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(54) **Title**: PHARMACEUTICAL COMPOSITION FOR MODIFIED DELIVERY OF ACTIVES

(57) **Abstract**: There is provided a modified release pharmaceutical dosage form for the delivery of the therapeutically active pharmaceutical ingredient wherein the dosage form comprises a swellable core comprising therapeutically active pharmaceutical ingredient and one or more swellable hydrophilic polymers, one or more rate controlling polymeric coating(s) surrounding the core; wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

PHARMACEUTICAL COMPOSITION FOR MODIFIED DELIVERY OF ACTIVES

Field of Invention

There is provided a modified release pharmaceutical dosage form for the delivery of the therapeutically active pharmaceutical ingredient, wherein the dosage form comprises a swellable core comprising therapeutically active pharmaceutical ingredient and one or more swellable hydrophilic polymers, one or more rate controlling polymeric coating(s) surrounding the core; wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

Background of the Invention

The modified release of active ingredients from the dosage form has been the major concern for numerous studies over the years. As against an immediate release, which dumps the active ingredient for absorption in GIT, the goal of modified release is to deliver therapeutically active pharmaceutical ingredients at desired rates over predetermined periods of time. The benefits provided by modified delivery of therapeutically active pharmaceutical ingredients for the treatment of diseases are well recognized in the art. These approaches may involve the use of rate controlling polymers (matrix and Geomatrix technology) and excipients including enteric coatings, osmotic delivery systems, gastric retentive drug delivery systems or implantable drug delivery devices.

Enteric coating of dosage forms is well known in the pharmaceutical field. Enteric coatings are coatings designed to prevent release of the enteric-coated drug in gastric fluid of the stomach and prevent exposure of the drug to the acidity of the gastric contents while the enteric-coated drug composition is in the stomach. After passing from the stomach into the intestine, the enteric coating dissolves and releases the drug into intestinal fluids.

Important technical ingredient in accordance with zero order kinetics as described in U.S. Patent No. 4,839,177, which discloses the use of hydrogels compressed to defined geometric forms. The polymer is mixed with biologically therapeutically active pharmaceutical ingredients to form a core, which is affixed to a "support platform" made of an insoluble polymeric material.

U.S. Patent No. 4,971,790 discloses osmotic dosage form utilizing a semipermeable wall containing exit means through the wall surrounding a core containing an osmotic agent, a neutral and ionizable hydrogel and a therapeutically active pharmaceutical ingredient.

US Patent 5,882,682 discloses a device for controlled delivery of therapeutically active pharmaceutical ingredient in dispersion, comprising compressed core, a polymer forming gelatinous microscopic particles upon hydration and a water insoluble coating with formed apertures surrounding the core.

US Patent 5,120,548 discloses a controlled release drug delivery device, comprised of swellable polymers, whose degree of swelling in an environment of use is controlled by swelling modulators blended within the polymers, surrounded by a micro porous coating or interspersed within individual matrices.

US Patent 5,422,123 discloses controlled release tablets consisting of a deposit core containing therapeutically active substance, a support-platform partially covering said deposit-core. The support platform comprises swellable and/ or gellable polymeric materials.

US Patent 5,626,874 discloses controlled release tablet having a lenticular form consisting of three layers with central core containing the active principle and two outer layers comprising gellable and/or erodible polymeric material. The central layer releases active principle through limited external annular surface exposed to the dissolution medium.

US Patent 4,946,686 discloses controlled drug delivery device comprising a core composition with plurality of controlled release solubility modulating units surrounded by a water insoluble coat. The coat comprising pore forming additive dispersed throughout. The water insoluble microporous wall surrounds the core.

US Patent 5,366,738 discloses device for controlled delivery of therapeutically active pharmaceutical ingredient as a gelatinous dispersion. The device consists of a core, a polymer forming gelatinous microscopic particles upon hydration, an agent to modulate the hydration of the polymer and an impermeable coating surrounding the core. The coat contains apertures releasing the therapeutically active pharmaceutical ingredient.

US Patent 4,814,183 discloses controlled drug delivery device comprising core composition containing water insoluble non-diffusible charged resins and diffusible, water-soluble ionizable therapeutically active pharmaceutical ingredient carrying the same charge as said resin entity. A wall having hole(s) surrounds the core for release of the therapeutic agent.

US Patent 6,372,255 discloses multi-layer tablet comprising at least two layers where the first outer layer allows immediate release of active substance and a second layer comprising inert porous polymeric matrix in which an active substance is dispersed, allows prolonged release of the active substance.

US Patent 5,972,389 discloses gastric-retained controlled-release oral drug dosage forms comprising plurality of particles of a solid-state drug dispersed in a swellable/erodible polymer.
US Patent 6,399,086 discloses controlled-release oral drug delivery system comprising beta-lactam antibiotic agent having a specific absorption site in the small intestine, in combination with a polymeric matrix.

US Patent 6,893,661 discloses controlled release pharmaceutical composition comprising a first intelligent polymer component comprising ethyl cellulose; and a second intelligent polymer component having opposite wettability characteristics.

US Patent 6,569,463 discloses pharmaceutical composition in the form of a solid carrier comprising a substrate and an encapsulation coat on the substrate.

US Patent 6,607,751 discloses controlled release pharmaceutical device providing sustained or pulsatile delivery of active substances, the device comprising microbial polysaccharide and cellulose ethers.

US Patents 6,720,005 and 6,733,784 disclose coated tablets which hydrate and expand upon swallowing such that coating ruptures around the belly-band surface of the tablet, thereby exposing the belly surface of the core tablet to hydrating and eroding liquids.

US Patent Application 20080213381 discloses oral drug delivery system comprising coating that is reliably removed fully or partially from one or more preselected surfaces of the system upon contact of the system with intestinal fluids.

US Patent Application 20080020041 discloses pharmaceutical formulation comprising leaky enteric coating, which releases a portion of a therapeutically active pharmaceutical ingredient from the core upon contacting with gastric fluid. The remaining portion of the therapeutically active pharmaceutical ingredient is released upon contacting intestinal fluid.

US Patent Application 20100297195 discloses controlled release formulation comprising a core comprising of lamotrigine and a hydrophilic rate controlling agent; a coating comprising of a pH-dependent polymer and a permeation enhancer; and a topcoat comprising of lamotrigine in immediate release form, wherein said coating does not include any orifice.

Though there are various techniques known in the literature for modified delivery of therapeutically active ingredient, still a need exists for a composition that will provide good bioavailability of therapeutically active pharmaceutical ingredients

of various classes and various pharmacokinetic profiles along with increased duration of action and decreased frequency of dosing. Different therapeutically active pharmaceutical ingredients on account of their different physicochemical properties exhibit large variation in their pharmacokinetic and pharmacodynamic profiles both *in vivo* and *in vitro*. Few of the therapeutically active pharmaceutical ingredients are highly soluble and show immediate effect while others have poor solubility and show different dissolution profile. Further, different excipients such as polymers in the dosage form contribute to the variation in the release of therapeutically active pharmaceutical ingredients from the dosage form. Some of the therapeutically active pharmaceutical ingredients show site-specific absorption or pH dependent absorption while others show absorption throughout the gastrointestinal tract.

The various modified release dosage forms known in the art are applicable to a particular category of drugs. There exists a need of a common platform technology, which can provide the optimized pharmacokinetic profiles of the dosage form by simple variation in the pharmaceutically acceptable excipients used therein. Such systems have not been known but are disclosed herein.

Summary of the invention

In one of the aspects of the invention there is provided a modified release pharmaceutical dosage form comprising:

a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and

b) one or more rate controlling polymeric coating(s) surrounding the core;

wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

In another aspect of the invention there is provided a modified release pharmaceutical dosage form comprising:
a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and
b) one or more rate controlling polymeric coating(s) surrounding the core; wherein said polymeric coating comprises one or more plasticizer(s);
wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

In yet another aspect of the invention there is provided a modified release pharmaceutical dosage form comprising:
a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and
b) one or more rate controlling polymeric coating(s) surrounding the core; wherein said polymeric coating comprises one or more wicking agent(s);
wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

In yet another aspect of the invention there is provided a modified release pharmaceutical dosage form comprising:
a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and
b) one or more rate controlling polymeric coating(s) surrounding the core;

wherein the shape of the dosage form is achieved in such a way that it provides leachable areas and wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

Embodiments of the present invention may comprise one or more pharmaceutically acceptable excipients selected form the group comprising of diluents, binders, disintegrants, surfactants, lubricants and glidants.

