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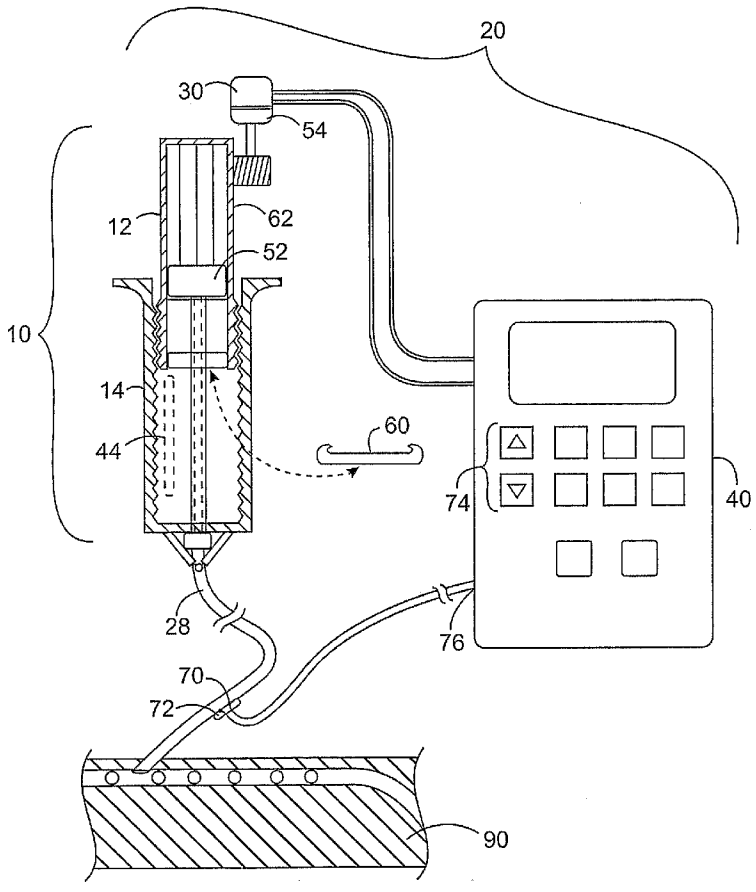
(54) Title: QUANTITATIVE CHRONOLOGICAL MEDICAL INFUSION DEVICE



(57) Abstract: The present invention is a medical infusion and aspiration system for delivering precisely timed and accurately calculated, pulsated delivery in high rates of flow delivering an effective profile of pulses tailored to provide momentary spikes of levels of freely available medicines based upon the uptake of the medicine and adjusted based on near real time measurements of the medicine or response of the patient. The system comprises a pumping mechanism (20), a cassette (10) and cartridge (12) having a reservoir area (18) wherein a plunger (16) rotates as it advances in reference to the cartridge (12) to provide additional accuracy and overcome the forces of inertia and slip-stick as well as eliminate backlash. The infusion is adjusted in both amount and duration between pulses to provide quantitatively controlled chronologically optimized infusion.

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QUANTITATIVE CHRONOLOGICAL MEDICAL INFUSION DEVICE

FIELD OF INVENTION

This invention relates to medical systems, and more specifically, to a medical infusion system which provides precise chronologically tuned and computed pulse delivery of infusions based upon the uptake characteristics of medicines and physiological responses of the patent, which device can also aspirate fluid and perform tests thereon, using a highly accurate, easily operated, disposable and reliable way to deliver any type of liquid or reagent, providing quantitative chronological delivery for treating a multitude of diseases and conditions, including cellular stimulation of metabolic pathways.

BACKGROUND OF THE INVENTION:

The historical means of delivering medicines have been arbitrarily divided into two types of delivery. The first is pharmaceutical delivery of compounds through chemically based systems using various carriers with specific chemical properties to control the uptake of the active chemicals. The chemical properties react in pre-designed responses to the tissues which are proximate and affected by the active, thus providing the modulated delivery of medicines.

The second means of delivering medicines uses various mechanical and electro-mechanical systems to modulate the delivery, which unlike chemical delivery systems, generally have limited direct interaction with the patient's tissues and are blind to the physiological responses to the compounds being administered.

Some medical devices which have attempted to use information from the physical response of the patient to adjust the medical delivery being infused, include a means for checking glucose by probe, and to help control Continuous Subcutanious Insulin Infusion such as the Medtronic wearable insulin pump with glucose reading information, as in Starkweather, US Patent No. 6,694,191 and another truly "closed loop" system such as the Miles Biostator device as in Clemens, US Patent No. 4,055,175. While the approach of these devices may constitute an improvement over devices which have no bio-feedback of the patent's response, they still fail to use uptake information to provide medicine in a quantitative chronological fashion.

SUMMARY

Accordingly, the present invention is a medical infusion and aspiration system delivering Quantitative Chronological infusions of accurate pulsatile delivery at high rates of flow. The system can provide a means to automatically avoid errors in concentration, reagent and medicine type, and avoid the problems of shear and other medicine degrading pressure problems. The system can avoid the slip-stick, chatter, overruns, and the problem of hysteresis by breaking the seating forces between Plunger and Cassette wall in a lateral motion that does not vary the delivery profile, and overcomes any limitations in the viscosity of the reagent. The system also can eliminate the need to dilute reagents to provide additional control for the limitations of accuracy in other systems. Other important characteristics of the invention include disposability, inexpensive cost and use by the manufacturer in glass lined or plastic, for the cartridge to act as both the pumping cartridge and the shipping and storage cartridge thus avoiding loss of reagent in the priming of an infusion device. The current invention also eliminates the need for withdrawing the medicine with a needle and achieves extraordinary accuracy without error correcting software or expensive volumetric measurement and control systems.

DESCRIPTION OF THE DRAWINGS

A preferred embodiment of the present invention is further described in connection with the accompanying drawings, in which:

FIG. 1 is a perspective view of a preferred embodiment of the medical infusion and aspiration system.

FIG. 2 is a perspective view of a preferred embodiment of the cartridge.

FIG. 3 is a perspective view of a preferred embodiment of the housing and plunger.

FIG. 4 is a perspective view of another preferred embodiment of the medical infusion and aspiration device.

FIG. 5 is a perspective view of a third preferred embodiment of the medical infusion and aspiration device.

FIG. 6 is a perspective view of a fourth preferred embodiment of the medical infusion and aspiration device.

FIG. 7 is a perspective view of a fifth preferred embodiment of the medical infusion and aspiration device.

