Abstract:

A novel oral gastroretentive pharmaceutical dosage form and methods for preparing a novel oral gastroretentive pharmaceutical dosage form are described in present invention. A present inventions also provide a novel gastroretentive dosage form that deliver one or more active substances at same or different release rate by same or different release mechanism for same or different period of time in same or different region of gastrointestinal tract from single drug delivery system, i.e. a dosage form that is relatively flexible with respect to how to obtain a desired release pattern of the same or different active substances.
TITLE OF THE INVENTION

A NOVEL ORAL GASTRORETENTIVE PHARMACEUTICAL DOSAGE FORM

FIELD OF THE INVENTION

[0001] A present invention relates to a novel oral gastroretentive pharmaceutical dosage form and methods for preparing a novel oral gastroretentive pharmaceutical dosage form.

BACKGROUND OF THE INVENTION

[0002] Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation, etc. Controlled drug therapy may reduce the required frequency of administration, ideally single doses at periodic intervals being sufficient, resulting in improved patient compliance. The main target is the improved efficiency in treatment. However, conventional controlled-release drug delivery systems are of only limited use for (1) drugs acting locally in the stomach, (2) drugs that are primarily absorbed in the stomach, (3) drugs that is poorly soluble at alkaline pH, (4) drugs with a narrow window of absorption, (5) drugs rapidly absorbed from the GI tract and (6) drugs that degrade in the colon.

[0003] Controlled-release drug delivery systems intended for prolonged gastric retention in the stomach are known in the art. Several systems are described in the art, implementing various mechanisms. These include flotation on the surface of gastric content, sinking to the bottom of the stomach, unfolding dosage forms, bioadhesive dosage forms, swelling or expandable dosage forms, and various delivery systems, comprising more than one of the above mechanisms.

[0004] U.S. Patent No. 3,976,764 discloses solid therapeutic preparations floatable in the gastric juice wherein the active ingredient is impregnated into a body of empty globular shell or a small granular lump of a material having high buoyancy. In this reference, outer surface of half-piece of capsule is separately coated with enteric coating material. Each of the openings of said coated half pieces are tamped with flat tablets and the gap between the contact area of the piece and the tamped tablet is sealed with a sealant of water insoluble material. However, method disclose for preparation of floatable pharmaceutical dosage form according to this invention is very difficult to manufacture at large scale because coating of only external surface of half-piece of capsule is not feasible at large scale production and furthermore, it is very difficult to seal gap between the contact area of the piece of capsule and the tamped tablet with a sealant of water insoluble material.

[0005] U.S. Patent No. 7,485,322 discloses a floating capsule dosage form having prolonged gastric residence time, wherein the capsule body and cap are assembled such as to encapsulate at least a tablet and granulate together with entrapped gas and is coated with a coating which is substantially insoluble or poorly soluble in an acidic medium. In this reference, the tablet and granulate comprise active and hydrophobic or lipophilic substances which helps in controlling the release. The active-release is controlled by a dual mechanism, one with the help of hydrophobic or lipophilic substances in the matrix of tablet and granulates, and second with the help of an outer coating layer.

[0006] WIPO published application WO2013054285A1 disclose a gastroretentive dosage system comprising: (a) a shell filled with the active ingredient in powder form; (b) an extended-release layer over the shell; and (c) an immediate-release layer comprising the active ingredient over the extended-release layer.

[0007] U.S. Pat. No. 5,198,229 discloses a fluid-imbibing drug delivery device having a first, low density such that it floats in the stomach contents for a predetermined prolonged period of time, during which prolonged period of time it dispenses a drug or other active agent to the stomach, and having a second, higher density such that the device exits the stomach at the end of the predetermined prolonged period of time.

[0008] However, to the best of our knowledge there is still a need to develop a technology that enables preparation of gastroretentive pharmaceutical dosage form in a relatively simple manner, preferably in a procedure involving relatively few steps and relatively simple equipment, and in an economical feasible manner. Moreover, it is desired to obtain a novel gastroretentive technology that deliver one or more active substances at same or different release rate by same or different release mechanism for same or different period of time in same or different region of gastrointestinal tract from single drug delivery system, i.e. a dosage form that is relatively flexible with respect to how to obtain a desired release pattern of the same or different active substances.

OBJECT OF THE INVENTION

[0009] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form which is floatable in the gastric fluid of the stomach while releasing drug or drugs contained therein into the gastric fluid of the stomach.

[0010] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form comprises single layer or multilayer core, wherein at least one layer of core is floatable in the gastric fluid of the stomach while releasing drug or
drugs contained therein into the gastric fluid of the stomach.

[0011] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form comprises multilayer core, wherein at least one layer of core is floatable in the gastric fluid of the stomach while releasing drug or drugs contained therein into the gastric fluid of the stomach at and least another layer of core is either gastroretentive layer or non gastroretentive layer releasing drug or drugs contained therein into stomach or other than stomach or in both i.e. stomach followed by intestine.

[0012] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form comprises multilayer core, wherein at least one layer of core is active ingredient composition layer and at least another layer of core is functional composition layer, wherein particular function is assign to each functional composition layer.

[0013] It is an object of present invention to provide the aforesaid a novel oral gastroretentive pharmaceutical dosage form that incorporate a suitable amount of each active substance (notably amount corresponding to daily dose and should be present in a specific weight ratio that is optimized with respect to therapeutic effect).

[0014] It is an object of present invention to provide aforesaid a novel oral gastroretentive pharmaceutical dosage form which is being capable to release drug or drugs in controlled release manner or in combination of immediate release and controlled release manner.

[0015] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form that comprises multi-layer core, wherein said dosage form is being able to release each layer independently of same or different active substances into the aqueous fluid with which it comes into contact at same or different release rate by same or different release mechanism for same or different period of time.

[0016] It is another object of present invention to design a novel oral gastroretentive pharmaceutical dosage form that comprises multi-layer core, wherein said dosage form is being able to release each layer independently of same or different active substances into same or different region of gastrointestinal tract.

[0017] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form which is divisible from specific region of dosage form into two or more segment without compromising with functionality of coating film.

[0018] It is an object of present invention to provide aforesaid a novel oral gastroretentive pharmaceutical dosage form comprising predetermined quantity of drug or drugs is administrable in part after dividing it into two or more segment, wherein each segment has a predetermined quantity of drug or drugs.

