PHARMACEUTICAL DOSAGE FORM FOR IN VIVO RETENTION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to Patent Application No. PCT/CN2024/081848 filed on March 15, 2024, which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] In some aspects, the present disclosure is directed to a pharmaceutical dosage form intended to provide a desired retention time in a subject based on geometric differences between dosage form states before and after administration. In some aspects, the provided oral pharmaceutical dosage form includes a swellable material that, upon swelling or expansion, drives the overall size of the oral pharmaceutical dosage form to expand, such that the oral pharmaceutical dosage form is retained in a stomach for a desired period of time. In some other aspects, the present disclosure is directed to a material for the oral pharmaceutical dosage form described herein. In some other aspects, the present disclosure is directed to a design method, a dosage form manufacturing method, for example, involving three-dimensional (3D) printing, injection molding, ultrasonic welding, or any combination thereof, and a method for delivering a drug to a subject, where the method includes administering the oral pharmaceutical dosage form described herein to the subject.

BACKGROUND

[0003] Conventional oral pharmaceutical dosage forms, when administered to a subject, are subject to natural forces, such as natural flow of liquids, semi-solids, and solids through a gastrointestinal system of the subject, and/or forces applied by the subject. As is the case with oral administration, such natural flow may vary between administrations to a specific subject and between groups of subjects, specifically depending on fluctuations relative to the time of administration, such as the timing of meal and/or beverage ingestion and the size of meal and/or beverage contents, as well as the current gastric phase and its remaining duration. Such

circumstances may lead to variability in, for example, the location of drug delivery, bioavailability, safety profile, and therapeutic efficacy of a pharmaceutical dosage form (e.g., an oral pharmaceutical dosage form) retained in a stomach for a period of time.

[0004] All references (including patent applications and publications) cited herein are incorporated herein by reference in their entireties.

SUMMARY

[0005] In some aspects, a pharmaceutical dosage form is provided. The pharmaceutical dosage form includes: a body structure, where the body structure forms an expandable material chamber, and the expandable material chamber includes an expandable material; an arm, where the arm is operably connected to the body, and the arm rotates around the body of the pharmaceutical dosage form by force provided by the expandable material; and a drug, where the pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the pharmaceutical dosage form is, at least in part, due to expansion of the expandable material in the presence of gastrointestinal fluid.

[0006] A pharmaceutical dosage form is provided. The pharmaceutical dosage form includes: a body extending in a Z axis direction, where the body includes an internal chamber and an expandable structure accommodated in the internal chamber, and the internal chamber includes a fluid inlet; an arm, where the arm is rotatable around the body; and a drug, where the pharmaceutical dosage form is configured to have a first state in which the pharmaceutical dosage form extends in the Z axis direction, and a second state in which the pharmaceutical dosage form extends in directions of XY axes and the Z axis direction simultaneously; the second state arises at least in part from expansion of the expandable structure; and the extension in the directions of the XY axes results from rotation of the arm about the body.

[0007] A pharmaceutical dosage form is provided. The pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form. The pharmaceutical dosage form includes: an arm and a body connected to the arm, where the arm is rotatable around the body, the body includes a pushing device, and the pushing device is triggered by an external condition and pushes the arm to rotate around the body

to form a post-administration state in an expanded form, where the pharmaceutical dosage form, when configured to have the pre-administration state in a compact form, includes an outer surface and an interior opposite to the outer surface; and a drug component, where the drug component is carried in the interior of the pharmaceutical dosage form, and when the pharmaceutical dosage form is in the post-administration state in an expanded form, the drug is at least partially exposed.

[0008] In some specific implementations, the Z axis may be regarded as a central axis of the pharmaceutical dosage form, and the X-axis and the Y-axis are axes perpendicular to the Z axis. A plane formed by the XY axes is a plane perpendicular to the Z axis.

[0009] In some specific implementations, the pushing device includes an expandable material.

[0010] In some specific implementations, the pushing device includes a gas-generating material.

[0011] In some specific implementations, the fluid inlet may be a through-hole located in the body and providing communication between the inside and outside of the body when the arm extends out of the body. In some specific implementations, the fluid inlet may be a separate water inlet hole provided in the body. In some specific implementations, the pushing device further includes a movable member.

[0012] In some specific implementations, the drug component is loaded on the arm and/or loaded on the body.

[0013] In some specific implementations, the body of the pharmaceutical dosage form is of an integral structure.

[0014] In some specific implementations, the pharmaceutical dosage form includes a first compartment for accommodating an expandable member, and a second compartment in communication with the first compartment.

[0015] In some specific implementations, the body structure of the pharmaceutical dosage form further includes a movable member, and the movable member is movable from the first compartment to the second compartment. When the pharmaceutical dosage form is configured to be in the pre-administration state in a compact form, the movable member is located within the first compartment. When the pharmaceutical dosage form is in the post-administration state in an expanded form, the movable member is at least partially accommodated within the second compartment.

[0016] In some specific implementations, the body structure of the pharmaceutical dosage

form further includes a fluid inlet in communication with the first compartment or the second compartment.

[0017] In some specific implementations, the body of the pharmaceutical dosage form is composed of a cover and a base. In some implementations, an inner wall of the base forms the first compartment, and an inner wall of the cover forms the second compartment. In some implementations, the body of the oral pharmaceutical dosage form includes one or more bases and one or more covers. In some specific implementations, the cover includes a first cover and a second cover.

[0018] In some specific implementations, the body of the pharmaceutical dosage form includes a semipermeable membrane that partially or wholly allows a liquid to enter. In some specific implementations, the body of the pharmaceutical dosage form is a semipermeable membrane. In some specific implementations, the body of the pharmaceutical dosage form has a pore/orifice that allows a liquid to enter.

[0019] In some specific implementations, the base of the pharmaceutical dosage form is composed of a semipermeable material or semipermeable membrane that partially or wholly allows a liquid to enter. In some specific implementations, the base of the body of the pharmaceutical dosage form is a semipermeable membrane. In some specific implementations, the base of the body of the pharmaceutical dosage form has a pore/orifice that allows a liquid to enter. In some specific implementations, an accommodating cavity formed by the semipermeable membrane includes a swellable material. In some specific implementations, the accommodating cavity formed by the semipermeable membrane further includes a drug and an osmotic pressure regulator, and the drug is released from the semipermeable membrane under the action of the osmotic pressure regulator. In some specific implementations, the osmotic pressure regulator may be a non-ionic osmotic pressure regulator or an ionic osmotic pressure regulator, and may be selected from one or more of the following materials: glucose, mannitol, sorbitol, glycerol, lactose, fructose, ammonium sulfate, betaine, sodium chloride, potassium chloride, calcium chloride, and potassium bromide.

[0020] In some specific implementations, the base and the cover of the body of the pharmaceutical dosage form are mated with each other by snap-fit, screw-threads, a mortise and tenon joint, binder bonding, riveting, ultrasonic welding, or heat staking.

[0021] In some specific implementations, the body of the pharmaceutical dosage form includes

two or more materials.

[0022] In some specific implementations, the base of the body of the pharmaceutical dosage form includes an opening at the top portion, and the opening is connected to the cover. In some specific implementations, the opening of the base of the oral pharmaceutical dosage form is configured to be circular, elliptical, rectangular, or polygonal, for example, triangular, quadrilateral, hexagonal, or octagonal. In some specific implementations, the opening of the base of the oral pharmaceutical dosage form has a diameter of 4 mm to 8 mm.

[0023] In some specific implementations, the base of the body of the pharmaceutical dosage form includes a bottom portion, and the bottom portion of the base is an arcuate surface. In some specific implementations, the bottom portion of the base of the oral pharmaceutical dosage form includes a material that allows a liquid to flow in. In some specific implementations, the bottom portion of the base of the oral pharmaceutical dosage form has a pore/orifice that allows a liquid to enter.

[0024] In some specific implementations, the orifice of the body or the base of the pharmaceutical dosage form has a diameter of 0.1 mm to 2 mm. In some specific implementations, the body or the base of the oral pharmaceutical dosage form has one or more orifices, specifically 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 15, 18, 20, or 30 orifices.

[0025] In some specific implementations, a channel formed by the bottom portion of the base of the pharmaceutical dosage form and the opening at the top portion of the base is a first directional channel. In some specific implementations, the opening at the top portion of the base of the oral pharmaceutical dosage form is located at a cross-section where the bottom portion of the cover is connected to the base.

[0026] In some specific implementations, the movable member is a piston. The swellable material, in the presence of a liquid (such as gastric fluid), absorbs the liquid and expands, and pushes the piston to move in a direction from the first compartment to the second compartment.

[0027] In some specific implementations, the swellable material includes sodium alginate (SA), hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), hydroxypropyl methylcellulose (HPMC), polyethylene oxide (PEO), polyvinyl alcohol (PVA), microcrystalline cellulose (MCC), croscarmellose sodium (CCNa), carboxymethyl cellulose sodium (CMC-Na), polyvinylpolypyrrolidone (PVPP), sodium carboxymethyl starch (CMS-Na), polyethylene glycol (PEG), or a mixture thereof.

[0028] In some specific implementations, the swellable material includes a gas-generating substance. In some specific implementations, the gas-generating substance includes an organic salt, an inorganic salt, or a mixture thereof. In some specific implementations, the swellable material is a spring. In some specific implementations, the swellable material is externally wrapped with an erodible material layer.

[0029] In some embodiments, the swellable material expands in volume by at least about 1.2 times upon exposure to gastrointestinal fluid. In some embodiments, the swellable material has a volume expansion rate of at least about 1.2 times within 30 minutes.

[0030] In some embodiments, an amount of the swellable material in the swellable material chamber is at least about 5 mg.

[0031] In some specific implementations, the swellable material has a swelling volume of about 10 mm^3 to about 50 mm^3.

[0032] In some specific implementations, the swellable material may be formed by prepressing. In some specific implementations, a bottom portion of the swellable material is configured into a shape conforming to the bottom portion of the base. In some specific implementations, the bottom portion of the swellable material is an arcuate surface.

[0033] In some specific implementations, the body structure forms a swellable material chamber, and the swellable material chamber further includes a cover and a base, where the cover is mated with the base to form an overall external structure of the swellable material chamber. In some specific implementations, the swellable material chamber includes a swellable material and a movable member.

[0034] In some specific implementations, the movable member in the swellable material chamber has a certain rigidity and strength. In some specific implementations, the movable member in the swellable material chamber is located between the swellable material and the opening of the base.

[0035] In some specific implementations, the movable member has a bottom portion close to the swellable material and a top portion close to the opening of the base. In some specific implementations, a surface area of the bottom portion of the movable member is greater than a surface area of the top portion of the movable member. In some specific implementations, the surface area of the bottom portion of the movable member is equal to the surface area of the top portion of the movable member. In some specific implementations, the surface area of the bottom

portion of the movable member is less than the surface area of the top portion of the movable member.

[0036] In some specific implementations, the movable member is configured as a cylinder, a T-shaped platform, a prism, a frustum of a pyramid, a frustum of a cone, or a frustum. In some specific implementations, the top portion of the movable member is provided with a hook structure. In some specific implementations, the bottom portion of the movable member is flat. In some specific implementations, the bottom portion of the movable member is provided with a groove.

[0037] In some specific implementations, the cover is configured to prevent the swellable material and the movable member from further moving, thereby retaining the arm in one or more extended positions.

[0038] In some specific implementations, the cover is optionally connected to the arm. In some specific implementations, the cover and the arm are configured as an interlocking structure, including a locking pin, a latch, or a pivot. In some specific implementations, an interior of the cover further includes a pin hole that cooperates with the locking pin of the arm.

[0039] In some specific implementations, the cover has a top portion, and the top portion of the cover forms part of an exterior of the body structure. In some specific implementations, the cover has a bottom portion, and the bottom portion of the cover is connected to the base. In some specific implementations, the cover has a side surface, and the side surface of the cover is a surface located between the top portion and the bottom portion of the cover.

