PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :
A61K 9/22, B65D 35/28

A1

(11) International Publication Number: **WO 94/18952**

(43) International Publication Date: 1 September 1994 (01.09.94)

(21) International Application Number: PCT/US94/01960

(22) International Filing Date: 25 February 1994 (25.02.94)

(30) Priority Data:
08/023,130 26 February 1993 (26.02.93) US

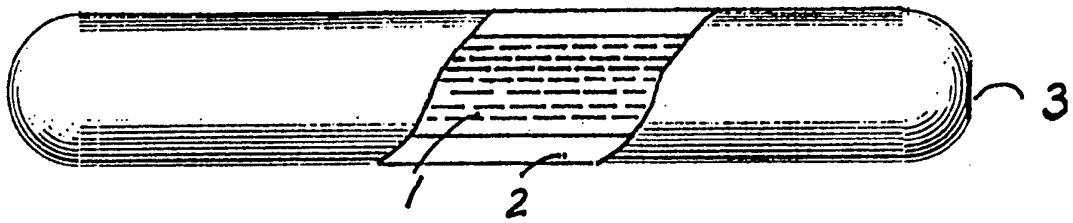
(71)(72) Applicant and Inventor: BETTINGER, David, S. [US/US]; 8030 Coventry, Grosse Ile, MI 48138 (US).

(74) Agents: DESCHERE, Linda, M. et al.; Barnes, Kisselle, Raisch, Choate, 3500 Penobscot Building, 645 Griswold Street, Detroit, MI 48226 (US).

(81) Designated States: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN, 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: PARENTERAL FLUID MEDICATION RESERVOIR PUMP



(57) Abstract

A fluid medication pump (1) comprises a reservoir (2) filled with fluid medication. The medication is continuously discharged over an extended period into the patient. The continuous discharge is obtained by a shrink polymer wall for the reservoir (2) which is powered by a shrink polymer. In the principal embodiment the device pumps from a reservoir (2) which is surgically implanted into the patient. A reservoir (2) depletion warning for surgically implanted pumps which creates a physiological indicator is also taught.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	**GB**	United Kingdom	**MR**	Mauritania
AU	Australia	**GE**	Georgia	**MW**	Malawi
BB	Barbados	**GN**	Guinea	**NE**	Niger
BE	Belgium	**GR**	Greece	**NL**	Netherlands
BF	Burkina Faso	**HU**	Hungary	**NO**	Norway
BG	Bulgaria	**IE**	Ireland	**NZ**	New Zealand
BJ	Benin	**IT**	Italy	**PL**	Poland
BR	Brazil	**JP**	Japan	**PT**	Portugal
BY	Belarus	**KE**	Kenya	**RO**	Romania
CA	Canada	**KG**	Kyrgystan	**RU**	Russian Federation
CF	Central African Republic	**KP**	Democratic People's Republic of Korea	**SD**	Sudan
CG	Congo			**SE**	Sweden
CH	Switzerland	**KR**	Republic of Korea	**SI**	Slovenia
CI	Côte d'Ivoire	**KZ**	Kazakhstan	**SK**	Slovakia
CM	Cameroon	**LI**	Liechtenstein	**SN**	Senegal
CN	China	**LK**	Sri Lanka	**TD**	Chad
CS	Czechoslovakia	**LU**	Luxembourg	**TG**	Togo
CZ	Czech Republic	**LV**	Latvia	**TJ**	Tajikistan
DE	Germany	**MC**	Monaco	**TT**	Trinidad and Tobago
DK	Denmark	**MD**	Republic of Moldova	**UA**	Ukraine
ES	Spain	**MG**	Madagascar	**US**	United States of America
FI	Finland	**ML**	Mali	**UZ**	Uzbekistan
FR	France	**MN**	Mongolia	**VN**	Viet Nam
GA	Gabon				

PARENTERAL FLUID MEDICATION RESERVOIR PUMP

TECHNICAL FIELD

This invention generally relates to a pump for dispensing parenteral fluid medication and more particularly to a pump which is surgically implanted to administer such medications by the induced flow of an internal reservoir over an extended period of time. In the main such implant devices find usage for the ambulatory patient requiring an extended regimen such as for a chronic condition or for birth control. About half of all ethical pharmaceuticals are consumed for a chronic condition. Such implant devices also find usage for the acute patient in transit where neither an IV gravity bag, nor continuous injections can be used.

BACKGROUND ART

Prior art on continuous medication where the reservoir is external to the patient includes

gravity feed,
power-driven pumps,
elastic bladder pumps,
gas pressurized pumps.

For an acute patient in transit, gravity IV may be cumbersome, power may be unavailable, or the duration of elastic bladders and gas pressure pumps may be too short.