[0019] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form which provide different release pattern. Example of such release pattern include, but are not limited to be, zero order release, release other than zero order, ascending order release, descending order release, conventional order release, release in specific location of gastrointestinal tract, release in two different location of gastrointestinal tract, etc.

[0020] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form, wherein size or dimension of oral gastroretentive pharmaceutical dosage form may be smaller compare to conventional dosage form to obtain such release pattern.

[0021] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form which delivers the drug or drugs in controlled manner from predefined surface area.

[0022] It is an object of present invention to design a novel oral gastroretentive pharmaceutical dosage form that provide different release patterns of one or more active substances from one or more composition layer of core that are optimized with respect to therapeutic effect.

[0023] It is an object of present invention to provide a novel oral gastroretentive pharmaceutical dosage form, which is easy to manufacture.

**SUMMARY OF THE INVENTION**

[0024] In preferred embodiment, an oral gastroretentive pharmaceutical dosage form comprising:

a) at least one container (S) having one or more aperture and a wall having an inside and an outside;

b) a core comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X);

c) encapsulate at least one preselected external surface of core within container (S) in such a way that it entrap air or create void between at least one inner surface of container (S) and at least one outer surface of core; and

d) water insoluble coating surrounding step (c) composition.

[0025] In specific embodiment, container (S) is capsule shell.

[0026] In preferred embodiment, a drug delivery system comprises a core, a said core comprising one or more composition layer, wherein at least one composition layer is active ingredient composition layer (L) comprises an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X).
In preferred embodiment, dosage form additionally comprising one or more inner coat on outer surface of core. In one embodiment, inner coat is swellable coat. In another embodiment, inner coat is non-swellable coat or insoluble coat.

In preferred embodiment, encapsulate at least one preselected external surface of core within container (S) in such a way that it entrap air or create void between at least one inner surface of container (S) and at least one outer surface of core which is at least sufficient to float the whole dosage form in gastric fluid of stomach for sufficient period of time.

In preferred embodiment, drug delivery system comprises a water insoluble coating in full or in part on outer surface of step (c) composition.

In preferred embodiment, an oral gastroretentive pharmaceutical dosage form comprising:

a) at least one insoluble container (C) having one or more aperture and a wall having an inside and an outside;

b) a core comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X); and

c) encapsulate at least one preselected external surface of core within insoluble container (C) in such a way that it entrap air or create void between at least one inner surface of insoluble container (C) and at least one outer surface of core.

In specific embodiment, insoluble container (C) is capsule shell.

In preferred embodiment, insoluble container (C) is made insoluble by chemical treatment, by high temperature, by high humidity, by ultraviolet (UV) and visible rays, by dyes, by making it from material which is either slowly soluble or soluble in aqueous environment after certain period of lag time or pH dependent soluble material, or by any other novel techniques for which the amount of information is limited.

In preferred embodiment, a drug delivery system comprises a core, a said core comprising one or more composition layer, wherein at least one composition layer is active ingredient composition layer (L) comprises an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X).

In preferred embodiment, encapsulate at least one preselected external surface of core within insoluble container (C) in such a way that it entrap air or create void between at least one inner surface of insoluble container (C) and at least one outer surface of core which is at least sufficient to float the whole dosage form in gastric fluid of stomach for sufficient period of time.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention which comprises container (S).

Figure 1A is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention comprising at least one container (S) (4) having one or more aperture and a wall having an inside and an outside, a core (5) comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients, encapsulate at least one preselected external surface of core (3) within container (S) (4) in such a way that it entrap air or create void (2) between at least one inner surface of container (S) (1) and at least one outer surface of core (3); and water insoluble coating (7) surrounding step (c) composition comprising pore forming agent (6).

Figure 1B is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention comprising at least one container (S) (4) having one or more aperture and a wall having an inside and an outside, a core (5) comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients, inner coat (8) surrounding core, encapsulate at least one preselected external surface of inner coated core (3) within container (S) (4) in such a way that it entrap air or create void (2) between at least one inner surface of container (S) (1) and at least one outer surface of inner coated core (3); and water insoluble coating (7) surrounding step (c) composition comprising pore forming agent (6).

Figure 1C is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention comprising at least one container (S) (4) having one or more aperture and a wall having an inside and an outside, a multilayer core (5) comprising three composition layer, wherein two composition layer is active ingredient composition layer (L) and another composition layer is functional composition layer (F), inner coat (8) surrounding multilayer core, encapsulate at least one preselected external surface of inner coated multilayer core (3) within container (S) (4) in such a way that it entrap air or create void (2) between at least one inner surface of container (S) (1) and at least one outer surface of inner coated multilayer core (3); and water insoluble coating (7) surrounding step (c) composition comprising pore forming agent (6).

Figure 2 is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention which comprises insoluble container (C).
Figure 2A is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention comprising at least one insoluble container (C) (4) having one or more aperture and a wall having an inside and an outside, a core (5) comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients, encapsulate at least one preselected external surface of core (3) within insoluble container (C) (4) in such a way that it entrap air or create void (2) between at least one inner surface of insoluble container (C) (1) and at least one outer surface of inner coated core (3).

Figure 2B is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention comprising at least one insoluble container (C) (4) having one or more aperture and a wall having an inside and an outside, a core (5) comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients, inner coat (6) surrounding core, encapsulate at least one preselected external surface of inner coated core (3) within insoluble container (C) (4) in such a way that it entrap air or create void (2) between at least one inner surface of insoluble container (C) (1) and at least one outer surface of inner coated core (3).

Figure 2C is a diagrammatic representation of an embodiment of novel oral gastroretentive dosage form of the present invention comprising at least one insoluble container (C) (4) having one or more aperture and a wall having an inside and an outside, a multilayer core (5) comprising three composition layer, wherein two composition layer is active ingredient composition layer (L) and another composition layer is functional composition layer (F), inner coat (8) surrounding a multilayer core, encapsulate at least one preselected external surface of inner coated multilayer core (3) within insoluble container (C) (4) in such a way that it entrap air or create void (2) between at least one inner surface of insoluble container (C) (1) and at least one outer surface of inner coated multilayer core (3).

Figure 3 is a diagrammatic representation of container (3) having one or more aperture (4) and a wall having an inside (1) and an outside (2).

Figure 4 is a diagrammatic representation of core (1) having outer/external surface (2).