FIG. 8 is a perspective view of an embodiment of the medical infusion and aspiration system having two cassettes being driven independently.

FIG. 9 is a perspective view of an embodiment of the medical infusion and aspiration system having two cassettes coupled by mechanical linkage.

FIG. 10 is a graph of the resulting infusion profile and free levels of medicine when starting with no or low backgrounds of medicines.

FIG. 11 is a graph of the resulting infusion profile and free levels of medicine when staring with a prior amount of medicine present in the body.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a unique pulse delivery system which delivers adjusted pulsed amounts of quantitatively precise actives, chronologically corrected to be most effective based upon the uptake characteristics of the medicine as well as the individual patient's real time response to the medicines or compounds being infused, hence the term Quantitative Chronological Medical Infusion Device.

The present invention is a medical infusion and aspiration system capable of accurate pulsatile delivery at high rates of flow and enabled to adjust the time between pulses and amount of delivery in each pulse to provide Quantitative Chronological Delivery. The present invention provides a means to provide changes in timing and amounts of delivery while automatically avoiding errors in concentration, reagent and medicine type, and avoiding the problems of shear and other medicine degrading pressure problems. The system also avoids the slip-stick, chatter, overruns, and the problem of hysteresis by breaking the seating forces between the plunger and cartridge wall in a lateral motion that does not vary the delivery profile by the viscosity of the reagent. The system also avoids loss of reagent in the priming of a separate infusion device and eliminates the tendency of reagents to separate when in a diluted environment. The invention is disposable, inexpensive and may be used by the manufacturer in glass lined or plastic, as both the pumping cartridge and the shipping and storage cartridge. The current invention, by acting as the storage container, also eliminates the need for withdrawing the medicine from a storage container with a needle and achieves extraordinary accuracy without error correcting software or expensive volumetric measurement and control systems.

In general, the current invention comprises a cassette cartridge pumping and

aspirating device. The cassette cartridge pumping and aspiration system comprise a cartridge, a housing, a plunger, a reservoir area where the reagent is contained, a neck opening in the plunger or cassette for the connection of the cartridge to a tube which travels to a point where infusion of the reagent in the reservoir takes place, and an in-line area where probes for sampling are located. The in-line area probes are used to provide input to a pumping device. The current invention has only one moving part in relation to the delivery mechanism and this simplicity allows for more accuracy and lower costs. It also allows for a single handed adaptation of the cartridge to the pumping device, freeing the other hand and avoiding accidental sticking with "sharps" such as needles which may be contaminated with blood or other materials.

Referring now to the figures, FIG. 1 is a perspective view of an embodiment of the invention showing a cassette 10, a pumping mechanism 20 and a motor 30. The cassette further comprises a cartridge 12, and a housing 14.

In a preferred embodiment, as seen in FIGS. 1 and 2, the cartridge 12 is cylindrical in shape and has a reservoir area 18, and encoded area 24. The cartridge 12 is preferably made from glass or plastic. For high-pressure situations, it is preferable that the cartridge 12 be made of steel or ceramics. It is preferable that the outer surface of the cartridge be partially threaded at the top and grooved for the remaining area to the end of the cartridge 26. Any standard or metric thread and groove sizes may be used.

The reservoir area 18 is preferably used for containing a reagent. The reservoir area 18 may be pre-filled, thereby enabling the seller to market pre-filled reagent cartridges which also act as the storage and transportation vehicle. The preferred embodiment eliminates expensive residue that is thrown away with a separate transportation bottle, as pre-filling allows for no waste. The preferred embodiment eliminates dilution requirements due to the accuracy of the pumping means. Cartridges which may be re-inserted can store the unused reagent for an appropriate period of time in the cartridge.

The housing is preferably opened along its center axis to remove cartridges, by means of a hinge 51 which is located off of center to allow the tube to run unobstructed up a plunger stanchion 16 and out of the cassette.

The neck opening 22 is preferably located in the plunger 52, or may be located on the bottom surface of the cartridge 12. The neck is preferably sized to connect an infusion tube 28 to the cartridge 12. Any conventional tube connection device may be used to

connect the infusion tube 28 to the cartridge 12. The opposite end of the infusion tube 28 is connected to the sensors and then to a vein in the patient 90.

It is preferable that the cartridge 12 also contains a cap as the container top which allows the cartridge 12 to act as the storage vessel for the reagent, and thereby avoids the additional steps of filling, mixing, diluting, measuring or wasting reagent in the handling of the fluid.

In the preferred embodiment of the invention, an optical or electromagnetic strip is located within an encoded area 24 on the cartridge 12. When the cartridge 12 is filled, an optical or electromagnetic strip with information on the contents and uses of the reagent is placed in the encoded area 24. The encoded area 24 is preferably located on the outer surface of the cartridge 12 in the area that is first inserted the housing 14.

It is preferable that optical reading of a bar code or other reading of the encoded area 24 will minimize dosage mistakes, as each cartridge can set the maximum allowable dose or delivery. When the cartridge 12 is placed in the system, it is preferable that rotational action provided when the cartridge is threadily attached to the housing 14 causes the encoded area 24 to be well aligned and easily read with the uniform motion of screwing the cartridge 12 into place. The preferred rotation, pre-determined position of the encoded area 24, and the ease of programming a unique character to each cartridge 12 allows the reagent to be mistake limiting. Furthermore, the preferred embodiment system requires a weight to be entered into a pumping device 40 for each patient, and when computed with the allowable dosing based on weight, greatly reduces the incidence of errors. Any conventional method of storing and retrieving data from the encoded area is preferably included in the present system to limit the incidence of errors.

It is preferable that the encoded area 24 comes into close proximity with a reading system as the cartridge 12 is loaded or is first used. The reading system may be any commercially available system capable of reading the encoded area 24. The pumping device 40 can be configured to store and use the encoded information in its operations, including a means to limit the profile of the infusion allowed without further intentional override of the profile.