Description of Drawings

Drawing figure (I-A) is a general view of a dosage form designed as donut shaped tablet for oral administration of therapeutically active pharmaceutical ingredient. Figure (I-B) shows regions 1, 4, 5, 8 of the inner peripheries and regions 2, 3, 6, 7 of the external peripheries of the donut shaped dosage form through which the controlled release of therapeutically active pharmaceutical ingredient occurs.

Drawings figures (II-A), (III-A) and (IV-A) are the general view of a centrally notched tablet dosage form for oral administration of therapeutically active pharmaceutical ingredient. Figures (II-B), (III-B) and (IV-B) show regions 1, 4, 5, 8 of the inner peripheries and regions 2, 3, 6, 7 of the external peripheries of the centrally notched dosage form through which the controlled release of therapeutically active pharmaceutical ingredient occurs.

Drawing figures (V-A), (VI-A), (VII-A) are the general view of a pillowed tablet dosage form for oral administration of therapeutically active pharmaceutical ingredient. Figures (V-B), (VI-B) and (VII-B) show regions 1,4,5,8 of the debossed area and regions 2,3,6,7 of the external peripheries of the pillowed dosage form through which the controlled release of therapeutically active pharmaceutical ingredient occurs.

Drawing figure (VIII-A) is the general view of a round beveled tablet dosage form, for oral administration of therapeutically active pharmaceutical ingredient. Figure (VIII-B) shows regions 1,2,3,4 of the beveled edges of the dosage form through which the controlled release of therapeutically active pharmaceutical ingredient occurs.

Drawing figure (IX-A) is the general view of oval shaped tablet dosage form for oral administration of therapeutically active pharmaceutical ingredient. Figure (IX-B) shows regions 1,2,3,4 of the oval dosage form through which the controlled release of therapeutically active pharmaceutical ingredient occurs.

Detailed Description of the Invention

The present inventors have now developed a modified release dosage form, comprising a core and coating surrounding the core wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

The core comprises one or more swellable hydrophillic polymers. The swellability i.e. intensity and duration of the swelling force developed by the swellable polymeric materials in the core is a major factor controlling the release of the therapeutically active pharmaceutical ingredient in the core when it comes in contact with aqueous fluids. In this respect the energy for activating, executing and regulating, the release of the therapeutically active pharmaceutical ingredient can be determined by the swelling force developed in the core when this comes into contact with water or with gastrointestinal fluids or with biological liquids. Said force has an intensity and duration which can vary in relation to the type and quantity of the polymeric materials used in formulating the core, and it lies between limits having a maximum value which occurs in the case of a core

mainly containing the swellable polymer and a minimum value when the core contains very little swellable polymer.

When the dosage form comes in contact with gastrointestinal fluid or water, this fluid or water gets permeated through outer coating into the core. The swellable polymer upon ingestion of fluid or water swells to a size that is at least twice its unswelled volume. Upon swelling, the pressure is built up in the core of the dosage form, which induces breaking or disruption of polymeric coat surrounding the core at weakened edges or at leachable areas or at peripheries of the dosage form. This results in the release of the therapeutically active pharmaceutical ingredient from the weakened edges or leachable areas or peripheries of the dosage form. The penetrating fluid causes release of the therapeutically active pharmaceutical ingredient in a gradual and prolonged manner by the process of dissolution of the therapeutically active pharmaceutical ingredient in the penetrating fluid and diffusion of the dissolved therapeutically active pharmaceutical ingredient back out of the swellable core. Thus, the technology achieves consistent release pattern through the designated areas and desirable dissolution profile. The dosage form developed helps to control initial burst release of therapeutically active pharmaceutical ingredient in acidic media.

The release kinetics of the therapeutically active pharmaceutical ingredient from the core may be dependent upon the relative magnitude of the rate of polymer swelling and the rate of polymer erosion. The kinetics of drug release from the dosage form may also be dependent at least in part upon the diffusion and/or erosion properties of excipients within the composition. The rate-limiting factor in the release of the therapeutically active pharmaceutical ingredient from the core may be dissolution of the therapeutically active pharmaceutical ingredient in the penetrating fluid and controlled diffusion of the therapeutically active pharmaceutical ingredient from the swellable core. The swelling core may render the dosage form sufficiently large to cause retention in the stomach during the fed mode; localizes the release of the drug to the stomach and small intestine so that the drug will have its full effect without colonic degradation, inactivation, or

loss of bioavailability. Further, it may retard the rate of diffusion of the drug long enough to provide multi-hour, controlled delivery of the drug into the stomach.

Suitable swellable hydrophilic polymers may comprise one or more of cellulose derivatives such as hydroxypropylmethyl cellulose (HPMC), hydroxypropyl cellulose, hydroxyethyl cellulose, methyl cellulose, ethyl cellulose, carboxymethyl cellulose, carboxyethyl cellulose, carboxymethylhydroxyethyl cellulose, microcrystalline cellulose, polyethylene oxides, polyvinylpyrrolidone (PVP), polyalkylene glycols, gelatine, polyvinyl alcohol, starch and derivatives thereof, acrylic acid polymers, polymethacrylates, polysaccharides such as xanthan gum, tragacanth gum, gum karaya, guar gum, acacia, gellan gum locust bean gum, alkali metal salts of alginic acid or pectic acid, sodium alginate, potassium alginate, ammonium alginate, chitosan, maleic anhydride copolymers, poly(ethyleneimine), polyurethane hydrogels, crosslinked polyacrylic acids and their derivatives, and mixtures thereof.

The swellable polymer may be present in an amount from about 5 to about 90% by weight, with respect to the mixture forming the core.

The term ‘modified release’ as used herein may interchangeably be used with prolonged release, extended release, controlled release, controlled delivery, slow release and sustained release. Further, the term ‘extended release’ also includes delayed release. Delayed release compositions involve the release of discrete amount(s) of drug some time after drug administration, e.g. enteric-coated products, and exhibit a lag time during which little or no absorption occurs. The extended release in the pharmaceutical composition may be achieved by one or more of coating or embedding in matrix using with hydrophilic or hydrophobic polymers or by attachment to ion-exchange resins.

The present invention provides a modified release pharmaceutical dosage form comprising a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and one or more rate controlling polymeric coating(s) surrounding the

core; wherein said polymeric coating comprises one or more plasticizer or wicking agent.

The term "plasticizer" as used herein includes any compounds capable of plasticizing or softening a polymer used in the invention. The plasticizers can be included in the dosage form to modify the characteristics of the polymers used in the coat(s) or core of the dosage form for convenient processing during manufacture of the coat(s) and/or the core of the dosage form. Once the coat(s) and/or core have been manufactured, certain plasticizers can function to increase the hydrophilicity of the coat(s) and/or the core of the dosage form in the environment of use. Plasticizers are molecular lubricants that reduce glass transition temperature of a polymer, which in turn helps to form the film of the polymer. Plasticizers are used for increasing the flexibility, durability, and stability of the coating surrounding the core. Plasticizers may also stimulate the dissolution. The area from which the polymer coating disrupts and the release of the active ingredient takes place depends on the quantity of the plasticizer present in the coating composition.

The suitable plasticizer may include one or more of citrate esters (example, triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate), pthalate esters (example, dimethyl phthalate diethyl pthalate, dibutyl pthalate, dihexyl phthalate, butyl octyl phthalate, diisononyl phthalate, butyl octyl phthalate, diethylhexyl phthalate, di-n-octyl phthalate, di-i-octyl phthalate, di-i-decyl phthalate, di-n-undecyl phthalate, di-n-tridecyl phthalate), dibutyl sebacate, dibutyl tartrate, glycerin, polyethylene glycols, propylene glycols, butyl phthalyl butyl glycolate, ethyl phthalyl ethyl glycolate, acetylated monoglycerides, polysorbates, glyceryl monostearate, gylcerol triacetate, triacetin, castor oil, mineral oils, rape seed oil, olive oil, sesame oil, polyhydric alcohols, sorbitol, tripropioin; diacetin, dioctyl azelate, epoxidized tallate, triisoctyl trimellitate, tri-2-ethylhexyl trimellitate, di-2-ethylhexyl adipate, di-2-ethylhexyl sebacate, di-2-ethylhexyl azelate, dibutyl sebacate, diethyloxalate, diethylmalate, diethylfumerate, dibutylsuccinate, diethylmalonate and mixtures thereof.