**DETAILED DESCRIPTION OF THE INVENTION**

It is well known that the success of a therapy depends not only on the correct choice of medicament but also on whether its formulation is optimum from the technical and biopharmaceutical viewpoint.

The gastroretentive drug delivery system not only reduce the number of administrations of active substance but also improve therapeutic efficacy of (1) drugs acting locally in the stomach, (2) drugs that are primarily absorbed in the stomach or at upper part of intestinal tract, (3) drugs that is poorly soluble at alkaline pH, (4) drugs with a narrow window of absorption, (5) drugs that degrade in the colon, and (6) Drugs that disturb normal colonic microbes.

**Drug Delivery System**

In present invention, the term "water insoluble excipient" is used to refer excipient which is insoluble in water at all pH or insoluble as such but soluble in presence of other excipients or insoluble in at least one region of gastrointestinal tract or insoluble in water at certain pH such as e.g. eudragit L100 55 is insoluble at pH below 5.5. So when the term "water insoluble excipient" is specified, it is to be understood as it is insoluble in water at all pH or insoluble in water at certain pH as such but soluble in presence of other excipients.

In present invention, the term "water soluble excipient" is used to refer excipients which are soluble in water at all pH or soluble in at least one region of gastrointestinal tract or soluble in water at certain pH such as e.g. Eudragit L100 55 is soluble at pH 5.5 or it above. So when the term "water soluble excipient" is specified, it is to be understood as it is soluble in water at all pH or soluble in water at certain pH.

In present invention, the term "water insoluble coating" is used to refer coating which is insoluble in water at all pH or insoluble as such but soluble in presence of other excipients or insoluble in at least one region of gastrointestinal tract or insoluble in water at certain pH such as e.g. coating of eudragit L100 55 is insoluble at pH below 5.5. So when the term "water insoluble coating" is specified, it is to be understood as it is insoluble in water at all pH or insoluble in water at certain pH as such but soluble in presence of other excipients.

Present invention provide a novel gastroretentive pharmaceutical dosage form which is floatable in the gastric fluid of the stomach while releasing drug or drugs contained therein into the gastric fluid of the stomach. Present invention provide a novel gastroretentive pharmaceutical dosage form, wherein whole dosage form is floatable in the gastric fluid of the stomach or part of dosage form is floatable in the gastric fluid of the stomach.

According to an embodiment of present invention, a novel gastroretentive pharmaceutical dosage form which is floatable in the gastric fluid of the stomach is being capable to release drug or drugs contained therein for prolong period of time into at least one region of GI tract, wherein at least one
region of GI tract is stomach. According to an embodiment of present invention, a novel gastroretentive pharmaceutical dosage form which is floatable in the gastric fluid of the stomach is being capable to release drug or drugs contained therein into two or more region of GI tract, wherein at least one region of GI tract is stomach and another region of GI tract is other than stomach.

[0052] According to an embodiment of present invention, a novel gastroretentive pharmaceutical dosage form is divisible from specific region of dosage form into two or more segments without altering the release of drug or drugs from dosage form. According to an embodiment of present invention, a novel gastroretentive pharmaceutical dosage form is divisible from specific region of dosage form into two or more segment without altering the release of drug or drugs from dosage form, wherein release of drug or drugs from segments are similar or not similar to release profile of a whole dosage form. In the present invention, the term “segment” is used to refer divided part of gastroretentive pharmaceutical dosage form.

[0053] According to an embodiment of present invention, a novel gastroretentive pharmaceutical dosage form is being capable to release drug or drugs contained therein in pulsatile manner or after specific period of time.

[0054] In preferred embodiment, the present invention provides a novel gastroretentive pharmaceutical dosage form, wherein it is a possible to obtain different release pattern from single dosage form. Example of such release pattern include, but are not limited to be, zero order release, release other than zero order, ascending order release, descending order release, pulsatile release, release after specific period of time, conventional release, release in specific location of gastrointestinal tract, release in two different location of gastrointestinal tract, etc.

[0055] In the embodiment, a novel oral gastroretentive pharmaceutical dosage form is being capable to deliver same or different active substances at same or different release rate by same or different release mechanism for same or different period of time in same or different region of gastrointestinal tract from single drug delivery system, i.e. a system that is relatively flexible with respect to how to obtain a desired release pattern of the same or different active substances from single drug delivery system.

[0056] In one embodiment, the present invention provides a novel gastroretentive pharmaceutical dosage form, wherein size or dimension of dosage form may be smaller compare to conventional dosage form to obtain such release pattern.

[0057] In preferred embodiment, a gastroretentive pharmaceutical dosage form is able to release drug or drugs at predetermined release rate from predefined surface for specific period of time.

[0058] In the present invention, the term "active ingredient composition layer" is used herein to refer composition layer that release the drug contained therein into immediate release or controlled release manner. The letter "L" is used in present invention to refer active ingredient composition layer. The term "controlled release" includes "delayed release", "extended release", "prolong release", "long-acting", "modified release", "slow release", "sustained release", "time release", "pulsatile release" and the like, all of which are understood to refer to a release which is later or slower than "immediate release or release after certain period of time."

[0059] In preferred embodiment, an oral gastroretentive pharmaceutical dosage form comprising:

a) at least one container (S) having one or more aperture and a wall having an inside and an outside;
b) a core comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X);
c) encapsulate at least one preselected external surface of core within container (S) in such a way that it entrap air or create void between at least one inner surface of container (S) and at least one outer surface of core; and
d) water insoluble coating surrounding step (c) composition.

[0060] In preferred embodiment, drug delivery system comprising one or more containers (S), a said container (S) has one or more aperture and a wall having an inside and an outside surface.

[0061] In another embodiment, container (S) is soluble in gastrointestinal fluid.

[0062] In specific embodiment, container (S) is capsule shell.

[0063] In preferred embodiment, a drug delivery system comprises a core, a said core comprising one or more composition layer, wherein at least one composition layer is active ingredient composition layer (L) comprises an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X).

[0064] In preferred embodiment, dosage form additionally comprising one or more inner coat on outer surface of core. In one embodiment, inner coat is swellable coat comprising at least one swellable excipient. In another embodiment, inner coat is non-swellable coat or insoluble coat comprising at least one excipients selected from group consisting of water soluble excipients, water insoluble excipients, pH dependent soluble material, enzyme degradable material or mixture thereof. In further embodiment,
inner coat is either insoluble or soluble. In some embodiment, inner coat is water insoluble coating optionally comprising water soluble pore forming agent. In specific embodiment, part of inner coat is being sandwich between inner surface of container and outer surface of core. In the present invention, dosage form additionally comprising one or more inner coat on outer surface of core, so when the term “core” is utilized in present invention, it is to be understood as it is either coated with inner coat or without inner coat.