In the preferred embodiment, the housing 14 consists of a cylindrical tube that is sealed at the upper end, as shown in FIG. 3. The housing 14 is preferably made of plastic, however, any suitable commercially available material may be used. The bottom 38 of the housing is preferably open and the inner surface 42 of the housing is threaded. Any

standard or metric thread size may be used. A plunger stanchion 16 is preferably connected to the sealed end 50 and is suspended in alignment with the central axis 36 of housing 14. The plunger stanchion is fixed to the housing and is mated with the plunger 52 when the cartridge 12 is inserted into the housing 14. The plunger 52 is fixed to the stanchion and is not allowed to rotate with the cartridge is turned. The housing 14 is sized to threadedly receive the cartridge 12. In the preferred embodiment, there is a plurality of openings 44 cut through the housing 14 parallel to the central axis 36 of housing 14. These openings 44 allow for normally trapped air to be exhausted as the plunger 16 either advances or retards. The plurality of openings 44 also creates an inspection window 46 within the housing 14. The inspection window 46 also allows access to the optical or electromagnetic strip within the encoded area 24. A lip 48 at the bottom 38 of the housing 14 provides for a manually removable protective cap like that used for the cartridge 60 used to protect the housing and the cartridge from contamination or damage to the plunger 16.

When the cartridge 12 is inserted into the housing 14 the plunger 52 engages the stanchion 16 to lock it into place and then when the cartridge is then engaged in the housing 14, the cartridge 12 is locked into place by the rotational engagement of the threads 26, 42. The locking of the meshed threads makes an accidental infusion by dropping or pressing on the plunger virtually impossible. The cartridge 12 will not siphon out of the pump, or accidentally deliver fluid when dropped or pushed against.

The preferred plunger 52 is a piston-type plunger and is made from plastic, however, any type of non-reactive material may be used. The plunger 52 is preferably connected to the sealed end 50 of the housing 14 and is aligned with the central axis of the housing. The plunger 52 preferably has a concave face to allow any air to first fill the neck space and be eliminated when the cartridge 12, is inserted into the housing 14, and is preferable sized to fit within the reservoir area 18, so there is very little dead space thus resulting in very little loss of reagent in the final stroke or at the end of treatment.

The plunger 52 and reservoir area 18 configuration may have a larger diameter in relationship to the depth the plunger travels, or a very small diameter and longer plunger travel, depending upon the flow characteristics desired for the application. In very viscous fluids, a different diameter would be helpful for both storage and delivery reasons.

In the preferred embodiment, a pumping mechanism 20 is used to rotate the cartridge with the stanchion 16 and the plunger 52, fixed to the housing 14. Grooves 62

on the side of the cartridge 12 mesh with the gearing mechanism driven by the motor 30, all of which are attached to the pumping device 40. The motor 30 rotates the cartridge 12 by attachment to the grooves 62 on the side of the cartridge, with the housing 14 fixed in relation to the motor or pumping device.

The pumping mechanism 20 comprises a gear linkage 54, a motor 30 and a pumping device 40. The pumping mechanism 20 may be actuated by any motor which rotably moves the stanchion 16 and plunger 52, or rotates the housing 14. The present invention allows for direct drive, stepper motor, spring or band action motor, or hand articulation to deliver the desired plunger rotation. The "motor" may also be a coordinated hand-eye movement or movement to a series of "click" points. In a preferred embodiment, the stanchion 16 and plunger 52 rotate in relation to the walls of the cassette 12.

In one embodiment, a motor 30 with either electromechanical or mechanical operation causes a rotation of the cartridge 12 with the stanchion 16 and plunger 52 fixed to the housing 14, giving both lateral and axial movement of the stanchion 16 and plunger 52 . The motor 30 can be controlled by Quantitative Chronological input from the probes 72 to cause the pumping and aspiration actions to take place as desired to achieve the free medicine profile. In the case of a mechanical motor, the settings may be made by a spring-like mechanism, with the number of turns and speed of the mechanism being governed by a simple clock mechanism.

The design of the motor 30 and assembly allow the pump mechanism 20 to be put above, at, or below the heart level, with no resulting change in the delivery profile. This allows the pump mechanism 20 to be worn or enclosed in several different tamper-proof or patient access limiting configurations.

The planes formed by the inner surface 42 of the housing 14 and part of the outer surface 26 of the cartridge are positioned so as to allow the cartridge 12 to begin turning as it is first attached, or after the plunger 52 is attached to the stanchion 16. The stanchion 16 may extend beyond the line of the housing 14 for purposes of easy snap-in connection and alignment of the plunger 52 and also the cartridge 12. The number of turns per meter or inch are adjusted to provide the desired rate of flow in both directions. The diameter of the cartridge and its separate housing are adjusted to provide different flow rates and to adjust for any necessary fluid dynamics which might be necessary to pump highly viscous liquids or pump fluids at high flow rates.

As the cartridge 12 is rotationally turned, the device infuses or aspirates liquid, depending on the rotational direction of rotation. The rotational movement of the present invention allows for bi-directional movement and provides accurate infusion or aspiration.

FIG. 4 shows an alternate embodiment of the device. In this embodiment, the cartridge 12 has an opening 22, where the infusion tube 28 is connected to the cartridge. The plunger 16 then rotates, due to the lands and groves meshed between the housing 14 and cartridge 12, causing the infusion and aspiration.

FIG. 5 shows another embodiment of the present invention. In this embodiment, a direct screwing system 64 interface is attached to the side of the cassette 10. The direct screwing system 64 accomplishes the rotational and axial movement of the plunger 52 by dual gearing of the internal rotational drive which automatically causes the plunger 16 to turn as the motor advances the plunger 16 downwards and upwards in order to infuse or aspirate.

FIG. 6 shows another embodiment of the present invention. FIG. 6 shows a rack 66 threaded surface, which allows the motor 30, when placed adjacent to the rack 66, to turn the housing 14. The plunger 16 remains stationary in relation to the motor 30 and rack 66, thereby causing the plunger 16 to move rotationally in reference to the cassette 10. The plunger sanction 68 may swing away for easy snap-in and snap-out action. FIG. 7 shows a further embodiment of the present invention. FIG. 7 shows a side screw 82 configuration for the cassette. FIG. 8 and FIG 9 show multiple cassettes.

FIG. 10 shows the infusion profile where the infusion begins with no background level of bioavailable medicine and the time between infusion X is maintained or changed Y with the concurrent amount of each pulse or bolus changed Z.

FIG. 11 shows the infusion profile where the infusion begins with some existing background level of bioavailable medicine and the time between infusion X is maintained or changed Y with the concurrent amount of each pulse or bolus changed Z.

In the preferred embodiment, the cartridge 12, when placed in the housing 14, causes the piston plunger 16 to move both forward and aft to aspirate for testing and then infuse, as well as rotate within the cassette 10 to break the forces of inertia and slip-stick as well as eliminate backlash. The infusion is delivered in pulses where the duration between pulses X is changed Y to increase, maintain or decrease the levels of free

medicine which causes beneficial responses to tissues by the medicines. Because the device avoids slip-stick, chatter and the forces of hysteresis, and has no gates or valves, it is designed to also be used in a bi-directional application, such as one of the preferred embodiments herein, where the precise amount being withdrawn may be tested and then re-inserted into the patient to the "zero" point.