The plasticizer(s) may be present in an amount from about 2 to about 20% by weight, with respect to the mixture forming the core.

Wicking agent as used herein is a material having the ability to draw water into the porous network of a delivery device. A wicking agent may do this with or without swelling. The wicking agents are characterized by having the ability to undergo physisorption with water. Physisorption is defined as a form of adsorption in which the solvent molecules can loosely adhere to surfaces of the wicking agent via Vander Waals interaction between the surface of the wicking agent and the adsorbed molecule. The function of the wicking agent is to carry water to surfaces inside the core of the tablet. For therapeutically active pharmaceutical ingredients with low solubility in water, the wicking agent aids in the delivery of partially solubilized therapeutically active pharmaceutical ingredient through the passageway in the semi-permeable coating.

Wicking agent incorporated into the polymeric coating material during processing of the dosage form erodes the dosage form after administration of the dosage form to the environment of use.

Suitable wicking agents may include one or more of colloidal silicon dioxide, porous silicon dioxide, fumed silicon dioxide, titanium dioxide, calcium silicate, magnesium aluminum silicate, low molecular weight polyvinylpyrrolidone, alumina, niacinamide, kaolin sodium lauryl sulfate, low molecular weight polyvinyl pyrrolidone, m-pyrol, bentonite, polyester, polyethylene and mixtures thereof.

The wicking agent(s) may be present in an amount from about 5 to about 35% by weight, with respect to the mixture forming the core.

In the present there is provided a modified release pharmaceutical dosage form wherein the shape of the dosage form is achieved in such a way that it provides leachable areas and wherein the core upon contact with gastrointestinal fluid swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the

combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

The dimensions of the dosage form including its size; shape does not have influence on the rate of release of the active agent from the dosage form. Different shapes of the dosage form may comprise one or more of round, oval, donut, pillowed shaped and centrally notched. When the dosage form comes in contact with gastrointestinal fluid or water, this fluid or water gets permeated through outer coating into the core. The swellable polymer upon ingestion of fluid or water swells to a size that is at least twice its unswelled volume. Upon swelling, the pressure is built up in the core of the dosage form, which induces breaking or disruption of polymeric coat surrounding the core at weakened edges or at leachable areas or at peripheries of the dosage form. This results in the release of the therapeutically active pharmaceutical ingredient from the weakened edges or leachable areas or peripheries of the dosage form. Thus technology achieves consistent release pattern through the designated areas and desirable dissolution profile. The dosage form developed helps to control initial burst release of therapeutically active pharmaceutical ingredient in acidic media.

Release of the drug from the dosage form depends on the area of disruption, which in turn depends on swellability of the hydrophillic polymer present in the core, plasticity of coat covering the core and/or quantity of wicking agent present in the coat covering the core.

Rate controlling polymer as used herein is defined to mean a functional polymer which can comprise one or more of pH independent polymer, pH dependent polymer, soluble polymer, insoluble polymer, lipids, lipidic materials or combinations thereof which when applied onto a dosage form can control or slow or modify the rate of release of the therapeutically active pharmaceutical ingredient when applied to an uncoated dosage form.
Suitable rate controlling polymers may include one or more of hydrophilic or hydrophobic polymers such as polyvinyl acetate, cellulose acetate, cellulose

acetate butyrate, cellulose acetate propionate, ethyl cellulose, a fatty acid, a fatty acid ester, an alkyl alcohol, a wax, shellac, rosin, zein (prolamine from corn), povidone, kollidon SR, a poly(meth)acrylate, microcrystalline cellulose or poly(ethylene oxide), polyuronic acid salts, cellulose ethers, xanthan gum, tragacanth gum, gum karaya, guar gum, acacia, gellan gum locust bean gum, alkali metal salts of alginic acid or pectic acid, sodium alginate, potassium alginate, ammonium alginate, hydroxypropyl cellulose, hydroxy ethyl cellulose, hydroxypropyl methyl cellulose, carboxyvinyl polymers, polymerized gelatin, shellac, methacrylic acid copolymer type C NF, cellulose butyrate phthalate, cellulose hydrogen phthalate, cellulose propionate phthalate, polyvinyl acetate phthalate (PVAP), cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate, dioxypropyl methylcellulose succinate, carboxymethyl ethyl cellulose (CMEC), hydroxypropyl methylcellulose acetate succinate (HPMCAS), and acrylic acid polymers and copolymers like methyl acrylate, ethyl acrylate, methyl methacrylate and/or ethyl methacrylate with copolymers of acrylic and methacrylic acid esters (Eudragit NE, Eudragit RL, Eudragit RS), pH dependent polymers such as methacrylic acid copolymer type C (Eudragit L 100 55), methacrylic acid copolymer type C (Eudragit L 30D 55), methacrylic acid copolymer type A (Eudragit L 100), methacrylic acid copolymer type C (Eudragit S 100) and mixtures thereof.

The rate controlling polymer(s) may be present in an amount form about 1.5% to about 5% by weight, with respect to the mixture forming the core.

The modified release dosage form disclosed in the invention releases therapeutically active pharmaceutical ingredients from the area of the dosage form by partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core. The technology achieves consistent release pattern through the designated areas and desirable dissolution profile. The

dosage form thus helps to control initial burst release of therapeutically active pharmaceutical ingredient in acidic media.

The term “area” of the dosage form used herein is defined as the region of the dosage form through which modified release of therapeutically active pharmaceutical ingredient occurs. The modified release of the active ingredient may occur through the regions of the inner peripheries and/ or the external peripheries and/ or through the weakened edges and/ or through leachable areas of the dosage form. The terms may interchangeably be used herein.

The term "dosage form" as used herein is defined to mean a pharmaceutical preparation in which doses of active drug are included.

The term "formulation" or "composition" as used herein refers to the drug in combination with pharmaceutically acceptable carriers and additional inert agents. This includes orally administrable formulations as well as formulations administrable by other means.

The term "core" as used here in is defined to mean any structure that is surrounded by a wall, membrane, or coating. The wall, membrane, or coating can be a functional or non-functional coating.

The term "active", "therapeutically active pharmaceutical ingredient", "active pharmaceutical agent", "active drug" or "drug" as used herein means any active pharmaceutical agent ("API"), including its pharmaceutically acceptable salts as well as in the anhydrous, hydrated, and solvated forms, in the form of prodrugs, and in the individually optically active enantiomers of the API as well as polymorphs of the API.

The modified release dosage forms of the invention can be constructed in many forms known to one of ordinary skill in the drug delivery arts and described in the prior art such as for example, "modified release matrix dosage forms", "normal release matrix dosage forms" coated with at least one "control-releasing coat",

"osmotic dosage forms", "multiparticulate dosage forms", and "gastric retention dosage forms". The USP considers that the terms controlled release, prolonged release and sustained release are interchangeable. Accordingly, the terms "modified-release", controlled-release", "control-releasing", "rate-controlled release", "prolonged-release", and "sustained-release" are used interchangeably herein. For the discussion herein, the definition of the term "modified-release" encompasses the scope of the definitions for the terms "extended release", "enhanced-absorption", "controlled release", and "delayed release".

"Controlled release dosage forms" or "control-releasing dosage forms", or dosage forms which exhibit a "controlled release" of therapeutically active pharmaceutical ingredient as used herein is defined to mean dosage forms administered once-or twice-daily that release the therapeutically active pharmaceutical ingredient at a controlled rate and provide plasma concentrations of the therapeutically active pharmaceutical ingredient that remain controlled with time within the therapeutic range of the therapeutically active pharmaceutical ingredient over about 12 to about 24-hour period. "Controlled release" or "control releasing" is defined to mean release of the drug gradually or in a controlled manner per unit time. For example, the controlled rate can be a constant rate providing plasma concentrations of the therapeutically active pharmaceutical ingredient that remain invariant with time within the therapeutic range of the therapeutically active pharmaceutical ingredient over at least about 12 hr to about 24 hour period.