[0065] In preferred embodiment, encapsulate at least one preselected external surface of core within one or more container (S) in such a way that it entrap air or create void between at least one inner surface of container (S) and at least one outer surface of core. In one embodiment, encapsulate at least one preselected external surface of at least one composition layer of core within container (S) in such a way that it entrap air or create void between at least one inner surface of container (S) and at least one outer surface of said composition layers of core. In preferred embodiment, entrapped air or void created between at least one inner surface of container (S) and at least one outer surface of core is at least sufficient to float the whole dosage form or at least one composition layer in gastric fluid of stomach for sufficient period of time. In some embodiment, container is being sandwich between outer surface of core and water insoluble coating. In some embodiment, container is being sandwich between inner insoluble coat and water insoluble coating, resulting into outer and inner surface of container may not be available for direct contact with aqueous media, so container may not dissolve rapidly which help in maintaining floating of dosage form for longer period of time.

[0066] In preferred embodiment, drug delivery system comprises a water insoluble coating in full or in part on outer surface of step (c) composition. In one embodiment, water insoluble coating comprises water insoluble excipients or mixture of water insoluble excipients and water soluble excipients in appropriate ratio. In another embodiment, coating is impermeable or permeable to active ingredients. In further embodiment, coating is impermeable or semipermeable to aqueous fluid. In one embodiment, coating is insoluble throughout drug release profile. In another embodiment, coating is insoluble for specific period of time or soluble after specific period of time. In further embodiment, coating is insoluble in one region of gastrointestinal tract but it may be soluble in another region of gastrointestinal tract. In preferred embodiment, coating further comprises one or more aperture. In preferred embodiment, drug delivery system further comprises drug coating and/or film coating surrounding outer surface of water insoluble coating.

[0067] In preferred embodiment, an oral gastroretentive pharmaceutical dosage form comprising:

a) at least one insoluble container (C) having one or more aperture and a wall having an inside and an outside;

b) a core comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X); and

c) encapsulate at least one preselected external surface of core within insoluble container (C) in such a way that it entrap air or create void between at least one inner surface of insoluble container (C) and at least one outer surface of core.

[0068] In preferred embodiment, drug delivery system comprising one or more insoluble container (C), a said insoluble container (C) has one or more aperture and a wall having an inside and an outside surface.

[0069] In one embodiment, insoluble container (C) is insoluble in at least one region of gastrointestinal tract. In another embodiment, insoluble container (C) is insoluble for specific period of time. In further embodiment, insoluble container (C) is permeable or impermeable to gastrointestinal fluid. So when the term "insoluble container" is utilized, it is to be understood as container is insoluble and impermeable, insoluble but permeable, insoluble in one region of gastrointestinal tract but soluble in another region of gastrointestinal tract or insoluble for specific period of time.

[0070] In specific embodiment, insoluble container (C) is capsule shell.

[0071] In preferred embodiment, insoluble container (C) is made insoluble by chemical treatment, by high temperature, by high humidity, by ultraviolet (UV) and visible rays, by dyes, by making it from material which is either slowly soluble or insoluble in aqueous environment after certain period of lag time or pH dependent soluble material, or by any other novel techniques for which the amount of information is limited.

[0072] In preferred embodiment, a drug delivery system comprises a core, a said core comprising one or more composition layer, wherein at least one composition layer is active ingredient composition layer (L) comprises an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X).

[0073] In preferred embodiment, encapsulate at least one preselected external surface of core within one or more insoluble container (C) in such a way that it entrap air or create void between at least one
inner surface of insoluble container (C) and at least one outer surface of core. In one embodiment, encapsulate at least one preselected external surface of at least one composition layer of core within insoluble container (C) in such a way that it entrap air or create void between at least one inner surface of insoluble container (C) and at least one outer surface of said composition layers of core. In preferred embodiment, entrapped air or void created between at least one inner surface of insoluble container (C) and at least one outer surface of core is at least sufficient to float the whole dosage form or at least one composition layer in gastric fluid of stomach for sufficient period of time. In preferred embodiment, drug delivery system further comprises drug coating and/or film coating surrounding outer surface of water insoluble coating.

[0074] In some embodiment, drug delivery system comprising a core, a said core comprises one or more composition layers as describes below.

[0075] In the present invention, when the term “composition layer” is utilized, it is to be understood as it is active ingredient composition layer (L) or functional composition layer (F) or both. In the present invention, when the term "container" is utilized, it is to be understood as it is either container (S) or insoluble container (C).

[0076] In preferred embodiment, drug delivery system comprises a core, a said core comprising one or more composition layer, wherein at least one composition layer is active ingredient composition layer (L). In one embodiment, a drug delivery system comprises a core, a said core comprising one or more active ingredient composition layers (L), wherein at least one active ingredient composition layer (L) release the drug or drugs contained therein in gastric fluid of stomach. In preferred embodiment, active ingredient composition layer (L) comprising one or more active ingredients (A) and optionally one or more pharmaceutically acceptable excipients (X) selected from group consisting of release rate controlling agent, swellable excipients, pH modifying agent, water soluble excipients, water insoluble excipients, gas generating agent, agent thereby mechanism of gastric retention of core is attained or mixture thereof.

[0077] In preferred embodiment, drug delivery system comprises a core, a said core comprising two or more composition layer, wherein at least one composition layer is active ingredient composition layer (L) and at least another composition layer is functional composition layer (F). In specific embodiment, a functional composition layer (F) is located at one end of core such as forming top or bottom part of core or at two opposite end of core such as forming top and bottom part of core. In specific embodiment, a functional composition layer (F) is being sandwich between two composition layers. In preferred embodiment, a said functional composition layer (F) comprises at least one pharmaceutically acceptable excipients (X) selected from group consisting of release rate controlling agent or swelling agent, swellable excipients, pH modifying agent, water soluble excipients, water insoluble excipients, gas generating agent, agent thereby mechanism of gastric retention of core is attained or mixture thereof. In some embodiments, functional composition layer may optionally comprise a drug.