In the preferred embodiments shown in FIGS. 1, 4, and 5, a sensor area 70 is located within the infusion tube 28. The sensor area 70 contains probes 72 designed to determine the chemical components and levels of desired substrates in the aspirated fluids. The information obtained by the probes 72 relayed to the pumping device 40 and is used to control or limit the infusion profile as contained in FIGS. 10 and 11. In prototype construction the probes were capable of emitting and receiving electromagnetic signals. However, any probe capable of relaying information to the pumping device may be used, including radio frequency, visible light, infrared radiation, and chemical testing which is photo sensitive or reactive to the desired substrates.

The bi-directional accuracy of the present invention allows the system to be used with any number of probes. It is preferable that the probes measure the properties of a sample, such as blood, and then allow the present invention to re-infuse that sample back into the patient after it has been tested, or if desired, by second flow direction, deposit that blood into a separate container or depository.

Referring to FIGS. 1, 4 and 5, the present invention also includes a pumping device 40. The pumping device 40 preferably has one, two, three or more sources of input and delivers Quantitative Chronological infusions FIGS. 10 and 11. The preferred pumping device includes, but is not limited to, an input system to drive the device 74, a sensor input for in-line measurement of substrates 76, an in-line occlusion pressure sensing system 78 and/or input from the reading of the encoded area 80. The sensor input 76 receives signals from the in-line sensor probes 72. The in-line occlusion pressure sensing system 78 determines the line pressure or back pressure on the motor. Other traditional pump features are intended to be incorporated into the pumping device 40.

In the preferred embodiment, the Rotational Velocity exceeds the Axial Velocity, although with sufficient diameter the difference in Rotational travel to Axial travel could be adjusted for the flow characteristics of the fluid to be infused and aspirated.

It is preferable that a second cassette and housing may be coupled and driven either independently or in mechanical linkage 80 with a cassette housing so as to have as

many infusion profiles, either in succession or concurrently as is desired for the given flow profiles and applications, as shown in FIGS. 8 and 9, with flows as shown in FIGS 10 and 11.

It is a desired effect of the present invention that certain deliveries via long catheters positioned in the patient may benefit from a very stable and accurate system which is not subject to the errors of conventional pumps, even when overcoming higher pressures within a given area.

Since the cartridge and plunger is also the pumping system, each time the cartridge and plunger are used, they are replaced, and the entire wearing aspects of the pumping system are replaced, thereby causing the product life cycles to be much greater. The entire fluid handling system is replaced with each use and sterilization and cleaning of parts is eliminated.

The purpose of the present invention is to provide a system of Quantitative Chronological Delivery, a term coined by the inventor. The apparent benefit to having timed pulses of individually controlled amounts, of almost any medicine, as an additional mode for delivery, was deemed by the Inventor to be a valid approach to medical infusion for any and perhaps all forms of infusion therapy. Part of the invention claimed is the use of the device in sequence of infusions which, while in the aggregate the amount medicine used is less, but by virtue of he pulses, accomplishes additional medical results.

The preferred embodiments described herein are illustrative only, and although the examples given include much specificity, they are intended as illustrative of only a few possible embodiments of the invention. Other embodiments and modifications will, no doubt, occur to those skilled in the art. The examples given should only be interpreted as illustrations of some of the preferred embodiments of the invention, and the full scope of the invention should be determined by the appended claims and their legal equivalents.

CLAIMS

What is claimed is:

1. A medical infusion and aspiration system, for accurate Quantitative Chronological Delivery of timed and individually controlled pulses using a known bioavailability uptake data of an infused medicine to deliver substantially optimal pulses which control or enhance the bioavailability or effectiveness of that medicine, and through pulse delivery, enhance the bioavailability or effectiveness by changing a duration between pulses and amount infused during each pulse irrespective of an existing levels of the infused medicine, which pulses are delivered by any conventional means of pumping.

2. The medical infusion device as in claim 1 containing:

at least one cassette having a cartridge, a housing, and a plunger, the cartridge having an outer cartridge surface, and a reservoir area; the outer cartridge surface having a grooved or threaded surface, the housing having an inner threaded surface;

an attachment for an infusion tube;

a pumping mechanism having a gear linkage, a motor and a pumping device delivering a pulsatile infusion of the infused medicine; and

an attachment for an in-line sensor probe.

3. The medical infusion and aspiration system of claim 2, wherein the outer cartridge surface is in threaded relationship to the housing inner threaded surface.

4. The medical infusion and aspiration system of claim 2, wherein the cartridge has a top side and a bottom side, the bottom side having a plunger opening.

5. The medical infusion and aspiration system of claim 4, wherein the infusion tube has a first end and a second end, the first end being connectively coupled to the plunger opening.

6. The medical infusion and aspiration system of claim 5, wherein the second end is connectively coupled to a vein of a patient.

7. The medical infusion and aspiration system of claim 2, wherein the cartridge is configured to receive a cap and a container top.

8. The medical infusion and aspiration system of claim 2, wherein the housing has at least one opening parallel to a central axis of the housing; wherein the at least one opening allows for trapped air to be exhausted and creates an inspection window.

9. The medical infusion and aspiration system of claim 2, wherein a bottom surface of the cartridge and housing have lips to receive a removable cover.

10. The medical infusion and aspiration system of claim 2, further comprising an encoded area located on the cartridge, the encoded area comprising an optical or electromagnetic strip.

11. The medical infusion and aspiration system of claim 10, further comprising a mechanism capable of reading the encoded area.

12. The medical infusion and aspiration system of claim 2, further comprising a stanchion coupled to the plunger, wherein the stanchion is aligned with a central axis of the housing and configured to capture the plunger fit within the reservoir area.

13. The medical infusion and aspiration system of claim 2, wherein the gear linkage connectively couples the motor to the cartridge outer surface.

14. The medical infusion and aspiration system of claim 13, wherein the motor causes both lateral and axial rotation of the plunger.

15. The medical infusion and aspiration system of claim 14, wherein the lateral and axial rotation of the plunger is bi-directional allowing for both infusion and aspiration.

16. The medical infusion and aspiration system of claim 2 wherein the in-line sensor probe is located in the infusion tube.