"Sustained-release dosage forms" or dosage forms which exhibit a "sustained-release" of the therapeutically active pharmaceutical ingredient as used herein is defined to mean dosage forms administered once-daily that provide a release of the therapeutically active pharmaceutical ingredient sufficient to provide a therapeutic dose soon after administration, and then a gradual release over an extended period of time such that the sustained-release dosage form provides therapeutic benefit over about 12 hr to about 24 hour period.

"Extended-or sustained-release dosage forms" or dosage forms which exhibit an "extended or sustained release" of the therapeutically active pharmaceutical ingredient as used herein is defined to include dosage forms administered once- or twice-daily that release the therapeutically active pharmaceutical ingredient slowly, so that plasma concentrations of the therapeutically active pharmaceutical ingredient are maintained at a therapeutic level for an extended period of time such that the extended or sustained-release dosage form provides therapeutic benefit over about 12 to about 24 hour period.

"Prolonged-release dosage forms" or dosage forms which exhibit a "prolonged release" of the therapeutically active pharmaceutical ingredient as used herein is defined to mean dosage forms administered once daily which provide for absorption of the therapeutically active pharmaceutical ingredient over a longer period of time than from a conventional, immediate release or uncoated normal release dosage form and which provide therapeutic benefit over at least about 12 hour to about 24 hour period.

"Delayed-release dosage forms" or dosage forms which exhibit a "delayed release" of the therapeutically active pharmaceutical ingredient as used herein is defined to mean dosage forms administered once-daily that do not effectively release drug immediately following administration but at a later time. Delayed-release dosage forms provide a time delay prior to the commencement of drug-absorption. This time delay is referred to as "lag time" and should not be confused with "onset time" which represents latency, that is, the time required for the drug to reach minimum effective concentration.

Said suitable therapeutically active pharmaceutical ingredient may comprise one or more of a single therapeutically active pharmaceutical ingredient, or may comprise plural therapeutically active pharmaceutical ingredients. Said therapeutically active pharmaceutical ingredient may comprise one or more of sedatives, hypnotics, anti-inflammatory agents, Antibiotics, Antidiabetics, Antihypertensives, Anti-Osteoporosis Agents, Antithrombotic Agents, Antivirals, Antifungals, Anticholinergic Agents, Anxiolytic Agents, Adrenergics,

Antipsychotics, Anti-Parkinsonism Agents, Anticonvulsants, Antiepileptics, CNS Stimulants, Antianginal Agents, Antiarrhythmics, Antihyperlipidemic Drugs, Diuretics, Antiasthmatics, Anticoagulants, Antianemia Agents, Vitamins, Hormones, Antihistaminics, Anticancer Agents, Antiallergics, Antiarthritis Agents, Antialzheimers' Agents, Vasopressin Antagonists, Anticonvulsants, Steroids, Anesthetics, Thrombolytics, Antacids, Proton Pump Inhibitors, Protease Inhibitors, Platelet Aggregation Inhibitors, Mucolytics, Antimalarials, Antiemetics, Laxatives, Expectorants, Enzymes, Contraceptives, Bronchodilators, Antitussives, Antimigraine Agents, Anthelmintics, and Anorexiants.

Non-limiting examples of suitable therapeutically active pharmaceutical ingredient may also comprise one or more of Lamotrigine, Amlodipine, Diazepam, Paracetamol, Aspirin, Ciprofloxacin, Dicyclomine, Celecoxib, Alendronate, Diacerein, Acyclovir, Fluconazole, Epinephrine, Divalproex, Methylphenidate, Flecainide, Metoprolol, Fenofibrate, Hydrochlorothiazide, Montelukast, Bicalutamide, Donepezil, Tolvaptan, Saquinavir, Bromhexine, Promethazine, Bisacodyl, Pancreatin, Ethinyl Estradiol, Salbutamol, Diphenhydramine, Sumatriptan, Diclofenac, Metronidazole, Orlistat, Ibuprofen, Indomethacin, Ketorolac, Tramadolol, Oxcarbazepine, Pioglitazone, Rosiglitazone, Miglitol, Vildagliptin, Sitagliptin, Repaglinide, Voglibose, Alprazolam, Chlorpromazine, Cimetidine, Pseudoephedrine, Naproxen, Piroxicam, Atenolol, Benazepril, Captopril, Lisinopril, Fosinopril, Enalapril, Furosemide, Indapamide, Atenolol, Felodipine, Cartenolol, Carvedilol, Cerivastatin, Diltiazem, Fluvastatin, Irbesartan, Candesartan, Methyldopa, Reserpine, Bupropion, Fluoxetine, Paroxetine, Escitalopram, Sertraline, Amitryptiline, Imipramine, Fexofenadine, Clopidogrel, Entacapone, Levodopa, Carbidopa, Levetiracetam, Venlafaxine, Duloxetine, Lisinopril, Losartan, Lovastatin, Niacin, Pravastatin, Ramipril, Simvastatin, Atorvastatin, Valsartan, Telmisartan, Sildenafil, Tadalafil, Vardenafil, Esomeprazole, Famotidine, Omeprazole, Pantoprazole, Rabeprazole, Ranitidine, Simethicone, Artesunate, Amodiaquine, Benazepril, Misoprostol, Metformin, Glipizide, Diltiazem HCl, Verapamil HCl, Labetalol HCl, Theophylline, Diclofenac Sodium, Aceclofenac, Naproxen sodium, Bupropion HCl, Metformin HCl, Duloxetine, Metoprolol

tartarate & succinate, Fexofinadine HCL, Pseudoephedrine HCL, Zolpidem tartarate, Tramadol HCl, Oxybutynin chloride, Alfuzosin, including pharmaceutically acceptable salts, hydrates, solvates, esters, prodrugs thereof.

The pharmaceutical dosage form disclosed herein can be present in the form of tablet, minitablets or caplet.

The modified release pharmaceutical composition may comprise one or more pharmaceutically acceptable excipients selected form the group comprising of diluents, binders, disintegrants, surfactants, lubricants and glidants.

Suitable binder may be selected from a group comprising one or more of, povidone, starch, stearic acid, gums, hydroxypropylmethyl cellulose and mixtures thereof.

Suitable diluent may be one or more of, microcrystalline cellulose, mannitol, calcium phosphate, calcium sulfate, kaolin, dry starch, powdered sugar and mixtures thereof.

Suitable disintegrant may be one or more of starch, croscarmellose sodium, crospovidone, sodium starch glycolate and mixtures thereof.

Suitable surfactants are those known to one of ordinary skill in the art and include but are not limited to one or more of polyoxyethylene glycerol esters of fatty acids, such as Tagats; polyoxylated castor oil, ethylene glycol esters, such as glycol stearate and distearate; propylene glycol esters, such as propylene glycol myristate; glyceryl esters of fatty acids, such as glyceryl stearates and monostearates; sorbitan esters, such as spans and tweens; polyglyceryl esters, such as polyglyceryl 4-oleate; fatty alcohol ethoxylates, such as Brij type emulsifiers; ethoxylated propoxylated block copolymers, such as poloxamers; polyethylene glycol esters of fatty acids, such as Labrafils, Labrafacs, and Labrasols; cremophores; glycerol monocaprylate/ caprate, such as Campmul CM

10; Gelucire, Capryol, Captex, Acconon, transcutol, triacetin, TPGS (d-alpha tocopheryl polyethylene glycol succinate) and mixtures thereof.

Suitable lubricant may be one or more of magnesium stearate, zinc stearate, calcium stearate, stearic acid, sodium stearyl fumarate, hydrogenated vegetable oil, glyceryl behenate and mixtures thereof.

Suitable glidant may be one or more of colloidal silicon dioxide, talc or cornstarch and mixtures thereof.

The pharmaceutical composition may be prepared by processes such as those known to one of ordinary skill in the art and include but are not limited to dry granulation, wet granulation and direct compression. The said process comprises of mixing of therapeutically active pharmaceutical ingredient with one or more pharmaceutically acceptable polymers along with one or more pharmaceutically acceptable excipients, compressing the blend into core and further coating with one or more rate controlling polymers.

While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention.

