(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 1 807 127 B1**

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
13.03.2013 Bulletin 2013/11

(21) Application number: **05803491.9**

(22) Date of filing: **04.11.2005**

(51) Int Cl.:
A61F 5/00 *(2006.01)* ***A61L 27/50*** *(2006.01)*
A61M 29/04 *(2006.01)* ***A61F 2/02*** *(2006.01)*
A61L 27/54 *(2006.01)* ***A61L 27/14*** *(2006.01)*

(86) International application number:
PCT/CA2005/001693

(87) International publication number:
WO 2006/047882 (11.05.2006 Gazette 2006/19)

(54) CONTROLLED DEGRADATION OF EXPANDABLE POLYMERS IN GASTRIC VOLUME REDUCTION TREATMENT

KONTROLLIERTER ABBAU VON EXPANDIERBAREN POLYMEREN BEI DER BEHANDLUNG ZUR REDUZIERUNG DES MAGENVOLUMENS

DEGRADATION COMMANDEE DE POLYMERES EXPANSIBLES DANS UN TRAITEMENT DE REDUCTION DU VOLUME GASTRIQUE

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR

(30) Priority: **05.11.2004 US 625092 P**
22.03.2005 US 666517 P

(43) Date of publication of application:
18.07.2007 Bulletin 2007/29

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EP 1 807 127 B1

Description

FIELD OF THE INVENTION

[0001] The present invention relates to the field of ingestible microelectronic dosage forms, and more specifically to ingestible, electronically-controlled and timed dosage forms comprising expandable polymeric material useful for weight control and the treatment of obesity.

BACKGROUND OF THE INVENTION

[0002] Weight control and treatments for obesity have been the subjects of a large amount of suggested diets, treatments and procedures, including, in the most severe cases of morbid obesity, device implantations and/or direct surgical interventions. Recent comprehensive statistics from the National Institutes of Health (USA) indicates that more that 40% of Americans are obese, with more than 20% of these individuals being morbidly obese. In addition, it can be estimated that at least twice as many people are seeking to control their body weight, and/or are adhering to diets or other weight-control mechanisms. This is particularly significant since obesity has been implicated as a leading cause of various clinical conditions, including cardiovascular diseases and diabetes.

[0003] Six major streams of research and development related to new treatments for obesity are currently available: (1) diet regiments, and diet-related supplements and treatments; (2) pharmacological treatment using specifically developed medications; (3) gastric stimulation using implantable electronic devices; (4) invasive surgical procedures related to gastric reduction; (5) intragastric balloons for reducing gastric volume and introducing a sensation of satiety and fullness; and (6) oral administration of cellulose or polymeric-based substances, which expand in the stomach and preclude their expulsion through the pylorus with the process of natural gastric peristalsis, thus introducing sensation of fullness and satiety. These expanded polymeric substances subsequently disintegrate chemically to allow for their expulsion from the body with natural gastrointestinal peristalsis.

[0004] Currently, there are very large numbers of various diets, diet supplements, diet regimens, and combinations thereof, and their numbers are growing dramatically. However, in many cases, these weight loss strategies do not work, or their success is very limited. The success of these techniques often varies widely between individuals, and they are often not sustainable. Weight-loss related pharmacological treatment based on specifically developed and clinically-tested drugs and/or health supplements has also not been very successful. Numerous such therapies have been associated with various side effects, some of which are quite serious and life-threatening. Therefore, commercially-available and clinically-proven diets and/or anti-obesity drugs and health supplements have yet to be developed.

[0005] Recently developed techniques for gastric stimulation (see for examples U.S. Patent Nos. 6,684,104, 6,615,084, 6,606,523, 6,600,953, 6,542.776, 6,535,764, and 6,449,511), involving surgical implantation of miniature microelectronic devices have been proposed as an avenue to tackle more severe cases of obesity, and particularly morbid obesity. The devices can administer electrical signals to the stomach and adversely affect normal propulsive gastric peristalsis. However, the procedures used for the positioning of the electrode as well as the implantation of the device remain invasive, and the long-term effect of the treatment remains unknown both in terms of sustainability and safety.

[0006] Surgical procedures related to gastric volume reduction are invasive measures to address the problem of obesity. Mortality rates of procedures like gastric bypass or direct gastric volume reduction can reach 2%, have prolonged recovery periods, and can be quite expensive.

[0007] Intragastric balloons or devices positioned in the stomach either surgically or endoscopically to reduce the effective gastric volume have been found effective in introducing early satiety and sensation of fullness, thus contributing to reduced food intake, which has been reliably related to sustainable weight loss (see for example U.S. Patent Nos. 4,739,758, 4,485,805, 4,899,747, 5,234,454, 5,993,473, and 6,579,301). More recently, wireless control of volume-controlling devices in the stomach has been suggested (see for example U.S. Patent Nos. 6,461,293, 6,454,699, 6,453,907, 6,460,543, and 6,450,946). However, these techniques remain invasive and can be associated with serious and sometimes life-threatening side-effects.

[0008] Most recently, the use of swellable polymers has been proposed to facilitate the reduction of gastric volume for treating obesity (see for example U.S. Patent Nos. 5,750,585, 6,271,278, German Pat. No. NDN-050003290517, and US Patent Application No. 20040192582). Compressed cellulose derivatives, or dehydrated hydrophilic polymers are introduced orally in the stomach, and expand to the point of not being able to pass through the pylorus, thus effectively achieving non-invasively what an intragastric balloon or another gastric volume-reducing device would achieve. However, the subsequent decomposition and/or degradation of these polymers to allow for expulsion through natural peristalsis can be very problematic. More specifically, the decomposition and/or degradation rate is not precisely controlled, and the volume and the number of the decomposing/degrading parts or portions is unknown. More importantly, since this decomposition is pharmacologically-based, its timing cannot be precisely controlled since it would depend on numerous external factors related to the gastric pH, enzyme content, peristaltic pattern, and the anatomy of the particular patient. Because of the uncontrolled nature of the decomposition, it is possible that the volume of the stomach may remain in an

expanded state for long intervals of time, which can lead to serious side-effects and significant discomfort. Moreover, improper decomposition and/or degradation may lead to serious complications such as small bowel obstructions.

[0009] US 2004/219186 A1 discloses an expandable gastric retention device having a dosage form of a capsule containing a polymeric foam carrying an active agent and a biodegradable coating around the foam, so that the active agent is released for a longer period in the stomach. The device is compressed to a size suitable for oral administration and expands in the stomach. It is possible to select the erosion period of the device in order to adjust the release of the active agent. This device is provided to at least partially suppress appetite.

[0010] Consequently, the need has arisen for non-invasive techniques or products that can be easily used for prolonged, and controlled reduction of gastric volume for use in facilitating weight loss, which address some of the problems encountered in the prior art.

SUMMARY OF THE INVENTION

[0011] According to a broad aspect of this invention, there is provided an orally administrable polymer-carrying unit for expanding in a stomach of a mammal to fill a space in the stomach, the polymer-carrying unit including: a carrier; a plurality of polymer molecules expandable in aqueous solutions, releasably coupled to the carrier; and means for selectively decoupling the polymer molecules from the carrier so that the polymer molecules and carrier are released in the stomach, as defined in claim 1.

[0012] The decoupling means can include a timer programmable to decouple the polymer molecules at selected intervals of time, resulting in a precisely timed, electronically controlled release of the polymer molecules. Moreover, the timer can be activated to decouple the polymer molecules when desired by using, for example, an external radio-frequency (RF) transmitter. In this embodiment, the decoupling means further comprises a miniature RF receiver. The timer and miniature RF receiver are both operably associated with the carrier. In one embodiment, the carrier has an internal cavity for housing the timer and RF receiver. In a further embodiment, the decoupling means further comprises a battery that may also be housed in the internal cavity of the carrier.

[0013] The polymer molecules can be selected from a large variety of different polymers, and can include a mixture of natural clay and/or various types of biocompatible polymers, for example, which is not meant to be limiting, superabsorbent and filler material such as Bentonite, microcrystalline hydrogels and polyolefins. Further, if desired, the polymer molecules can be biodegradable to facilitate the release of the carrier and polymer molecules from the stomach. The polymer-carrying unit may also further include at least one active agent, which can be releasably associated with either the carrier or the polymer molecules, or both. The active agent may be selected from a wide group of agents, which include, but are not limited to, enzymatic agents, medicinal agents, chemical agents, or combinations thereof. The polymer molecules may be releasably coupled to the carrier by means of electric forces, magnetic forces, electrostatic forces, electromagnetic forces, frictional forces, a fiber, or piezoelectric hinges.

[0014] According to another broad aspect of this invention, there is provided an orally administrable polymer-carrying unit for expanding in a stomach of a mammal to fill a space in the stomach, the polymer-carrying unit including: a carrier having at least one outer surface; at least one coupling member having a first surface and a second surface; a plurality of polymer molecules expandable in the presence of an aqueous solution associated with the first surface of the coupling member; a coupling means for releasably coupling the second surface of the coupling member to the outer surface of the carrier; and a decoupling means for selectively decoupling the carrier from the coupling member, as defined in claim 4.

[0015] The carrier may adopt a wide variety of different shapes, which can include, but are not limited to, sphere-like, triangular-like, pyramid-like, and cube-like shapes. Moreover, the coupling means can be selected from, but are not limited to, an electromagnetic force, a frictional force, piezoelectric hinges, or combinations thereof. The decoupling means, which may be operably associated with the carrier, can also be quite diverse, and can comprise a timer, a battery, a radio-frequency receiver, or combinations thereof. In one embodiment, the carrier comprises an internal cavity and the decoupling means comprises an electronic device selected from the group consisting of a timer, a battery, a radio-frequency receiver, or combinations thereof, housed within the internal cavity. In one embodiment, the coupling means can be a frictional force and the decoupling means can be an electromagnet operatively associated with the outer surface of the carrier and means for activating the electromagnet to create a magnetic field. In this embodiment, the coupling member can include a material that can be repelled by the magnetic field. In another embodiment, the coupling means can be a piezoelectric hinge and the decoupling means can produce an electric voltage to control motion of the piezoelectric hinge.

[0016] As mentioned, the polymer molecules can be a mixture of Bentonite and/or a biocompatible polymer, and can be biodegradable. The polymer-carrying unit may also further include at least one active agent, which can be releasably associated with either the carrier or the polymer molecules, or both. The active agent may be selected from a wide group of agents, which include, but are not limited to, enzymatic agents, medicinal agents, chemical agents, or combinations thereof.

[0017] According to another broad aspect of this invention, there is provided an arrangement of polymer-carry-

ing units, the arrangement comprising a first unit and a second unit, wherein the outer surface of the first unit is releasably coupled to the outer surface of the second unit by means of electric forces, magnetic forces, electrostatic forces, electromagnetic forces, or a combination thereof.

[0018] According to another broad aspect of this invention, there is provided an orally administrable dosage form, the dosage form comprising: one or more polymer-carrying unit or an arrangement of polymer-carrying units and at least one pharmaceutically acceptable excipient. The dosage form may be a capsule, which can be coated with a pH-sensitive coating layer. The pH-sensitive coating layer can be formulated to prevent dissolution prior to the dosage form reaching the stomach.

[0019] According to another broad aspect of this invention, there is provided an orally administrable polymer-carrying unit comprising: a carrier having an outer surface and an inner surface, the inner surface forming an internal cavity; at least one fiber for releasably supporting a plurality of sacs, the sacs containing polymer molecules, the fiber being threaded into or through the internal cavity of the carrier so that at least one segment of the fiber is located within the internal cavity; a decoupling means located in the internal cavity for decoupling the sacs from the carrier by cutting the internal segment of the fiber so that the sacs are released from the carrier, as defined in claim 13. In one embodiment, the decoupling means comprises an electrical wire located in the internal cavity of the carrier, the electrical wire being heated when desired to melt and cut the internal segment of the fiber. The polymer molecules can be a mixture of Bentonite and/or various types of biocompatible polymers, for example, which is not meant to be limiting, super-absorbent and filler material such as microcrystalline, hydrogels and polyolefins. The polymer molecules can also be biodegradable. According to another broad aspect of this disclosure there is provided a method for the non-invasive reduction of gastric volume, the method comprising the steps of: (a) orally administering at least one polymer-carrying unit as described above; (b) contacting the polymeric-carrying unit with gastric juice to allow for the polymer molecules to expand and prevent the polymer-carrying unit from exiting the stomach; and (c) after a desired period of time, selectively decoupling the polymer molecules from the unit so that exit from the stomach is permitted.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] The present invention, both as to its organization and manner of operation, may best be understood by reference to the following description, and the accompanying drawings of various embodiments wherein like reference numerals are used throughout the several views, and in which:

FIG. 1A is a schematic view of one embodiment of a polymer-carrying unit according to the invention, with the polymer molecules and sacs in an expanded state.

FIG. 1B is a schematic view of the polymer-carrying unit of FIG. 1A in an encapsulated state.

FIG. 2 is a schematic view of the polymer-carrying unit of FIG. 1A, where the fiber has one cut.

FIG. 3 is a schematic view of the polymer-carrying unit of FIG. 1A, where the fiber has two cuts.

FIG. 4 is a schematic view of another embodiment of a polymer-carrying unit according to the invention having two fibers.

FIG. 5 is a schematic view of the polymer-carrying unit of FIG. 4, where each of the fibers have one cut.

FIG. 6 is a schematic view of the polymer-carrying unit of FIG. 4, where each of the fibers have two cuts.

FIG. 7 is a schematic view of one embodiment of a decoupling means according to the invention.

FIG. 8 is a schematic view of another embodiment of a polymer-carrying unit according to the invention.

FIG. 9 is a schematic view of another embodiment of a polymer-carrying unit according to the invention.