17. The medical infusion and aspiration system of claim 16, wherein the in-line sensor probe determines a chemical component or level of one or more substrates in an aspirated fluid.

18. The medical infusion and aspiration system of claim 17, wherein the inline sensor probe transmits information concerning the chemical component or level of one or more substrates to the pumping device.

19. The medical infusion and aspiration system of claim 18, wherein the information provided adjusts a duration between pulses of fluid and amount of fluid pulsed to provide Quantitative Chronological Delivery changes to stimulate certain tissues with less active ingredient.

20. The medical infusion and aspiration system of claim 2, wherein the at least one cassette comprises two or more cassettes which are coupled and driven independently or in mechanical linkage.

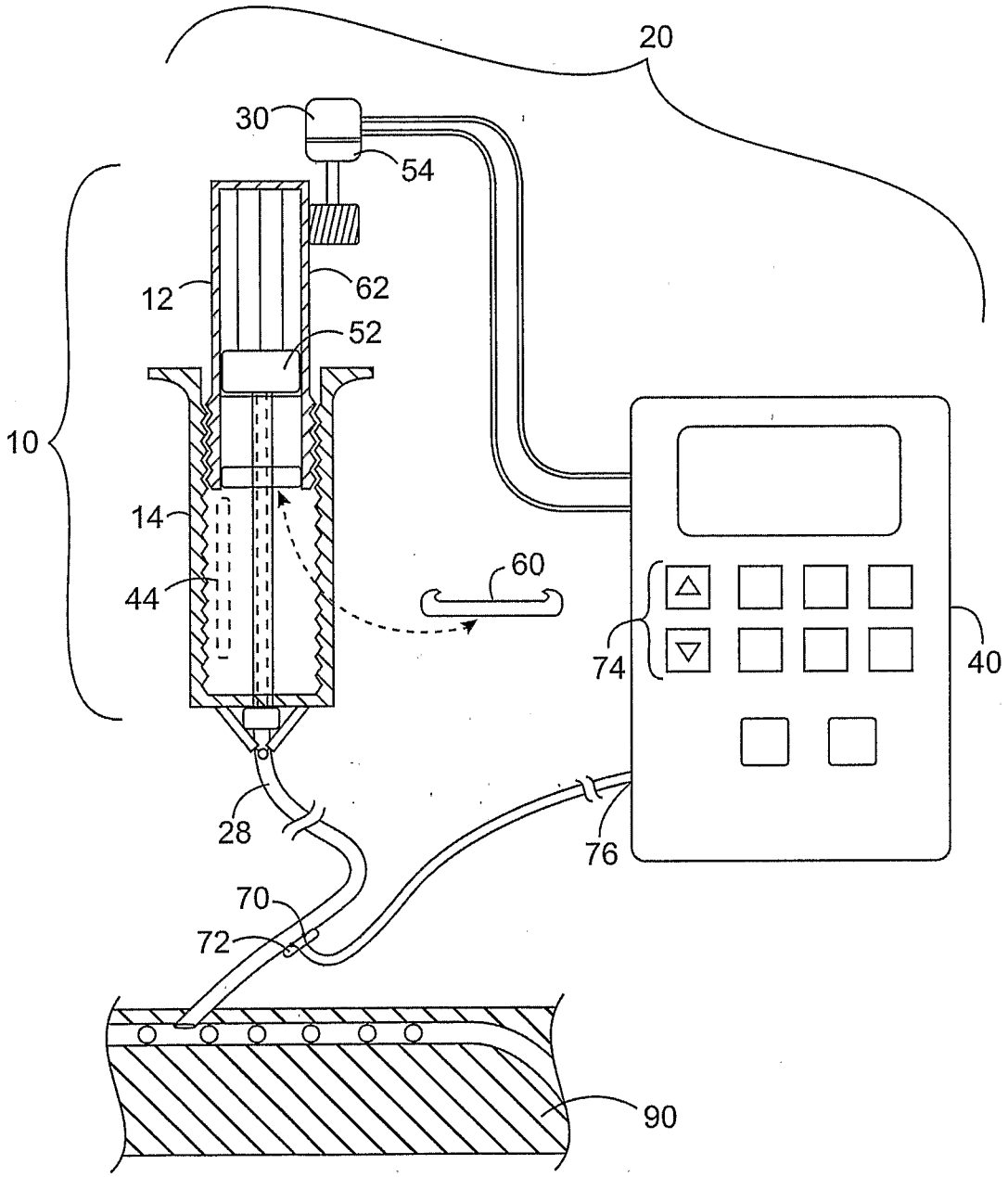

FIG. 1

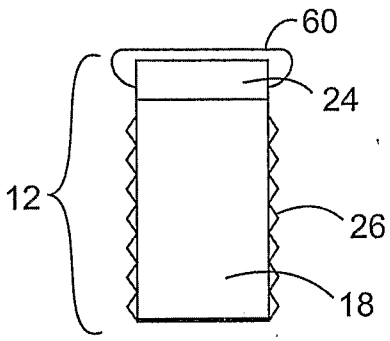

FIG. 2

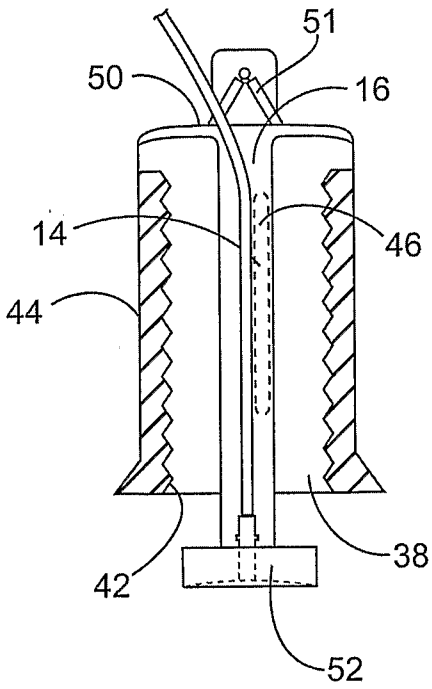

FIG. 3

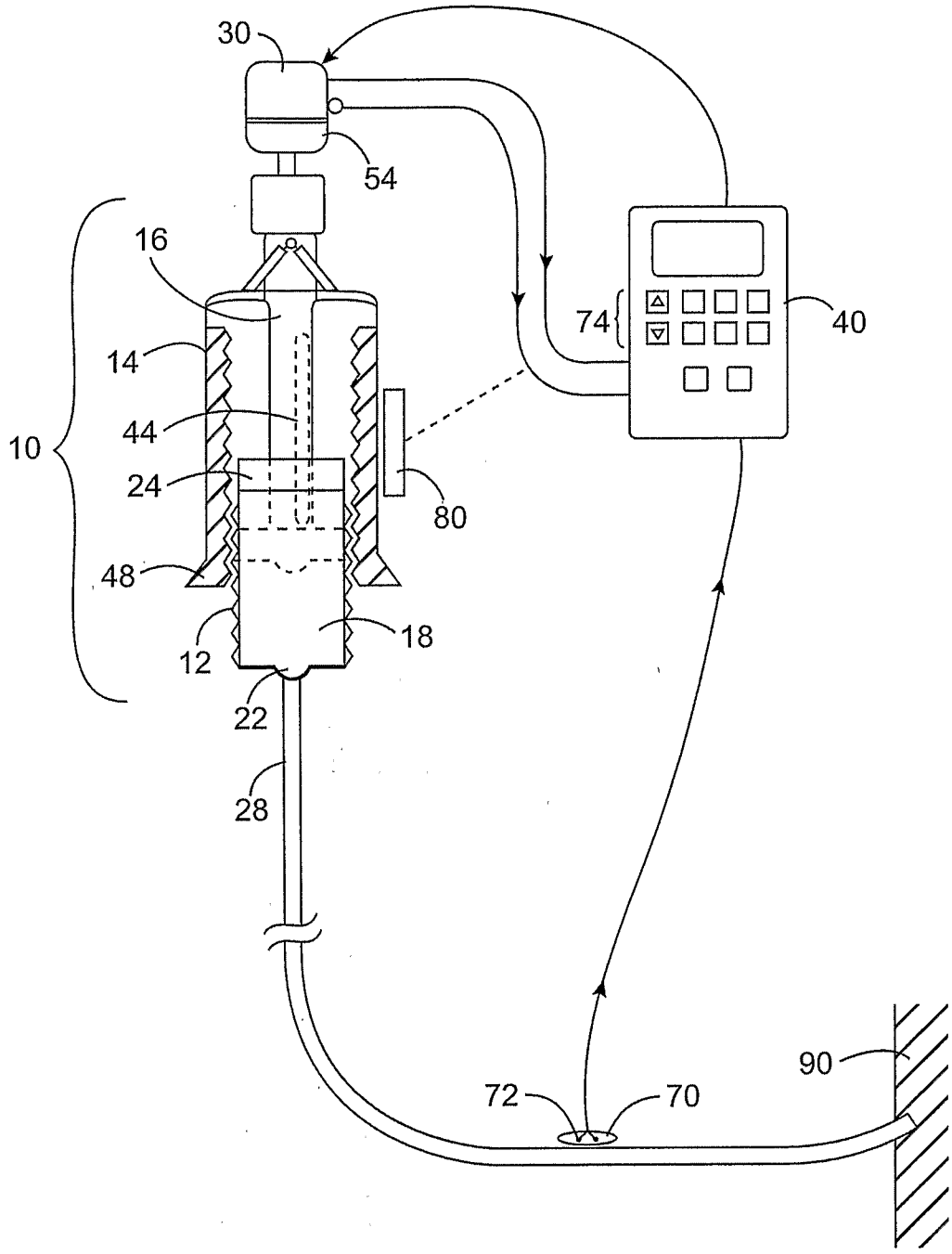

FIG. 4

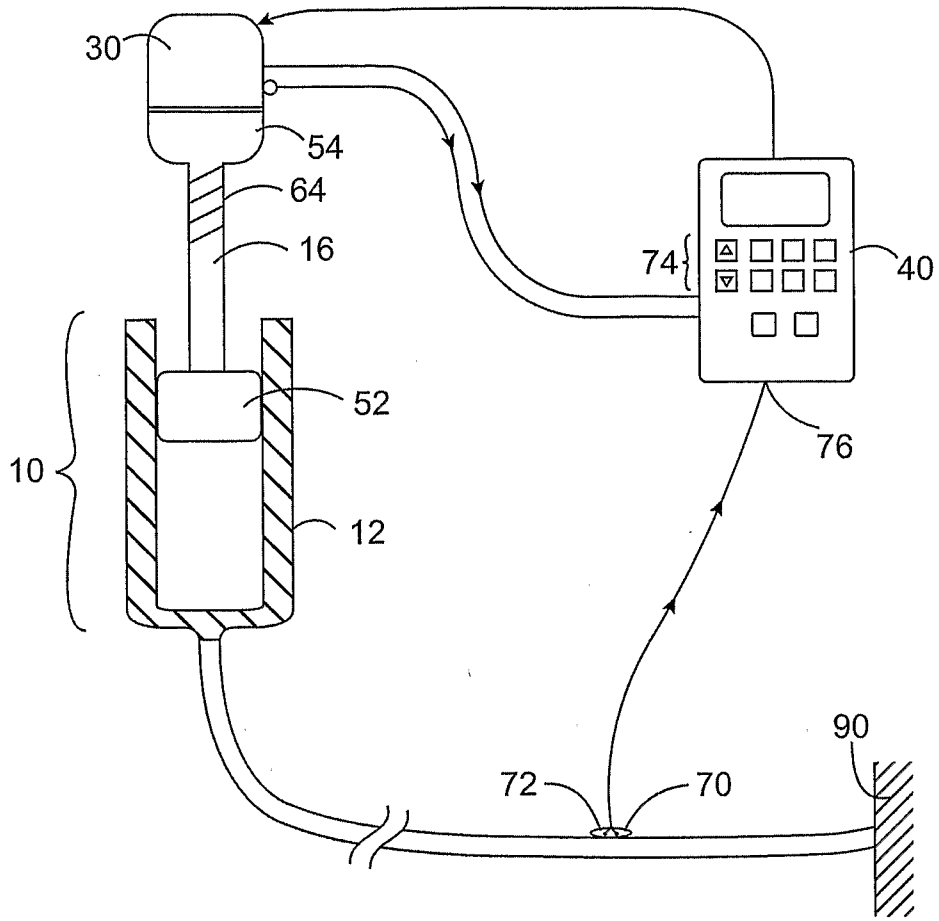

FIG. 5

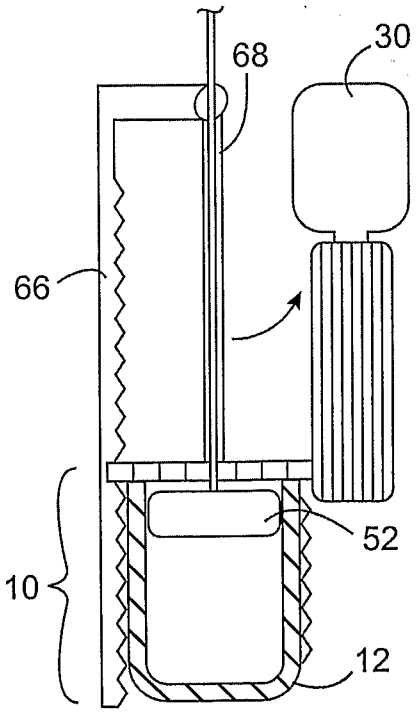

FIG. 6

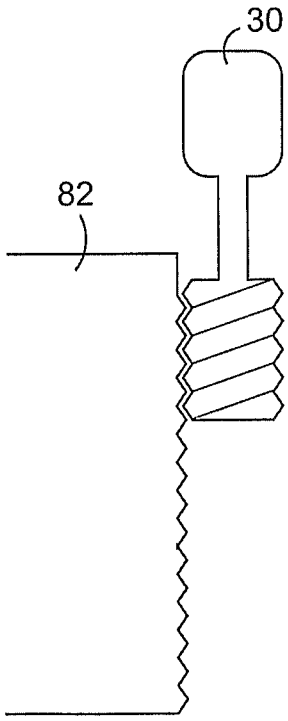

FIG. 7

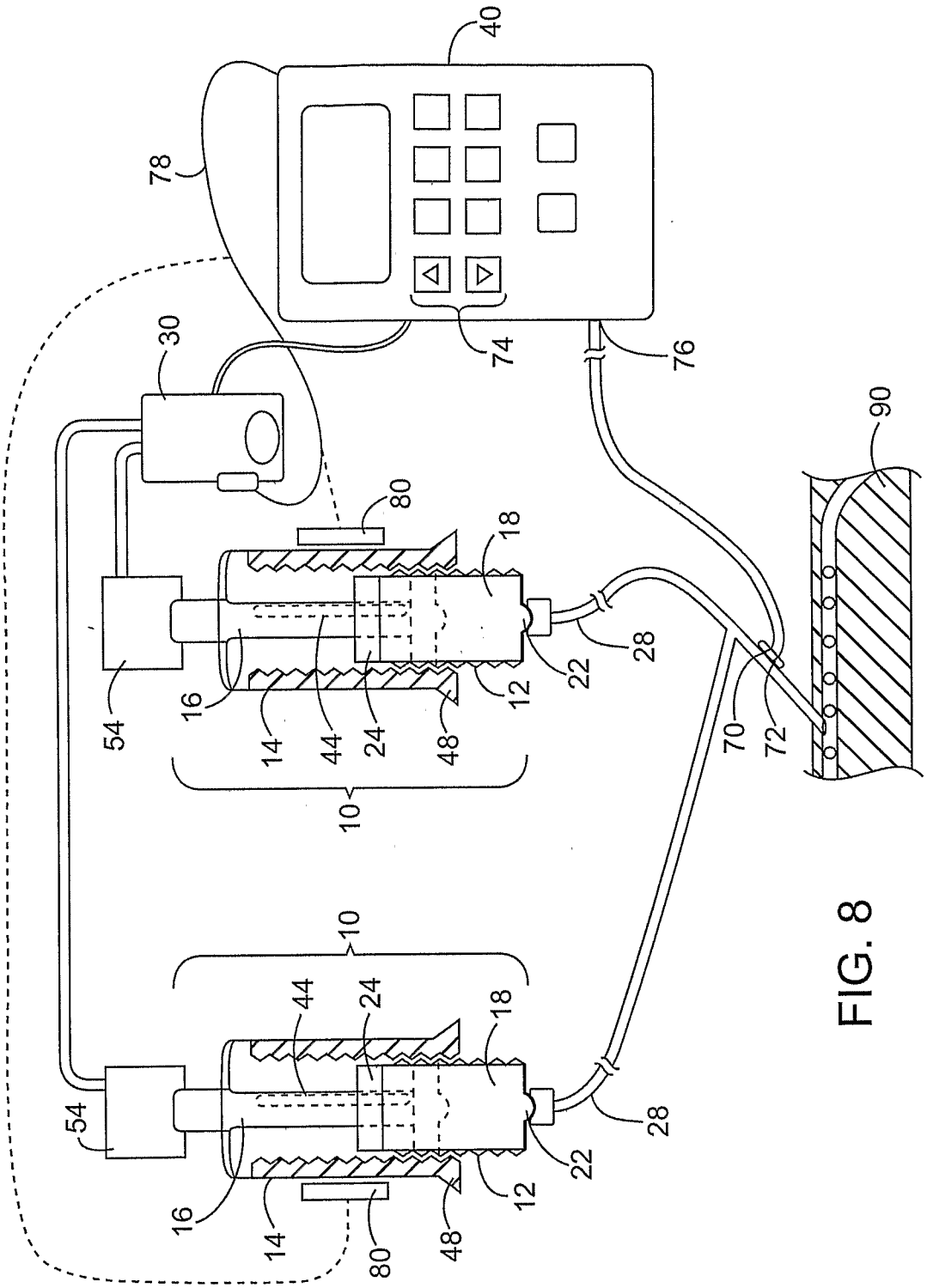
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FIG. 8