Example 1

Table 1 - Lamotrigine Extended Release Tablets 200mg

Sr. No.	Ingredient	Qty (%w/w)
	Core formula	
1	Lamotrigine	10-70
2	HPMC	15-90
3	Lactose monohydrate	5-50
4	Purified water	qs
5	Magnesium stearate	0.25-5
	Coating formula	
1	Methacrylic copolymer type C	1.5 - 5
2	Triethyl citrate	2 - 20
3	Talc	5-50
4	Polysorbate 80	0-5
5	Iron oxide red	0-5
6	Povidone (PVK K30)	5 - 35
7	Colloidal silicon oxide	5 - 35
8	Purified water	Qs

Lamotrigine Extended Release tablet is a donut shaped tablet similar to shown in Figure (I-A)

Procedure:

Agents No. 1, 2, 3 & 4 are sifted and mixed using rapid mixing granulator. The premix is granulated with purified water or suitable solvent. The granules are dried using suitable fluidized bed dryer followed by milling using multimill. The granules are sized using 20# mesh ASTM (840 micron size mesh) and lubricated with lubricant in double cone blender. The blend is compressed to form core tablets followed by coating the tablet using enteric polymer like, Methacrylic copolymer type C (Eudragit L 30 D55) using suitable wicking agents viz. Povidone (PVK K30), Colloidal silicon oxide (Aerosil200).

Table 2 – Drug release in different dissolution apparatus

Time in Hrs	USP Type I	USP Type II
	% Release	% Release
1hr	8	10
3hr	22	21
5hr	36	42
8hr	59	62
10hr	72	75
12hr	85	91
15hr	97	95

Table 2 provides drug release from the composition described in the example I using different dissolution apparatus.

For USP Type I, dissolution was studied using 900 ml of 0.1 N Hydrochloric acid as a dissolution media with rotation speed of 100 rpm at a temperature of 37℃±0.5℃.

For USP Type II, dissolution was studied using 900 ml of 0.1 N Hydrochloric acid as a dissolution media with rotation speed of 50 rpm at a temperature of 37℃±0.5℃.

Table 3 – Drug release in USP Type III Dissolution apparatus

Time in Hrs	Dissolution Media	% Release in individual Dissolution Media	Cumulative % Release
2 hrs	0.1 N HCL	12	12
2 hrs	4.5 pH Acetate	15	27
2 hrs	5.5 pH Acetate	18	45
2 hrs	6.8 pH Phosphate	19	64
2 hrs	6.8 pH Phosphate	14	78
5 hrs	6.8 pH Phosphate	23	101

Table 3 provides drug release from the composition described in the example I using USP Type III dissolution apparatus. Dissolution was studied using 250 ml of different dissolution medias mentioned in the table 3 with 15 dips per minute at a temperature of 37°C±0.5°C.

Table 4 - Effect of various punch sizes and shapes on release pattern for composition of example 1.

Time in Hrs	**Circular Punch** (Figures: I-A, II-A, III-A, IV-A, V-A, VI-A, VII-A)	**Circular punch** Beveled edges (Figure: VIII-A)	**Oval Punch** (Figure: IX-A)
	% Release	**% Release**	**% Release**
1 hr	12	11	8
3hr	30	27	23
5hr	40	47	37
8hr	60	66	55
10hr	71	77	72
12hr	82	85	82
15hr	97	96	98

Table 4 describes effect of punch dimensions on the drug release from the composition described in the example I using different punches. Dissolution was studied using 900 ml of 0.1 N Hydrochloric acid as a dissolution media with rotation speed of 50 rpm at a temperature of 37°C±0.5°C.

Example 2

Table 5 – Alfuzosin hydrochloride Extended Release Tablets 10mg

Sr. No.	**Ingredient**	**Qty (%w/w)**
	Core formula	
1	Alfuzosin Hydrochloride	5.0

2	HPMC	45.0
3	Hydroxy propyl cellulose	27.5
4	Mannitol	21.25
5	Colloidal silicon oxide	0.5
6	Hydrogenated Castor oil	0.25
7	Magnesium stearate	0.1
	Extragranular	
8	Hydrogenated Castor oil	0.25
9	Magnesium stearate	0.15
	Coating formula	**Qty %w/w**
1	Methacrylic copolymer type C	60.0
2	Triethyl citrate	9.0
3	Talc	12.7
4	Yellow Iron oxide	0.3
5	Povidone (PVK K30)	6.0
6	Colloidal silicon oxide	12.0
7	Purified water	q.s

Alfuzosin hydrochloride extended release tablet is a centrally notched tablet similar to shown in Figure (II-A)

Procedure:

Alfuzosin Hydrochloride, HPMC (Methocel K100M premium CR), Hydroxy propyl cellulose (HPC-M), Mannitol and Colloidal silicon oxide (Aerosil200) were sifted and mixed together. Above blend was lubricated with Hydrogenated Castor oil and magnesium stearate in blender. This mixture was compacted and granules were formed. The granules were further lubricated with Hydrogenated Castor oil and magnesium stearate and compressed to form core tablets. Tablets were coated using Methacrylic copolymer type C (Eudragit L 30D 55) using suitable wicking agents like Colloidal silicon oxide (Aerosil200), Povidone (PVK K30).

Table 6 – Drug release in different dissolution apparatus

Time in Hrs	USP Type II
	% Release
1hr	6
2hr	20
5hr	35
10hr	63
12hr	75
15hr	87
20hr	101

Table 6 provides drug release from the composition described in the example 2 using different dissolution apparatus.

For USP Type II, dissolution was studied using 900 ml of 0.1 N Hydrochloric acid as a dissolution media with rotation speed of 100 rpm at a temperature of 37℃±0.5℃.

Example 3

Table 7 - Venlafaxine Hydrochloride Extended Release Tablets 150mg

Sr. No.	Ingredient	Qty (%w/w)
	Core formula	
1	Venlafaxine Hydrochloride	50.0
2	HPMC	32.33
3	Xanthan gum	11.66
4	Povidone	5.0
5	Purified water	q.s
6	Magnesium stearate	1.0
	Coating formula	**Qty %w/w**

1	Methacrylic copolymer type A	54.0
2	Triethyl citrate	5.41
3	Talc	22.9
4	Titanium dioxide	2.5
5	Povidone (PVK K30)	4.0
6	Colloidal silicon oxide (Aerosil200)	10.83
7	Purified water	q.s

Venlafaxine hydrochloride extended release tablet is a pillowed tablet similar to shown in Figure (V-A)

Procedure:

Venlafaxine Hydrochloride, HPMC (Methocel K100M premium CR) and Xanthan gum (Xantural 75) were sifted and mixed together. This mixture was granulated using Povidone (PVK K30). Granules were dried and lubricated with suitable lubricant and compressed to form core tablets. These tablets were further coated using Methacrylic copolymer type C (Eudragit L 100) and colloidal silicon oxide (Aerosil200), Povidone (PVK K30).

Table 8 – Drug release in different dissolution apparatus

Time in Hrs	**USP Type I**
	% Release
2hr	12
4hr	18
8hr	36
12hr	56
15hr	86
20hr	100

Table 8 provides drug release from the composition described in the example 3 using different dissolution apparatus.

For USP Type I, dissolution was studied using 900 ml of water as a dissolution media with rotation speed of 100 rpm at a temperature of 37℃±0.5℃.

Example 4

Table 9 – Bupropion Hydrochloride Extended Release Tablets 150mg

Sr. No.	Ingredient	Qty (%w/w)
	Core formula	
1	Bupropion Hydrochloride	50.0
2	HPMC	30.0
3	Povidone	16.6
4	Purified water	q.s
5	Glyceryl behenate	3.33
	Coating formula	**Qty %w/w**
1	Methacrylic copolymer type C	52.0
2	Triethyl citrate	5.2
3	Talc	18.2
4	Iron oxide red	1.0
5	Povidone	5.2
6	Silicon dioxide	18.4
7	Purified water	q.s

Bupropion hydrochloride extended release tablet is a pillowed tablet similar to shown in Figure (VII-A)

Procedure:

Bupropion Hydrochloride, HPMC (Methocel K4M premium CR) and Povidone (PVP K90) were mixed together and granulated using purified water. Granules were dried and lubricated with suitable lubricant and compressed to form core tablets. These tablets were further coated using Methacrylic copolymer type C (Eudragit L 100) and silicon oxide (Aerosil200), Povidone (PVK K30).

