the membrane and returning the blood to a patient.

29. The method of claim 28 wherein the dilution product is formed by combining an aqueous diluent with an acid concentrate and the alkalizer/buffer concentrate.

30. The fluid of claim 29 wherein the aqueous diluent is combined with the acid concentrate prior to combination with the alkalizer/buffer concentrate.

31. The method of claim 28 wherein the dialysate fluid is maintained at a temperature of about 35-40°C.

32. The method of claim 28 wherein the dialysate fluid is contacted with a membrane at a rate of about 200 to 1000 milliliters of fluid per minute.

33. The method of claim 28 wherein the acid concentrate further comprises magnesium ion and calcium ion in an amount sufficient to result in the addition of about 0.1 to 6 mEq/L, independently, of each ion in the dialysate fluid.

34. A two package concentrate for a 45X dialysis machine that can be diluted with purified water to form a physiologically compatible dialysate fluid, which comprises:

(a) a first package comprising an aqueous alkalizer buffer comprising a bicarbonate salt; and

(b) an acid concentrate comprising a source of acid in sufficient concentration to provide at least 1 millimole of acid in the final diluted dialysate fluid.

35. The concentrate of claim 34 wherein the source of acid comprises hydrochloric acid, acetic acid, citric acid, lactic acid, pyruvic acid, formic acid, fumaric acid, succinic acid or mixtures thereof.

36. The concentrate of claim 34 wherein the bicarbonate salt is present at a concentration of about 40 to 95 grams per liter.

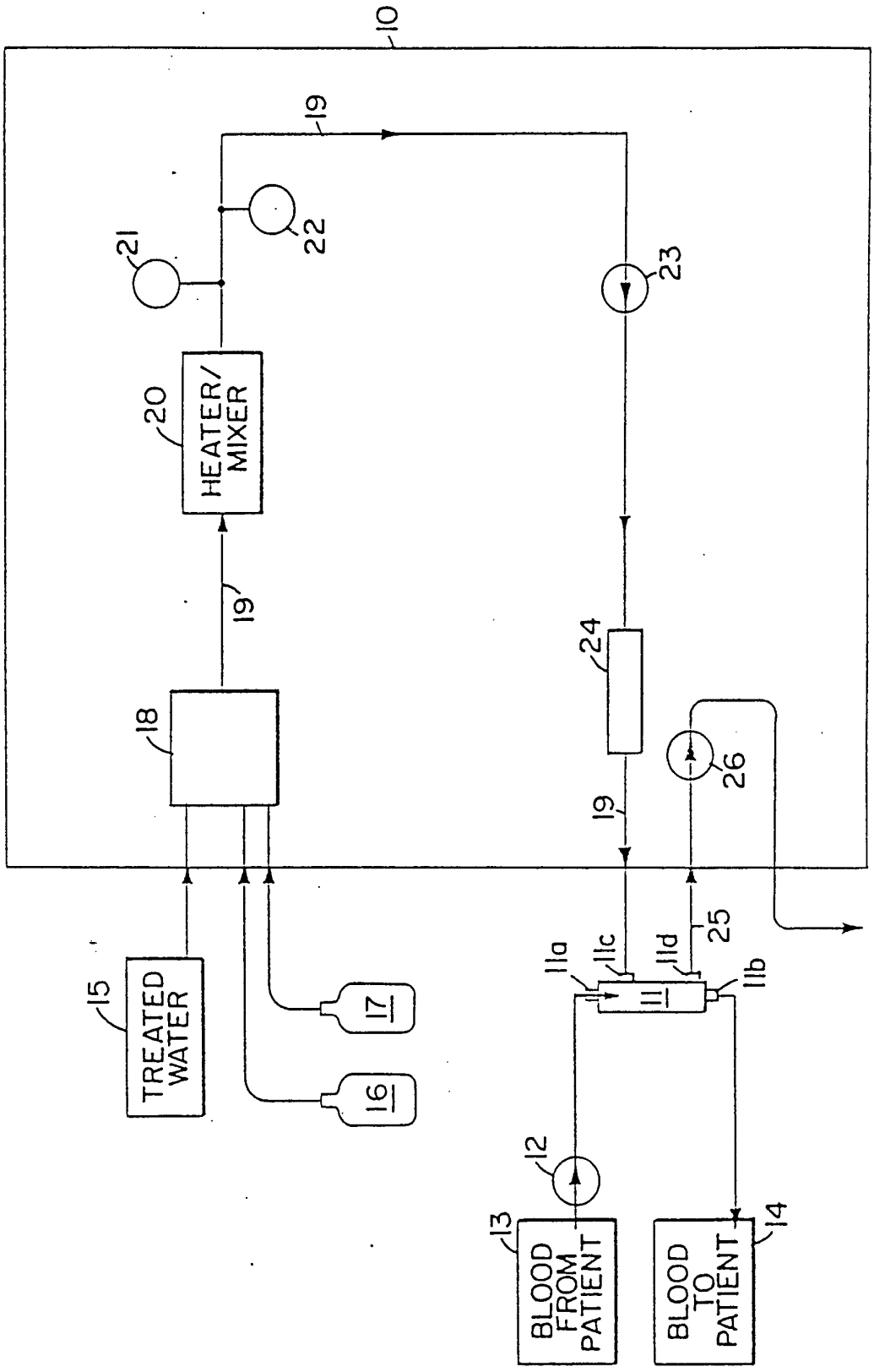
37. A two package concentrate for a 36.83X dialysis machine that can be diluted with purified water to form a physiologically compatible dialysate fluid, which comprises:

(a) a first package comprising an aqueous alkalizer buffer comprising a bicarbonate salt; and

(b) an acid concentrate comprising a source of acid in sufficient concentration to provide at least 1 millimole of acid in the final diluted dialysate fluid.

38. The concentrate of claim 37 wherein the source of acid comprises hydrochloric acid, acetic acid, citric acid, lactic acid, pyruvic acid, formic acid, fumaric acid, succinic acid or mixtures thereof.

39. The concentrate of claim 37 wherein the bicarbonate salt is present at a concentration of about 40 to 95 grams per liter.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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/04351

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61K 9/00, 9/08; B01D 61/00
US CL :210/646, 647; 514/832, 833; 252/1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 210/646, 647; 514/832, 833; 252/1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 4,366,881 (Babb et al.) 29 June 1982 See entire document	1-33
A	US, A, 4,399,036 (Babb et al.) 16 August 1983 See entire document	1-39
X	Renasol/Centrisol brochure issued January 1989 (Minneapolis, Minnesota), Renal Systems See entire document	34-39

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"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
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 19 July 1993	Date of mailing of the international search report 03 AUG 1993
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