Prior art on continuous medication where the reservoir is internal to the patient as an indwelling implant includes

osmotic powered pumps,
exuding or diffusion controlled polymers,
eroding systems, and
power-driven pumps.

Osmotic implant durations are limited to 30 days. Exuding implants have durations of up to five years, but have decreasing sloped delivery curves as shown in the

1992 Physicians' Desk Reference, page 2484. Eroding implants are difficult to develop because the drug, the vehicle, and the binder must all be compatible, and predictably benign when absorbed. Power-driven pump implants are complex and expensive.

DISCLOSURE OF INVENTION

It is a general object of this invention to overcome the aforementioned drawbacks of prior art medication dispensing systems. It is another general object of this invention to teach the continuous dispensing of medication by shrink polymer pumps. It is another object of this invention to dispense fluid medication at a reliable, flat delivery rate. It is a further object of this invention to provide an inexpensive pump which takes up little volume of space because the package is the pump. It is another object of this invention to provide a universal infuser implant pump for all intravenous, intramuscular, or subcutaneous extended-regimen drugs including hormones, cardiovascular, antibiotics, and psychotropics. It is still another object of this invention to provide a pump capable of programmable multi-drug sequencing. It is yet another object of this invention to provide a safe drug dispenser with safeguards for patient self-monitoring and pump disablement.

In keeping with these objects and others which will become apparent hereinafter, one feature of this invention resides, briefly stated, in a disposable parenteral fluid medication pump comprising an elongated reservoir having an enclosing wall; said reservoir having at least one closable outlet through which a flowable fluid is induced to administer a medication; and wherein said reservoir wall is made of shrink polymer material which when activated results in a reduction in the interior volume of said reservoir forcing said flowable fluid through said outlet; and wherein said shrink polymer material is

activated by heat, aging, light, chemical agent, oxygen, or a combination. Such shrink polymers are well known and their use in general dispensing is taught by Bettinger in U.S. Patent No. 5,188,260.

In accordance with one embodiment of this invention as an implant pump wherein the pump is surgically implanted for such periods as may be required for the medication or medications resident in the charge with the duration of the implantation achieved by the shrink-polymers selected. For example, poor patient compliance with oral medication during the treatment of tuberculosis leads to drug resistance and contagion. A 60 day duration implant dispensing antibiotics by age-shrinkage would be a major step toward regaining control of the disease. Because most shrink polymers are temperature responsive, the fixed ambient temperature of the patient's body provides a flat delivery curve.

It will be understood by one skilled in the art that said pump implant may be prepared with one end drawn to a point to facilitate insertion in flesh and which by shape memory achieves after implantation a more rounded and thereby less irritating shape.

It will also be understood by one skilled in the art that said implant pump may be coated with polymers which enhance biocompatability.

It will also be understood by one skilled in the art that the dispensing status of such a subcutaneous semi-transparent implant can be visually monitored by the use of dye for all or a portion of the charge together with the proper external application of a light of selected strength and spectrum to penetrate the skin and make visible the dye.

In accordance with a second embodiment of this invention wherein the reservoir of said implant pump is charged by the insertion of a prefilled flexible tube, bag, sack, or pouch containing the fluid to be administered. The

shrink-polymer implant pump may thus be stored separately awaiting application and activation.

In accordance with a third embodiment of this invention, when during administration said shrink polymer pump is activated by the patients body temperature then insulation means are provided for maintaining a uniform temperature at the reservoir site by shielding said pump from temperature variations.

In accordance with a fourth embodiment of this invention, wherein the reservoir outlet is mounted in communication with a means for continuous administering medication such as a hollow tube for site targeting or multi-drug sequencing. For site targeting a subcutaneous site allows status monitoring with said hollow tube dispensing end placed directly within a tumor. For multi-drug sequencing, drugs may be arranged in linear array within either said hollow tube or said pump of small diameter and programmed by concentration, and amount to satisfy a complex regimen of months or years.

In accordance with a fifth embodiment of this invention, wherein said pump has a magnetic, externally activated, disabling device. It will be understood by one skilled in the art that a hypodermic can be used to pierce the skin and the pump wall to withdraw a portion of the charge to also forestall short-term dispensing.

In accordance with a sixth embodiment of this invention, wherein said pump which achieves in its post-dispensing state, a relaxed shape in which the opposing internal surfaces are adjacent and parallel, so as to minimize any residual undispensed charge.

In accordance with an independent embodiment of this invention, any surgically implanted medication dispenser internal to the patient wherein at or near the exhaustion of the medication the implant dispenses a drug which creates a perceptible or observable physiological change in the patient as an indicator for medication

exhaustion or implant removal.

For example the medication exhaustion indicator wherein the indicator drug is methylene blue would color the urine, alerting the patient to seek further medical care and implant removal.