FIG. 10 is a schematic view of another embodiment of a polymer-carrying unit according to the invention.

FIG. 11 is a schematic view of one embodiment of a decoupling means according to the invention.

FIG. 12 is an exploded view of a portion of the decoupling means of FIG. 11.

FIG. 13 is a schematic view of one embodiment of a decoupling means according to the invention.

FIG. 14 is an exploded view of a portion of the decoupling means of FIG. 13.

FIG. 15 is a schematic view of one embodiment of a decoupling means according to the invention.

FIG. 16 is an exploded view of a portion of the decoupling means of FIG. 15.

FIG. 17 is a schematic view of one embodiment of an arrangement of polymer-carrying units according to the invention.

FIG. 18 is a schematic view of one embodiment of

an arrangement of polymer-carrying units according to the invention.

FIG. 19 is a schematic view of one embodiment of an arrangement of polymer-carrying units according to the invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0021] An orally administrable polymer-carrying unit for expanding in a stomach of a mammal to fill a space in the stomach, as described herein, includes at least a carrier; a plurality of polymer molecules expandable in aqueous solutions that are releasably coupled to the carrier; and means for selectively decoupling the polymer molecules from the carrier so that the polymer molecules and carrier are released in the stomach. When the polymer-carrying unit expands in the stomach, the expanded size of the unit is such that passage of the unit through the pylorus is prevented, which can result in the attainment of a sensation of satiety for a specified period of time when the stomach remains filled with the unit.

[0022] After a desired amount of time has passed, the decoupling means can be activated in a timed and controlled manner to allow for the disintegration of the polymer-carrying unit by selectively releasing the polymer molecules from the carrier. This disintegration can allow the disintegrated parts of the unit to now pass through the pylorus, and empty from the stomach. The decoupling means can vary widely and can either be pre-programmed before ingestion or programmed after ingestion. Thus, only certain sections of the polymer-carrying unit can be allowed to disintegrate at one time. This can be particularly useful for the facilitation of weight loss and the treatment of obesity. The polymer-carrying unit can be a non-invasive treatment for obesity that can be timed and controlled, which can result in less discomfort to the subject ingesting the unit.

[0023] In the embodiment as illustrated in FIGS. 1-3 and the embodiment as illustrated in FIGS. 4-6, the polymer-carrying unit, referred to generally as element 10 and 110, respectively, includes a carrier 12 having an outer surface 68 and an inner surface 70, with the inner surface forming an internal cavity 72. In this embodiment, polymer molecules 22 are carried in a plurality of sacs 76 that are releasably coupled to the carrier 12 by at least one fiber 74. The decoupling means 26 for selectively decoupling polymer-containing sacs 76 is located in internal cavity 72 and operates to cut fiber 74 to release the sacs. Desirably, fiber 74 is arranged so as to maximize coverage of carrier 12 with sacs 76. If desired, sacs 76 can be supported by fiber 74 through rings 80, as shown in FIGS. 1-6.

[0024] In the embodiment illustrated in FIGS. 1-3, fiber 74 can be threaded through internal cavity 72 of the carrier to form a closed loop so that at least one segment of fiber 74 is located within the internal cavity. Fiber 74 can enter carrier 12 at first location 82 through apertures 84 and 86, forming an internal fiber segment 120, and also at second location 88, through apertures 90 and 92, forming internal fiber segment 122. Of course, if desired, more than two locations can also be used.

[0025] In the embodiment illustrated in FIGS. 4-6, at least two fibers 74, 75 can be connected to carrier 12. As shown in FIG. 13, one fiber 75 can be connected to carrier 12 at aperture 86 of first location 82, and aperture 92 of second location 88, while the other fiber 74 can be connected to carrier 12 at aperture 84 of first location 82 and aperture 90 of second location 88. In this manner, both fibers 74, 75 can have a segment 124, 126, 128, 130 located within internal cavity 72, which may facilitate cutting, as will be discussed below.

[0026] In the embodiments illustrated in FIGS. 1-6, polymer molecules 22 can include any polymer that can expand when in contact with aqueous solutions, and can include, but are not limited to, natural clays (for example, which is not meant to be limiting, Bentonite), microcrystalline hydrogels, polyolefins, polyvinyl alcohol, poly (ethyloxazoline), polyvinylacetate-polyvinylalcohol copolymers, poly(2-hydroxyethylacrylate), poly(2-hydroxyethylmethacrylate), polyacrylic acid, and copolymers thereof, polysaccharides, water soluble proteins, polynucleic acids, or a combination thereof. Polymer molecules 22 can be made, if desired, of polyacrylic acid and a crosslinker by solution or suspension polymerization, using the type and quantity of crosslinker to control the swelling capacity and the gel modulus. The synthesis and use of such polymer molecules have been previously described in the following references: (1) Buchholz and Peppas, Superabsorbent Polymers, ACS Symposium Series, 1994; (2) Buchholz and Graham, Modern Superabsorbent Polymer Technology, John Wiley & Sons, 1998; and (3) Biocompatible/Biodegradable Materials (Tutorial). Sigma-Aldrich, 2005, available online at: http://www.sigmaaldrich.com/Area of Interest/Chemistry/Materials Scienc e/BiocompatibleBiodegradable/Tutorial.html.

[0027] Sacs 76 can be made of an expandable permeable liner. The permeable liner should be able to allow aqueous solutions to enter sacs 76 and contact polymer molecules 22 to allow for their expansion. In one embodiment, sacs 76 can be made from natural cellulose fiber or specialty fiber through spun laced process, spun-bonded polypropylene or absorbable haemostatic oxidised regenerated cellulose (commercially available under the name Curasel), and are initially folded, containing the non-expanded polymer molecules. It may be desirable that the material used to construct sacs 76 be expandable, so as to concurrently expand with polymer molecules 22. As a safety feature, sacs 76 may be made of biodegradable material, so as to allow for biodegradation after several days. Moreover, fiber 74, 75 and rings 80 can also be made of a biocompatible material, which can include, but are not limited to, P-767, Azdel fiber or unreinforced Nylon 612. However, it may be desirable to

select a material for fiber 74, 75 capable of withstanding the maximum peristaltic force present in the stomach to prevent release of sacs 76.

[0028] Decoupling means 26, which can be located within internal cavity 72, can be used to cut an internal segment of fibers 74 and/or 75 to decouple or release sacs 76 when exit from the stomach is desirable. As shown in FIGS. 2, 3, 5 and 6, fibers 74 and/or 75 can be cut either at one location or at more than one location. Of course, additional cuts can also be made if desired. One way of cutting can be melting the internal segment of the fiber. Once fibers 74 and/or 75 is/are cut, sacs 76 can become separated from polymer-carrying unit 10.

[0029] Decoupling means 26 can take a variety of different forms. In the embodiment illustrated in FIG. 7, decoupling means 26 can include an electrical wire 100. When appropriate electric current flows through wire 100, its temperature in the area where it contacts fibers 74 and/or 75 increases, and the fiber(s) melts. Fibers 74 and/or 75 is/are preferably comprised of a material having a low melting point. In one embodiment, fibers 74 and/or 75 can have a melting point of about 45°C to about 180°C, for example, P-767, Azdel fiber or unreinforced Nylon 612. An electronically-controlled microheater 102 can be used to provide electrical wire 100 with the required energy to cut fiber 74. In one embodiment, microheater 102 can generate sufficient energy to raise the temperature of electrical wire 100 to about 10°C above the melting point of fiber 74, by allowing an impulse current of appropriate magnitude to flow through the wire. Wire 100 can be connected to an output electronic stage 83, which can be controlled by at least one timer 85 (as shown in FIG. 7). An RF receiver 87 and battery 89 can also be used to control wire 100 in a timed and controlled manner. The timer(s), which can be pre-programmed, or can be controlled by the RF receiver, can be coupled to an electronic output stage designed with standard power transistors, which can deliver the necessary current to the electrical wire, so that the microheater increases its temperature above the melting point of the fiber, holding the sacs containing the expanded polymer molecules. For example, which is not meant to be limiting, fiber 74 can be cut at several locations, wherein each cut is performed over a certain period of time to allow for partial disintegration, or in embodiments including more than one fiber, i.e., fibers 74, 75, only one fiber may cut at a certain time. If desired, separate electronic devices may be used for each fiber 74, 75, or for each cut.

[0030] In the embodiment illustrated in FIG. 1B, polymer-carrying unit 10 can be contained within a shell 81, with sacs 76 in a folded conformation to facilitate oral administration. Shell 81 can be made of a variety of different materials, which can include, but are not limited to, pH-sensitive materials that will only dissolve under certain conditions, for example, the pH of the stomach. The material used to make the shell can be the same material, for example, gelatine or cellulose, used to make pharmaceutical capsules known in the art. Various sizes of shells can be used, as long as they are swallowable by the patient.

[0031] FIGS. 8, 9, and 10 illustrate, in a schematic view, other embodiments of polymer-carrying units, 210a, 210b and 210c according to this invention, which can be used to facilitate weight loss and to treat obesity, wherein the polymer molecules are releasably coupled to each unit by different coupling means. Accordingly, each unit will have a decoupling means specific for the particular coupling means.

[0032] In general, each polymer-carrying unit 210a, 210b, 210c includes a carrier 212 having an outer surface 214, at least one coupling member 216 having a first surface 218 and a second surface 220, a plurality of polymer molecules 222 associated with first surface 218 of coupling member 216, and a coupling means 224 for releasably coupling second surface 220 to outer surface 214. Each unit further comprises a decoupling means for selectively decoupling carrier 212 from coupling member 216, which decoupling means will be discussed in more detail below. Decoupling means can allow for polymer-carrying unit 210a, 210b, 210c to disintegrate and pass through the pylorus after a certain, controllable period of time.

[0033] Carrier 212 can be made of a wide variety of different materials, which can include, but are not limited to electrically non-conductive silicon and other biocompatible materials such as composite acrylics. The carrier can adopt a wide variety of different shapes. For example, which is not meant to be limiting, carrier 212 can adopt a sphere-like shape, a triangular-like shape, a pyramid-like shape, or a cube-like shape. Preferably, the carriers comprises internal cavity 272, as shown in FIGS. 8-13, which houses the necessary electronics. The electronics can be insulated and may be further encapsulated within the internal cavity of the carrier using electrically non-conductive silicon and other biocompatible materials such as composite acrylics.

[0034] As discussed above for the embodiments shown in FIGS. 1-6, polymer molecules 22 can include any polymer that can expand when in contact with aqueous solutions, and can include, but are not limited to, natural clays (for example, which is not meant to be limiting, Bentonite), microcrystalline hydrogels, polyolefins, polyvinyl alcohol, poly(ethyloxazoline), polyvinylacetate-polyvinylalcohol copolymers, poly(2-hydroxyethylacrylate), poly(2-hydroxyethylmethacrylate), polyacrylic acid, and copolymers thereof, polysaccharides, water soluble proteins, polynucleic acids, or a combination thereof. Moreover, they can be prepared using a variety of different methods, also discussed above.

[0035] In the embodiments illustrated in FIGS. 8-10, polymer molecules 22 can be coupled to first surface 218 of coupling member 216 through a variety of different methods. In one embodiment, polymer molecules having high densities can be deposited onto the first surface of the coupling member directly. In another embodiment, the polymer molecules may be coupled to the first surface

using glue. The glue may be selected from a wide variety of different glues, which can include, but are not limited to, medical glues such as medical grade cyanoacrylate adhesive. In another embodiment (not shown), the polymer molecules may be inserted into a sac made from a permeable absorbable liner. This liner may be made from a variety of different products, which can include, but are not limited to, medical gauze and the like. The sac may then be attached to the first surface of the coupling member through different ways, including, but not limited to, suturing and/or gluing.

[0036] FIGS. 8-13 illustrate that coupling member 216 can be coupled to outer surface 214 in a wide variety of different ways through coupling means 224, which can include, but is not limited to, a frictional force (FIGS. 8, 9, 11, 13, and 14) and piezoelectric hinges (FIGS. 10, 15, and 16), or combinations thereof. Decoupling means, which can be used to decouple coupling member 216 from outer surface 214 can include, but is not limited to, means for producing an electromagnetic force, means for producing electromagnetically-induced vibrations, means for producing piezoelectricity, and various electronic devices, which can include, but are not limited to, timers, microcontrollers, power transistors with high impulse current delivery capabilities, batteries and/or radio-frequency receivers and transmitters. These devices may be used to program the unit to disintegrate after a desired amount of time prior to ingestion or after ingestion. For example, which is not meant to be limiting, radio-frequency receivers can receive a signal from a transmitter and allow for the activation of decoupling means after ingestion of polymer-carrying unit 210a, 210b, 210c. Alternatively, again without limiting, the timer(s) can be pre-programmed to initiate the disintegration of the device after a certain period of time, and without the need for external communication with a transmitter.

[0037] FIGS. 11 and 12 are illustrative of one embodiment of a decoupling means, referred to generally as element numeral 226a, useful with the polymeric-carrying unit as illustrated in FIG. 8. In the unit of FIG. 8, coupling means 224 comprises a frictional force that is created by the outer surface 214 of the carrier tightly meshing with coupling member 216. In order to prevent separation of coupling member 216 to outer surface 214, the frictional force should desirably be of sufficient strength to overcome normal peristaltic movement in the stomach. In one embodiment, the frictional force is set to be at least 2 Newtons. This value may be calculated assuming that a maximum peristaltic pressure of 150 mmHg exerted on a fully expanded polymer on a coupling member 216 having dimensions of 1 cm square is about 1.5 Newtons. Of course, this value may be different depending on the dimensions of coupling member 216. As shown in FIG. 11, outer surface 214 includes at least two projections 228 and 230, which can engage indent 232 of coupling member 216 and can create a sufficiently strong mechanical frictional force.