Table 10 – Drug release in different dissolution apparatus

Time in Hrs	USP Type II
	% Release
1hr	20
4hr	44
5hr	85
8hr	97

Table 10 provides drug release from the composition described in the example 4 using different dissolution apparatus.

For USP Type II, dissolution was studied using 900 ml of water as a dissolution media with rotation speed of 50 rpm at a temperature of 37℃±0.5℃.

Example 5

Table 11 - Divalproex sodium Extended Release Tablets 125mg

Sr. No.	Ingredient	Qty (%w/w)
Core formula		
1	Divalproex sodium	48.0
2	Microcrystalline Cellulose	7.69
3	Hypromellose	25.0
4	Hydroxy propyl cellulose	7.69
5	Purified water	q.s
6	Silicon dioxide	1.92
7	Talc	1.92
8	Glyceryl behenate	3.84
Coating formula		
1	Methacrylic copolymer type C	52.0
2	Triethyl citrate	5.2

3	Talc	18.2
4	Iron oxide red	1.0
5	Povidone (PVK K30)	5.2
6	Silicon dioxide	18.4
7	Purified water	q.s

Divalproex sodium extended release tablet is a round beveled tablet similar to shown in Figure (VIII-A)

Procedure:

Divalproex, microcrystalline cellulose, hypromellose and hydroxypropylcellulose were sifted and mixed together. This mix was granulated using purified water. The granules were dried and suitably sized. The sized granules were lubricated with lubricant and compressed into core tablets. These core tablets were further enteric coated with Methacrylic copolymer type C (Eudragit L 30 D55) and suitable wicking agents like Silicon dioxide (Slyloid FP244), Povidone (PVK K30).

Table 12 – Drug release in different dissolution apparatus

Release in 0.1N HCl	
Time in Hrs	**USP Type II**
	% Release
45min	5
3hr	15
9hr	42
12hr	63
15hr	77
18hr	93
21hr	98

Table 12 provides drug release from the composition described in the example 5 using different dissolution apparatus.

For USP Type II, dissolution was studied using 500 ml of 0.1 N Hydrochloric acid with 75mMol SDS as a dissolution media for 24 hours with rotation speed of 100 rpm at a temperature of 37℃±0.5℃.

Example 6

Table 13 - Carbamazepine Extended Release Tablets 125mg

Sr. No.	Ingredient	Qty (%w/w)
Core formula		
1	Carbamazepine	55.5
2	Mannitol	8.47
3	Hypromellose	20.83
4	Sodium lauryl sulphate	2.08
5	Eudragit RL 30D	12.5
6	Colloidal silicon dioxide	5.55
7	Sodium stearyl fumarate	2.08
Coating formula		
1	Methacrylic copolymer type C	40.0
2	Triethyl citrate	5.0
3	Talc	19.0
4	Iron oxide yellow	1.0
5	Povidone (PVK K30)	20.0
6	Colloidal silicon dioxide	15.0
7	Purified water	q.s

Carbamazepine extended release tablet is oval shaped tablet similar to shown in Figure (IX-A)

Procedure:

Carbamazepine, Mannitol, Hypromellose and Sodium lauryl sulphate were sifted and mixed together. This mix was granulated using purified water. The granules were dried and suitably sized. The sized granules were lubricated with lubricant and compressed into core tablets. These core tablets were further enteric coated

with Methacrylic copolymer type C (Eudragit L 30 D55) using suitable wicking agents like Colloidal silicon dioxide & Povidone (PVK K30).

Table 14 – Drug release in different dissolution apparatus

Time in Hrs	USP Type I
	% Release
1hr	6
3hr	14
6hr	23
8hr	35
10hr	59
12hr	71
18hr	87
24hr	99

Table 14 provides drug release from the composition described in the example 6 using different dissolution apparatus.

For USP Type I, dissolution was studied using 900 ml of water as a dissolution media with rotation speed of 100 rpm at a temperature of 37℃±0.5℃.

Example 7

Table 15 - Lamotrigine Extended Release Tablets 50 mg

Sr. No.	Ingredient	Qty (% w/w)
Core formula		
1	Lamotrigine	13.51
2	Methocel K 100L V Premium CR	16.08
3	Methocel E4M Premium CR	22.7
4	Lactose monohydrate (Pharmatose 200M)	41.82
5	Purified Water	q.s.

6	Magnesium Stearate	0.47
7	Opadry Clear YS-1R-7006	1.41
Coating formula		
Enteric Coating 1		
1	Methacrylic acid polymer (Eudragit L 30D-55)	1.57
2	Purified Water	q.s.
3	Triethyl citrate	0.16
4	Polysorbate 80	0.002
5	Talc	0.78
6	Iron Oxide	0.029
7	Calcium Silicate (Florite RE) (20% of dried Enteric Polymer wt.)	0.31
Enteric Coating 2		
8	Opadry Enteric 94S54507 Pink	14.74
9	Isopropyl Alcohol	q.s
10	Methylene Chloride	q.s

Procedure:

API, Methocel K100LV premium CR, Methocel E4M Premium CR and Lactose monohydrate were sifted through 40 # mesh ASTM and dry mixed in Rapid mixer granulator. The dry mix was granulated with purified water in Rapid Mixer Granulator (RMG). Granules were dried in FBD at 60°C inlet temp for 15 minutes. Granules were sized. Further were sized. Further dried for 20 minutes and co-milled and finally passed through 20 # ASTM. Granules were lubricated with Magnesium Stearate in DCB for 3 minutes. Lubricated blend was compressed into tablets.

Table 15 – Drug Dissolution in different media.

Release in pH 6.8 phosphate buffer	
Time in Hrs	**USP Type II**
	% Release
Acid Stage 2 hrs	1
Buffer Stage1 hrs	3
2hr	9
3hr	16
5hr	30
7hr	46
10hr	65
13hr	80
15hr	88

Table 15 provides drug release from the composition described in the example 7 using USP type II dissolution apparatus.

Dissolution was studied using Official Media (Acid Stage: 0.01 M HCl, Buffer Stage: Trisodium Phosphate Buffer, pH 6.8 ± 0.5% SLS. (Add 200mL of 0.0205 M sodium phosphate solution containing 2.25% w/v SLS to 700 mL of HCl) with rotation speed of 100rpm at a temperature of 37℃±0.5℃.

We claim -

1. A modified release pharmaceutical dosage form comprising:
   a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and
   b) one or more rate controlling polymeric coating(s) surrounding the core;

   wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

2. The modified release pharmaceutical dosage form of claim 1, wherein the swellable hydrophilic polymers may include one or more of cellulose derivatives such as hydroxypropylmethyl cellulose (HPMC), hydroxypropyl cellulose, hydroxyethyl cellulose, methyl cellulose, ethyl cellulose, carboxymethyl cellulose, carboxyethyl cellulose, carboxymethylhydroxyethyl cellulose, microcrystalline cellulose, polyethylene oxides, polyvinylpyrrolidone, polyalkylene glycols, gelatine, polyvinyl alcohol, starch and derivatives thereof, acrylic acid polymers, polymethacrylates, polysaccharides such as xanthan gum, tragacanth gum, gum karaya, guar gum, acacia, gellan gum locust bean gum, alkali metal salts of alginic acid or pectic acid, sodium alginate, potassium alginate, ammonium alginate, chitosan, maleic anhydride copolymers, poly(ethyleneimine), polyurethane hydrogels, crosslinked polyacrylic acids, derivatives and mixtures thereof.

3. The modified release pharmaceutical dosage form of claim 2, wherein the swellable hydrophilic polymer is hydroxypropyl methylcellulose.