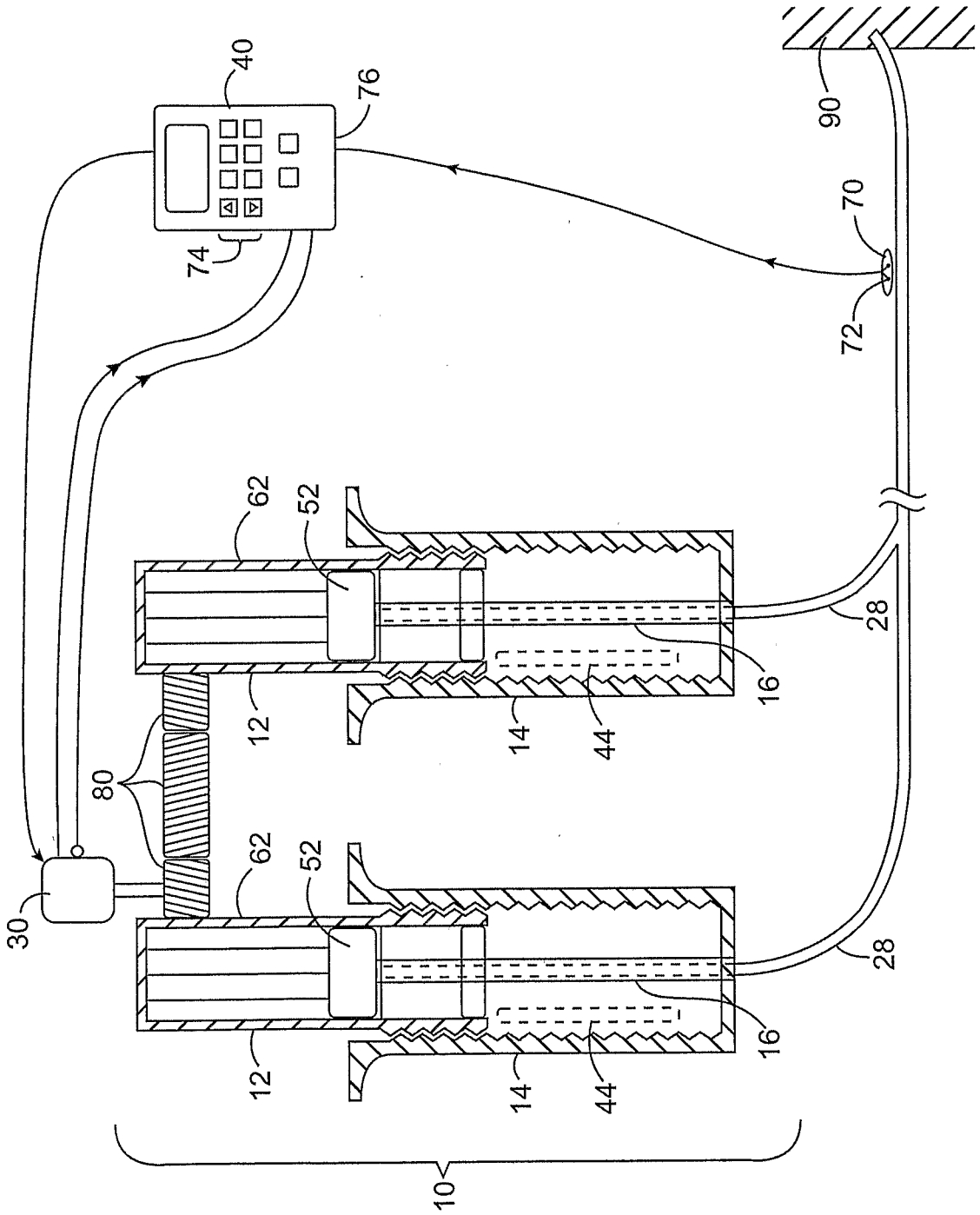

FIG. 9

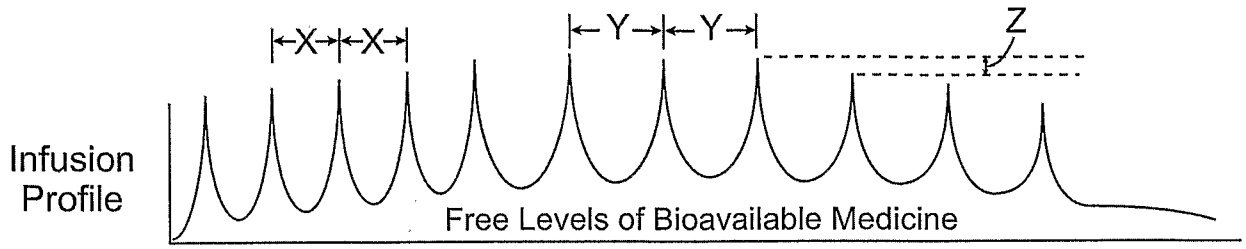
X
X
Y
Y
Z
Infusion Profile
Free Levels of Bioavailable Medicine

FIG. 10

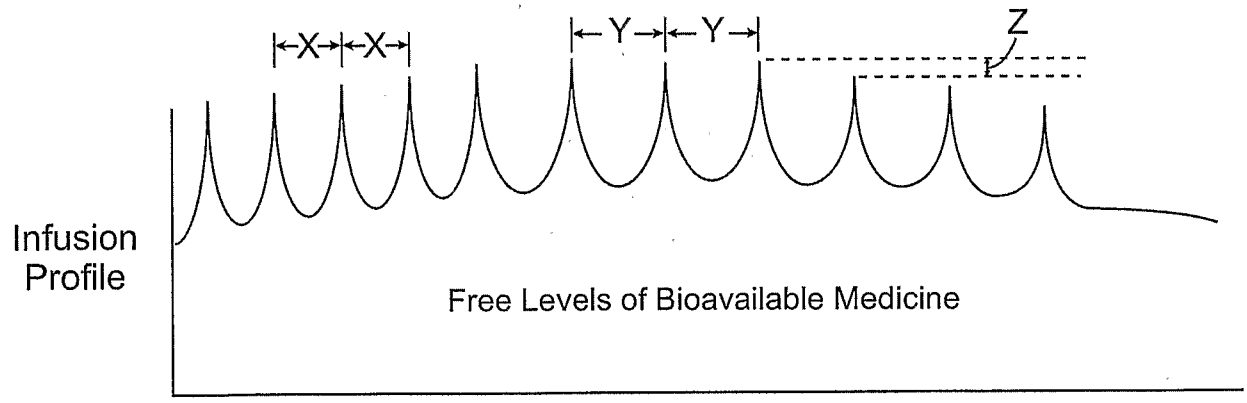
X
X
Y
Y
Z
Infusion Profile
Free Levels of Bioavailable Medicine

FIG. 11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/14890

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61M 1/00
US CL : 604/152
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. : Please See Continuation Sheet

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 6,565,535 B2 (ZAIAS et al) 20 May 2003, see Figures 1-9.	1-20

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

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"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)

"O" document referring to an oral disclosure, use, exhibition or other means

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"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

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search
21 August 2005 (21.08.2005)

Date of mailing of the international search report
09 SEP 2005

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/14890

Continuation of B. FIELDS SEARCHED Item 1:
604/152, 27, 29, 30-35, 43, 519, 65-67, 80, 81, 131, 134, 135, 151, 154, 155, 187, 218, 224, 245, 537, 902, 186, 189, 198; 128/dig. 1, dig. 12, dig. 13; 600/561-563, 565, 568