[0040] In some specific implementations, the top portion of the cover is provided with an orifice. In some specific implementations, the orifice in the top portion of the cover is configured to match the shape of the arm close to the connecting end. In some specific implementations, a quantity of orifices in the top portion of the cover is the same as a quantity of arms. In some specific implementations, the quantity of orifices in the top portion of the cover is one or more, specifically 2, 3, 4, 5, 6, 7, or 8. In some specific implementations, the top portion of the cover is in the shape of a three-leaf clover, a four-leaf clover, or a petal. In some specific implementations, the orifice in the top portion of the cover is in the shape of a trumpet, a rectangle, or a round arch.

[0041] In some specific implementations, the top portion of the cover is flat. In some specific implementations, the top portion of the cover is provided with a reinforcing rib. In some specific implementations, the reinforcing ribs at the top portion of the cover are in the shape of a cross, *, #, or a grid.

[0042] In some specific implementations, an inner surface of the cover matches the shape of the top portion of the movable member.

[0043] In some specific implementations, an inner surface of the top portion of the cover matches the shape of the top portion of the movable member.

[0044] In some specific implementations, the bottom portion of the cover mates with the top portion of the base. In some specific implementations, part of an inner surface of the side surface of the cover mates with part of an outer surface of the top portion of the base. In some specific implementations, part of an outer surface of the side surface of the cover mates with part of an inner surface of the top portion of the base.

[0045] In some specific implementations, the bottom portion of the cover includes an opening. In some specific implementations, the opening at the bottom portion of the cover of the oral pharmaceutical dosage form is configured into a shape the same as that of the top portion of the movable member. In some specific implementations, the opening at the bottom portion of the cover of the oral pharmaceutical dosage form is configured to be circular, elliptical, rectangular, or polygonal, for example, triangular, quadrilateral, hexagonal, or octagonal. The opening at the bottom portion of the cover of the oral pharmaceutical dosage form has a diameter of 4 mm to 8 mm.

[0046] In some specific implementations, the cross-section of the bottom portion of the cover is configured as discontinuous arcs on a circumference. In some specific implementations, a quantity of arcs in the cross-section of the bottom portion of the cover is the same as a quantity of arms. In some specific implementations, the quantity of arcs in the cross-section of the bottom portion of the cover is a plurality, specifically 2, 3, 4, 5, 6, 7, or 8. In some specific implementations, the cross-section of the bottom portion of the cover is configured to be a complete shape. In some specific implementations, the cross-section of the bottom portion of the cover is configured in the shape of a circle, a circular ring, an ellipse, an elliptical ring, a rectangle, a rectangular ring, a polygon, or a polygonal ring.

[0047] In some specific implementations, a channel formed between the bottom portion and the top portion of the cover is a second directional channel.

[0048] In some specific implementations, after coming into contact with a liquid (e.g., gastric fluid), the swellable material absorbs water and swells to push the movable member to move along the first channel to the second channel until the movable member moves to a position close to the

top portion of the cover, thereby pushing the arm to rotate around the body of the oral pharmaceutical dosage form, such that the oral pharmaceutical dosage form changes from a pre-administration compact state to an expanded state.

[0049] In some specific implementations, the body of the oral pharmaceutical dosage form includes a first cover and a second cover, where the first cover includes a first top surface, a first bottom surface, and a first side surface located between the first top surface and the first bottom surface. The second cover includes a second top surface, a second bottom surface, and a second side surface located between the second top surface and the second bottom surface. In some specific implementations, the second bottom surface of the second cover mates with the top portion of the base. In some specific implementations, the first bottom surface of the first cover mates with the second top surface of the second cover. In some specific implementations, the second bottom surface of the second cover mates with the top portion of the base, and the first bottom surface of the first cover mates with the second top surface of the second cover. In some specific implementations, the first side surface of the first cover and the second side surface of the second cover partially or wholly mate with the inner surface of the top portion of the base. In some specific implementations, a connecting portion between the arm and the body is located between the first cover and the second cover.

[0050] In some specific implementations, the side surface of the cover is provided with an aperture. In some specific implementations, the aperture in the side surface of the cover is in communication with the orifice in the top portion of the cover. In some specific implementations, when the oral pharmaceutical dosage form is in a pre-administration compact state, the aperture in the side surface of the cover is in the same shape as a portion where the cover is in contact with the arm.

[0051] In some specific implementations, an engagement feature is provided between components constituting the pharmaceutical dosage form. In some specific implementations, the engagement feature includes a form-fit surface or a mechanical snap-fit assembly or a binder.

[0052] In some specific implementations, the binder optionally includes one or more of the following materials: dextrin, xanthan gum, maltodextrin, povidone, methylcellulose, ethylcellulose, zein, fructose, poloxamer, sodium alginate, pregelatinized starch, hydroxypropyl cellulose, hydroxypropyl methylcellulose, carbomer, starch, gum arabic, microcrystalline cellulose, sodium lauryl sulfate, sucrose, cellulose acetate, polysorbate, glucose, dextran, compressible sugar,

carrageenan, modified starch, tragacanth, and honey.

[0053] In some specific implementations, the arm includes a connecting end that is in contact with the body. In some specific implementations, the arm includes a connecting end that mates with the aperture in the side surface of the cover when the oral pharmaceutical dosage form is in a pre-administration compact state. In some specific implementations, the arm includes an extension section that extends away from the body from the connecting end when the oral pharmaceutical dosage form is in an expanded state. In some specific implementations, the arm includes a distal end of the arm farthest from the body when the oral pharmaceutical dosage form is in an expanded state.

[0054] In some specific implementations, the connecting end of the arm is connected to the body. In some specific implementations, the connecting end of the arm is connected to the cover.

[0055] In some specific implementations, the arm rotates around a rotation axis, where a direction of the rotation axis is perpendicular to an extension direction of the arm.

[0056] In some specific implementations, the connecting end of the arm is provided with a pin structure. The pin at the connecting end of the arm mates with a pin hole inside the body, such that the arm is rotatable around the rotation axis. In some specific implementations, the pin structure is a cylinder or a prism, such as a triangular prism, a quadrangular prism, a pentagonal prism, a hexagonal prism, or an octagonal prism.

[0057] In some specific implementations, the connecting end of the arm has a width of 0.5 mm to 2 mm. In some specific implementations, a ratio of the width of the connecting end of the arm to a width of the extension section of the arm ranges from 1:0.5 to 1:5. In some specific implementations, a ratio of the width of the connecting end of the arm to a width of the extension section of the arm ranges from 1:1 to 1:5. A ratio of the width of the connecting end of the arm to a length of the arm ranges from 1:10 to 1:20. In some specific implementations, the connecting end of the arm is configured as an L shape. In some specific implementations, when the oral pharmaceutical dosage form is in an expanded state, the connecting end of the arm is rotatable within the aperture in the side surface of the cover. In some specific implementations, when the oral pharmaceutical dosage form is in an expanded state, the connecting end of the arm mates with the hook structure at the top portion of the movable member.

[0058] In some specific implementations, when the oral pharmaceutical dosage form is in an expanded state, the connecting end of the arm has an inner angle β of the arm close to a base end,

and an inner angle γ of the arm close to the top portion of the cover. In some specific implementations, the inner angle β of the arm ranges from 0° to 180°. In some specific implementations, the inner angle β of the arm ranges from 0° to 120°. In some specific implementations, the inner angle β of the arm ranges from 0° to 70°. In some specific implementations, the inner angle β of the arm ranges from 70° to 120°. In some specific implementations, the inner angle γ of the arm ranges from 0° to 180°. In some specific implementations, the inner angle γ of the arm ranges from 0° to 30°. In some specific implementations, the inner angle γ of the arm ranges from 0° to 90°. In some specific implementations, the inner angle γ of the arm ranges from 30° to 90°.

[0059] In some specific implementations, the connecting end of the arm is the shape of a cylinder, a cone, a frustum of a cone, a prism, a pyramid, or a frustum of a pyramid. In some specific implementations, the connecting end of the arm has a width of 0.5 mm to 2 mm. In some specific implementations, the connecting end of the arm has a length of 2 mm to 10 mm. In some specific implementations, the connecting end of the arm is provided with a reinforcing rib. In some specific implementations, the reinforcing rib of the arm has a thickness of 1 mm to 3 mm.

[0060] In some specific implementations, the extension section of the arm is the shape of a cylinder, a cone, a frustum of a cone, a prism, a pyramid, or a frustum of a pyramid. In some specific implementations, when the oral pharmaceutical dosage form is in a pre-administration compact state, an outer surface of the extension section of the arm forms part of the outer surface of the pharmaceutical dosage form. In some specific implementations, when the oral pharmaceutical dosage form is in the pre-administration compact state, an inner surface of the extension section of the arm is close to a central axis of the body. In some specific implementations, the inner surface of the extension section of the arm is provided with a recess. In some specific implementations, the extension section of the arm has a width of 2 mm to 5 mm. In some specific implementations, the extension section of the arm has a length of 8 mm to 18 mm. In some specific implementations, the extension section of the arm is provided with a reinforcing rib. In some specific implementations, the reinforcing rib of the extension section of the arm has a thickness of 1 mm to 3 mm.

[0061] In some specific implementations, the distal end of the arm is in a curved state. In some specific implementations, an outer surface of the distal end of the arm is an arcuate surface. In some specific implementations, the outer surface of the distal end of the arm is a smooth

continuous curved surface.

[0062] In some specific implementations, there are at least two arms, which rotate around the body of the same oral pharmaceutical dosage form. In some specific implementations, there are 2, 3, 4, 5, 6, 7, or 8 arms. In some specific implementations, the arms include a first arm, a second arm, a third arm, and a fourth arm.

[0063] In some specific implementations, the arms each have a length of 5 mm to 22 mm, specifically 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22 mm.

[0064] In some specific implementations, the arms are configured as being distributed around a body axis. In some specific implementations, the arms are in contact with each other in a pre-administration compact state, forming a folded state. In some specific implementations, when the arms are in an unfolded state after administration, the arms are unfolded outward from the axis, to form a petal-like shape.

[0065] In some specific implementations, in the post-administration state of the arms, angles between adjacent arms are equal and are selected from the group consisting of 180°, 120°, 90°, 72°, 60°, and 45°.

[0066] In some specific implementations, a directional channel is configured to guide the movement of the arm by using the swellable material. In some specific implementations, the directional channel includes a swellable material and a movable member. In some specific implementations, the directional channel is configured to push the movable member to move by using the swellable material, to push open the arms for unfolding. In some implementations, the directional channel includes a straight channel. In some specific implementations, the directional channel includes a curved channel. In some implementations, a cross-section of the directional channel is circular, elliptical, square, rectangular, or capsule-shaped.

[0067] In some embodiments, the post-administration state of the pharmaceutical dosage form occurs within 2 hours or less after the pharmaceutical dosage form is administered to a subject.

[0068] In some embodiments, the gastric retention time of the pharmaceutical dosage form ranges from about 6 hours to about 3 months.

[0069] In some embodiments, a maximum cross dimension of the pharmaceutical dosage form in the pre-administration state is 24 mm or less.

[0070] In some embodiments, at least two perpendicular dimensions of the pharmaceutical dosage form are 20 mm or greater in the post-administration state.

[0071] In some embodiments, the body of the pharmaceutical dosage form further includes a central post, and in the pre-administration state, an axial length of the central post does not exceed an axial length of the arm.

[0072] In some embodiments, the central post carries the drug.

[0073] In some embodiments, the pharmaceutical dosage form further includes a restraining member, which is configured to inhibit extension of the arm in the pre-administration state. In some embodiments, the restraining member is an erodible restrainer, which is disposed on an outer side of the pharmaceutical dosage form. In some embodiments, the erodible restrainer of the pharmaceutical dosage form is a continuous erodible coating coated on the outer surface of the pharmaceutical dosage form. In some embodiments, the erodible restrainer may be a localized erodible coating that covers only a partial region of the arm. In some embodiments, the erodible restrainer of the oral pharmaceutical dosage form is an erodible ring. In some embodiments, the erodible restrainer of the pharmaceutical dosage form is a capsule shell, a capsule body, or a capsule cap.