[0078] In preferred embodiment, particular function is assign to each functional composition layer (F) such as, but not to be limited:

a) Functional composition layer as immediate release layer in core composition

b) Functional composition layer act as time release or delay release composition layer for one or more active ingredient composition layer in core composition, i.e. functional composition layer allow the release of drug or drugs from active ingredient composition layer after specific period of time or in specific location of gastrointestinal tract

c) Functional composition layer as barrier composition layer to separate composition layer

d) Functional composition layer as additional/supportive gastroretentive layer in core composition

e) Functional composition layer as divisible composition layer in core composition to divide dosage form into two or more segments without compromise with functionality of coating intended for particular function.

[0079] In some embodiment, core comprises two or more functional composition layer (F), wherein particular function assign to each functional composition layer (F) is similar or different. In specific embodiment, component of functional composition layer is selected based on function assign to each functional composition layer (F) in dosage form.

[0080] In preferred embodiment, functional composition layer act as immediate release layer, wherein said functional composition layer comprises drug or drugs and one or more swellable excipients and/or pH modifying agent.

[0081] In preferred embodiment, functional composition layer act as time release or delay release composition layer for one or more drug composition layer in core composition, wherein said functional composition layer comprises at least one excipients
selected from group consisting of pH modifying agent, water soluble excipients, water insoluble excipients or mixture thereof. In one embodiment, functional composition layers (F) allow the release of drug or drugs form active ingredients composition layer after specific period of time or in specific location of gastrointestinal tract.

[0082] In preferred embodiment, functional composition layer act as barrier composition layer to separate two composition layer, wherein said functional composition layer comprises at least one excipients selected from group consisting of swellable excipients, pH modifying agent, water soluble excipients, water insoluble excipients or mixture thereof.

[0083] In preferred embodiment, functional composition layer act as additional/supportive gastroretentive layer in core composition, wherein said functional composition layer comprises at least one agent thereby mechanism of gastric retention is attained.

[0084] In preferred embodiment, functional composition layer act as divisible composition layer in core composition, wherein said functional composition layer is placebo composition layer, i.e. drug free composition layer. In one embodiment, divisible composition layer comprises at least one excipients selected from group consisting of swellable excipients, pH modifying agent, water soluble excipients, water insoluble excipients or mixture thereof. In preferred embodiment, a drug delivery system is divisible at functional composition layers (F) into two or more segments without compromise with functionality of coating film intended for particular purpose. In preferred embodiment, divided segment yields a predetermined quantity of drug or drugs. In preferred embodiment, a drug delivery system can be administered in part after dividing it into two or more segments. In one embodiment, releases of drug or drugs from divided segments are similar or not similar to release profile of a whole dosage form.

[0085] In preferred embodiment, an oral gastroretentive pharmaceutical dosage form can be matrix or reservoir system to release drug. In reservoir system, drug release occurs through porous polymeric membrane while in matrix system, drug release by dissolution, diffusion or erosion process. In some embodiment, a dosage form release the drug or drugs in sustained manner from predefined surface.

[0086] In one embodiment, composition layers of core encapsulate within container are gastroretentive in the gastric fluid of the stomach. In another embodiment, composition layer of core without encapsulation are either gastroretentive or non-gastroretentive in gastric fluid of stomach.

Components of Gastroretentive Pharmaceutical Dosage Form - Container:

[0087] In a preferred embodiment of the present invention, the container is capsule shell.

[0088] In the present invention, when the term "capsule shell" is used, it is to be understood as it is part of capsule or whole capsule. Part of capsule means either body part or cap part of capsule. Whole capsule shell means capsule having both cap and body part.

[0089] In one embodiment, the capsule shell is typically a hollow shell of generally cylindrical shape having a diameter and length sufficient so that the composition layers of core fits appropriately in the empty capsule. The clearance between the capsule shell and the composition layers of core is preferably from about +1.0 mm to about 0 mm. According to a specifically preferred embodiment of the present invention, the clearance between the capsule shell and the composition layers of core is in the range of from about +0.5 mm to about -0.5 mm.

[0090] The capsule shell comprising a material, wherein said material is selected from group consisting of, but are not to be limited, gelatin, starch, casein, chitosan, soya bean protein, gum Arabic, safflower protein, alginites, gelan gum, carrageenan, xanthan gum, phtalated gelatin, succinated gelatin, cellulosephthalate-acetate, polyvinylacetate, cellulose derivatives include, but not to be limited, hydroxypropyl methylcellulose, hylromellose phthalate, carboxy-methyl cellulose, polyvinylacetate-phthalate, polymericates of acrylic or methacrylic esters, sodium alginate, carrageenan, polyvinylpyrolidone, natural or synthetic materials or mixtures thereof. In specific embodiment, material composition for capsule shell is selected from group consisting of gelatin and its derivative, cellulose and its derivatives and starch and its derivatives.

[0091] In some embodiment, container (S) is soluble in gastrointestinal fluid.

[0092] In some embodiment, insoluble container (C) is insoluble in at least one region of gastrointestinal tract. In specific embodiment, capsule shell materials may be made insoluble by chemical treatment, by high temperature, by high humidity, by ultraviolet (UV) and visible irradiation, by dyes, by making it from material which is either slowly soluble or soluble in aqueous environment after certain period of lag time or pH dependent soluble material, or by any other novel techniques for which the amount of information is limited. Radiation crosslinking includes crosslinking by electron beams, ultraviolet, γ-irradiation, x-rays, and other means.
Chemical crosslinking is carried out by exposing the polymers to the crosslinking composition or molecule that contains a plurality of functional groups that are reactive with functional groups on the polymer such as e.g. cross linking with cross linking agent, e.g glutaraldehyde.

Active Substance:

[0093] In preferred embodiment of present invention, the core comprises one or more active ingredient composition layers (L), wherein active ingredient (A) in any of one composition layers may be the same or different from the active ingredient (A) in any of the other composition layers.

[0094] The terms "drug", "active substance", "active ingredient", "active agent", "drug substance", "pharmacologically active agent", "therapeutically active substance", "physiologically active agent" or "drug substance in physiologically active form" are used interchangeably herein to refer to a chemical compound that induces a desired pharmacological or physiological effect. The terms also encompass pharmaceutically acceptable derivatives of those active agents specifically mentioned herein, including, but not to be, limited, salts, solvates, polymorphs, hydrates, complexes with one or more molecules, produgs, active metabolites, analogs, and the like. The letter "A" is used herein to denote "Active substance". When the terms "drug", "active substance", "active ingredient", "active agent", "drug substance", "pharmacologically active agent", "therapeutically active substance", "physiologically active agent" or "drug substance in physiologically active form" are used, or when a particular drug, for example Sertraline, is identified, it is to be understood as including the active agent as well as pharmaceutically acceptable salts, solvates, polymorphs, hydrates, complexes with one or more molecules, produgs, active metabolites, analogs and like.