[0038] To break the frictional force holding coupling member 216 to outer surface 214, an electromagnet can be used as decoupling means 226a, as illustrated in FIGS. 11 and 12. As shown in FIGS. 11 and 12, a wire 234 is wrapped around the outer surface 214 of carrier 212. Coupling member 216 can be made of a biocompatible material with high magnetic permeability, AISI Type 316L Stainless Steel. Outer surface 214 and coupling member 216 can be repelled from one another by inducing an electrical current through wire 234 surrounding outer surface 214. In one embodiment, this electrical current is set to be strong enough so that the resulting magneto-motive force overcomes coupling means 224 (i.e., the frictional forces keeping outer surface 214 and coupling member 216 together).

[0039] As shown in FIG. 12, the electromagnet can include N turns of wire 234 carrying a current I around a core of outer surface 214 of cross-sectional area S and constant permeability μ_c. The repelling force exerted on coupling member 216, assuming that the member has permeability μ_b and cross-section S_b, can be calculated as follows. It should be noted that the following calculation assumes that a gap is present between coupling member 216 and outer surface 214 (as shown in FIGS. 8, 11 and 12), and that this gap has the same cross-sectional area as outer surface 214 (see Fig. 12).

[0040] If it is assumed that coupling member 216 is slightly separated from outer surface 214 by an air gap of width Z, the magnetic flux Φ passing through the core and the gap can be obtained as a magnetic voltage drop around the entire magnetic circuit, which subsequently can be related to the magneto-motive force produced by the electromagnet. Φ is expressed as:

$$\Phi = NI/(Rc+Rb+2Rg)$$

where $Rc=Lc/(\mu_c*S)$ $Rb=Lb/(\mu_b*Sb)$ and $Rg=z/(\mu_0*S)$ are the reluctances of the core of outer surface 214, coupling member 216 and the air gap, respectively. The repelling force, Fm, acting on coupling member 216 can be expressed as:

$$Fm = -(\Phi^2)/(\mu_0*S)$$

[0041] Since the magnetic permeabilities of outer surface 214 and coupling member 216 are much larger than μ_0, the equivalent reluctance can be mainly dominated by the air gaps reluctance. Lengths Lc and Lb can be set to 1cm, and S and Sb can be sections of 1 mm x 1cm.

[0042] The force required to repel coupling member 216 should be larger than the mechanical friction holding the member to outer surface 214 (which can be estimated to be 2 Newtons). If such a repelling force is needed for a 0.25 mm gap between outer surface 214 and coupling member 216, 100 windings of the electromagnet would

be required for a 1 A impulse current.

[0043] As discussed above, decoupling means 226a can be activated after a certain amount of time has passed. FIG. 11 illustrates that decoupling means 226a, including the electromagnet discussed above, can be activated through a plurality of electronic devices. In this embodiment, carrier 12 has an internal cavity 272 for housing these electronic devices. These electronic devices can include, but are not limited to, a timer 236, a battery 238, and/or a radio-frequency (RF) receiver 240. As shown in FIG. 11, timer 236, battery 238 and RF receiver 240 are all electronically connected. Further, timer 236 can be connected to outer surface 214, which has wire 234 wrapped around it, through wires 242 to allow for controlled repulsion of coupling member 216 from outer surface 214. To protect the electronic devices, it may be desirable to cover each device with an insulating material, such as nylon or silicon. In one embodiment, the insulating material is oxide.

[0044] In one embodiment (not shown), separate electronic devices can be used to control the decoupling of each coupling member from the carrier of the polymer-carrying unit. By having a separate electronic timing control, different disintegration patterns can be used. For instance, a separation to two parts consisting of Y/2 units might occur after 2 hours, a separation to 4 smaller parts consisting of Y/4 units might occur after 3 hours, etc.

[0045] In the polymeric-carrying unit embodiment shown in FIG. 9, coupling means 224 includes frictional force. It is understood that the frictional force must be of sufficient strength to prevent separation of coupling member 216 from outer surface 214. In this embodiment, outer surface 214 can further include at least two pegs 244 and 246, which can engage indents 248 and 250, respectively, of coupling member 216 and thus create a sufficiently strong mechanical frictional force.

[0046] To break the frictional force holding coupling member 216 to outer surface 214, an electromagnet is used in decoupling means, the decoupling means referred to generally as element numeral 226b, as illustrated in FIGS. 13 and 14. As illustrated in FIGS. 13 and 14, an electromagnet 252 can be embedded within outer surface 214. Electromagnet 252 can be formed by wrapping a wire 254 around a ferromagnetic core 256 in multiple windings, while coupling member 216 can embed at least one biocompatible permanent magnet 258, for example bonded Neodymium Iron Boron.

[0047] In this embodiment of decoupling means 226b, outer surface 214 and coupling member 216 can be repelled from one another by inducing vibrations due to the magnetic interaction between permanent magnet 258 embedded in coupling member 216 and electromagnet 252 embedded in outer surface 214. Specifically, an alternating electrical current flowing through wire 254 of electromagnet 252 can cause the poles of the electromagnet to alternate, thus repelling or attracting coupling member 216 to outer surface 214 until these vibrations become strong enough so that the friction force holding them together is overcome. It may be desirable that this electrical current be sufficiently strong to ensure that the resulting magneto-motive force can introduce sufficiently strong vibrations to overcome coupling means 224.

[0048] As shown in FIG. 14, electromagnet 252 can consist of N windings of single-loop wire 254 with a winding radius of r, carrying an alternating current I around a core of cross-sectional area S and constant permeability μ_c. Assuming permanent magnet 258 embedded in coupling member 216 is made from bonded Neodimium Iron Boron of dimensions 0.5 x 0.5 cm, giving a magnetic field Bo = 0.7 T, and electromagnet 252 embedded in outer surface 214 has similar dimensions with 10 to 20 windings, then the magnetic field produced by the electromagnet $Bi = \mu_c NI/2r$ can also reach the same value, which for convenience will be labeled with B. Consequently, outer surface 214 and coupling member 216 can be subjected to dynamic attraction and repulsion changing with the alternating current controlling electromagnet 252. Thus, vibrations can be introduced with maximum repelling and attracting force of F = I.r.B.

[0049] As discussed above for decoupling means 226a, decoupling means 226b can also be controlled through a variety of electronic devices such as timer 236, battery 238 and/or RF receiver 240. Moreover, the electronic devices can allow selective disintegration of polymer-carrying unit 210, by uncoupling coupling member 216 from outer surface 214 only at certain, specific locations on the unit.

[0050] In the embodiment shown in FIG. 10, coupling means 224a includes piezoelectric hinges 260, while decoupling means includes electrodes which produce an electric voltage. Piezoelectric hinges 260 can be used to couple coupling member 216 to outer surface 214, and are hingedly connected to outer surface 214. The piezoelectric hinges can be made of a zinc oxide-based biocompatible piezoelectric material, for example one produced by Gredmann, San Jose, CA. In one embodiment, piezoelectric hinges 260 can have dimensions of about 2 to about 3 mm in height, and about 0.2 to about 0.5 mm in width. In one embodiment, piezoelectric hinges 260 can adopt a general "r"- like conformation.

[0051] As shown in more detail in FIGS. 15 and 16, coupling member 216 includes a plurality of apertures 264 through which piezoelectric hinges 260 can be inserted to couple coupling member 216 to outer surface 214. As discussed above, it may be desirable that piezoelectric hinges 260 exert a holding force sufficiently greater than the maximal peristaltic force in the stomach to prevent decoupling of coupling member 216 and outer surface 214.

[0052] To displace piezoelectric hinges from a coupling position to an uncoupling position in apertures 264, an electric voltage can be applied through electrodes 262 of the decoupling device shown in FIG. 16, referred to generally as element numeral 226c. In one embodiment, by applying electric voltage to piezoelectric hinges 260, a displacement ranging between 10 to 20% from the cou-

pling position to the uncoupling position can be produced, which can allow for the piezoelectric hinges to detach from coupling member 216 and exit through apertures 264 in coupling member 216. In the uncoupling position, piezoelectric hinges 260 can no longer engage and retain coupling member 216, which can be released from outer surface 214.

[0053] Decoupling means 226c useful in the embodiment illustrated in FIG. 10, can be controlled through a variety of electronic devices such as timer 236, battery 238 and/or RF receiver 240, as shown in FIGS. 10 and 15. Moreover, the electronic devices can allow selective disintegration of polymer-carrying unit 210, by uncoupling coupling member 216 from outer surface 214 only at certain, specific locations on the unit.

[0054] FIGS. 17-19 illustrate further embodiments according to the invention. In these embodiments, a plurality of polymer-carrying units can be interconnected to form an arrangement. In the embodiment illustrated in FIG. 17, one of the outer surfaces 314 of polymer-carrying unit 310a is extended by means of a spacer 317 and has a wire 334 operably attached at its extremity. Another polymer-carrying unit 310b also has an extended outer surface 314, which is extended by means of spacer 317 and is adapted to frictionally receive the extended outer surface of polymer-carrying unit 310a as described above. Decoupling means can be used to decouple the polymer-carrying units as described above. Moreover, as discussed above, decoupling means dedicated only to the decoupling of one unit from another may be used to allow for partial disintegration of the arrangement.

[0055] In the embodiment shown in FIG. 18, outer surface 314 of polymer-carrying unit 310c is extended by means of a spacer 317. Outer surface 314 can include electromagnet 352 embedded at its extremity. Outer surface 314 of polymer-carrying unit 310d is also extended by means of spacer 317 and the outer surface extremity includes a biocompatible permanent magnet 358 embedded therein. Outer surface 314 of polymer-carrying unit 310c further includes pegs 344 and 346, which are frictionally received by the outer surface of polymer-carrying unit 310d, as described above. Decoupling means can be used to decouple the polymer-carrying units, as described above. Moreover, as discussed above, decoupling means dedicated only to the decoupling of one unit from another may be used to allow for partial disintegration of the arrangement.

[0056] In the embodiment illustrated in FIG. 19, one of the outer surfaces 314 of polymer unit 310f can be extended by means of a spacer 317, and can include piezoelectric hinges 360. One of the outer surface 314 of polymer-carrying unit 310e can also be extended by a spacer 317 and can include apertures 364 for receiving the hinges, as described above. Decoupling means can be used to decouple the units as described above. Moreover, as described above, decoupling means dedicated only to the decoupling of one unit from another may be used to allow for partial disintegration of the arrangement.

[0057] It may be desirable to include spacers 317 within polymer-carrying unit 10 in order to allow for the addition of various active agents. Active agents may be selected from the group consisting of enzymatic agents, medicinal agents, chemical agents, or combinations thereof. For example, which is not meant to be limiting, it may be desirable to deliver various pharmaceutical agents that also facilitate weight loss, or enzymes that may accelerate degradation of polymer molecules 322. However, the active agents can also be added to sacs 376, or associated with polymer molecules 322.

[0058] According to another embodiment of this invention, there is provided an orally-administrable pharmaceutical dosage form including at least one polymer-carrying unit and, if desired, a pharmaceutically acceptable excipient such as binders, fillers and disintegrants, for example, starch. The pharmaceutical dosage form may take various forms, which include, but are not limited to, liquids, soft substances, powder-like substances, and hard pharmaceutical substances such as soft capsules, hard capsules and tablets. In one embodiment, the pharmaceutical dosage form is a capsule. In another embodiment, the capsule can be coated with a pH-sensitive coating. The pH-sensitive coating may prevent dissolution until the stomach reached, to prevent contact between polymer molecules 22 and aqueous solutions.

[0059] The administration of a polymer-carrying unit or a dosage form including at least one polymer-carrying unit can be used as a non-invasive technique for the reduction of gastric volume. The unit or a dosage form including at least one unit can be administered by mouth, where it will reach the stomach. Once in the stomach, the polymer molecules can be contacted with aqueous solutions, which will result in their expansion. The expanded polymer molecules, which cannot pass through the pylorus, can fill a significant portion of the volume of the stomach, resulting in the attainment of a feeling of satiety. After a desired period of time has passed, polymer molecules can be selectively decoupled from the unit, or portions of the dosage form can be selectively decoupled from one another, in order for the decoupled portions to exit the stomach through normal peristaltic movement.

Claims

1. An orally administrable polymer-carrying unit for expanding in a stomach of a mammal to fill a space in the stomach, the polymer-carrying unit comprising:

   (a) a carrier;
   (b) a plurality of polymer molecules, expandable in the presence of an aqueous solution, releasably coupled to the carrier by means of at least one fiber; and
   (c) means for selectively decoupling the polymer molecules from the carrier so that the polymer

molecules and carrier are released in the stomach.

2. The polymer-carrying unit of claim 1, wherein the decoupling means comprises a timer programmable to decouple the polymer molecules at selected intervals of time or when desired.

3. The polymer-carrying unit of claim 1, further comprising at least one active agent releasably associated with either the carrier or the polymer molecules, or both.

4. An orally administrable polymer-carrying unit for expanding in a stomach of a mammal to fill a space in the stomach, the polymer-carrying unit comprising:

(a) a carrier having at least one outer surface;
(b) at least one coupling member having a first surface and a second surface;
(c) a plurality of polymer molecules, expandable in the presence of an aqueous solution, associated with the first surface of the at least one coupling member;
(d) a coupling means for releasably coupling the second surface of the at least one coupling member to the outer surface of the carrier, wherein the coupling means is selected from the group consisting of means for producing an electromagnetic force, means for producing a frictional force, piezoelectric hinges, or combinations thereof; and
(e) a decoupling means for selectively decoupling the at least one coupling member from the carrier.