[0074] In some embodiments, the erodible restrainer is eroded within about 30 minutes after administration to a subject.

[0075] In some implementations, the drug is selected from one or more of small molecule compounds, polypeptides, proteins, nucleic acids, antibodies, cell-containing hydrogels, probiotics, or analogs thereof. In some implementations, an active material of the drug is selected from one or more of small molecule compounds, polypeptides, and proteins.

[0076] In some embodiments, the drug is selected from one or more of riociguat, aceclofenac, bicalutamide, carbamazepine, carvedilol, clotrimazole, cinnarizine, danazol, dapsone, estradiol, ezetimibe, glibenclamide, fenofibrate, griseofulvin, ibuprofen, itraconazole, ketoconazole, mefenamic acid, naproxen, nevirapine, nifedipine, nitrofurantoin, nomegestrol acetate, phenytoin sodium salt, piroxicam, praziquantel, rifampicin, sulfamethoxazole, trimethoprim, verapamil, levodopa, carbidopa, pregabalin, apixaban, tofacitinib, metformin hydrochloride, sitagliptin, diclofenac, ciprofloxacin, gabapentin, risperidone, rosuvastatin, memantine hydrochloride, gabapentin, tapentadol, oxycodone, acetaminophen, levetiracetam, dapagliflozin, aripiprazole, lenalidomide, pioglitazone, valsartan, sacubitril, cetirizine, clozapine, domperidone, dipyridamole, compound gentamicin sulfate, ranitidine, Corydalis Rhizoma, vitamin B2, norfloxacin, diltiazem, ropinirole, gentamicin sulfate, mifepristone, and salts and stereoisomers thereof.

[0077] All references cited herein, including patent applications and publications, are incorporated herein by reference in their entireties.

[0078] A person skilled in the art will also appreciate that changes may be made to the forms and details of the implementations described herein without departing from the scope of the present disclosure. Furthermore, although various advantages, aspects, and objects have been described with reference to various implementations, the scope of the present disclosure should not be limited by reference to these advantages, aspects, and objects.

BRIEF DESCRIPTION OF DRAWINGS

[0079] FIG. 1 illustrates a pharmaceutical dosage form including a two-arm structure, where FIG. 1a is an exemplary view of the pharmaceutical dosage form in a compact state, and FIG. 1b is an exemplary view of the pharmaceutical dosage form in an expanded state.

[0080] FIG. 2 is a side cross-sectional view of a pharmaceutical dosage form including a three-arm structure in an expanded state.

[0081] FIG. 3 is a side cross-sectional view of another pharmaceutical dosage form including a three-arm structure in an expanded state.

[0082] FIG. 4 is a perspective view of a pharmaceutical dosage form including a five-arm structure in an expanded state.

[0083] FIG. 5 is a schematic structural diagram of an arm.

[0084] FIG. 6 is a schematic structural diagram of a movable member.

[0085] FIG. 7 is a schematic structural diagram of a cover.

[0086] FIG. 8 is a schematic structural diagram of a base.

[0087] FIG. 9a to FIG. 9c are top views of a pharmaceutical dosage form including a four-arm structure in an expanded state.

[0088] FIG. 10 illustrates another pharmaceutical dosage form including a four-arm structure, where FIG. 10a and FIG. 10c are exemplary views of the pharmaceutical dosage form in a compact state, and FIG. 10b and FIG. 10d are exemplary views of the pharmaceutical dosage form in an expanded state.

[0089] FIG. 11 illustrates another pharmaceutical dosage form including a two-arm structure, where FIG. 11a is an exemplary view of the pharmaceutical dosage form in a compact state, and

FIG. 11b is an exemplary view of the pharmaceutical dosage form in an expanded state.

[0090] FIG. 12 illustrates a test result of expansion of a pharmaceutical dosage form.

[0091] FIG. 13a and FIG. 13b are schematic structural diagrams of an arm.

[0092] FIG. 14 is a diagram illustrating an expanded state of a four-arm pharmaceutical dosage form.

[0093] FIG. 15 illustrates an X-ray image of a pharmaceutical dosage form in a canine body.

[0094] FIG. 16 is an exemplary diagram of a five-arm pharmaceutical dosage form in an expanded state.

DETAILED DESCRIPTION

[0095] In some aspects, an oral pharmaceutical dosage form provided herein includes a swellable material that, upon swelling, drives the overall size of the oral pharmaceutical dosage form to expand, such that the oral pharmaceutical dosage form is retained in a stomach for a desired period of time. The oral pharmaceutical dosage form provided herein is based, at least in part, on the inventors' unique insights and discoveries regarding oral pharmaceutical dosage form designs and mechanisms that provide an oral pharmaceutical dosage form that is small enough to facilitate administration to a patient and has sufficient size increase in the stomach to inhibit passage through the pylorus for a desired period of time (that is, the oral pharmaceutical dosage form is retained in the stomach for a relatively long period of time, for example, 6 hours to 3 months). In some aspects, the oral pharmaceutical dosage form of this application includes one or more arms driven by expansion of a swellable material, where the oral pharmaceutical dosage form maintains sufficient mechanical stability after size increase to be retained in the stomach for a relatively long period of time without interfering with a normal gastric function. The pharmaceutical dosage form of this application may be further configured to release, according to any desired drug release profile of one or more drugs (e.g., an immediate release profile, a sustained release profile, a delayed-sustained release profile, a pulsatile release profile, a zero-order release profile, or any combination thereof), the drug(s) therefrom.

[0096] Accordingly, in some aspects, an oral pharmaceutical dosage form for gastric retention is provided. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms a swellable material chamber, and the swellable material chamber includes a

swellable material; an arm, where the arm is operably connected to the body, and the arm rotates around the body of the oral pharmaceutical dosage form by force provided by the swellable material; and a drug. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the swellable material in the presence of gastrointestinal fluid.

[0097] I. Definitions

[0098] For the interpretation of this specification, the following definitions will apply, and where appropriate, terms used in the singular will also include the plural, and vice versa. If any of the following definitions conflicts with any document incorporated herein by reference, the definitions listed herein shall prevail.

[0099] The term "subject" as used herein refers to a mammal, including but not limited to a human, a bovine, an equine, a feline, a canine, a rodent, a rat, a mouse, a dog, or a primate. In some embodiments, the subject is a human subject.

[0100] The terms "including", "having", "containing", "comprising", and other similar forms and grammatical equivalents thereof, as used herein, are intended to be equivalent in meaning and are open-ended, as any one or more items in these terms are not meant to be an exhaustive list of such one or more items, or limited to the one or more items listed. For example, an article "including" components A, B, and C may be composed of (i.e., including only) components A, B, and C, or may include not only the components A, B, and C, but also one or more other components. Accordingly, it is intended and understood that "including" and similar forms thereof, and grammatical equivalents thereof, include the disclosure of embodiments consisting "essentially of" or "consisting of".

[0101] The terms "body axis", "central axis of the body" and other similar forms and grammatical equivalents thereof, as used herein, are intended to denote a central axis in a direction of a long side.

[0102] As used herein, the term "perpendicular dimension" and other similar forms and grammatical equivalents thereof are intended to mean the dimension of the pharmaceutical dosage form that is perpendicular to a maximum cross dimension.

[0103] Where a range of values is provided, it may be understood that, unless otherwise clearly

specified by the context, every intervening value between upper and lower limits of the range and any other stated or intervening value within the stated range is encompassed within the disclosure, subject to any expressly excluded limitations within the stated range. If the range includes one or both of the limits, a range not including one or both of the included limits is also included in the disclosure.

[0104] References herein to "about" a value or parameter include (and describe) variations pointing to the value or parameter itself. For example, a description referring to "about X" includes a description of "X".

[0105] As used herein, including in the appended claims, the singular forms "a", "an", "or" and "the" include plural referents unless the context clearly dictates otherwise.

[0106] II. Pharmaceutical dosage form

[0107] In some aspects, the present disclosure is directed to a pharmaceutical dosage form intended to achieve desired retention in a subject based on geometric differences between dosage form states before and after administration, such as a change in size of one or more dimensions. In some aspects of the description provided herein, an oral pharmaceutical dosage form is exemplified. However, it should be understood that the teachings of such a dosage form can be readily extrapolated to other pharmaceutical dosage forms, such as a dosage form suitable for vaginal or rectal administration, or even other pharmaceutical dosage forms in similar environments. In some aspects, an oral pharmaceutical dosage form for gastric retention and components thereof are provided herein. The oral pharmaceutical dosage form provided herein is configured with a swellable material, including one or more portions of the swellable material composed of the same or different materials, such that the swellable material swells upon exposure to gastrointestinal fluid and provides force to drive an increase in the size of the oral pharmaceutical dosage form. The increase in the size of the oral pharmaceutical dosage form results in the oral pharmaceutical dosage form being retained in the stomach for a relatively long period of time since the oral pharmaceutical dosage form cannot easily pass through the pylorus.

[0108] In some embodiments, the pharmaceutical dosage form or the components thereof expand due to body fluid. For example, in some embodiments, the body fluid is gastrointestinal fluid.

[0109] In some embodiments, an oral pharmaceutical dosage form for gastric retention is provided. The oral pharmaceutical dosage form includes: a body structure, where the body

structure forms a swellable material chamber, and the swellable material chamber includes a swellable material; an arm, where the arm is operably connected to the body, and the arm rotates around the body of the oral pharmaceutical dosage form by force provided by the swellable material; and a drug, where the oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the swellable material in the presence of gastrointestinal fluid.

[0110] In some specific implementations, the swellable material is a chemical material. In some specific implementations, the swellable material chamber includes a swellable material, a movable member, and an orifice, where the movable member has certain rigidity, and the swellable material pushes the movable member to move toward the orifice, thereby pushing the arm to be unfolded. In some specific implementations, the movable member is pushed out of the orifice. In some specific implementations, the movable member moves in a direction of the orifice until the movable member is blocked by a cover. In some specific implementations, the movable member has greater rigidity than the swellable material.

[0111] In some embodiments, an oral pharmaceutical dosage form for gastric retention is provided. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms a swellable material chamber, the swellable material chamber includes a swellable material, and the swellable material is at least partially wrapped with a semipermeable membrane; and a first arm, a second arm, a third arm, and a fourth arm, where the arms are operably connected to the body. The first arm, the second arm, the third arm, and the fourth arm are configured such that each of the arms rotates around a body axis by force provided by the swellable material. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention. The expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the swellable material in the presence of gastrointestinal fluid.

[0112] In some embodiments, an oral pharmaceutical dosage form for gastric retention is provided. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms a swellable material chamber, and the swellable material chamber includes a swellable material and a movable member structure, where the body structure includes a base, a

cover, and a directional channel formed by a bottom portion of the base and an opening in a top portion of the base, and the base is composed of a semipermeable membrane. Arms include a first arm, a second arm, a third arm, and a fourth arm. The arms are operably connected to the body. The swellable material absorbs a liquid and expands, and a provided force pushes the movable member to move in the directional channel closer to a top portion of the cover. The first arm, the second arm, the third arm, and the fourth arm are configured such that each of the arms rotates around a body axis through pushing by the movable member. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention. The expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the swellable material in the presence of gastrointestinal fluid.

[0113] In some embodiments, an oral pharmaceutical dosage form for gastric retention is provided. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms a swellable material chamber, and the swellable material chamber includes a swellable material; an arm, where the arm is operably connected to the body, and the arm rotates around the body of the oral pharmaceutical dosage form by force provided by the swellable material; and a drug. The oral pharmaceutical dosage form further includes an erodible restrainer, which is configured to inhibit extension of the arm in the pre-administration state. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the swellable material in the presence of gastrointestinal fluid.