[0095] In specific embodiments, drugs that may be used in the pharmaceutical composition of the present invention may be selected from the group consisting, but are not limited to be, of Alzheimer's disease, anesthetics, acromegaly agents, analgesics, centrally-acting analgesics, antiasthmatics, anabolic agents, appetite suppressants, anti-inflammatory, non-steroids anti-inflammatory, anticancer agents, anticoagulants and antithrombotic agents, anticonvulsants, antidepressants antiemetics, antihypertemics, antiepileptics, antimigraine, antiglaucoma, antihistamines, anti-infective agents, antiparkinsons, antplatelet agents, antirheumatic agents, antispasmodics and anticholinergic agents, antitussives, carbonic anhydrase inhibitors, cardiovascular agents, antiobesity, lipid modifying agents, cholinesterase inhibitors, treatment of CNS disorders, CNS stimulants, contraceptives, cystic fibrosis management, antipsychotics, dopamine receptor agonists, endometriosis management, anxiolytics, antiasthmatics, erectile dysfunction therapy, fertility agents, corticosteroid, gastrointestinal agents, Decongestant, cough suppressant, immunomodulators and immunosuppressives, memory enhancers, migraine preparations, muscle relaxants, anaesthetics, nucleoside analogues, opioids, osteoporosis management, adrenergics, parasympathomimetics, expectorants, antinauseants, prostaglandins, active substances against amoebiasis and other protozoal diseases; psychotherapeutic agents, antidepressants, sedatives, hypnotics and tranquilizers, drugs used for skin ailments, steroids and hormones and drugs used to treat narcolepsy and attention deficit hyperactivity disorder. In one embodiment, drugs that may be used in the pharmaceutical composition of the present invention may be selected from active substance associated with abuse syndromes include opioids, CNS depressants, CNS stimulants, cannabinoids, nicotine-like compounds, glutamate antagonists and N-methyl-D-aspartate (NMDA) antagonists.

[0096] The active substance can be in various forms, such as uncharged or charged molecules, molecular complexes, crystalline forms, amorphous form, polymorphous form, polymorphous complex, complexes, solvates, anhydrates, if relevant isomers, enantiomers, racemic mixtures and pharmaceutically acceptable salts. Derivatives of active substances such as esters, ethers and amides which have solubility characteristics suitable for use herein can be used alone or mixed with other drugs. After release of the derivative from the drug delivery system it may be converted by enzymes, hydrolysed by body pH or other metabolic processes to the parent drug or to another biologically active form.

[0097] In one embodiment, a pharmaceutical composition of the invention may in addition be suitable for the delivery of peptides, polypeptides, hormones, proteins, antibodies and microorganisms, either living, attenuated or dead.

[0098] In preferred embodiment of present invention, the drug substance (A) may also include new chemical entity for which the amount of information is limited. In such cases, the dosage form regimen needs to evaluate based on preclinical and clinical trials.

Release rate controlling excipients:

[0099] A suitable water soluble or water insoluble release rate controlling excipient is selected from group consisting of cellulose derivatives include, but are not limited to be, methyl cellulose, ethyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose,
hydroxyethyl methylcellulose, cellulose acetate phthalate, microcrystalline cellulose, ethylhydroxyethylcellulose, ethylmethylcellulose, cellulose propionate, cellulose nitrate, cellulose acetate, hydroxyethylcellulose, hydroxyethylpropylcellulose, carboxymethylcellulose and sodium carboxymethylcellulose, ethyl cellulose; glycerol palmitostearate, beeswax, glycowax, castor wax, carnauba wax, glycerol monostearate, hydrogenated vegetable oils, vegetable oils, stearyl alcohol, acetylated hydrogenated soybean oil glycerides, castor oil, glycerol behenic acid ester, glyceryl monooleate, glyceryl monostearate, propylene glycol monostearate, cetyl alcohol, natural and synthetic glycerides, waxes, fatty acids, fatty alcohol, lipid, steryl alcohol, sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate, sorbitan monostearate, sorbitan sesquioleate, sorbitan trioleate, sorbitan tristearate, polyacrylamide derivatives, methacrylic acid derivatives; vinyl pyrrolidone polymers such as polyvinylpyrrolidone and copolymers of vinyl pyrrolidone and vinyl acetate; Polyalkylene oxide and copolymer thereof, alkylene oxide homopolymers; gums of plant, animal, mineral or synthetic origin, polyactic acid or polyglycolic acid and copolymers thereof, methacrylates, Polyacrylic acid and copolymer thereof, a co-polymer of methacrylate-galactomannan etc., Polyvinyl alcohols, glycercinated gelatin, cocoa butter, macrogol esters, macrogol Stearate, phosphate esters, amides, phthalate esters, glyceryl cocoate oleyl alcohol, myristyl alcohol, sucrose octaacetate, diacetylated monoglycerides, diethylen glycol monostearate, ethylene, polyoxethylene 50 stearate, macrogol ethers, cetomacrogol 1000, laurmacrogols, poloxamers; and mixtures thereof. In one embodiment, an active ingredient composition layer (L) may comprise one or more release rate controlling excipients mentioned above in an amount ranging from about 2% to about 90%, by weight of the composition or layer.

Swellable Excipients:

[00100] The swelling agent is generally used in an amount ranging from about 0.5% to about 95% by weight of composition or layer. The swellable excipient that may be used may be a highly swellable excipient selected from vinylpyrrolidone polymers such as crospovidone; cellulose and cellulose derivatives such as carboxymethyl celluloses, crosslinked carboxymethylcelluloses and their alkali salts; sodium starch glycolate, starch and starch derivatives, resins and mixtures thereof. The highly swellable excipient is preferably used in an amount ranging from about 1% to about 40% by weight of composition or layer. The swellable excipient that may be used may be a moderately swellable excipient and may be used in an amount ranging from about 4% to about 80% by weight of composition or layer, preferably about 5% to about 50% by weight of composition or layer.