5. The polymer-carrying unit as claimed in claim 4, the carrier having a shape selected from the group consisting of sphere-like shape, triangular-like shape, cube-like shape, or pyramid-like shape.

6. The polymer-carrying unit as claimed in claim 4, wherein the decoupling means comprises an electronic device selected from the group consisting of a timer, a battery, a radio-frequency receiver, or combinations thereof, the electronic device being operably associated with the carrier.

7. The polymer-carrying unit as claimed in claim 4, wherein the coupling means comprises means for producing a frictional force and the decoupling means comprises an electromagnet operatively associated with the outer surface of the carrier and means for activating the electromagnet to create a magnetic field.

8. The polymer-carrying unit as claimed in claim 4, wherein the coupling means is at least one piezoelectric hinge and the decoupling means produces an electric voltage.

9. The polymer-carrying unit as claimed in claim 4, further comprising an active agent releasably associated with the carrier, the coupling member, the polymer molecules, or a combination thereof.

10. An arrangement of polymer-carrying units as claimed in claim 4, the arrangement comprising a first unit and a second unit, wherein the outer surface of the first unit is releasably coupled to the outer surface of the second unit by means of electric forces, magnetic forces, electrostatic forces, electromagnetic forces, or a combination thereof.

11. An orally administrable dosage form, the dosage form comprising:

(a) one or more polymer-carrying unit as claimed in claim 1 or 4, or one or more arrangements of polymer-carrying units of claim 10; and
(b) at least one pharmaceutically acceptable excipient.

12. The orally administrable dosage form of claim 11, wherein the dosage form is a capsule.

13. An orally administrable polymer-carrying unit for expanding in a stomach of a mammal to fill a space in the stomach, the polymer-carrying unit comprising:

(a) a carrier having an outer surface and an inner surface, the inner surface forming an internal cavity;
(b) at least one fiber for releasably supporting a plurality of sacs, the sacs containing expandable polymer molecules, the fiber being threaded into or through the internal cavity of the carrier so that at least one segment of the fiber is located within the internal cavity;
(c) a decoupling means located in the internal cavity for decoupling the sacs from the carrier by cutting the internal segment of the fiber so that the sacs are released.

14. The polymer-carrying unit of claim 13, wherein the decoupling means comprises an electrical wire operably associated with the carrier, the electrical wire being heated when it is desirable to melt and cut through the internal segment of the fiber.

15. The polymer-carrying unit of claim 13, wherein the unit is encapsulated in a shell.

16. A unit as claimed in claim 1 or 4, wherein the polymer molecules are a mixture of a natural clay and a biocompatible polymer.

17. A unit as claimed in claim 1, 4 or 13, wherein the polymer molecules are biodegradable.

18. The polymer-carrying unit of claim 13, wherein the polymer molecules are a mixture of Bentonite and a biocompatible polymer.

Patentansprüche

1. Oral zu verabreichende polymertragende Einheit zur Expansion in einem Magen eines Säugetiers, um einen Raum in dem Magen auszufüllen, die polymertragende Einheit umfassend:

(a) einen Träger;
(b) eine Vielzahl von Polymermolekülen, die in Anwesenheit einer wässrigen Lösung expandieren können und die mithilfe von mindestens einer Faser lösbar an den Träger gekoppelt sind; und
(c) ein Mittel zum wahlweisen Abkoppeln der Polymermoleküle von dem Träger, so dass die Polymermoleküle und der Träger in dem Magen freigesetzt werden.

2. Polymertragende Einheit gemäß Anspruch 1, wobei das Abkopplungsmittel einen Zeitgeber umfasst, der so programmiert werden kann, dass die Polymermoleküle in ausgewählten Zeitintervallen oder auf Wunsch abgekoppelt werden.

3. Polymertragende Einheit gemäß Anspruch 1, des Weiteren umfassend mindestens einen Wirkstoff, der lösbar mit entweder dem Träger oder den Polymermolekülen oder mit beiden verknüpft ist.

4. Oral zu verabreichende polymertragende Einheit zur Expansion in einem Magen eines Säugetiers, um einen Raum in dem Magen auszufüllen, die polymertragende Einheit umfassend:

(a) einen Träger mit mindestens einer äußeren Oberfläche;
(b) mindestens ein Kopplungselement mit einer ersten Oberfläche und einer zweiten Oberfläche;
(c) eine Vielzahl von Polymermolekülen, die sich in Anwesenheit einer wässrigen Lösung ausdehnen können und mit der ersten Oberfläche des mindestens einen Kopplungselements verknüoft sind;
(d) ein Kopplungsmittel zum lösbaren Koppeln der zweiten Oberfläche des mindestens einen Kopplungselements an die äußere Oberfläche des Trägers, wobei das Kopplungsmittel aus der Gruppe ausgewählt ist, welche umfasst: Mittel zum Erzeugen einer elektromagnetischen Kraft, Mittel zum Erzeugen einer Reibungskraft, piezoelektrische Scharniere oder Kombinationen von diesen; und
(e) ein Abkopplungsmittel zum wahlweisen Abkoppeln des mindestens einen Kopplungselements von dem Träger.

5. Polymertragende Einheit gemäß Anspruch 4, wobei der Träger eine Form aufweist, die aus der Gruppe ausgewählt ist, welche umfasst: kugelartige Form, dreiecksartige Form, würfelartige Form oder pyramidenartige Form.

6. Polymertragende Einheit gemäß Anspruch 4, wobei das Abkopplungsmittel eine elektronische Einrichtung umfasst, die aus der Gruppe ausgewählt ist, welche umfasst: einen Zeitgeber, eine Batterie, einen Funkfrequenzempfänger oder Kombinationen von diesen, wobei die elektronische Einrichtung im Betriebszustand mit dem Träger verknüpft ist.

7. Polymertragende Einheit gemäß Anspruch 4, wobei das Kopplungsmittel Mittel zum Erzeugen einer Reibungskraft umfasst und das Abkopplungsmittel einen Elektromagneten umfasst, der im Betriebszustand mit der äußeren Oberfläche des Trägers verknüpft ist, und Mittel zum Aktivieren des Elektromagneten zum Erzeugen eines Magnetfelds.

8. Polymertragende Einheit gemäß Anspruch 4, wobei es sich bei dem Kopplungsmittel um mindestens ein piezoelektrisches Scharnier handelt und das Abkopplungsmittel eine elektrische Spannung erzeugt.

9. Polymertragende Einheit gemäß Anspruch 4, des Weiteren umfassend einen Wirkstoff, der lösbar mit dem Träger, dem Kopplungselement, den Polymermolekülen oder einer Kombination von diesen verknüpft ist.

10. Anordnung von polymertragenden Einheiten gemäß Anspruch 4, die Anordnung umfassend eine erste Einheit und eine zweite Einheit, wobei die äußere Oberfläche der ersten Einheit mithilfe von elektrischen Kräften, magnetischen Kräften, elektrostatischen Kräften oder einer Kombination von diesen lösbar an die äußere Oberfläche der zweiten Einheit gekoppelt ist.

11. Oral zu verabreichende Dosisform, die Dosisform umfassend:

(a) eine oder mehrere polymertragende Einheiten gemäß Anspruch 1 oder 4 oder eine oder mehrere Anordnungen von polymertragenden Einheiten gemäß Anspruch 10; und
(b) mindestens einen pharmazeutisch akzeptablen Trägerstoff.

12. Oral zu verabreichende Dosisform gemäß Anspruch 11, wobei es sich bei der Dosisform um eine Kapsel handelt.

13. Oral zu verabreichende polymertragende Einheit zur Expansion in einem Magen eines Säugetiers, um einen Raum in dem Magen auszufüllen, die polymertragende Einheit umfassend:

(a) einen Träger mit einer äußeren Oberfläche und einer inneren Oberfläche, wobei die innere Oberfläche einen inneren Hohlraum bildet;
(b) mindestens eine Faser zum lösbaren Festhalten einer Mehrzahl von Beuteln, die expansionsfähige Polymermoleküle enthalten, wobei die Faser in den inneren Hohlraum des Trägers hinein oder durch diesen hindurch gefädelt ist, sodass sich mindestens ein Segment der Faser innerhalb des inneren Hohlraums befindet;
(c) ein Abkopplungsmittel, das sich in dem inneren Hohlraum befindet, zum Abkoppeln der Beutel von dem Träger durch Durchtrennen des inneren Segments der Faser, so dass die Beutel freigesetzt werden.

14. Polymertragende Einheit gemäß Anspruch 13, wobei das Abkopplungsmittel einen elektrischen Draht umfasst, der im Betriebszustand mit dem Träger verknüpft ist, wobei der elektrische Draht auf Wunsch beheizt werden kann, um das interne Segment der Faser zu schmelzen und zu durchtrennen.

15. Polymertragende Einheit gemäß Anspruch 13, wobei die Einheit in einer Schale eingekapselt ist.

16. Einheit gemäß Anspruch 1 oder 4, wobei es sich bei den Polymermolekülen um eine Mischung aus einem natürlichem Lehm und einem biokompatiblen Polymer handelt.

17. Einheit gemäß Anspruch 1, 4 oder 13, wobei die Polymermoleküle biologisch abbaubar sind.

18. Polymertragende Einheit gemäß Anspruch 13, wobei es sich bei den Polymermolekülen um eine Mischung aus Bentonit und einem biokompatiblen Polymer handelt.

Revendications

1. Une unité porteuse d'un polymère pouvant être administrée par voie orale destinée à s'étendre dans un estomac d'un mammifère de façon à remplir un espace dans l'estomac, l'unité porteuse d'un polymère comprenant :

(a) un vecteur,
(b) une pluralité de molécules polymères, expansibles en présence d'une solution aqueuse, couplées de manière libérable au vecteur au moyen d'au moins une fibre, et
(c) un moyen de découplage de manière sélective des molécules polymères du vecteur de sorte que les molécules polymères et le vecteur soient libérés dans l'estomac.

2. L'unité porteuse d'un polymère selon la Revendication 1, où le moyen de découplage comprend une horloge programmable destinée à découpler les molécules polymères à des intervalles temporels sélectionnés ou lorsque souhaité.

3. L'unité porteuse d'un polymère selon la Revendication 1, comprenant en outre au moins un agent actif associé de manière libérable à soit le vecteur ou les molécules polymères, ou les deux.

4. Une unité porteuse d'un polymère pouvant être administrée par voie orale destinée à s'étendre dans un estomac d'un mammifère de façon à remplir un espace dans l'estomac, l'unité porteuse d'un polymère comprenant :

(a) un vecteur possédant au moins une surface extérieure,
(b) au moins un élément de couplage possédant une première surface et une deuxième surface,
(c) une pluralité de molécules polymères, expansibles en présence d'une solution aqueuse, associées à la première surface du au moins un élément de couplage,
(d) un moyen de couplage destiné à coupler de manière libérable la deuxième surface du au moins un élément de couplage à la surface extérieure du vecteur, où le moyen de couplage est sélectionné dans le groupe se composant d'un moyen de production d'une force électromagnétique, d'un moyen de production d'une force de frottement, de charnières piézoélectriques, ou de combinaisons de ceux-ci, et
(e) un moyen de découplage destiné à découpler de manière sélective le au moins un élément de couplage du vecteur.

5. L'unité porteuse d'un polymère selon la Revendication 4, le vecteur possédant une forme sélectionnée dans le groupe se composant d'une forme sphérique, d'une forme triangulaire, d'une forme cubique ou d'une forme pyramidale.

6. L'unité porteuse d'un polymère selon la Revendication 4, où le moyen de découplage comprend un dispositif électronique sélectionné dans le groupe se composant d'une horloge, d'une batterie, d'un récepteur à radiofréquence, ou de combinaisons de

ceux-ci, le dispositif électronique étant associé de manière opérationnelle au vecteur.

7. L'unité porteuse d'un polymère selon la Revendication 4, où le moyen de couplage comprend un moyen de production d'une force de frottement et le moyen de découplage comprend un électro-aimant associé de manière opérationnelle à la surface extérieure du vecteur et un moyen d'activation de l'électro-aimant de façon à créer un champ magnétique.

8. L'unité porteuse d'un polymère selon la Revendication 4, où le moyen de couplage est au moins une charnière piézoélectrique et le moyen de découplage produit une tension électrique.

9. L'unité porteuse d'un polymère selon la Revendication 4, comprenant en outre un agent actif associé de manière libérable au vecteur, à l'élément de couplage, aux molécules polymères, ou à une combinaison de ceux-ci.

10. Un agencement d'unités porteuses d'un polymère selon la Revendication 4, l'agencement comprenant une première unité et une deuxième unité, où la surface extérieure de la première unité est couplée de manière libérable à la surface extérieure de la deuxième unité au moyen de forces électriques, de forces magnétiques, de forces électrostatique, de forces électromagnétiques, ou d'une combinaison de celles-ci.

11. Une forme de dosage pouvant être administrée par voie orale, la forme de dosage comprenant :

(a) une ou plusieurs unités porteuses d'un polymère selon la Revendication 1 ou 4, ou un ou plusieurs agencements d'unités porteuses d'un polymère selon la Revendication 10, et
(b) au moins un excipient pharmaceutiquement acceptable.

12. La forme de dosage pouvant être administrée par voie orale selon la Revendication 11, où la forme de dosage est une capsule.

13. Une unité porteuse d'un polymère pouvant être administrée par voie orale destinée à s'étendre dans un estomac d'un mammifère de façon à remplir un espace dans l'estomac, l'unité porteuse d'un polymère comprenant :

(a) un vecteur possédant une surface extérieure et une surface intérieure, la surface intérieure formant une cavité interne,
(b) au moins une fibre destinée à prendre en charge de manière libérable une pluralité de poches, les poches contenant des molécules polymères expansibles, la fibre étant enfilée dans ou au travers de la cavité interne du vecteur de sorte qu'au moins un segment de la fibre se situe à l'intérieur de la cavité interne,
(c) un moyen de découplage situé dans la cavité interne destiné à découpler les poches du vecteur par un découpage du segment interne de la fibre de sorte que les poches soient libérées.