[0114] As described herein, the oral pharmaceutical dosage form includes a plurality of mechanism modules that can be cooperatively assembled with each other or be integrally formed. Other sections are provided below to teach an exemplary mechanism related to providing gastric retention by the oral pharmaceutical dosage form, as well as some aspects of the oral pharmaceutical dosage form. This modular description is not intended to limit the scope of the description provided herein, and based on the teachings provided herein, a person of ordinary skill in the art will readily understand that the description includes any combination of modules combined to form an oral pharmaceutical dosage form that achieves gastric retention.

[0115] A. Exemplary pharmaceutical dosage form

[0116] To illustrate and explain the subject matter provided herein, some pharmaceutical dosage forms, such as an oral pharmaceutical dosage form, are described below. As previously described, the basic teachings described herein enable various movable arm mechanisms to provide an increase in the size of the oral pharmaceutical dosage form, such that the oral pharmaceutical dosage form cannot easily pass through the pylorus for a desired period of time, thereby exhibiting a gastric retention period. In some aspects, the oral pharmaceutical dosage form taught herein includes a mechanism for post-administration size increase.

[0117] An exemplary pharmaceutical dosage form of FIG. 1 is provided. In a pre-administration state shown in FIG. **1a**, the pharmaceutical dosage form is in a compact state. Viewed externally, the oral pharmaceutical dosage form includes a body 1 and arms 2. The body 1 includes a compartment unit, which refers to one or more cavities formed inside the body, and the cavities may or may not be in communication with the outside of the body. One end of each of the arms 2 is connected to the body, and the other end thereof extends away from the body. The pharmaceutical dosage form is designed to have two forms: a compact form before administration and an expanded form after administration. After entering the subject, the drug will change from a compact form to an expanded form within 5 to 120 minutes, depending on different uses and designs. The compartment unit of the body 1 includes an expandable material 5 and a movable member 6. The expandable material deforms when a preset trigger condition is reached, such as an increase in volume or length, enabling the movable member 6 to move. After being squeezed by the expandable material, the movable member 6 generates a moving force to push the arm 2 to move or rotate, and the pharmaceutical dosage form changes from a compact form to an expanded form, as shown in FIG. 1b. The expandable material 5 may be a swelling tablet that expands after absorbing water, or may be a gas-generating tablet that releases gas after absorbing water or other substances, or may be a spring structure. In some embodiments, the arm 2 can rotate around the body 1, and the component connecting the arm 2 to the body is located in a second compartment 4 of the compartment unit. The expandable material 5 and the movable member 6 are located in a first compartment 3 of the compartment unit. There is an orifice between the first compartment 3 and the second compartment 4, and the movable member 6 can enter the second compartment 4 from the first compartment 3 through the orifice to push the arm 2 to rotate around the body 1 until the pharmaceutical dosage form is in an expanded state.

[0118] In some specific implementations, the component connecting the arm 2 to the body 1

is located in the second compartment 4 of the compartment unit, the second compartment 4 includes at least one hole, one end of the arm 2 is located in the second compartment 4, and the other end thereof extends out of the body 1 through the hole. In another implementation, the component connecting the arm 2 to the body 1 is located outside the second compartment 4. The second compartment 4 includes at least one hole, and the movable member 6 can extend out of the body 1 through the hole. When the pharmaceutical dosage form is placed in a fluid environment, the fluid can enter the compartment unit through the hole.

[0119] In some specific implementations, the first compartment 3 and the second compartment 4 are in seamless transition. In some specific implementations, spaces of the first compartment 3 and the second compartment 4 are inconsistent in size, and preferably, the space of the first compartment 3 is larger than the space of the second compartment 4. In some specific implementations, in an expanded state of the pharmaceutical dosage form, a length from a distal end of one arm to a farthest point of the pharmaceutical dosage form is not less than 12 mm. More preferably, an expanded length of the pharmaceutical dosage form refers to the length from the distal end of one arm to the distal end of the farthest arm, and the expanded length is not less than 15 mm, or not less than 20 mm, or not less than 25 mm, or not less than 30 mm. A maximum length of the pharmaceutical dosage form in a compact state is not greater than 10 mm, or not greater than 14 mm, or not greater than 16 mm, or not greater than 18 mm, or not greater than 20 mm, or not greater than 22 mm.

[0120] In some specific implementations, in order to prevent dysphagia in a user when the pharmaceutical dosage form is used as an oral pharmaceutical dosage form, and to prevent the pharmaceutical dosage form from passing through the pylorus during gastric retention, a maximum dimension of the oral pharmaceutical dosage form in an expanded state is greater than a maximum dimension thereof in a compact state. In a preferred implementation, the maximum dimension in the expanded state is less than or equal to 2 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.9 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.8 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.7 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension

in the expanded state is less than or equal to 1.6 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.5 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.4 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.3 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.2 times the maximum dimension in the compact state; or in another preferred implementation, the maximum dimension in the expanded state is less than or equal to 1.1 times the maximum dimension in the compact state.

[0121] FIG. 2 is an implementation structure of another pharmaceutical dosage form according to the present invention. The pharmaceutical dosage form includes three arms 2a, 2b, and 2c. In this embodiment, a connecting end of each arm 2 enters a second compartment 4 through an opening 7 of a body, and the opening 7 may also serve as a fluid inlet. The body 1 in this embodiment may be integrally formed by injection molding or 3D printing. The arm 2 may alternatively be formed through printing simultaneously with the body 1 in a layer-by-layer stacking manner during 3D printing. The three arms 2a, 2b, and 2c have the same angle therebetween, and are spaced 60° apart from each other.

[0122] As shown in FIG. 2, the pharmaceutical dosage form includes a central axis ca. The pharmaceutical dosage form extends in a direction of the central axis ca in a compact state. When the pharmaceutical dosage form is in an expanded state, a central axis aa of each arm is substantially perpendicular to the central axis of the pharmaceutical dosage form. The three arms are almost in the same plane. In another optional embodiment, when the pharmaceutical dosage form is in an expanded state, an angle formed by the central axis aa of the arm and the central axis ca of the pharmaceutical dosage form may be an acute angle, a right angle, or an obtuse angle, with a preferred range of 45° to 155°, and a more preferred range of 60° to 135°, or 75° to 120°. Angles between the three arms and the central axis may be the same or different, that is, in the case of a side view, highest points of the three arms may or may not be on the same straight line.

[0123] In the embodiment shown in FIG. 2, each of the arms 2 sequentially includes a connecting end 21 connected to the body, an extension section 22, and a distal end 23 in a direction from the central axis ca. In some embodiments, the connecting end 21, the extension section 22,

and the distal end 23 have different thicknesses. In some embodiments, the drug may be carried on the extension section 22. In some embodiments, the connecting end 21 is connected to the body by a pivot. An outer side surface 22a of the extension section 22 is almost parallel to the central axis aa of the arm 2a, and an outer side surface 21a of the connecting end 21 forms an included angle of less than 30° with the central axis aa, with a more preferred range being less than 20°.

[0124] FIG. 3 is an implementation structure of another pharmaceutical dosage form according to the present invention. The pharmaceutical dosage form includes three arms 2a, 2b, and 2c. The pharmaceutical dosage form structure includes a body 1, and arms 2a, 2b, and 2c connected to the body 1. In this embodiment, a connecting end of each arm 2 enters a second compartment 4 through an opening 7 of the body, and in addition to the opening 7, the body 1 includes one or more water inlets 10. In a preferred embodiment, the water inlet 10 is in communication with a first compartment. In another preferred embodiment, a plurality of water inlets 10 are in communication with the first compartment and the second compartment respectively. The arm 2 sequentially includes a connecting end 21 connected to the body, an extension section 22, and a distal end 23 in a direction from a central axis. In this embodiment, the distal end 23 of the arm 2 includes a protrusion 211. When the arms 2 are in a compact state, the protrusions 211 at the distal ends of the three arms 2a, 2b, and 2c abut against each other, to resist deformation of the pharmaceutical dosage form caused by its own internal stress or external force, and to extend the shelf life. Preferably, an outer contour of each of the protrusions 211 is triangular or isosceles trapezoidal, and under this structure, the arms resist deformation without interfering with the unfolding of each other. Preferably, the outer contour of each of the protrusions 211 is in smooth transition, and under this structure, the arms do not cause physical damage to a mucosal surface after being expanded into a body cavity, and there is no risk of bleeding during drug retention, resulting in higher safety.

[0125] In some embodiments, an outer contour of the pharmaceutical dosage form in a compact state may be regarded as an outer surface. Preferably, the outer contour is capsule-shaped, or may be designed into different shapes such as a cylinder and a circle as needed. The outer surface of the pharmaceutical dosage form in a compact state does not contain a drug, or the drug is not exposed to the outer surface. When the pharmaceutical dosage form is placed in an environment containing liquid water, an internal pushing device of the pharmaceutical dosage form starts to work, and an expandable material expands after absorbing water, driving a movable arm

to rotate. Once the movable arm starts to rotate, the compact state begins to transform into an expanded state, and a drug-containing component located inside the pharmaceutical dosage form begins to be exposed to the aqueous environment, and the drug begins to be released in a preset manner. The drug-containing component may be carried at any position of the pharmaceutical dosage form as needed, such as on the movable arm, or in a cavity formed by the movable arm, or on the body.

[0126] FIG. 4 is an implementation structure of another pharmaceutical dosage form according to the present invention. The pharmaceutical dosage form includes five arms. As shown in FIG. 4, angles between any two of the five arms are consistent, and in the expanded state, an angle α between two arms is 36°. The pharmaceutical dosage form includes a body 1 extending in a Z axis direction. The body includes an internal chamber and an expandable structure accommodated in the internal chamber, and the internal chamber includes a fluid inlet. In the compact state of the pharmaceutical dosage form, the five arms all extend in the Z axis direction. After the arms of the drug are opened, the arms extend around XY axes, that is, extend in a direction parallel to the XY axes or at a certain included angle with the XY axes. In a preferred embodiment, a plane where a plurality of arms are located is parallel to or coincides with a plane where the XY axes are located. In another embodiment, a certain angle may be provided between each of extension directions of the plurality of arms and the plane where the XY axes are located. If the angles between the extension directions of the plurality of arms and the plane where the XY axes are located are the same, a shape similar to a cone or a trumpet mouth is presented. If the angles between the extension directions of the plurality of arms and the plane where the XY axes are located are different, it means that heights of all the arms on the Z axis are also different. In some embodiments, if the angles between the extension directions of the plurality of arms and the plane where the XY axes are located are different, it means that projections of all the arms on the Z axis are also at different heights.

[0127] In this embodiment, the drug is located on the arms. In one embodiment, a drug (API) and a polymer or only the drug forms drug particles 55. A preparation method for the drug particles 55 may be implemented by adopting the prior art, such as incorporating the drug into a polymer matrix and forming the drug particles by hot melt extrusion, or preparing the drug particles by melting and casting. The size and dimensions of the drug particles 55 may range from the nanometer scale to the millimeter scale. The dimensions and drug loading of the drug particles

may be designed according to drug selection, solubility, a release profile, and other requirements, based on common general knowledge in the field. In one embodiment, the drug particles may be uniformly distributed on the arms and continuously released according to the erosion of the arms. In one embodiment, the drug particles may be distributed on surfaces of the arms. In one embodiment, the drug particles may be located on protrusions and connecting ends of the arms.

[0128] Each of the drug particles 55 contains a drug and a matrix. The matrix material may be a water-soluble matrix or a water-insoluble material. The matrix material may be microcrystalline cellulose, synthetic polymers such as poly(vinyl chloride), poly(vinyl acetate), copolymers of vinyl acetate and ethylene, polystyrene, or the like. The matrix material may further include a release modifier, such as hydroxypropyl cellulose (HPC), hydroxypropyl methylcellulose (HPMC), methylcellulose, poly(N-vinyl-2-pyrrolidone) (PVP), poly(ethylene oxide) (PEO), poly(vinyl alcohol) (PVA), xanthan gum, carrageenan, lactose, sucrose, glucose, mannitol, and other such natural and synthetic materials.