Gas Generating Agent:

[01001] The composition layers may also comprise gas generating agent in an amount ranging from about 0.5% to about 60% by weight of composition or layer. Gas generating agents may help in release of insoluble or poorly soluble drug or drugs, disintegration of composition layer and may act as a agent thereby mechanism of gastric retention is achieved. Gas generating agents that may be used in the present invention include carbonates such as calcium carbonate, bicarbonates such as sodium or potassium bicarbonate, sulfites such as sodium sulfite, sodium bisulfite, or sodium metabisulfite, and the like. These salts may be used alone or in combination with an acid source as a gas generating couple. The acid source may be an edible organic acid, a salt of an edible organic acid, acidic components such as acrylic polymers, or mixtures thereof. Examples of organic acids that may be used include citric acid, malic acid, succinic acid, tartaric acid, fumaric acid, maleic acid, ascorbic acid, glutamic acid, and their salts, and mixtures thereof.

pH modifying Agent:

[01002] According to present invention, pH modifying agents are acidic agent or alkalizing agent. pH modifying alkalizing agent include, but are not to be limited, magnesium oxide, meglumine, sodium oxide, sodium hydroxide, sodium bicarbonate, potassium citrate, sodium citrate, sodium carbonate, potassium bicarbonate, potassium carbonate, calcium carbonate, magnesium hydroxide, magnesium carbonate, sodium borate, aluminum oxide, aluminum hydroxide, ammonium Carbonate, monoethanolamine, diethanolamine, triethanolamine, Potassium Hydroxide, Sodium Phosphate Dibasic and Trolamine. pH modifying acidic agent include, but are not to be limited, ascorbic acid, benzoic acid, boric acid, citric acid, EDTA and derivative thereof like disodium edetate, trisodium edetate, tetrasodium edetate, disodium calcium edetate and like, edetic acid, erythorbic acid, fumaric acid, lactic acid, lauric acid, linoleic acid, malic acid, myristic acid, oleic acid, palmitic acid, sorbic acid, succinic acid and tartaric acid. pH modifying agent can be added as acidic agent alone or alkalizing agent alone or mixture thereof in dosage form composition.

Water soluble excipients:

[01003] According to present invention, water soluble excipients include natural, synthetic or semi synthetic water soluble material. A said water soluble material are selected from group consisting of
polymer, sugar, salts, salts of organic acid, acid and polysaccharide. Water soluble polymer include, but are not to be limited, cellulose derivatives include, but are not limited to be, methyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxyethyl methylcellulose, ethylhydroxyethylcellulose, ethylmethylcellulose, hydroxyethylpropylcellulose, sodium carboxymethylcellulose, polyacrylamide derivatives, methacrylic acid derivatives; vinyl pyrrolidone polymers such as polyvinylpyrrolidone; Starch derivative, Polyalkylene oxide and copolymer thereof, alkylene oxide homopolymers; gums of plant, animal, mineral or synthetic origin, methacrylates, Polyacrylic acid and copolymer thereof, Polyvinyl alcohols, polyethylene glycol, poloxamer; and mixtures thereof. Preferred sugars include dextrose, glucose, arabinose, ribose, arabinose, xylose, lyxose, xylo, allose, altrose, inositol, glucose, sorbitol, mannose, gulose, Glycerol, idose, galactose, talose, trehalose, mannotol, erythritol, ribitol, xylitol, maltitol, isomalt, lactitol, sucrose, raffinose, maltose, fructose, lactose, dextrin, dextran, amylose and xylan. Water soluble salts include sodium chloride, potassium chloride, calcium chloride or magnesium chloride, lithium chloride, lithium, sodium or potassium hydrogen phosphate, lithium, sodium or potassium dihydrogen phosphate, salts of organic acids such as sodium or potassium acetate, magnesium succinate, sodium benzoate, sodium citrate or sodium ascorbate. Preferred acids include ascorbic acid, 2-benzene carboxylic acid, benzoic acid, fumaric acid, citric acid, maleic acid, serbic acid, sorbic acid, edic acid, ethic acid, glutamic acid, toluene sulfonic acid, water-soluble amino acids such as glycine, leucine, alanine, or methionine and tartaric acid; and like. Polysaccharides are polymeric carbohydrate molecules composed of long chains of monosaccharide units bound together by glycosidic linkages and on hydrolysis give the constituent monosaccharides or oligosaccharides. They range in structure from linear to highly branched. Examples include storage polysaccharides such as starch and glycogen, and structural polysaccharides such as cellulose and chitin.

Water insoluble excipients:
[0104] According to present invention, water insoluble excipients include natural, synthetic or semi synthetic water insoluble material. Natural, synthetic or semi synthetic water insoluble material include, but are not to be limited, cellulose derivatives include cellulose acetate phthalate, microcrystalline cellulose, cellulose acetate, HPMC phthalate, microcrystalline cellulose, ethyl cellulose, glycerol palmitostearate, Wax include microcrystalline wax, beeswax, glycowax, castor wax, carnauba wax; glycerol monostearate, hydrogenated vegetable oils, vegetable oils, stearyl alcohol, acetylated hydrogenated soybean oil glycerides, castor oil, glycerol behenic acid ester, glycercy monooleate, glycercy monostearate, propylene glycol monostearate, cetyl alcohol, natural and synthetic glycerides, fatty acids, fatty alcohol, lipid, steryl alcohol, sorbitan monolaurate, sorbitan monooleate, sorbitan monopalmitate, sorbitan monostearate, sorbitan sesquioleate, sorbitan trioleate, sorbitan tristearate, polyacrylamide derivatives, methacrylic acid derivatives such polymethacrylate and its copolymer; Polivinyl Acetate, copolymers of vinyl pyrrolidone and vinyl acetate; vinyl acetate and copolymer thereof, ethyl vinyl acetate, modified starch like pregelatinised starch, polyactic acid or polyglycolic acid and copolymers thereof, methacrylates, Polyacrylic acid and copolymer thereof, a co-polymer of methacrylate-galactomannan etc., cocoa butter, macrogol Stearate, diethylene glycol monostearate, polyoxyethylene 50 stearate, dibasic calcium phosphate and mixtures thereof.