14. L'unité porteuse d'un polymère selon la Revendication 13, où le moyen de découplage comprend un fil électrique associé de manière opérationnelle au vecteur, le fil électrique étant chauffé lorsqu'il est souhaitable de faire fondre et de couper au travers du segment interne de la fibre.

15. L'unité porteuse d'un polymère selon la Revendication 13, où l'unité est encapsulée dans une enveloppe.

16. Une unité selon la Revendication 1 ou 4, où les molécules polymères sont un mélange d'argile naturel et d'un polymère biocompatible.

17. Une unité selon la Revendication 1, 4 ou 13, où les molécules polymères sont biodégradables.

18. L'unité porteuse d'un polymère selon la Revendication 13, où les molécules polymères sont un mélange de bentonite et d'un polymère biocompatible.

Figure 1

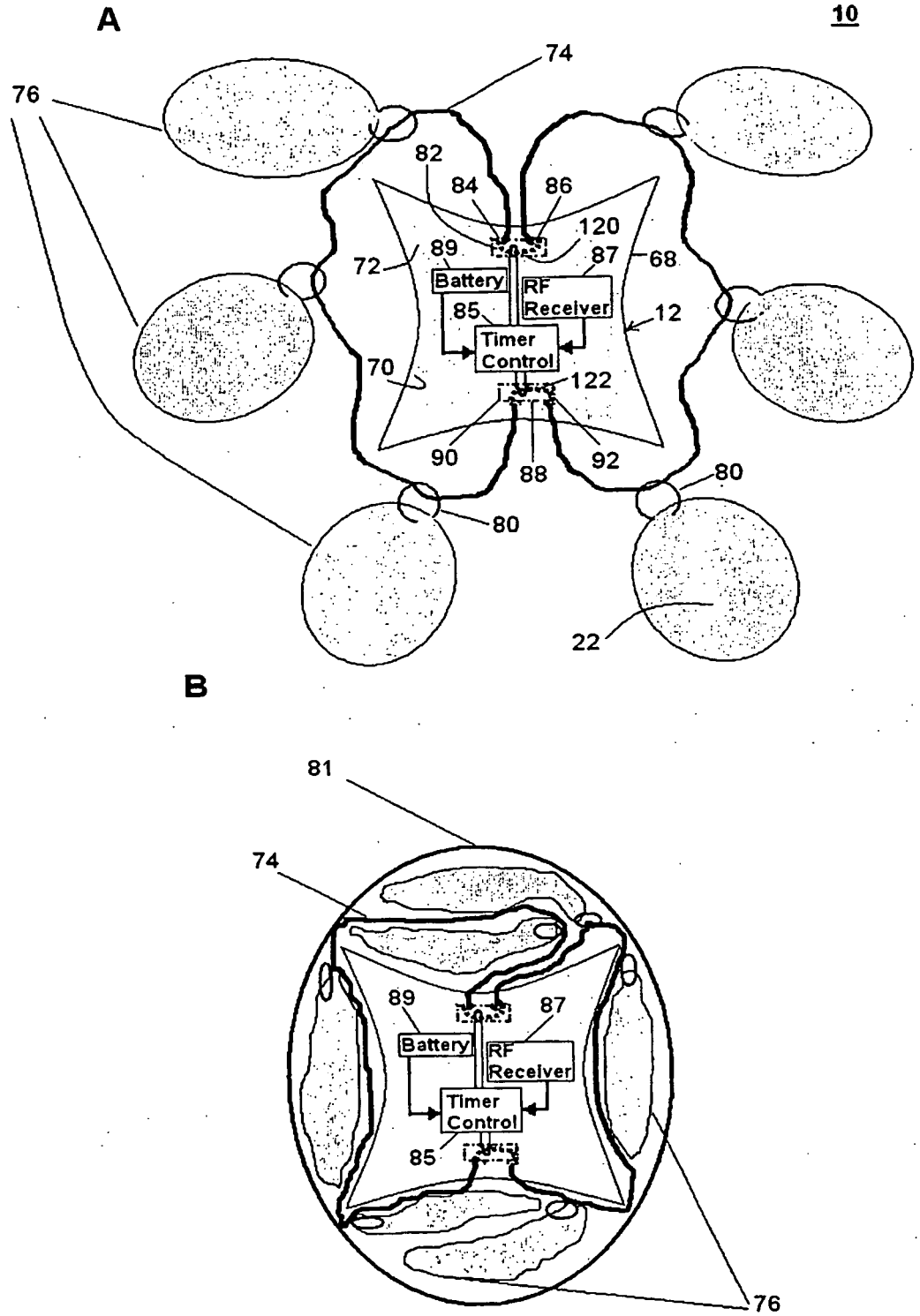

A
10
74
76
82
84
86
120
89
87
68
72
Battery
RF Receiver
85
12
Timer Control
70
122
90
88
92
80
80
22
B
81
74
89
87
Battery
RF Receiver
Timer Control
85
76

Figure 2.

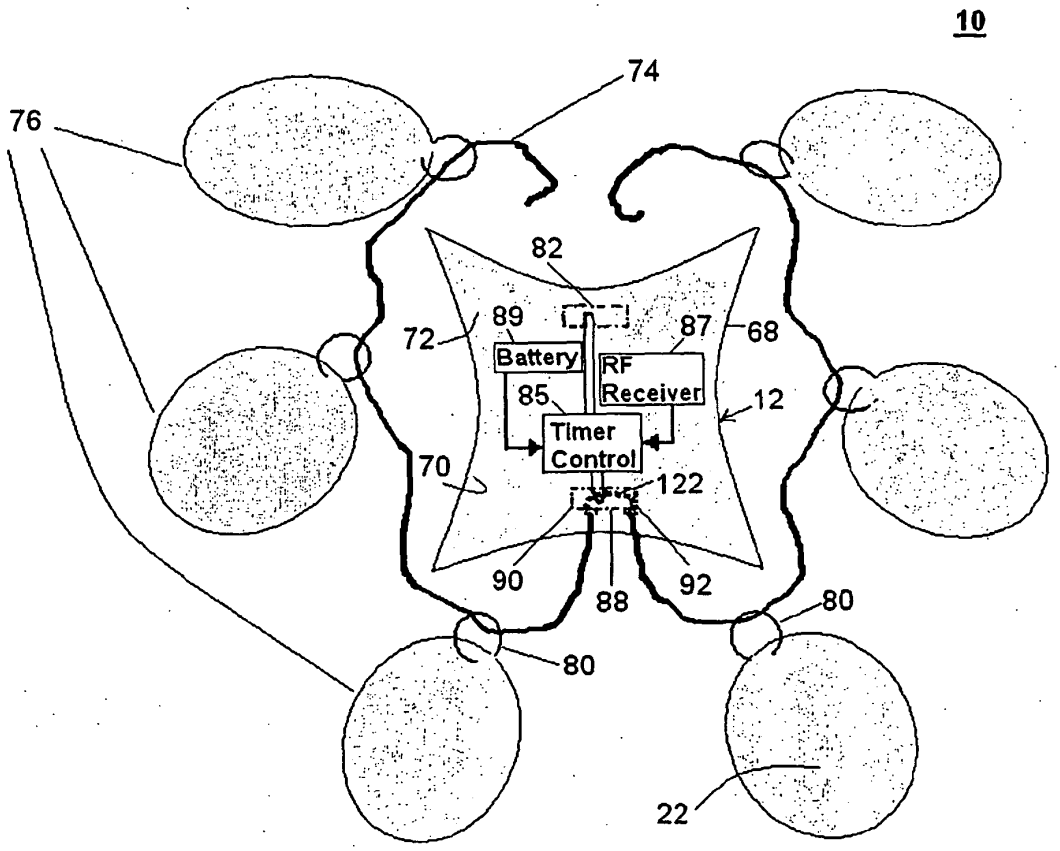
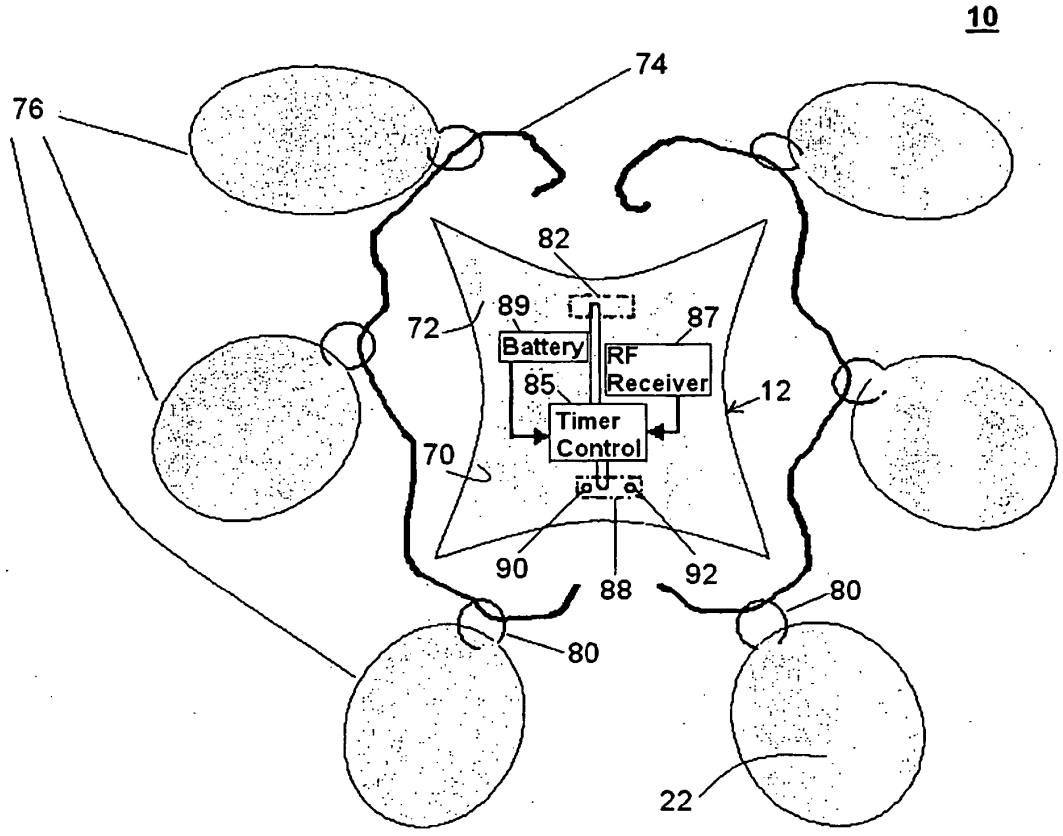

10
74
76
82
89
72
87
68
Battery
RF
Receiver
85
12
Timer
Control
70
122
90
88
92
80
80
22

Figure 3.


10
74
76
82
89
72
87
Battery
RF
Receiver
85
12
Timer
Control
70
90
88
92
80
80
22

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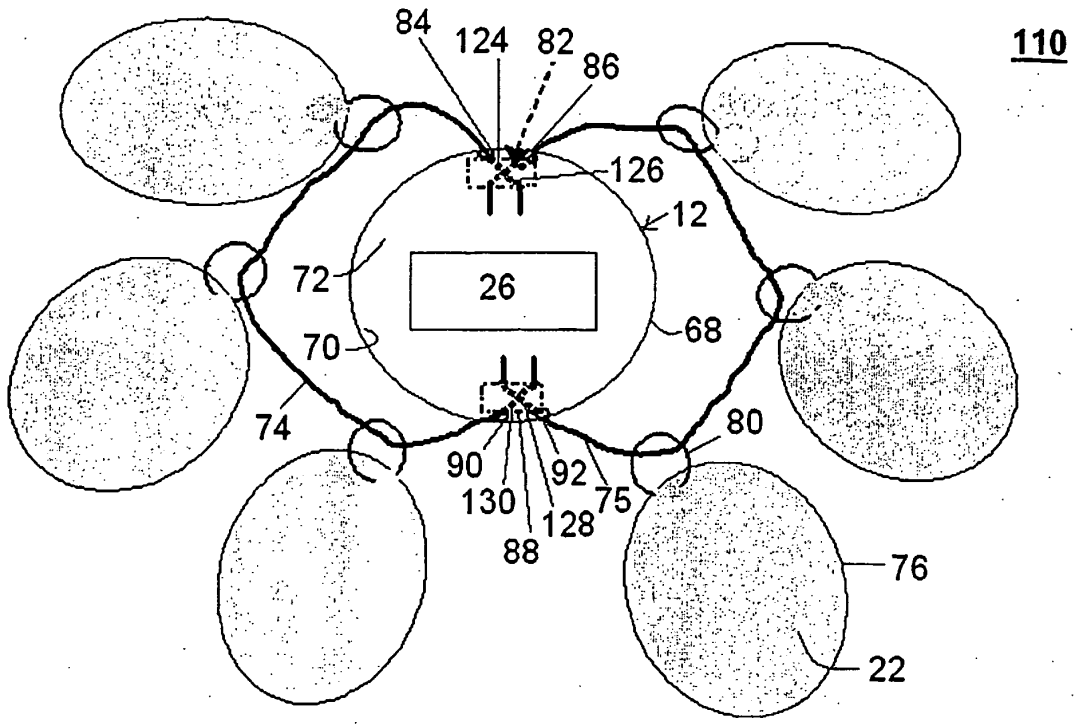