[0129] FIG. 5 to FIG. 8 are schematic structural diagrams of various components forming the pharmaceutical dosage form in one embodiment.

[0130] FIG. 5 is a schematic structural diagram of a movable arm. As shown in FIG. 5, the movable arm 2 includes a connecting end 21, an extension section 22, and a distal end 23. In one embodiment, a protrusion 211 extends from the distal end 23. The connecting end 21 includes a pivot 233 connected to the body, and a neck 232 connected to the pivot. The neck 232 is connected to the extension section 22 through a transition section 231. In some embodiments, the width of the neck may be the same as the widths of the extension section 22 and the transition section 231. In some embodiments, the width of the neck may be slightly smaller than that of the extension section 22. The inventors have found that if a ratio of the width of the extension section to the width of the neck is set within a range of less than or equal to 5:1, it can not only meet mechanical strength requirements, but also minimize the interference received by the movable arm during unfolding. In one embodiment, the extension section 22 of the movable arm 2 includes a drug-carrying groove 221, which may be configured to be filled with a single drug or a mixture of a drug and other pharmaceutical excipients. In one embodiment, the drug or the mixture of a drug and other pharmaceutical excipients may be disposed on the surface of the movable arm 2. In one embodiment, it may be formed from a drug, or by blending a drug with a material for fabricating the movable arm 2.

[0131] A pushing member 234 is included adjacent to a pivot of the connecting end 21. The pushing member 234 is configured to abut against the movable member, and when the movable member moves directionally, the pushing member 234 is pushed to rotate around the pivot. The pushing member 234 includes a bottom surface connected to the connecting end 21 and a side surface 234a. In a preferred embodiment, the pushing member 234 includes four side surfaces 234a, and the four side surfaces 234a are triangular or trapezoidal separately or simultaneously. In a preferred embodiment, the pushing member 234 is a hemispherical member.

[0132] The protrusion 211, the distal end 23, and the extension section 22 of the movable arm are all rounded or passivated, and all contact surfaces or contact corners with the body cavity have no sharp edges, which improves the safety of a pharmaceutical preparation.

[0133] FIG. 6a and FIG. 6b are different schematic structural diagrams of a movable member. As shown in FIG. 6, the movable member 6 includes a bottom member 61 and a top member 62. In a preferred embodiment, a maximum width of the bottom member 61 is greater than that of the top member. In some embodiments, a bottom surface of the bottom member 61 is annular or circular. The top member is a cylinder. In a preferred embodiment, the bottom member 61 and the top member 62 are rounded, and the top member 62 further includes an arcuate top 64. In a preferred embodiment, a top surface of the top member 62 is a flat surface. The top member 62 of the movable member primarily functions as a guide. As the volume of the expandable material within the first compartment varies, force acting on any point of the bottom member 61 of the movable member 6 may be converted into directional displacement of the movable member 6. In some preferred embodiments, the bottom member 61 of the movable member 6 matches an internal space of the first compartment, that is, the shape of the bottom member 61 is the same as the shape of the first compartment, and the bottom surface dimension of the bottom member 61 is slightly smaller than the cross-sectional dimension of the first compartment, so as to ensure that a moving direction of the movable member is basically parallel to or coincides with the central axis. In some preferred embodiments, the height of the top member 62 is greater than or equal to the height of the bottom surface of the connecting end of the arm, so as to prevent the movable member 6 of the pharmaceutical preparation from returning to the first compartment again from the second compartment.

[0134] In a preferred embodiment, an overall outer contour of the movable member 6 is cylindrical, that is, the bottom member 61 and the top member 62 are consistent in shape and

dimension. In a preferred embodiment, the overall outer contour of the movable member 6 is columnar, and a side surface thereof includes an engagement feature. In this embodiment, the engagement feature is at least one groove or rib 65 located on the side surface of the movable member 6. In this embodiment, the first compartment has a side wall with the same shape as the movable member 6, and the rib 65 is accommodated in a space formed by the side wall, or the side wall is accommodated in a space formed by the groove 65. When the volume of the expandable material in the first compartment changes, the movable member 6 moves from the first compartment to the second compartment. When the movable member 6 completely enters the second compartment, the groove or the rib 65 prevents the movable member 6 from returning to the first compartment. FIG. 7 is a schematic structural diagram of a cover. As shown in FIG. 7, the cover 8 includes openings 7, and a quantity of the openings 7 is consistent with the quantity of arms. An interior of the cover 8 includes a cavity to form a second compartment 4. In a compact state, the second compartment 4 is configured to accommodate at least a portion of the connecting end of the movable arm, such as a pushing member. In an expanded state, the second compartment 4 is configured to accommodate at least a part of the movable member 6. The cover 8 includes an upper top surface 83, and a lower top surface located inside the second compartment 4. The shape of the lower top surface matches the shapes of the arcuate top and the top member 62 of the movable member. When the movable member enters the second compartment 4 from the first compartment 3, the pushing member 234 is subjected to force from the movable member 6, rotates around the pivot, and rotates from the space inside the second compartment 4 to the opening 7. Since the shape of the lower top surface matches the shapes of the arcuate top and the top member 62 of the movable member, the movable member cannot return to the first compartment 3 after entering the second compartment 4. In some preferred embodiments, the lower top surface in the second compartment 4 may further include an engagement feature for fixing the movable member, and the engagement feature may be a mechanical structure, a binder, a magnetic structure, or other means. For example, a snap-fit blind hole or a snap-fit through hole may be provided in the lower top surface in the second compartment 4, and a snap-fit member that matches the shape of the snap-fit blind hole or snap-fit through hole may be arranged on the top member of the movable member. When the snap-fit member of the movable member enters a snap-fit hole, the two cannot be separated unless an excessive external force is applied.

[0135] In another implementation of the cover 8, the cover 8 has only one opening, and the

top member 62 of the movable member 6 may extend out through the opening to abut against an arm located on the outer surface of the cover 8. After being subjected to force, the arm moves or rotates, enabling the pharmaceutical dosage form to change from a pre-administration state in a compact form to a post-administration state in an expanded form. In this implementation, the arm may be provided with a hinge connected to the outer surface of the cover 8.

[0136] A pivot hole 82 is provided in the second compartment 4, and is configured to accommodate the pivot of the arm. In some preferred embodiments, the second compartment 4 and the pivot hole 82 are in communication with an external space through the opening 7. The cover 8 further includes several snap-fit members 81 for engaging with the base. In some preferred embodiments, the width of the opening 7 includes a first width L1 close to the outer side surface and a second width L2 close to the center, where L1 is greater than or equal to L2, to reduce contact and friction that may occur between the arm and the cover 8 during expansion of the arm.

[0137] In another preferred embodiment, the cover 8 may be designed from an integral structure into an upper cover and a lower cover. When the upper cover and the lower cover are closed, a second compartment and a pivot hole are formed. The lower cover may be an annular structure or a bottom surface, and the shape and dimension of the annular structure or the bottom surface may match the upper surface of the top member of the movable member. The engagement feature for the movable member may alternatively be arranged on the bottom surface of the lower cover.

[0138] FIG. 8 is a schematic structural diagram of a base. As shown in FIG. 8, the base 9 includes a wall 91 forming a first compartment 3, and a water inlet 10 located in the wall 91. The base 9 further includes a snap-fit groove 91 for snap-fit connection with the cover 8.

[0139] Each component constituting the pharmaceutical dosage form in FIG. 5 to FIG. 8 may be composed of pharmaceutical excipients, and may be selected from one or more of the following materials: ammonium methacrylate copolymer, ammonium methacrylate B type copolymer, stearic acid, ethyl cellulose (EC), titanium dioxide, cellulose acetate phthalate (CAP), poly(lactide-co-glycolide) (PLGA), ethylene-vinyl acetate copolymer, polyethylene (PE), polycaprolactone (PCL), polylactic acid (PLA), allulose acetate butyrate (CAB), cellulose acetate (CA), polyvinyl acetate (PVAc), polyvinylacetal diethylaminoacetate (AEA), poly(butyl methacrylate-co-(2-dimethylaminoethyl) methacrylate-co-methyl methacrylate) and poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride), or a combination thereof. The

material composition of each component may further include any one or more of a plasticizer and another additive, such as a filler, a binder, a lubricant, a glidant, and a disintegrant. In some specific implementations, the additive is selected from clay, SiC nanoparticles, Ni powder, carbon nanotubes, carbon fibers, carbon black, graphene, metal oxides (e.g., Fe_3O_4, TiO_2, ZnO), silver (Ag) nanoparticles, gold (Au) nanoparticles, silver and gold nanoparticles, nanorods, nanowhiskers, nanowires, and cellulose nanocrystals. In some embodiments, each component constituting the pharmaceutical dosage form may be made of an imaging material, or include a component formed of an imaging material.

[0140] In another preferred embodiment, the wall of the base 9 is composed of a semipermeable material or a semipermeable membrane. The base 9 made of a semipermeable material or a semipermeable membrane is not provided with a water inlet 10.

[0141] FIG. 9 is a top view of an expanded structure of another pharmaceutical dosage form according to the present invention. The pharmaceutical dosage form includes four arms. The pharmaceutical dosage form in FIG. 9a includes a body, and arms 20a, 20b, 20c, and 20d. In the top view of the expanded structure, it can be seen that a connecting end 201 of each of the arms is connected to the body through an opening 700. The connecting end includes a pushing member 260. A width of an extension section 240 is greater than a width of the connecting end 201. In some embodiments, one or more drug-carrying grooves 240 may be provided in an inner side surface of the extension section 240. As shown in FIG. 9a, in the top view of the expanded structure, it can be seen that the drug-carrying groove 240 is exposed to a plane perpendicular to the central axis ca of the pharmaceutical dosage form, which is beneficial for precisely controlling the release of the drug. In the compact state, the four arms are closed, the drug-carrying grooves 240 are located in the internal spaces of the four arms, and no drug is exposed to the outer surface of the pharmaceutical dosage form. In this embodiment, a bottom portion of each of the drug-carrying grooves 240 includes an imaging layer, and a drug-containing layer is located above the imaging layer. The imaging layer can track the unfolding of the arms of the drug and its retention at different positions after the drug enters a human or animal body.

[0142] In another preferred embodiment, a compartment within the body can also serve as a drug-carrying groove, and the drug can be released through the opening 700 or another through hole.

[0143] As shown in FIG. 9b, in some embodiments, the pharmaceutical dosage form further

includes a reinforcing rib. For example, a reinforcing rib 301 may be arranged on the upper top surface of the body, or a reinforcing rib 302 may be arranged on the inner side surface of the connecting end of the arm, or a reinforcing rib 302 may be arranged on the outer side surface of the connecting end of the arm.

[0144] The reinforcing rib may be in the shape of a straight line, a cross, *, #, Ω, U, or a grid.

[0145] As shown in FIG. 9c, in some embodiments, reinforcing ribs 302 of the pharmaceutical dosage form are arranged at necks of the arms 20a, 20b, 20c, and 20d. In the unfolded state of the arms, the reinforcing ribs 302 located at the necks each abut against or are close to an outer wall of the body, and have better resistance to lateral bending. In some embodiments, a reinforcing rib 301 of the pharmaceutical dosage form is arranged on an inner wall of the cover of the body.