4. The modified release pharmaceutical dosage form of claim 1, wherein the rate controlling polymers may include one or more of hydrophilic or hydrophobic polymers selected from the group consisting of polyvinyl acetate, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, ethyl cellulose, a fatty acid, a fatty acid ester, an alkyl alcohol, a wax, shellac, rosin, zein (prolamine from corn), povidone, kollidon SR, a poly(meth)acrylate, microcrystalline cellulose or poly(ethylene oxide), polyuronic acid salts, cellulose ethers, xanthan gum, tragacanth gum, gum karaya, guar gum, acacia, gellan gum locust bean gum, alkali metal salts of alginic acid or pectic acid, sodium alginate, potassium alginate, ammonium alginate, hydroxypropyl cellulose, hydroxy ethyl cellulose, hydroxypropyl methyl cellulose, carboxyvinyl polymers, polymerized gelatin, shellac, methacrylic acid copolymer type C NF, cellulose butyrate phthalate, cellulose hydrogen phthalate, cellulose propionate phthalate, polyvinyl acetate phthalate (PVAP), cellulose acetate phthalate (CAP), cellulose acetate trimellitate (CAT), hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate, dioxypropyl methylcellulose succinate, carboxymethyl ethyl cellulose (CMEC), hydroxypropyl methylcellulose acetate succinate (HPMCAS), and acrylic acid polymers and copolymers like methyl acrylate, ethyl acrylate, methyl methacrylate and/or ethyl methacrylate with copolymers of acrylic and methacrylic acid esters (Eudragit NE, Eudragit RL, Eudragit RS), pH dependent polymers such as methacrylic acid copolymer type C (Eudragit L 100 55), methacrylic acid copolymer type C (Eudragit L 30D 55), methacrylic acid copolymer type A (Eudragit L 100), methacrylic acid copolymer type C (Eudragit S 100) and mixtures thereof.

5. The modified release pharmaceutical dosage form of claim 4, wherein the rate controlling polymer is methacrylic acid copolymer.

6. The modified release pharmaceutical dosage form of claim 1, wherein the rate controlling polymer(s) is present in an amount form about 1.5% to about 5% by weight, with respect to the mixture forming the core.

7. The modified release pharmaceutical modified release pharmaceutical dosage form of claim 1, wherein the dosage form comprises one or more of pharmaceutically acceptable excipients selected form the group consisting of diluents, binders, disintegrants, surfactants, lubricants and glidants.

8. The modified release pharmaceutical dosage form of claim 1, wherein the dosage form comprises one or more of tablet, minitablets or caplet.

9. The modified release dosage form of claim 1, wherein shape of the dosage form comprises one or more of round, oval, donut, pillowed shaped and centrally notched.

10. A modified release pharmaceutical dosage form comprising:
    a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and
    b) one or more rate controlling polymeric coating(s) surrounding the core; wherein said polymeric coating comprises one or more plasticizer(s);

    wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

11. The modified release pharmaceutical dosage form of claim 10, wherein the suitable plasticizer may include one or more of citrate esters (example, triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate), phthalate esters (example, dimethyl phthalate diethyl phthalate, dibutyl phthalate, dihexyl phthalate, butyl octyl phthalate, diisononyl phthalate, butyl octyl phthalate, diethylhexyl phthalate, di-n-

octyl phthalate, di-i-octyl phthalate, di-i-decyl phthalate, di-n-undecyl phthalate, di-n-tridecyl phthalate), dibutyl sebacate, dibutyl tartrate, glycerin, polyethylene glycols, propylene glycols, butyl phthalyl butyl glycolate, ethyl phthalyl ethyl glycolate, acetylated monoglycerides, polysorbates, glyceryl monostearate, glycerol triacetate, triacetin, castor oil, mineral oils, rape seed oil, olive oil, sesame oil, polyhydric alcohols, sorbitol, tripropioin; diacetin, dioctyl azelate, epoxidized tallate, triisoctyl trimellitate, tri-2-ethylhexyl trimellitate, di-2-ethylhexyl adipate, di-2-ethylhexyl sebacate, di-2-ethylhexyl azelate, dibutyl sebacate, diethyloxalate, diethylmalate, diethylfumerate, dibutylsuccinate or diethylmalonate.

12. The modified release pharmaceutical composition of claim 11, wherein the plasticizer is triethyl citrate.

13. The modified release pharmaceutical composition of claim 10, wherein the plasticizer(s) is present in an amount form about 2% to about 20% by weight, with respect to the mixture forming the core.

14. The modified release pharmaceutical modified release pharmaceutical dosage form of claim 10, wherein the dosage form comprises one or more pharmaceutically acceptable excipients selected form the group comprising of diluents, binders, disintegrants, surfactants, lubricants and glidants.

15. The modified release pharmaceutical dosage form of claim 10, wherein the dosage form comprises one or more of tablet, minitablets and caplet.

16. The modified release dosage form of claim 10, wherein shape of the dosage form comprises one or more of round, oval, donut, pillowed shaped and centrally notched.

17. A modified release pharmaceutical dosage form comprising:

a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and
b) one or more rate controlling polymeric coating(s) surrounding the core; wherein said polymeric coating comprises one or more wicking agent(s);

wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

18. A modified release pharmaceutical dosage form of claim 17, wherein the suitable wicking agent may include one or more of colloidal silicon dioxide, porous silicon dioxide, fumed silicon dioxide, titanium dioxide, calcium silicate, magnesium aluminum silicate, low molecular weight polyvinylpyrrolidone, alumina, niacinamide, kaolin sodium lauryl sulfate, low molecular weight polyvinyl pyrrolidone, m-pyrol, bentonite, polyester, and polyethylene.

19. The modified release pharmaceutical composition according to claim 17, wherein the wicking agent(s) is present in an amount from about 5 to about 35% by weight with respect to the mixture forming the core.
20. The modified release pharmaceutical modified release pharmaceutical dosage form of claim 17, wherein the dosage form comprises one or more pharmaceutically acceptable excipients selected form the group comprising of diluents, binders, disintegrants, surfactants, lubricants and glidants.

21. The modified release pharmaceutical dosage form of claim 17, wherein the dosage form comprises one or more of tablet, minitablets and caplet.

22. The modified release dosage form of claim 17, wherein shape of the dosage form comprises one or more of round, oval, donut, pillowed shaped and centrally notched.

23. A modified release pharmaceutical dosage form comprising:
    a) a core comprising therapeutically active pharmaceutical ingredient or pharmaceutically acceptable salts thereof, one or more swellable hydrophilic polymers; and
    b) one or more rate controlling polymeric coating(s) surrounding the core;

    wherein the shape of the dosage form is achieved in such a way that it provides leachable areas and wherein the core upon contact with gastrointestinal fluids swells and exerts a pressure which causes partial disruption of the rate controlling coating surrounding the core and modified release is achieved by the combination of swellability and rate controlling ability of polymer in core and area of disruption of rate controlling polymer surrounding the core.

24. The modified release dosage form of claim 23, wherein shape of the dosage form comprises one or more of round, oval, donut, pillowed shaped and centrally notched.