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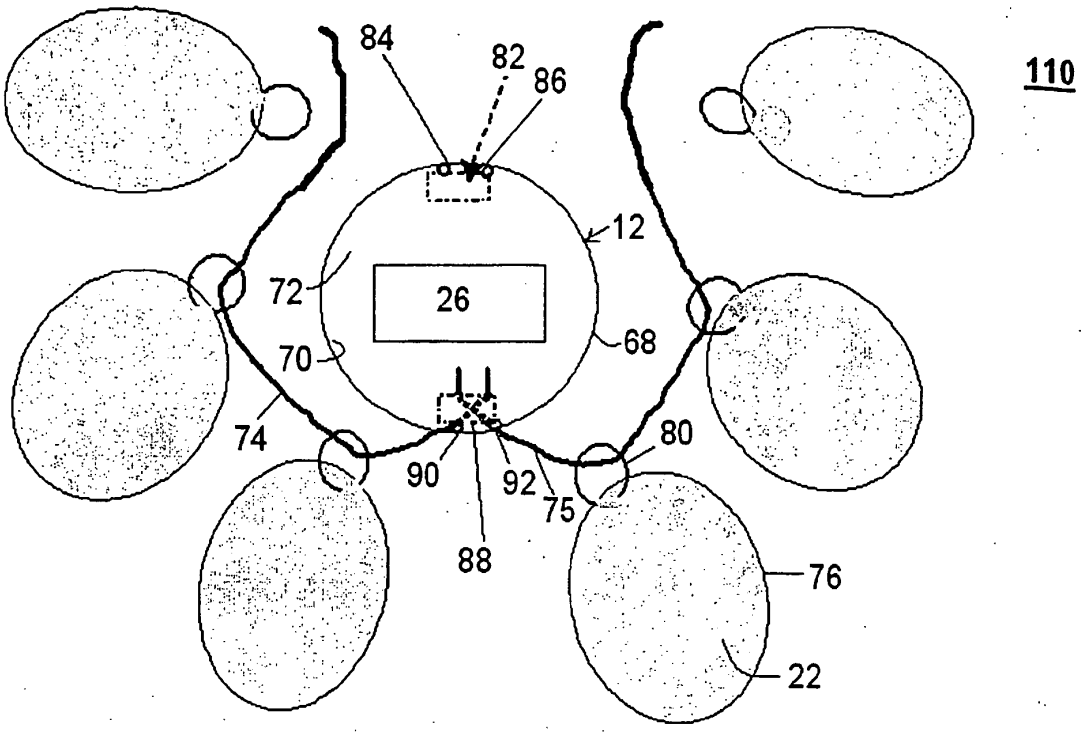

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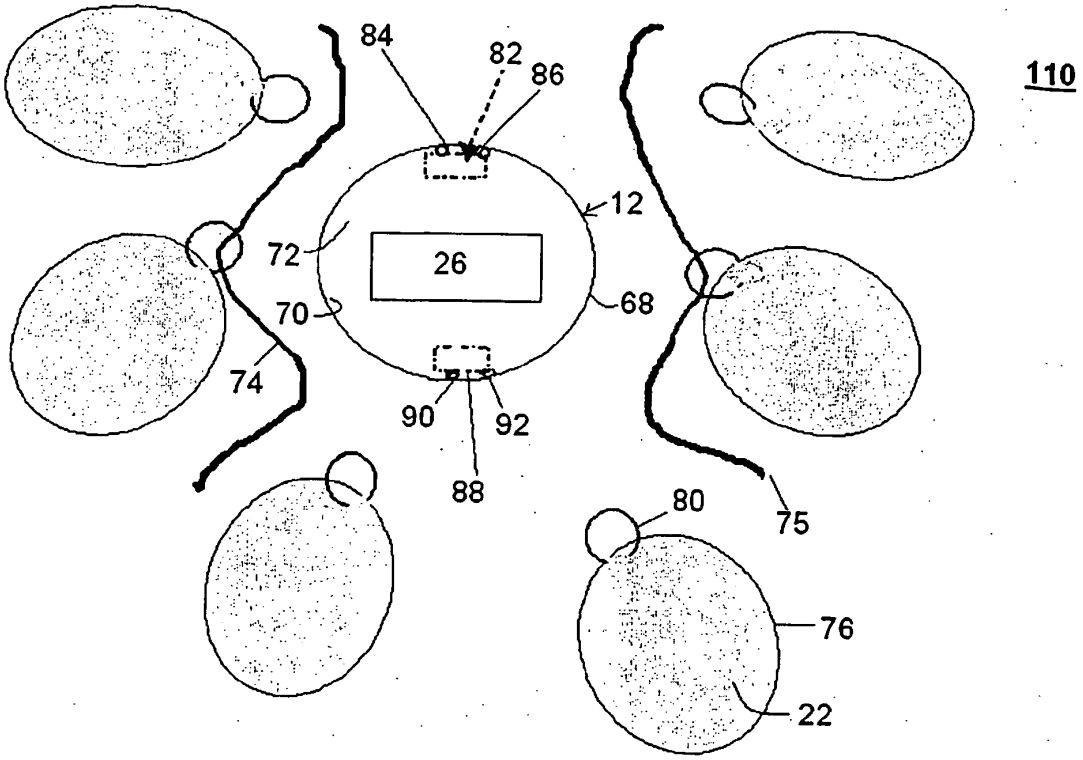

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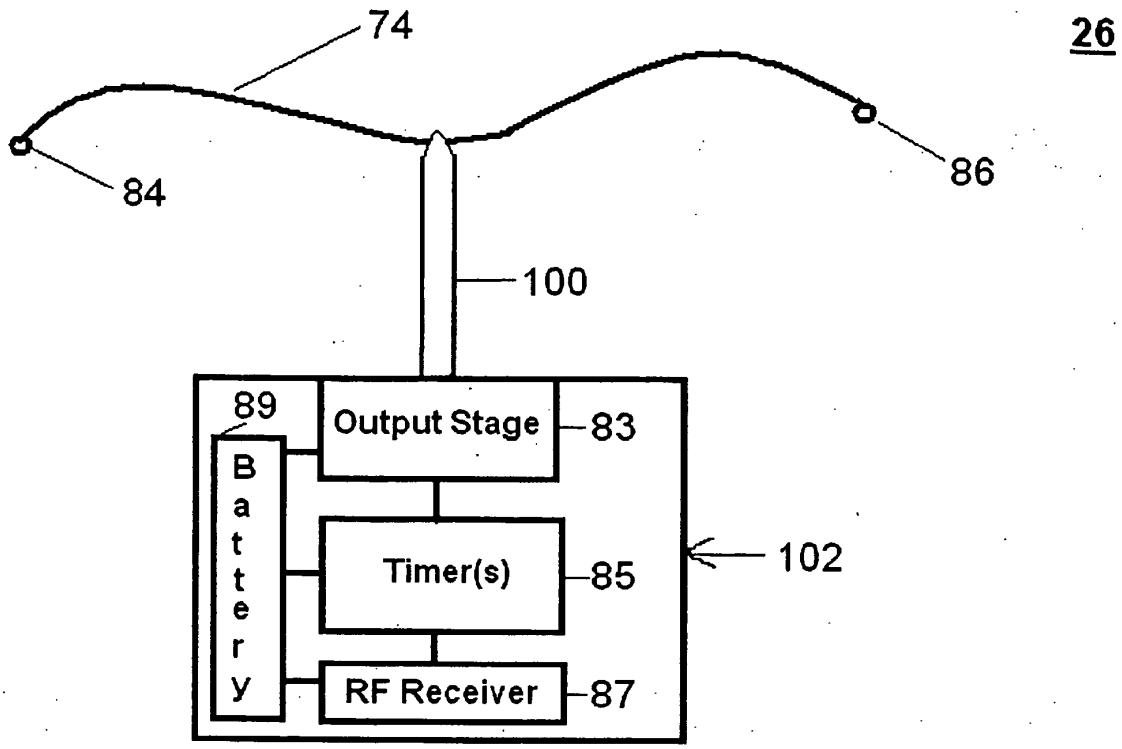
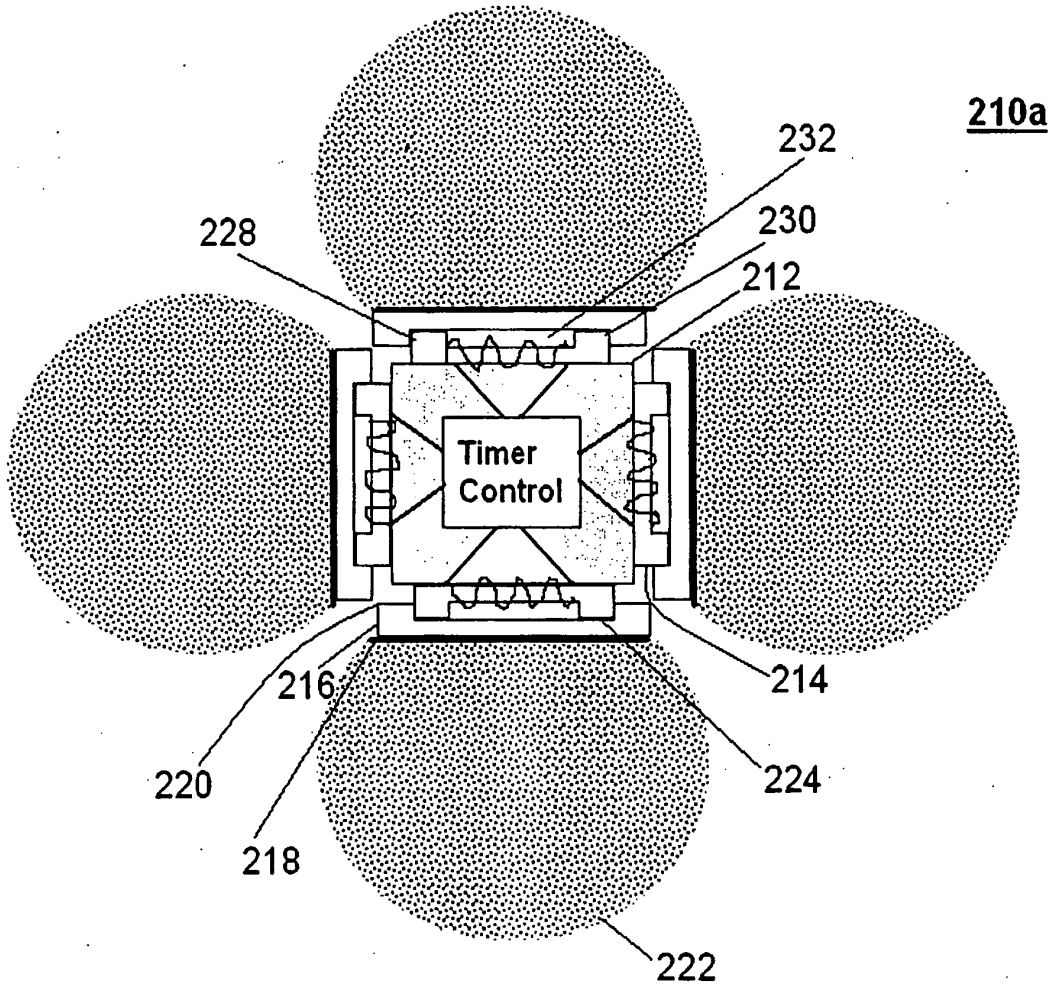

74
26
84
86
100
89
Output Stage
83
Battery
Timer(s)
85
102
RF Receiver
87

Figure 8.



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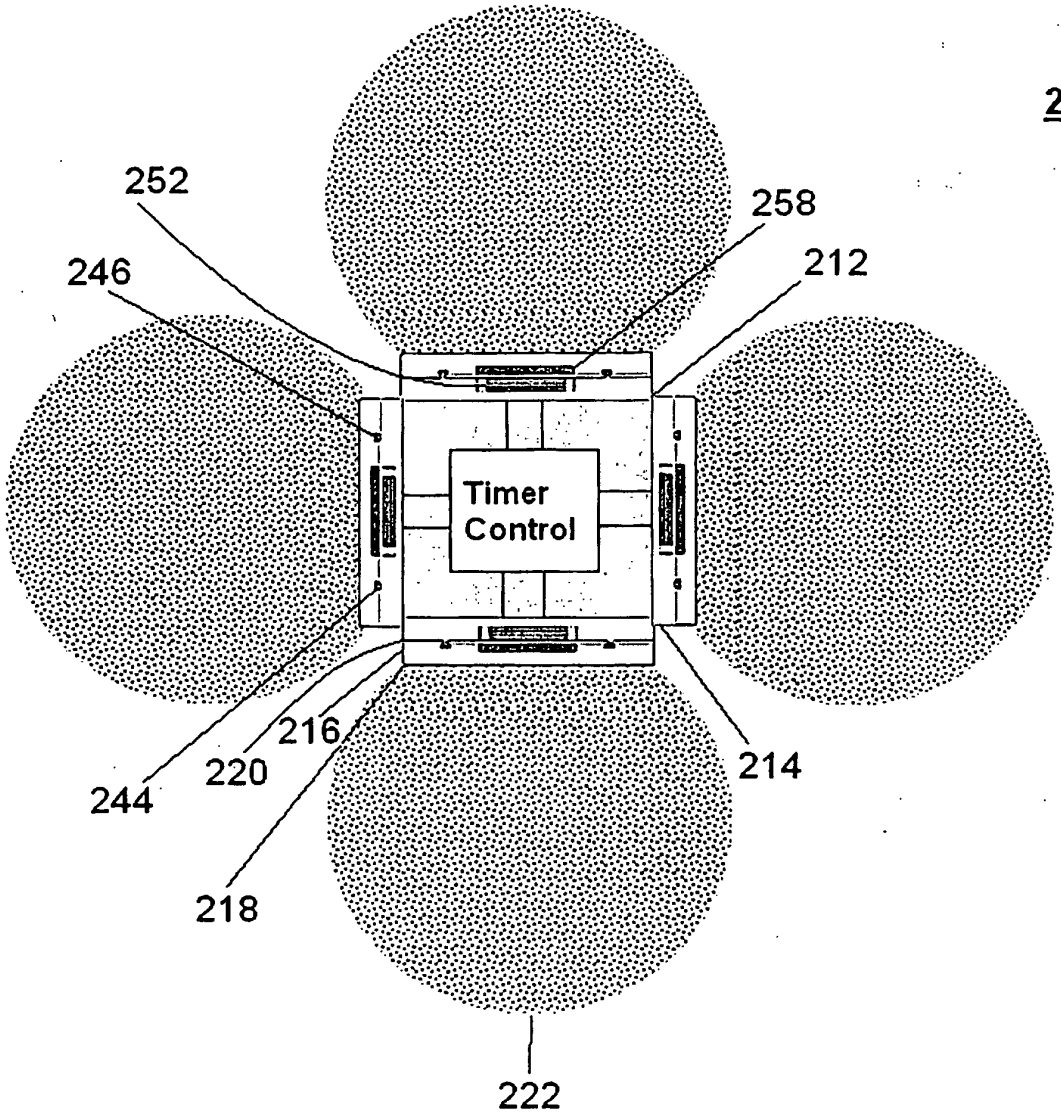