BRIEF DESCRIPTION OF DRAWINGS

FIG. 1 is an elevation and partial section through an embodiment of a pump used as a surgical implant.

FIG. 2 is a transverse section through a pump prior to shrinkage dispensing.

FIG. 3 through FIG. 5 are transverse sections through pumps after shrinkage dispensing which revert to shapes of varying dispensing efficiency.

FIG. 6 is a section through the wall of a pump showing a disabling plug removable by external magnetic means.

FIG. 7 is a longitudinal section through a pump showing the magnetic plug in a displaced position.

FIG. 8 is a transverse section through a pump prior to shrinkage dispensing showing the prefilled container for the charge.

FIG. 9 is a schematic showing a small diameter tube connected to the pump for multi-drug sequencing.

FIG. 10 is a schematic showing a small diameter pump for multi-drug sequencing.

BEST MODES OF CARRYING OUT THE INVENTION

Referring now to the drawings, reference numeral 1 identifies a first embodiment pump in FIG. 1. As the pump shrinks it constricts the volume of the reservoir 2 thereby dispensing fluid 2 through the outlet at 3.

In FIG. 2 the pump 4 in its unconstricted state when implanted takes the form in section of a cylinder containing a reservoir 5.

In FIG. 3 the pump 6 is shown in a depleted state when final shape of the pump 6 has been determined to be a cylinder. In this case the cylindrical shape has shrunken radially. If the shrink polymer has had a 50% dimensional reduction, then the reservoir has retained about 50% of its charge as unused follower fluid.

FIG. 4 shows an embodiment of the pump 8 which minimizes the reservoir volume at depletion by utilizing the shape memory of the polymer material at the two lobes to bring the two opposing faces 9 and 10 of the internal surface into parallel.

It will be understood by one skilled in the art that multiple lobes may follow the rule taught by this invention of bringing opposing faces into parallel. In FIG. 5 a three lobe pump 11 has dispensed its charge aided by the thickened ends of lobes 12, 13, 14 to increase the strength required of the shape memory polymer at the lobe ends 12.

In FIG. 6 the pump wall 15 has an additional outlet closed by a plug 17 with a magnetic core 16. Immediate short term cessation of drug dispensing is accomplished by applying a strong magnet to the implant to rotate the plug 17 inward. When plug 17 is dislocated, a free flowing inert follower fluid 18 is dispensed rather than a more viscous charge.

In FIG. 7 the plug 17 is displaced from pump 18 after an external magnet acts on magnetic core 18.

In FIG. 8 the pump 5 is charged with a container 18, prefilled with medication prior to dispensing.

In FIG. 9 a small diameter hollow tube 20 is connected to pump 19 for multi-drug sequencing. The non-misable medications are shown schematically as alternating charges in the tube 20.

In FIG. 10 the pump 21 is formed as a long, small-diameter, tubular, multi-drug sequencer. The non-misable medications are shown schematically as alternating charges in the pump 21.

CLAIMS

What is claimed as new and desired to be protected by Letter Patent is set forth in the appended claims.

1. A disposable parenteral fluid medication pump comprising an elongated reservoir having an enclosing wall;

said reservoir having at least one closable outlet through which a flowable fluid is induced to administer a medication; and

wherein said reservoir wall is made of shrink polymer material which when activated results in a reduction in the interior volume of said reservoir forcing said flowable fluid through said outlet; and

wherein said shrink polymer material is activated by heat, aging, light, chemical agent, oxygen, or a combination.

2. The pump of claim 1 wherein the pump is made of age activated, shrink polymers which are biocompatible with surgical implantation in a patient for such periods as may be required for the medication or medications resident in the charge.

3. The pump of claim 1 wherein the reservoir outlet is mounted in communication with a means for continuous administering medication such as a hollow tube for site-targeting and multi-drug sequencing.

4. The implant pump of claim 2 wherein said pump has an additional outlet closed by a plug having a magnetic core, which when externally activated by a magnet, dislocates said plug, releasing an inert follower fluid, rather than the charge.

5. The pump of claim 1 wherein the reservoir is

charged by the insertion of a container, prefilled with the medication to be administered.

6. The pump of claim 1 which achieves in its post dispensing state a relaxed shape in which the opposing internal walls are adjacent and parallel so as to minimize any residual undispensed charge.

7. The pump of claim 1 wherein said pump of small diameter contains linear programmed medication for multi-drug sequencing.