[0146] FIG. 10a and FIG. 10b illustrate an implementation structure of another pharmaceutical dosage form according to the present invention, including a cross-sectional view in a compact state and a cross-sectional view in an expanded state. The pharmaceutical dosage form includes four arms. The pharmaceutical dosage form includes a body, and arms 20a, 20b, 20c, and 20d (not shown in the figure). The body includes a base 30, a cover 40, and a pushing plunger 50. In the compact state, the pushing plunger 50 is located in a first compartment 70. The arms 20a, 20b, 20c, and 20d each include a connecting end and a protrusion 211 away from the connecting end. Each arm includes a rotation center Ra located at the connecting end, and the arm can rotate by 45° to 135° around the rotation center Ra. The connecting end includes an outer side surface 200a, a bottom surface 200b, and an inner side surface 200c. The bottom surface 200b and the inner side surface 200c extend to form a pushing member 90. In some preferred embodiments, in the compact state, the outer side surface 200a of the connecting end is substantially flush with an outer side surface 42 of the body. In some preferred embodiments, in the compact state, the outer side surface 200a of the connecting end does not exceed the outer side surface 42 of the body. An angle β formed by the outer side surface 200a and the bottom surface 200b of the connecting end is greater than or equal to 90°, so as to facilitate the rotation center Ra being closer to the direction of the central axis. An angle γ between the bottom surface 200b of the connecting end and the side surface 200c of the pushing member is less than 90°, more preferably less than 60°. In the compact state, the pushing member 90 of the connecting end is located in a second compartment 80. In the expanded state, the connecting end rotates around Ra, and the pushing member 90 moves from the second compartment 80 to a position of an opening.

[0147] FIG. 10c is a cross-sectional view of another four-arm pharmaceutical dosage form in a compact state. The pharmaceutical dosage form includes a body, and arms 20a, 20b, 20c, and 20d (not shown in the figure). The body includes an expandable material 5 located in a first compartment, a movable member 6, and a water inlet 10 located on the body. The body further includes a second compartment, and the second compartment accommodates a connecting end 200 of each of the arms. The arm includes a drug component 800 accommodated in a drug-carrying groove. An interior of the movable member 6 may include a cavity, and the drug component 800 may be loaded in the cavity. In some preferred embodiments, the cavity of the movable member 6 has only one opening, and the opening of the cavity faces the expandable material 5. After the pharmaceutical dosage form enters a body cavity of a human or an animal, body fluid comes into contact with the expandable material 5 through the water inlet 10, and after expanding, the expandable material 5 pushes the movable member 6 into the second compartment. The connecting end 200 of the arm is pushed by the movable member 6 to be unfolded. The drug component 800 on the arm may be an immediate-release drug component or a sustained-release drug component, and is released after the arm is unfolded. The expandable material 5 may be selected from materials that erode after expansion, and a specific erosion rate can be selected according to a required retention time. After the expandable material 5 is fully or partially eroded, the body fluid enters the cavity of the movable member 6, and the drug component 800 located inside the cavity begins to be released.

[0148] In some preferred embodiments, a reinforcing rib 303 is arranged on a peripheral side surface 200a of the connecting end of the arm. The reinforcing rib 303 can serve as an engagement feature between the arm and the body after the arm is unfolded. In some preferred embodiments, the reinforcing rib 303 is configured to provide stability to the arm in an unfolded state. The arm rotates by 90° around a pivot from a pre-administration state in a compact form to reach a post-administration unfolded state, and the reinforcing rib 303 abuts against an outer surface of the body, that is, the reinforcing rib 303 comes into contact with the outer surface of the body. When the pharmaceutical dosage form is located in the human stomach and is subjected to an external force, such as an excessive force on the arm due to gastric peristalsis or food factors, the reinforcing rib 303 can share the force and provide stability for the overall expanded structure.

[0149] In some preferred embodiments, the bottom surface 200b of the connecting end includes an engagement feature 280 for engagement with an engagement feature on the pushing

plunger 50. In the expanded state, the pushing plunger 50 moves from the first compartment 70 to the second compartment 80, and the pushing member 90 synchronously moves from the second compartment 80 to the position of the opening. The engagement feature on the pushing plunger 50 mates with the engagement feature 280 on the bottom surface 200b of the connecting end to lock the arm, so that the arm cannot return from the second compartment 80 to the first compartment 70. In some preferred embodiments, the engagement feature on the pushing plunger 50 and/or the engagement feature 280 on the bottom surface 200 of the connecting end may be made of an erodible material. When a preset retention time is reached, the engagement feature disappears, and the pushing plunger 50 can return from the second compartment 80 to the first compartment 70. The arms 20a, 20b, 20c, and 20d are not supported by an external force, and can fold or close with an external environment, thereby ending the retention.

[0150] In some preferred embodiments, the engagement feature on the pushing plunger 50 is an annular groove, and the annular groove extends a full circle along an outer surface of the pushing plunger 50. This embodiment can overcome the failure of the engagement feature caused by the rotation of the pushing plunger 50 around the central axis in the first compartment 70 and/or the second compartment 80.

[0151] In some preferred embodiments, a peripheral surface of the pushing plunger 50 may be provided with a binder, and the binder may be bonded to the bottom surface of the arm to support an unfolded form of the arm. The binder is selected from one or more of the following materials: dextrin, xanthan gum, maltodextrin, povidone, methylcellulose, ethylcellulose, zein, fructose, poloxamer, sodium alginate, pregelatinized starch, hydroxypropyl cellulose, hydroxypropyl methylcellulose, carbomer, starch, gum arabic, microcrystalline cellulose, sodium lauryl sulfate, sucrose, cellulose acetate, polysorbate, glucose, dextran, compressible sugar, carrageenan, modified starch, tragacanth, and honey.

[0152] In some preferred embodiments, the engagement feature may alternatively be disposed in the internal space of the body, such as on the inner wall of the base 30. For example, the inner wall of the first compartment 70 formed by the base 30 is provided with a sloped section with an inclined angle. When entering the second compartment 80 from the first compartment 70 along the sloped section, the pushing plunger 50 cannot return to the first compartment 70 due to the presence of the sloped section.

[0153] In some preferred embodiments, protrusions 211 of the arms 20a, 20b, 20c, and 20d

are in contact with each other in pairs in a compact state. In some other preferred embodiments, there are erodible components between the protrusions 211 of the arms 20a, 20b, 20c, and 20d. The erodible components may each be shaped as a quadrilateral matching the shapes of the protrusions 211, to retain the arms in the compact state and prevent premature unfolding before or during administration.

[0154] In some preferred embodiments, the entire pharmaceutical dosage form may be loaded in a capsule shell, and only after the capsule ruptures, dissolves or disintegrates can water enter the expandable material chamber through the fluid inlet.

[0155] In some preferred embodiments, as shown in FIG. 10d, the shape of the movable member 6 also constitutes an engagement feature. In a preferred embodiment, the movable member 6 includes a bottom member 61 and a top member 62. In this embodiment, the top member 62 is a flat top. A height value of the top member 62 is greater than or equal to a length value of the bottom surface 200b of the connecting end of the arm. In a preferred embodiment, the height value of the top member 62 is about 1.1 to 1.3 times the length value of the bottom surface 200b of the connecting end of the arm. The height value of the top member 62 being greater than or equal to the length value of the bottom surface 200b of the connecting end of the arm can prevent the movable member 6 from returning to the first compartment after the movable member engages with the connecting end of the arm. In a preferred embodiment, an included angle of less than or equal to 90° is formed between a peripheral surface of the top member 62 of the movable member 6 and a top surface of the bottom member 61. In a preferred embodiment, this included angle δ ranges from 89° to 70°.

[0156] FIG. 11a and FIG. 11b are cross-sectional views of another pharmaceutical dosage form according to the present invention in a compact state and an expanded state, respectively. As shown in FIG. 11a, the pharmaceutical dosage form includes a body 1010 and a movable arm 1020. The body forms a first compartment 1030 and a second compartment 1040. The first compartment 1030 and the second compartment 1040 communicate through an orifice. An expandable material 1050 is located in the first compartment 1030. In the compact state, the first compartment 1030 further includes a movable member 1060. The movable member 1060 may be shaped as a plunger, a hollow cylinder, or another configuration that can be properly accommodated within the first compartment 1030.

[0157] In some embodiments, the upper top surface of the body 1010 is further provided with

a central post 1011. The central post 1011 can enhance mechanical properties of the pharmaceutical dosage form, and maintain the length along the central axis within a preset range when the pharmaceutical dosage form transitions from the compact state to the expanded state. In the structure of a two-arm pharmaceutical dosage form, the design incorporating the central post 1011 enables the pharmaceutical dosage form to extend at least along a YZ plane in the expanded state. In the structure of a three-arm pharmaceutical dosage form or a pharmaceutical dosage form with more arms, the design incorporating the central post 1011 enables the pharmaceutical dosage form to extend along both an XY plane and the YZ plane simultaneously in the expanded state.

[0158] In some embodiments, the central post 1011 is a drug-carrying post. The central post 1011 may be provided with at least one drug-carrying groove, or a drug-carrying layer may be coated on the surface of the central post, or the central post as a whole may be of an erodible structure containing drug particles, or the central post may be of a layered structure including a drug-containing layer and an erodible structure, and so on.

[0159] In some embodiments, in the compact state, the central post 1011 is located in an accommodating space formed by a plurality of arms 1020, and the length of the central post 1011 is less than the length of each of the arms. In the expanded state, after the arms 1020 move, a drug in the central post 1011 is exposed to body fluid, and the drug begins to be released.

[0160] In some embodiments, the pharmaceutical dosage form further includes a restraining member 1070. The restraining member 1070 may be designed as a capsule shell, a restraining ring, a restraining band, a restraining cover, or the like. In a preferred embodiment, the restraining member 1070 is made of a material that dissolves in a short time, such as polyvinylpyrrolidone, TEC, gelatin, hydroxypropyl methylcellulose, and pullulan. In different embodiments, restraint duration can be controlled by geometric features of the restraining member.

[0161] In some embodiments, the restraining member 1070 can release the inhibition on the movement of the movable arm within 45 minutes. In a more preferred embodiment, the restraining member 1070 can release the inhibition within 35 minutes, or within 25 minutes. In a more preferred embodiment, the restraint duration of the restraining member 1070 is not less than 5 minutes, or not less than 8 minutes, or not less than 12 minutes, or not less than 15 minutes. An appropriate time to release the inhibition can ensure that the drug does not prematurely expand in the oral cavity or esophagus, and rapidly transitions from the compact state to the expanded state upon reaching a predetermined position, thereby preventing the drug from passing through the

gastric pylorus while in the compact state.

[0162] In some embodiments, portions of the oral pharmaceutical dosage form can be produced, for example, by three-dimensional printing, injection molding, ultrasonic welding, or any combination thereof, and then assembled to form a pre-administration oral pharmaceutical dosage form. For example, in some embodiments, the base, the cover, and the movable arms may be prepared separately, and these components are subsequently assembled to form an oral pharmaceutical dosage form.

[0163] B. Components and materials of the pharmaceutical dosage form

[0164] The pharmaceutical dosage forms described herein include one or more features that generate force that facilitates the change of the pharmaceutical dosage form from a pre-administration state to a post-administration state. In some embodiments, the pharmaceutical dosage form includes a swellable material. The swellable material described herein is configured to expand in the presence of gastrointestinal fluid and generate force applied to the arms, or the swellable material pushes the movable member to move toward the top portion of the cover within the directional channel, and the force applied to the arms causes the arms to rotate around the body and be unfolded into a petal-like shape, so that the oral pharmaceutical dosage form transforms into an expanded post-administration form.

[0165] In some specific implementations, the swellable material and/or the swellable material is configured to expand at a desired rate and/or with a desired force. For example, in some embodiments, the swellable material and/or the swellable material is configured to swell or expand rapidly upon contact with gastrointestinal fluid (including contact of the oral pharmaceutical dosage form with gastrointestinal fluid) to prevent the oral pharmaceutical dosage form from passing through the stomach prior to a required gastric retention period for retention in the stomach. In some embodiments, the swellable material and/or the swellable material is configured to swell or expand with a necessary force to move components of the oral pharmaceutical dosage form to a gastric retention state, for example, to move one or more movable arms.