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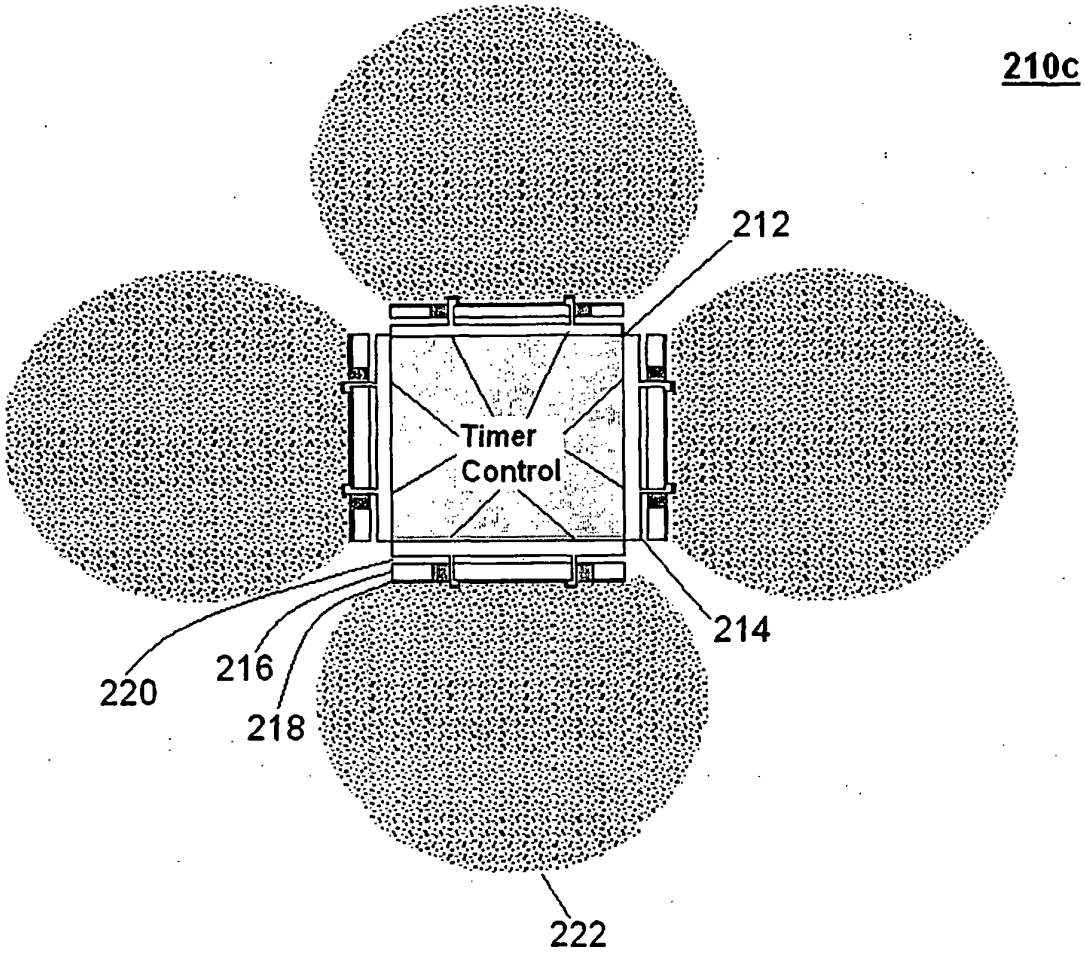

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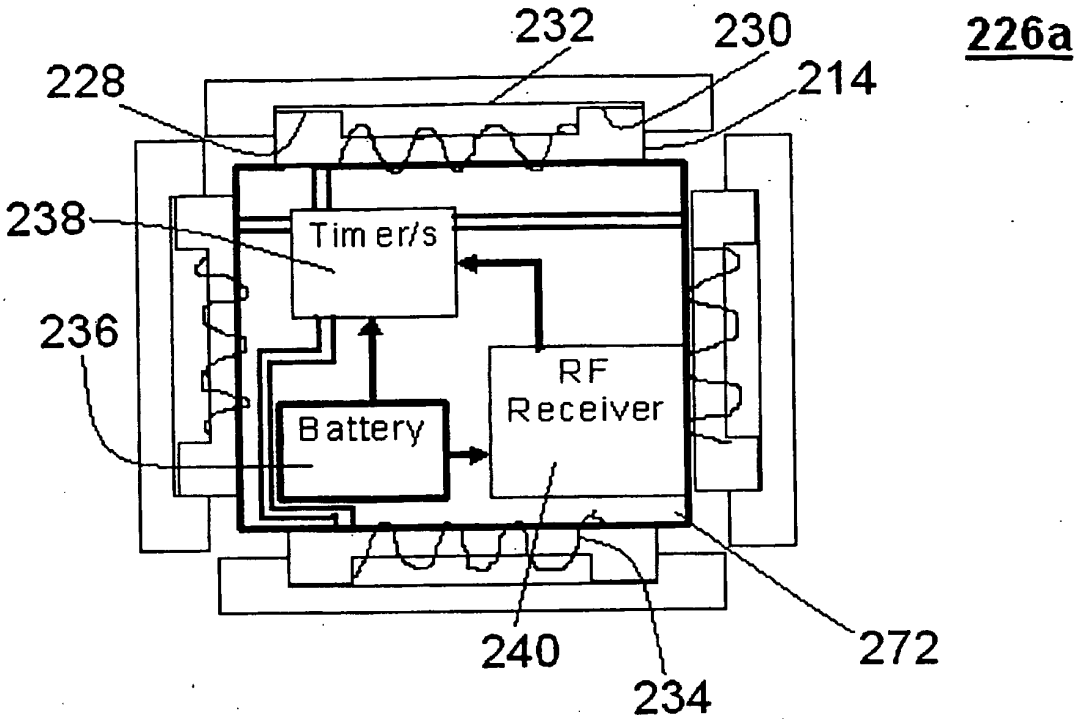
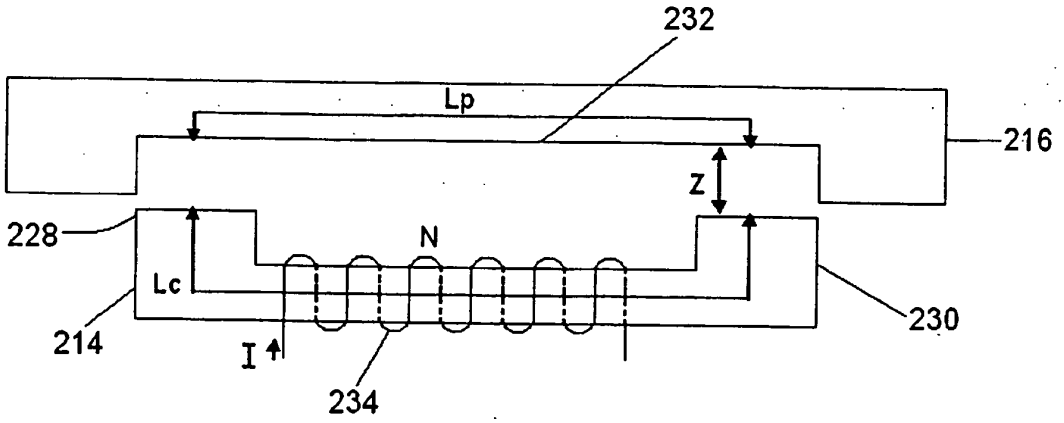

232
230
226a
228
214
238
Timer/s
236
RF
Receiver
Battery
240
234
272

Figure 12.



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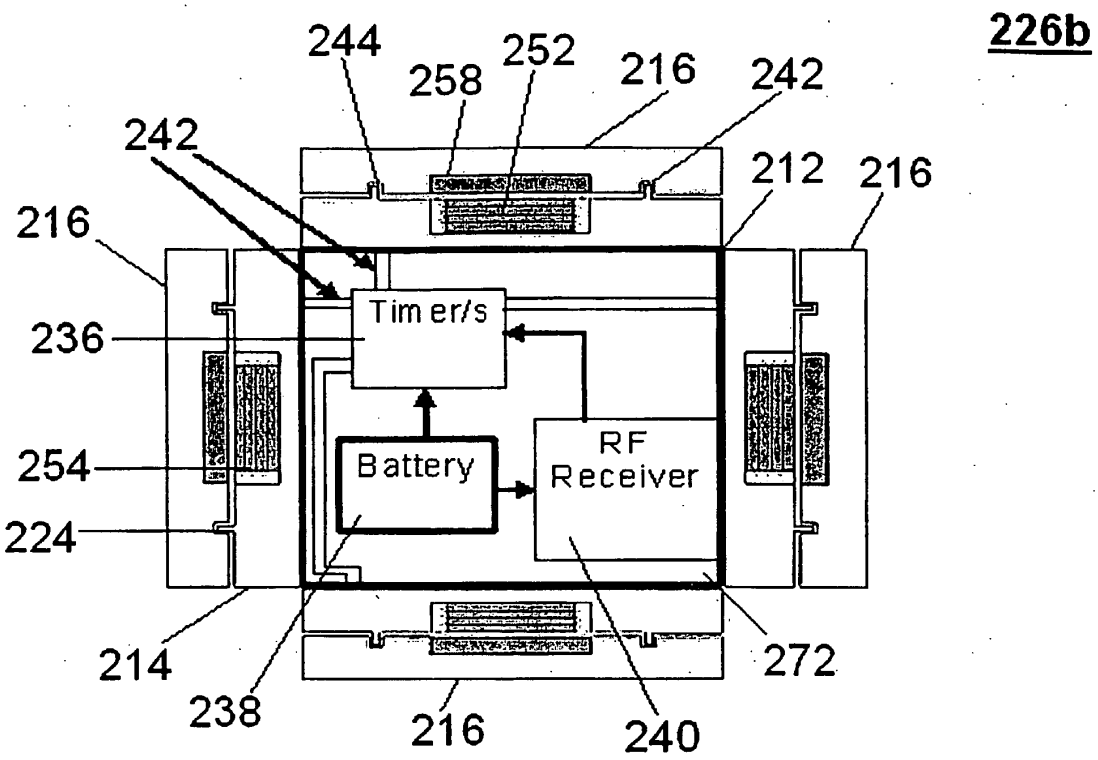
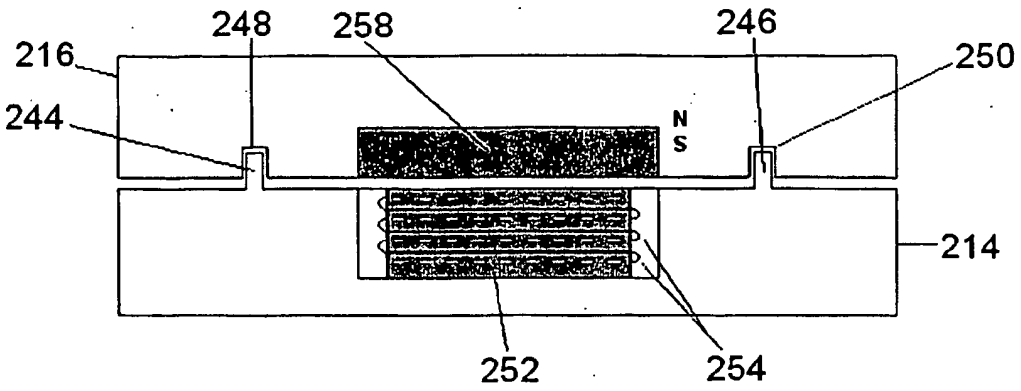

226b
244
258
252
216
242
242
212
216
216
236
Timer/s
254
Battery
RF
Receiver
224
214
238
216
240
272

Figure 14.