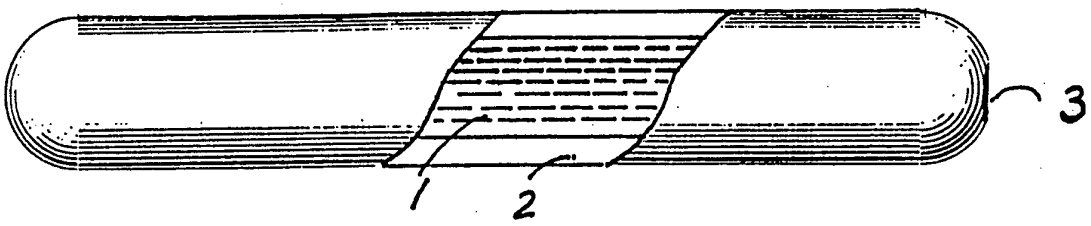


FIG. 1

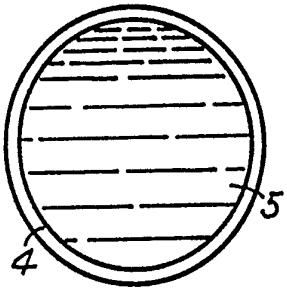


FIG. 2

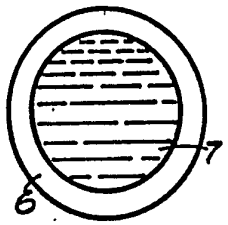


FIG. 3

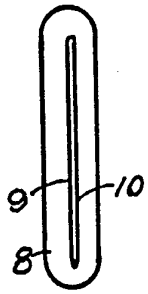


FIG. 4

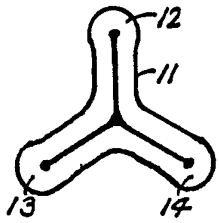


FIG. 5

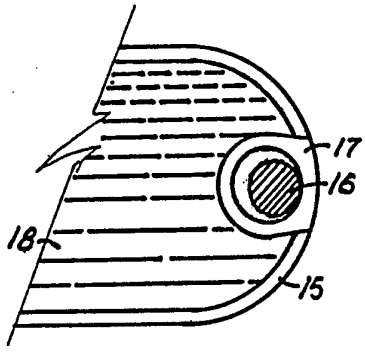


FIG. 6

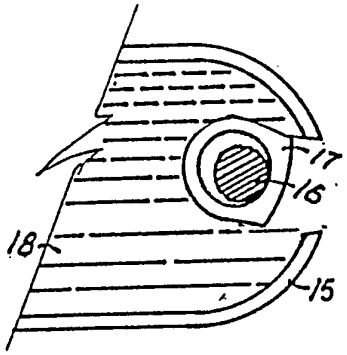


FIG. 7

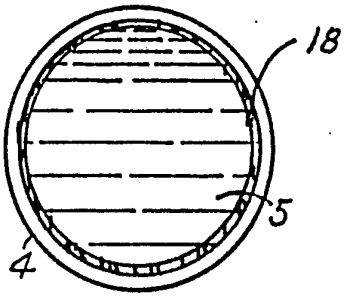


FIG. 8

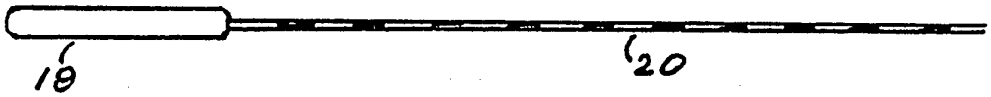


FIG. 9

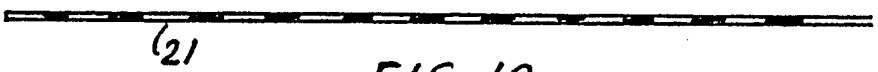


FIG. 10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/01960

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :A61K 9/22; B65D 35/28

US CL :222/95, 107; 424/423; 428/35.1; 604/890.1, 891.1

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. : 604/891.1, 890.1, 892.1, 132; 222/95, 107, 386.5; 424/420, 421, 423, 424, 425; 428/35.1

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

NONE

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

APS S RESERVIOR (P) (SHRINK (5A) POLYMER)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 5,053,032, (BARCLAY ET AL.), 01 October 1991. See entire document.	NONE
A	US, A, 5,019,372, (FOLKMAN ET AL.), 28 May 1991. See entire document.	None
A	US, A, 4,957,119, (DE NIJS), 18 September 1990. See entire document.	None
A	US, A, 4,304,232, (MICHAELS), 08 December 1981. See entire document.	None
A	US, A, 4,192,308, (MICHAELS), 11 March 1980. See entire document.	None
A	US, A, 4,180,073, (MICHAELS), 25 December 1979. See entire document.	None

[X] 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

06 APRIL 1994

Date of mailing of the international search report

25 MAY 1994

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JOHN G. WEISS

Telephone No. (703) 308-2702

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/01960

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 3,710,795, (HIGUCHI ET AL.), 16 January 1973. See entire document.	None