[0166] In some specific implementations, upon exposure to gastrointestinal fluid, the volume of the swellable material increases by at least about 1.2 times, for example, at least about 1.3 times, 1.4 times, 1.5 times, 1.6 times, 1.7 times, 1.8 times, 1.9 times, or 2.0 times. In some embodiments, expansion occurs within about 1 hour, for example, within any of about 50 minutes, 40 minutes, 30 minutes, 20 minutes, 10 minutes, or 5 minutes. In some embodiments, the swellable material

expands by at least about 1.2 times within 30 minutes, for example, at least about 1.3 times in volume within 30 minutes upon exposure to gastrointestinal fluid, 1.4 times within 30 minutes, 1.5 times within 30 minutes, 1.6 times within 30 minutes, 1.7 times within 30 minutes, 1.8 times within 30 minutes, 1.9 times within 30 minutes, or 2.0 times within 30 minutes. In some embodiments, the swellable material reaches a substantially fully swollen state (e.g., absorbing at least about 90% of the fluid volume) within about 1 hour or less, for example, within about 50 minutes, 40 minutes, 30 minutes, 20 minutes, 10 minutes, or 5 minutes.

[0167] In some specific implementations, the swellable material, during swelling, at least partially conforms to the shape of the directional channel and/or the orifice or a portion thereof. In some specific implementations, when the swellable material expands, the swellable material pushes the movable member to move toward the top portion of the cover within the directional channel. In some specific implementations, the swellable material is partially or completely surrounded by the base. In some specific implementations, the swellable material is completely or partially surrounded by a semipermeable material.

[0168] The terms "semipermeable", "semipermeable membrane" or "semipermeable material" refer to a membrane through which water can readily diffuse, while solutes dissolved in water generally cannot readily diffuse through the membrane relative to a rate at which water diffuses through the membrane.

[0169] In some specific implementations, the swellable material is selected from sodium alginate (SA), hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), hydroxypropyl methylcellulose (HPMC), polyethylene oxide (PEO), polyvinyl alcohol (PVA), microcrystalline cellulose (MCC), croscarmellose sodium (CCNa), carboxymethyl cellulose sodium (CMC-Na), polyvinylpolypyrrolidone (PVPP), sodium carboxymethyl starch (CMS-Na), polyethylene glycol (PEG), or a mixture thereof. In some embodiments, HPC includes L-HPC or H-HPC, or a combination thereof.

[0170] In some specific implementations, the swellable material includes a material selected from the group consisting of: polyvinyl acetate (PVAc), povidone, hydroxypropyl methylcellulose phthalate, methacrylic acid copolymer, ethyl cellulose (EC), hydroxypropyl methylcellulose (HPMC), tocopheryl polyethylene glycol succinate (TPGS), polycaprolactone (PCL), polyethylene (PE), guar gum, polyetheretherketone (PEEK), polyphenylsulfone (PPSU), polysulfone (PSU), polypropylene (PP), ethylene vinyl acetate (EVA), poly(methyl methacrylate)

(PMMA), polylactic acid (PLA), polyglycolide (PGA), poly(lactic-co-glycolic acid) (PLGA), or combinations thereof.

[0171] In some specific implementations, the swellable material includes a material selected from the group consisting of: cross-linked polymers and shape memory materials. In some embodiments, the swellable material includes a material selected from the group consisting of: a poly(ethylene oxide)-poly(ethylene glycol) (PEO-PEG) cross-linked polymer, polycaprolactone-polyethylene glycol-polycaprolactone (PCL-PEG-PCL), hydroxypropyl cellulose, polyethylene oxide (PEO), such as high molecular weight PEO, sodium alginate, carbomer, high molecular weight hydroxypropyl cellulose (HPC), high molecular weight hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), high molecular weight polyvinyl alcohol (PVA), polyvinyl acetate (PVAc) and polyvinylpyrrolidone (PVP) 80/20, a methacrylate copolymer, an aminoalkyl methacrylate copolymer, aminoalkyl methacrylate copolymer E, hydroxypropyl methylcellulose acetate succinate (HPMCAS), hydroxypropyl methylcellulose phthalate (HPMCP), or a combination thereof. In some specific implementations, the shape-memory material is selected from polyurethane; block copolymers of polyethylene terephthalate (PET) and poly(ethylene oxide) (PEO); block copolymers containing polystyrene and poly(1,4-butadiene); ABA triblock copolymers prepared from poly(2-methyl-2-oxazoline) and polytetrahydrofuran; polynorbornene (e.g., Norsorex, developed by CdF Chemie/Nippon Zeon); composites of polynorbornene and partially substituted polyhedral oligomeric silsesquioxane (POSS); composites composed of polycyclooctene (PCOE) and poly(5-norbornene-exo,exo-2,3-dicarboxylic anhydride) (PNBEDCA); polyester-urethanes; composite materials formed by combining polyols (soft segments) and diisocyanates with chain extenders (hard phase) (poly(ε-caprolactone) (PCL), poly(ethylene adipate) (PEA) ethylene glycol); combinations of polyester-polyurethane (PUR) and PCL and ethylene oxide–ethylene terephthalate segment copolymers; PUR based on PUR (ε-caprolactone) and oligo(p-dioxanone); poly(p-dioxanone)-b-poly(tetramethylene glycol) multiblock copolymers; poly(methyl methacrylate)-poly(ethylene glycol) (PMMA-PEG) semi-interpenetrating networks (IPN); a crosslinked polymer of poly(cyclohexyl methacrylate) (PCHMA) backbones and difunctional PCL polymers; polymers with short PEG side chains grafted onto PCL backbones; Nafion®; copoly(ester-urethane) networks; covalently crosslinked poly[ethylene-co-(vinyl acetate)] (cPEVA); combinations of PCL and poly(tetramethylene ether) glycol (PTMEG); or combinations thereof. In some specific implementations, the material may

have various properties, including a swellable material and a shape memory material.

[0172] In some specific implementations, the swellable material further includes a salt or a mixture of salts, for example, to promote the absorption of gastrointestinal fluid to facilitate swelling. In some embodiments, the salt is selected from the group consisting of sodium salts, magnesium salts, and potassium salts. In some embodiments, the sodium salt is sodium sulfate.

[0173] In some specific implementations, the swellable material further includes a gas-generating substance, for example, to generate carbon dioxide by contact with gastrointestinal fluid, and in some embodiments, the gas-generating substance is selected from a carbonate, a bicarbonate, or a combination thereof.

[0174] In some specific implementations, the amount of swellable material in the swellable material chamber is at least about 5 mg, for example, at least about 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 75 mg, 100 mg, 125 mg, 150 mg, 175 mg, or 200 mg.

[0175] In some specific implementations, the swellable material has a swelling volume of about 10 mm^3 to about 50 mm^3. In some specific implementations, the swellable material has a swelling volume of at least about 5 mm^3, for example, any one of at least about 10 mm^3, 15 mm^3, 20 mm^3, 25 mm^3, 30 mm^3, 35 mm^3, 40 mm^3, 45 mm^3, or 50 mm^3.

[0176] In some specific implementations, the swellable material may be printed by a three-dimensional printing process, injection molding, ultrasonic welding, or any combination thereof, as described in other aspects of the present disclosure. In some specific implementations, the swellable material is a thermoformable material.

[0177] In some specific implementations, the body includes two or more components, which are configured as the body. In some embodiments, the body includes one or more bases and one or more covers. In some specific implementations, the body includes two or more materials. In some embodiments, the body of the oral pharmaceutical dosage form is of an integral structure. In some embodiments, the body may be partially or entirely composed of a semipermeable membrane. In some embodiments, the base and the cover are mated to form an integral structure by snap-fit, screw-threads, a mortise and tenon joint, binder bonding, riveting, 3D printing, or injection molding. In some embodiments, the base surrounds a portion of the cover. In some embodiments, the cover is configured to prevent the swellable material, the plunger, or the movable member from further moving, thereby retaining the arm in one or more extended positions. In some embodiments, the cover is in the shape of a reserved orifice, including a trumpet shape, a circular shape, a

semicircular shape, a square shape, and an elliptical shape. In some embodiments, the cover is provided with reinforcing ribs in the shape of a cross, *, or #. In some specific implementations, the body may be printed by a three-dimensional printing process, injection molding, ultrasonic welding, or any combination thereof, as described in other aspects of the present disclosure. In some specific implementations, the body is composed of a thermoformable material.

[0178] In some specific implementations, the body is connected to the arm. In some specific implementations, the cover is connected to the arm. In some specific implementations, a locking structure is provided between the cover and the arm, including a locking pin, a latch, and a pivot. In some embodiments, the swellable material chamber surrounds the swellable material; the swellable material chamber may be of any dimension and/or shape.

[0179] As described herein, the oral pharmaceutical dosage form includes one or more arms, such as any of 1, 2, 3, 4, 5, 6, 7, 8, or 10. The arm may be designed using several mechanisms of swelling based on the swellable material, and the oral pharmaceutical dosage form may implement one or more such mechanisms. In some embodiments, the arm or a portion thereof is configured to slide within a directional channel. In some embodiments, the arm is configured to rotate along an axis. In some embodiments, at least two movable arms or oral pharmaceutical dosage forms have different movement mechanisms. In some embodiments, at least two arms of the oral pharmaceutical dosage form have the same movement mechanism. In some embodiments, at least two arms of the oral pharmaceutical dosage form are configured such that at least a portion of each arm can be extended out of or farther beyond the body of the oral pharmaceutical dosage form by using force provided by the swellable material. In some embodiments, at least two arms of the oral pharmaceutical dosage form are configured such that at least a portion of each arm can be extended out of or farther beyond the body of the oral pharmaceutical dosage form through pushing by the movable member.

[0180] In some specific implementations, the distal end of the arm is curved. In some specific implementations, when the oral pharmaceutical dosage form is in an expanded state, the connecting end of the arm is provided with an inner angle α of the arm close to the base, and an inner angle β of the arm close to the top portion of the cover, where the inner angle α of the arm ranges from 70° to 120°, for example, 70°, 75°, 80°, 85°, 90°, 95°, 100°, 105°, 110°, 115°, or 120°; and the inner angle β of the arm ranges from 30° to 90°, for example, 30°, 35°, 40°, 45°, 50°, 55°, 60°, 65°, 70°, 75°, 80°, 85°, or 90°. In some specific implementations, the arms are in contact with

each other before administration to be in a folded state. In some specific implementations, the outer surface of the arm is a smooth continuous curved surface.

[0181] In some specific implementations, the oral pharmaceutical dosage form further includes an erodible restrainer configured to inhibit extension of one or more arms for a period of time. Generally, the erodible restrainer is configured to facilitate oral administration of the oral pharmaceutical dosage form, for example, by preventing one or more arms from extending prematurely before entering the stomach of a subject. In some embodiments, the erodible restrainer is eroded within about 30 minutes after administration to a subject, for example, within any one of about 25 minutes, 20 minutes, 15 minutes, 10 minutes, or 5 minutes.

[0182] In some specific implementations, the erodible restrainer may be a capsule shell, a restraining ring, a restraining band, a restraining cover, or the like. The erodible restrainer is formed from a material selected from the group consisting of polyvinylpyrrolidone, TEC, gelatin, hydroxypropyl methylcellulose, and pullulan.

[0183] In some specific implementations, a component of the oral pharmaceutical dosage form, such as the body or the movable arm, includes an insoluble substance and a pH-sensitive erodible material, for example, a material that does not erode or erodes slowly at the pH of the stomach, and can erode after leaving the stomach. In some specific implementations, the body or the arm of the pharmaceutical dosage form includes a material selected from the group consisting of: ammonium methacrylate copolymer, ammonium methacrylate copolymer type B, stearic acid, ethyl cellulose (EC), titanium dioxide, cellulose acetate phthalate (CAP), poly(lactide-co-glycolide) (PLGA), ethylene-vinyl acetate copolymer, polyethylene (PE), polycaprolactone (PCL), polylactic acid (PLA), allulose acetate butyrate (CAB), cellulose acetate (CA), polyvinyl acetate (PVAc), polyvinylacetal diethylaminoacetate (AEA), poly(butyl methacrylate-co-(2-dimethylaminoethyl) methacrylate-co-methyl methacrylate) and poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride), or a combination thereof.