Agent thereby mechanism of gastric retention is attained:
[0105] Agent thereby mechanism of gastric retention is attained comprises at least one material selected from group consisting of gas generating agent, low density material, high density material, partially or completely hollow or porous material or mixture thereof. List of gas generating agent is already discuss above. Partially or completely hollow or porous materials include cellulotic polymers, cellulose ether polymers, methacrylate polymers, waxes or combinations thereof. Suitable low density materials include, but are not to be limited, polyvinyl alcohol-polyethylene glycol graft copolymers, acrylic acid polymers, Wax, methacrylic acid copolymers, polyvinyl alcohol, polyvinyl acetate, polysaccharides, cellulose based polymers or combinations thereof. High density materials include, but are not to be limited, barium sulphate, zinc oxide, iron powder, titanium dioxide etc.

[0106] General procedure of manufacturing gastroretentive dosage form:

a) Compression of core tablets
b) Optionally apply inner coat surrounding step (a) core tablets
c) Encapsulate at least one preselected outer surface of step (b) inner coated tablet within container in such a way that it entrap air or create a void between at least one inner surface of container and at least one outer surface of inner coated tablet
d) Coat the step (c) composition with water insoluble coating

EXAMPLE

[0107] Certain aspects of the present invention may be better understood as illustrated by the following examples, which are meant by way of illustration and not limitation.

[0108] Example 1

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Name</th>
<th>Qty/tab (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core Tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Sertraline HCl</td>
<td>12.05</td>
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<tr>
<td>2</td>
<td>Mannitol</td>
<td>47.35</td>
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<tr>
<td>3</td>
<td>Microcrystalline Cellulose</td>
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<tr>
<td>4</td>
<td>Magnesium Stearate</td>
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<tr>
<td>Inner Coat</td>
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<tr>
<td>5</td>
<td>Ethyl Cellulose</td>
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<tr>
<td>6</td>
<td>Hypromellose E5</td>
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</tr>
<tr>
<td>Encapsulation</td>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>Capsule Shell</td>
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<tr>
<td>Water Insoluble Coating</td>
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<td></td>
</tr>
<tr>
<td>8</td>
<td>Ethyl Cellulose</td>
<td>3.04</td>
</tr>
<tr>
<td>9</td>
<td>Hypromellose E5</td>
<td>2.02</td>
</tr>
</tbody>
</table>

Procedure:
1. Core Tablet: Sertraline HCl, lactose, microcrystalline cellulose and magnesium stearate were mixed in polybag and tablets were compressed.
2. Inner Swellable Coat: Coating solution was prepared by dissolving ethyl cellulose and hypromellose E5 in mixture of IPA:DCM (1:1) and step (1) core tablets were coated.
3. Inner Insoluble Coat: Coating solution was prepared by dissolving ethyl cellulose and hypromellose E5 in mixture of IPA:DCM (1:1) and step (2) tablets were coated.
4. Encapsulation: Half part of outer surface of step (3) inner coated tablet was encapsulated within capsule shell in such a way that void was created between inner surface of capsule and outer surface of inner coated tablets.
5. Water Insoluble Coating: Step (4) encapsulated tablets were further coated with step (3) solution.

[0109] Example 2

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Name</th>
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</tr>
</thead>
<tbody>
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<td>Core Tablet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Sertraline HCl</td>
<td>12.05</td>
</tr>
<tr>
<td>2</td>
<td>Hypromellose K100M</td>
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</tr>
<tr>
<td>3</td>
<td>Mannitol</td>
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<tr>
<td>4</td>
<td>Magnesium Stearate</td>
<td>0.84</td>
</tr>
<tr>
<td>Inner Swellable Coat</td>
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<td></td>
</tr>
<tr>
<td>5</td>
<td>Crospovidone</td>
<td>5.73</td>
</tr>
<tr>
<td>6</td>
<td>Povidone K30</td>
<td>1.01</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>Ethyl Cellulose</td>
<td>2.02</td>
</tr>
<tr>
<td>8</td>
<td>Hypromellose E5</td>
<td>1.35</td>
</tr>
<tr>
<td>Encapsulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Capsule Shell</td>
<td>7.23</td>
</tr>
</tbody>
</table>

Water Insoluble Coating
| 10     | Ethyl Cellulose  | 3.04            |
| 11     | Hypromellose E5  | 2.02            |
CLAIMS:
We claim:
1. An oral gastroretentive pharmaceutical dosage form comprising:
   a) at least one container (S) having one or more aperture and a wall having an inside and an outside;
   b) a core comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients (X);
   c) encapsulate at least one preselected external surface of core within container (S) in such a way that it entrap air or create void between at least one inner surface of container (S) and at least one outer surface of core; and
   d) water insoluble coating surrounding step (c) composition.
2. An oral gastroretentive pharmaceutical dosage form comprising:
   a) at least one insoluble container (C) having one or more aperture and a wall having an inside and an outside;
   b) a core comprising an active ingredients (A) and optionally other pharmaceutically acceptable excipients; and
   c) encapsulate at least one preselected external surface of core within insoluble container (C) in such a way that it entrap air or create void between at least one inner surface of insoluble container (C) and at least one outer surface of core.
3. An oral gastroretentive pharmaceutical dosage form according to claim 1 and claim 2, wherein container is capsule shell.
4. An oral gastroretentive pharmaceutical dosage form according to claim 1 and claim 2, wherein a core comprising one or more composition layer, wherein at least one composition layer is active ingredient composition layer (L) comprises at least one active ingredient (A).
5. An oral gastroretentive pharmaceutical dosage form according to claim 1 and claim 2, wherein a core comprising two or more composition layer, wherein at least one composition layer is active ingredient composition layer (L) and at least another composition layer is functional composition layer (F).
6. An oral gastroretentive pharmaceutical dosage form according to claim 5, wherein functional composition layer (F) act as immediate release layer, time release or delay release layer for active ingredient composition layer (L), barrier layer, divisible composition layer or additional/supportive gastroretentive layer.
7. An oral gastroretentive pharmaceutical dosage form according to claim 1 and claim 2, wherein dosage form comprises inner coat on outer surface of core.
8. An oral gastroretentive pharmaceutical dosage form according to claim 7, wherein part of inner coat being sandwich between outer surface of core and inner surface of container.
9. An oral gastroretentive pharmaceutical dosage form according to claim 7, wherein inner coat is swellable coat, non-swellable coat or insoluble coat.
10. An oral gastroretentive pharmaceutical dosage form according to claim 1 comprising water insoluble coating, wherein coating is insoluble in water at all pH or insoluble in water at certain pH or insoluble for specific period of time or insoluble as such but soluble in presence of other excipients.