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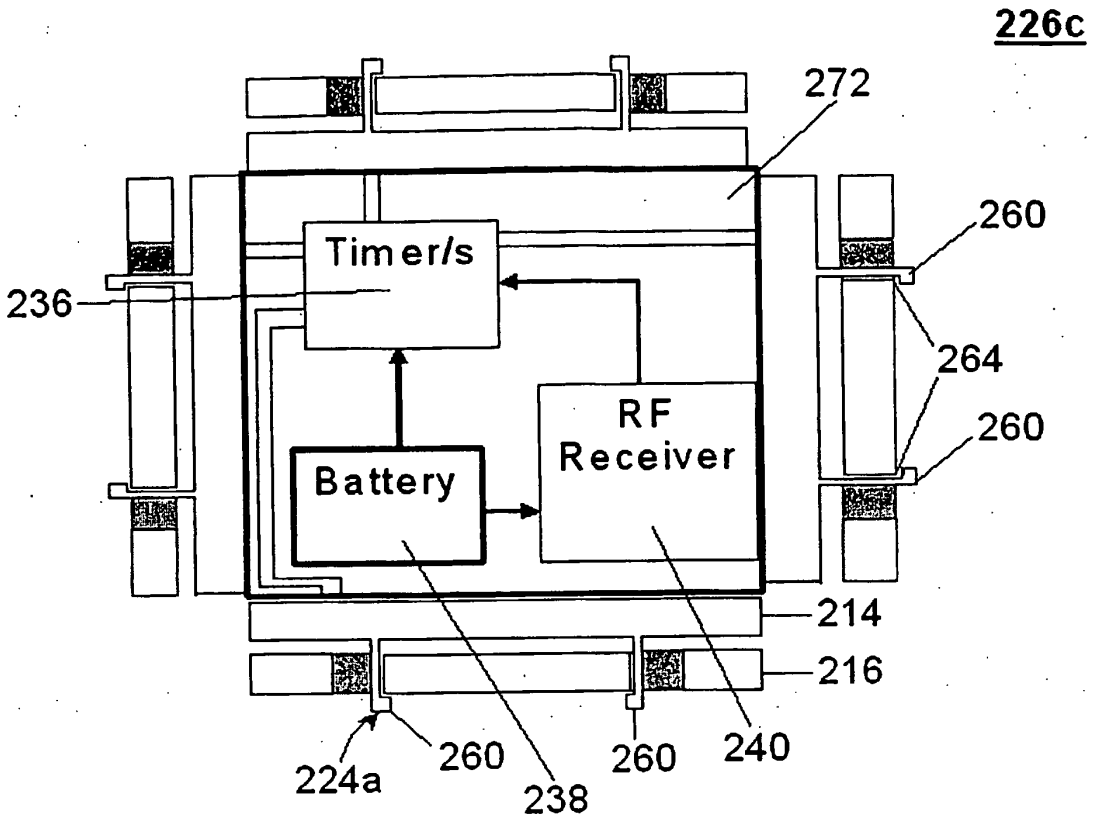
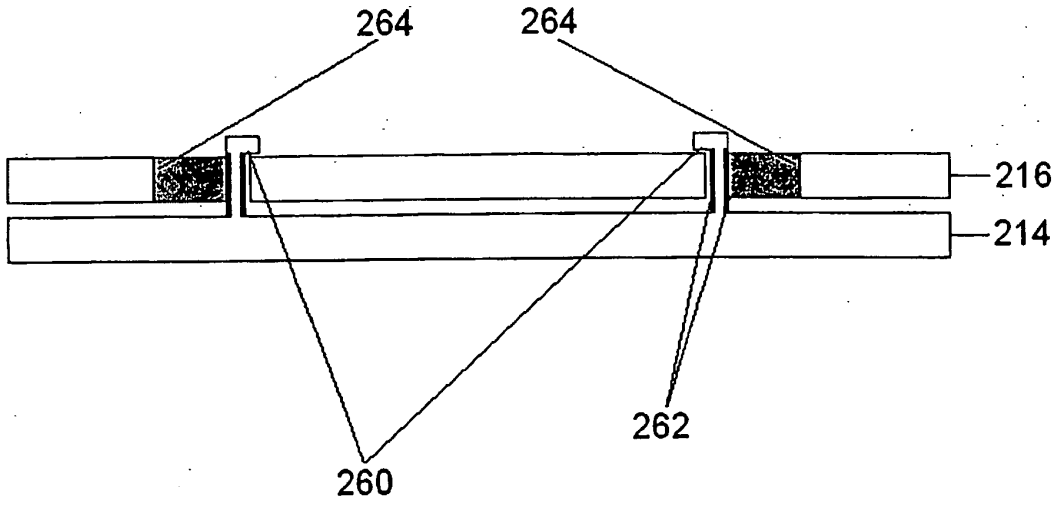

226c
272
260
236
Timer/s
264
RF
Receiver
260
Battery
214
216
224a
260
260
240
238

Figure 16.



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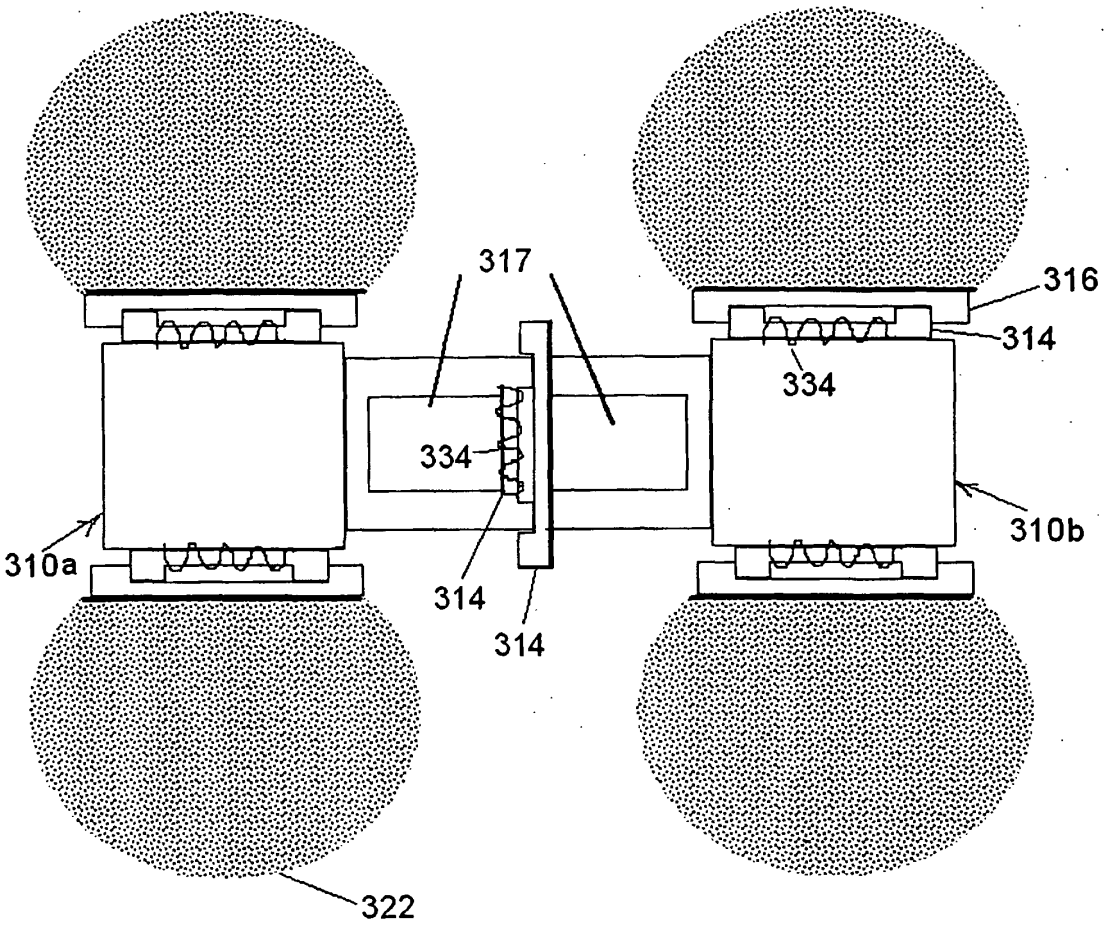

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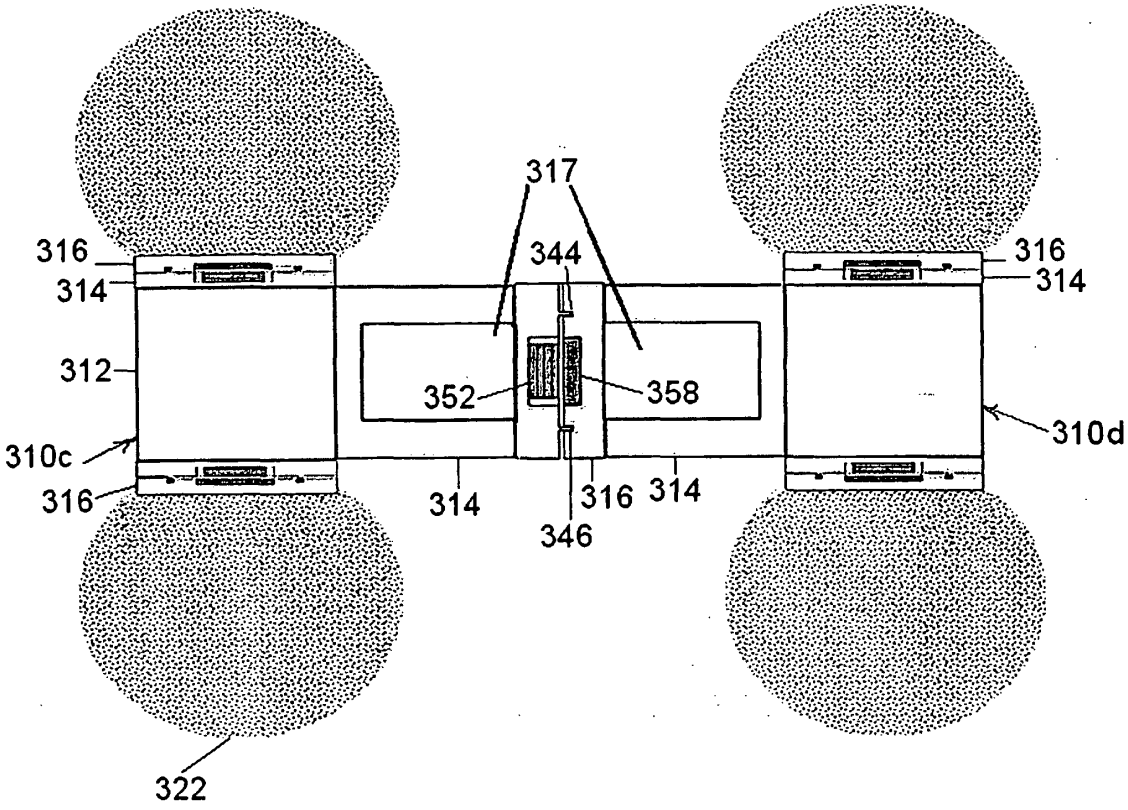
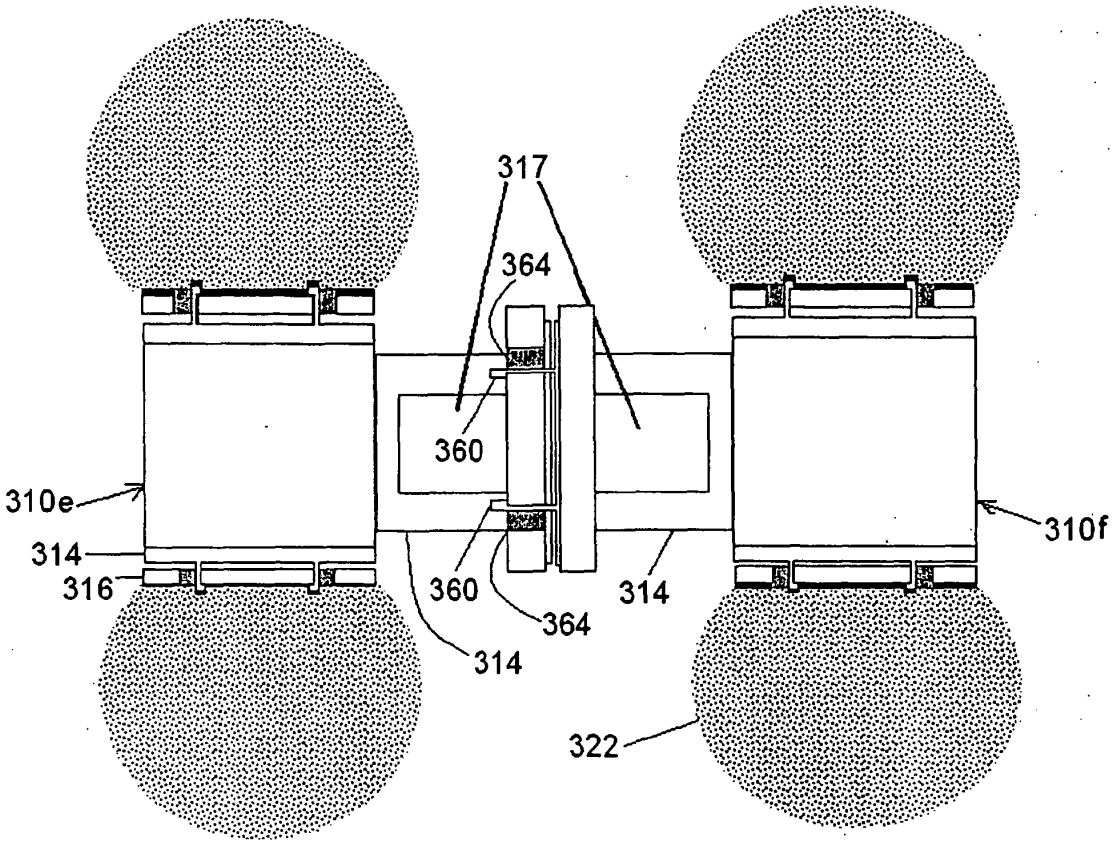

317
316
344
316
314
314
312
352
358
310d
310c
316
314
316
314
346
322

Figure 19.



REFERENCES CITED IN THE DESCRIPTION

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