FIGURE (I-A): Donut shaped tablet

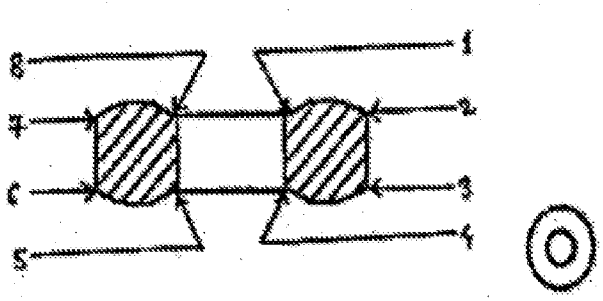

FIGURE (I-B): Regions of Donut shaped tablet through which release occurs

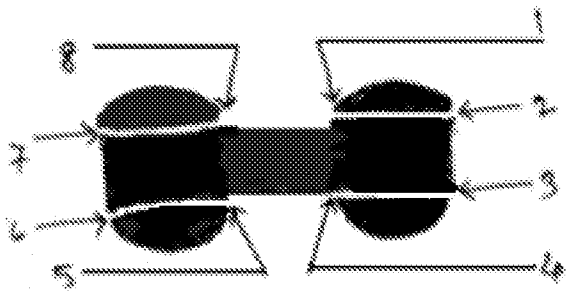

FIGURE (II-A): Centrally notched tablet dosage form

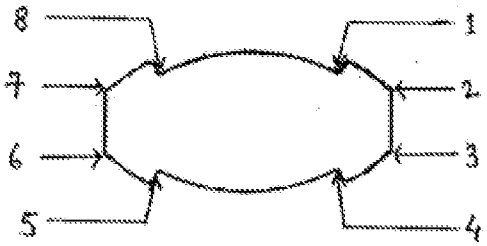

FIGURE (II-B): Regions of Centrally notched tablet through which release occurs

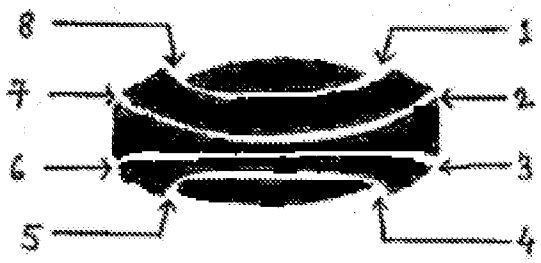

FIGURE (III-A): Centrally notched tablet dosage form

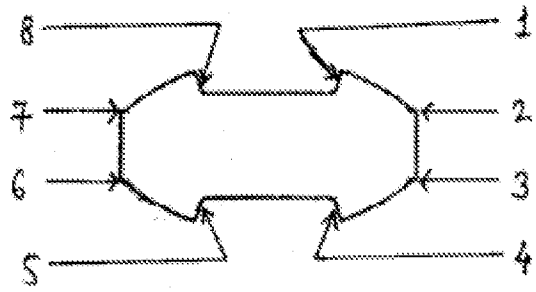

FIGURE (III-B): Regions of Centrally notched tablet through which release occurs

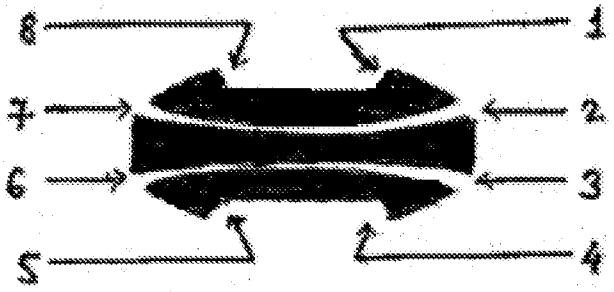

FIGURE (IV-A): Centrally notched tablet dosage form

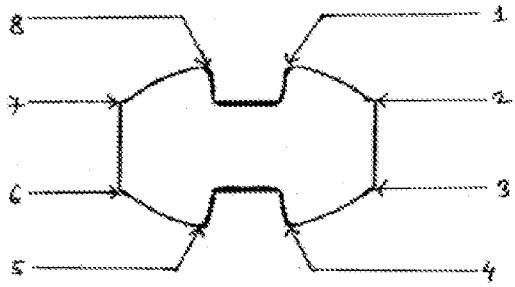

FIGURE (IV-B): Regions of Centrally notched tablet through which release occurs

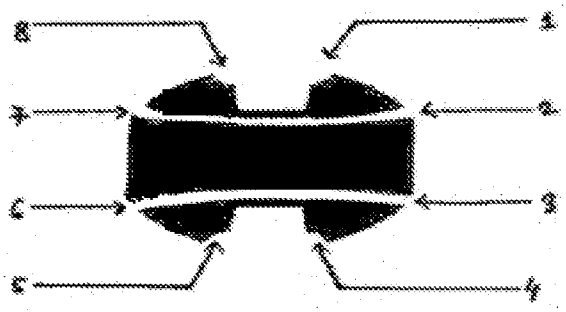

FIGURE (V-A): Pillowed tablet dosage form

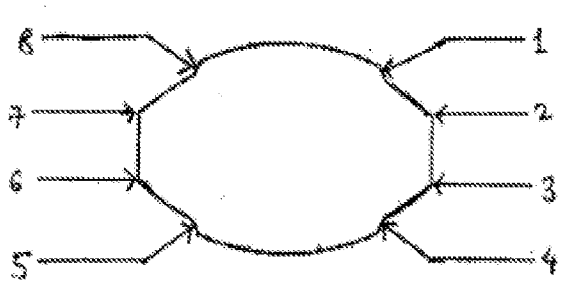

FIGURE (V-B): Regions of Pillowed tablet through which release occurs

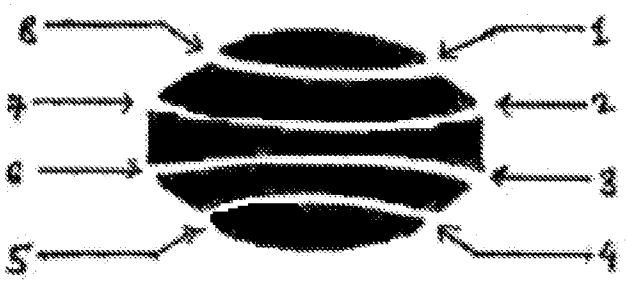

FIGURE (VI-A): Pillowed tablet dosage form

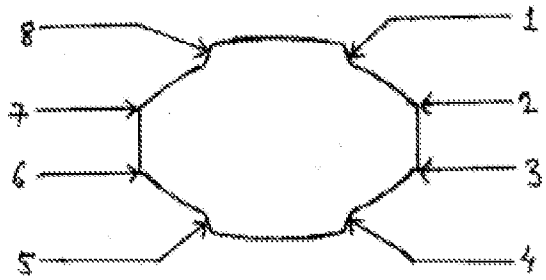

FIGURE (VI-B): Regions of Pillowed tablet through which release occurs

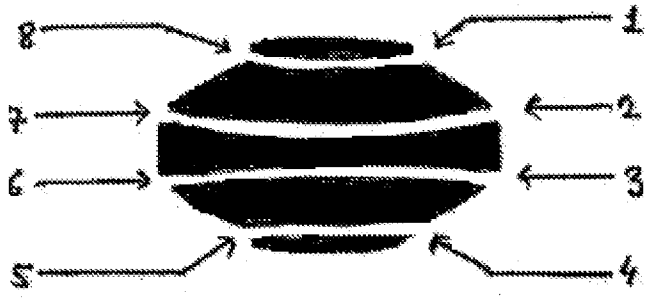

FIGURE (VII-A): Pillowed tablet dosage form

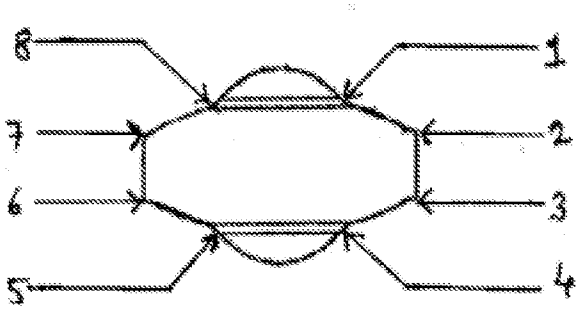

FIGURE (VII-B): Regions of Pillowed tablet through which release occurs

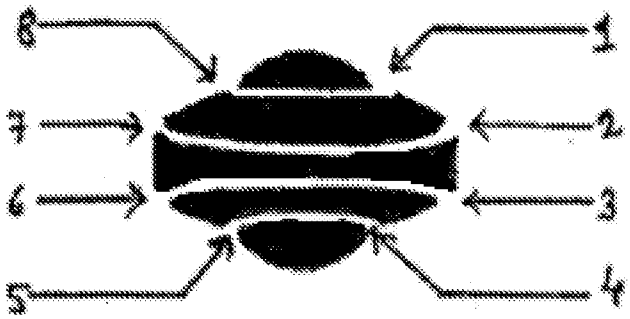

FIGURE (VIII-A): Round beveled tablet

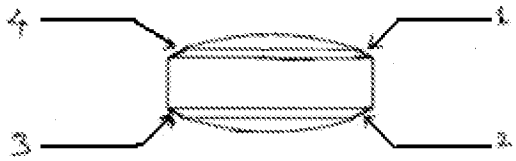

FIGURE (VIII-B): Regions of a round beveled tablet through which release occurs

FIGURE (IX-A): Oval shaped tablet dosage form

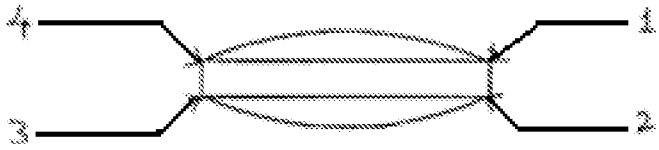

FIGURE (IX-B): Regions of oval shaped tablet through which release occurs