[0184] In some specific implementations, a material of a component of the pharmaceutical dosage form, such as the body or the arm, is a thermoplastic material. In some specific implementations, the thermoplastic material is a thermoplastic polymer. In some specific implementations, the thermoplastic material includes any one or more of a plasticizer and another additive, such as a filler, a binder, a lubricant, a glidant, and a disintegrant. In some specific implementations, the additive is selected from clay, SiC nanoparticles, Ni powder, carbon

nanotubes, carbon fibers, carbon black, graphene, metal oxides (e.g., Fe_3O_4, TiO_2, ZnO), silver (Ag) nanoparticles, gold (Au) nanoparticles, silver and gold nanoparticles, nanorods, nanowhiskers, nanowires, and cellulose nanocrystals.

[0185] In some specific implementations, the body is configured to have a wall thickness (e.g., from a swellable material compartment to an outer portion of the oral pharmaceutical dosage form or from the directional channel to the outer portion of the oral pharmaceutical dosage form) of at least about 0.3 mm for example, at least about 0.3 mm, for example, at least about 0.6 mm, 0.7 mm, 0.8 mm, 0.9 mm, 1.0 mm, 1.1 mm, 1.2 mm, 1.3 mm, 1.4 mm, 1.5 mm, 1.6 mm, 1.7 mm, 1.8 mm, 1.9 mm, 2.0 mm, 2.1 mm, 2.2 mm, 2.3 mm, 2.4 mm or 2.5 mm. In some embodiments, the body is configured to have a wall thickness (e.g., from the swellable material compartment to the outer portion of the oral pharmaceutical dosage form or from the directional channel to the outer portion of the oral pharmaceutical dosage form) of about 0.3 mm to about 2.5 mm, for example, any of about 0.5 mm to about 2.2 mm or about 0.4 mm to about 1.2 mm.

[0186] In some specific implementations, the body or at least a portion thereof is composed of a semipermeable membrane. The semipermeable membrane material is selected from the group consisting of: polyamide, polyamide ester, cellulose acetate, polyetherketone membrane, polypropylene, polyether, polyethersulfone, polyimide, polyesteramide, polyesteramide-imide copolymer, polyether carbonate, fluoropolymers such as polyvinyl fluoride, tetrafluoroethylene-hexafluoropropylene copolymer, polyvinyl alcohol, cellulose acetate, polymethacrylate, polyvinyl chloride, polyethylene, polyoxysilane, ethylene-vinyl acetate copolymer, silicone rubber, ethyl cellulose, acrylic resin, cellulose acetate phthalate, carboxymethylethyl cellulose, hydroxypropyl methylcellulose acetate succinate, hydroxypropyl methylcellulose phthalate, polyvinyl alcohol acetate phthalate, polyvinyl acetate, shellac, nanopores, such as graphene oxide membrane, aluminum oxide, silicon membrane, polyester, and polyester carbonate.

[0187] In some specific implementations, the binder is selected from the group consisting of: dextrin, xanthan gum, maltodextrin, povidone, methylcellulose, ethylcellulose, zein, fructose, poloxamer, sodium alginate, pregelatinized starch, hydroxypropyl cellulose, hydroxypropyl methylcellulose, carbomer, starch, gum arabic, microcrystalline cellulose, sodium lauryl sulfate, sucrose, cellulose acetate, polysorbate, glucose, dextran, compressible sugar, carrageenan, modified starch, tragacanth, and honey.

[0188] In some specific implementations, the arm is configured to have a thickness of about 1

mm to about 2 mm, for example, about 1.1 mm to about 1.6 mm.

[0189] In some specific implementations, the oral pharmaceutical dosage form includes a component, and the component is a plunger or a movable member. For example, the plunger is configured to be pushed by the swellable material into contact with one or more arms. In some embodiments, the plunger has a wall thickness of about 0.3 mm to about 2.5 mm, for example, about 0.4 mm to about 2.2 mm. In some implementations, the plunger has a wall thickness of at least about 0.3 mm, for example, at least about 0.4 mm, 0.5 mm, 0.6 mm, 0.7 mm, 0.8 mm, 0.9 mm, 1.0 mm, 1.1 mm, 1.2 mm, 1.3 mm, 1.4 mm, 1.5 mm, 1.6 mm, 1.7 mm, 1.8 mm, 1.9 mm, 2.0 mm, 2.1 mm, 2.2 mm, 2.3 mm, 2.4 mm or 2.5 mm.

[0190] In some specific embodiments, an included angle of less than or equal to 90° is formed between a peripheral surface of the top member 62 of the movable member 6 and a top surface of the bottom member 61. The included angle δ may be 89°, 88°, 87°, 86°, 85°, 84°, 83°, 82°, 81°, 80°, 79°, 78°, 77°, 76°, 75°, 74°, 73°, 72°, 71°, or 70°.

[0191] C. Loading one or more drugs in an oral pharmaceutical dosage form

[0192] The oral pharmaceutical dosage forms described herein include one or more drugs. In some embodiments, the oral pharmaceutical dosage form includes two or more drugs, for example, any of 3, 4, or 5 drugs. The drug in the oral pharmaceutical dosage form may be released at any time point during the life cycle of the oral pharmaceutical dosage form. For example, in some embodiments, the oral pharmaceutical dosage form is configured and formulated to release the drug in the stomach of a subject. In some embodiments, substantially all, for example, at least about 70%, 75%, 80%, 85%, 90%, 95%, or 100% of the drug is released in the stomach. In some embodiments, the pharmaceutical dosage form is configured to release the drug after leaving the stomach.

[0193] In some embodiments, the drug is a poorly water-soluble drug. In some embodiments, the poorly water-soluble drug is a Biopharmaceutics Classification System (BCS) Class II active pharmaceutical ingredient (API), for example, a drug with high permeability and low solubility. In some embodiments, the poorly water-soluble drug is a Biopharmaceutics Classification System (BCS) Class IV active pharmaceutical ingredient (API), for example, a drug with low permeability and low solubility. In some embodiments, the drug is a Biopharmaceutics Classification System (BCS) Class III active pharmaceutical ingredient (API), for example, a drug with low permeability and high solubility. In some embodiments, the drug is selected from one or more of riociguat,

aceclofenac, bicalutamide, carbamazepine, carvedilol, clotrimazole, cinnarizine, danazol, dapsone, estradiol, ezetimibe, glibenclamide, fenofibrate, griseofulvin, ibuprofen, itraconazole, ketoconazole, mefenamic acid, naproxen, nevirapine, nifedipine, nitrofurantoin, nomegestrol acetate, phenytoin sodium salt, piroxicam, praziquantel, rifampicin, sulfamethoxazole, trimethoprim, and verapamil hydrochloride, or salts and stereoisomers thereof.

[0194] The oral pharmaceutical dosage form may be configured to release the drug based on any desired release profile, and be expanded to release one or more drugs, where each drug has any desired release profile. Typically, because the oral pharmaceutical dosage form described herein is designed to be retained in the stomach for a relatively long period of time, the release profile of at least one drug will be configured based on the expected gastric retention of the oral pharmaceutical dosage form. In some embodiments, when two or more drugs are in the oral pharmaceutical dosage form, the oral pharmaceutical dosage form is configured to release each drug according to a desired release profile. In some embodiments, the oral pharmaceutical dosage form is configured such that all (or substantially all, for example, at least about 90%) of the drug content in the oral pharmaceutical dosage form (or a portion thereof) is released during the expected gastric retention of the oral pharmaceutical dosage form. In some embodiments, the oral pharmaceutical dosage form is configured to release a certain amount of drug content (e.g., a second drug) in the oral pharmaceutical dosage form after the oral pharmaceutical dosage form or a component thereof is expected to exit the stomach. In some embodiments, the oral pharmaceutical dosage form is formulated and configured such that the drug is released according to a delayed release profile, a sustained release profile, a delayed-sustained release profile, a zero-order release profile, a first-order release profile, an immediate release profile plus a sustained release profile, an immediate release profile plus a delayed release profile, an immediate release profile plus a delayed-sustained release profile, a pulsatile release profile, an iterative pulsatile release profile, an immediate release profile plus a pulsatile release profile, or a combination thereof.

[0195] The oral pharmaceutical dosage form described herein may be configured and formulated to release the drug according to a desired drug release profile using various technologies. In some embodiments, drug release from the oral pharmaceutical dosage form is based on the erosion of a drug-containing material, for example, when the drug-containing material is exposed to gastrointestinal fluid. In some specific embodiments, the drug-containing material is

configured as a layer having a predetermined surface area, and the layer has the surface area exposed to gastrointestinal fluid, a thickness, and a drug mass fraction, where these characteristics of the drug-containing material achieve the desired drug release. In some embodiments, the drug-containing material is in the form of a multilayer structure. In some embodiments, the drug-containing material is embedded, including being partially embedded in a material of a component of the pharmaceutical dosage form. Providing the design, configuration, and materials of such a drug-containing material to achieve the desired drug release is known in the art. For example, refer to U.S. Patent No. 10,350,822, which is incorporated herein in its entirety.

[0196] In some embodiments, the oral pharmaceutical dosage form is configured with a drug-containing compartment, where the compartment has an orifice for releasing the drug from the oral pharmaceutical dosage form. In some specific implementations, the orifice is blocked by an erodible material (e.g., a plug). In some embodiments, a feature that blocks the orifice, such that the drug is retained within a compartment of the oral pharmaceutical dosage form, is configured to no longer block the orifice at a desired time. For example, in some embodiments, the drug-containing compartment is sealed with an erodible plug, where the erodible plug dissolves at a specific time after administration to a subject, thereby releasing the drug from the oral pharmaceutical dosage form. The release time may be based on the thickness of the plug and/or the material of the plug, and the like. The drug-containing compartment may be configured in any component. In some embodiments, the oral pharmaceutical dosage form includes a plurality of drug-containing compartments. In some specific implementations, the component is a non-erodible material, such as an insoluble shell material. In some embodiments, the component erodes after the drug leaves the drug-containing compartment, for example, after the oral pharmaceutical dosage form leaves the stomach.

[0197] In some embodiments, the oral pharmaceutical dosage form is configured such that the drug will leach or diffuse from the material.

[0198] In some embodiments, the drug is loaded on one or more arms; and in some embodiments, each movable arm is loaded with the drug. In some embodiments, the drug is loaded on one or more covers. In some embodiments, the drug is loaded in a swellable material chamber.

[0199] D. Characteristics of the oral pharmaceutical dosage form providing gastric retention in a post-administration state

[0200] As described herein, the swelling of one or more swellable materials or a portion

thereof increases the dimension of the oral pharmaceutical dosage form, thereby allowing the drug to be retained in the stomach for a relatively long period of time. In some embodiments, the post-administration state of the oral pharmaceutical dosage form is referred to as a gastric retention state. A person of ordinary skill in the art will readily appreciate that characteristics of the oral pharmaceutical dosage form, such as size, can be dynamic and vary over time during the swelling of the swellable material or a portion thereof. Descriptions of some states of the oral pharmaceutical dosage form, such as the post-administration gastric retention state, are not intended to limit the disclosure herein to a static embodiment of the pharmaceutical dosage form.

[0201] In some embodiments, when the oral pharmaceutical dosage form is in an expanded state (e.g., a gastric retention state), the size of the oral pharmaceutical dosage form is a size that inhibits and/or prevents the oral pharmaceutical dosage form from reaching the duodenum through an aspect of the pylorus (e.g., the pyloric antrum, the pyloric canal, or the pyloric orifice formed by the pyloric sphincter). In some embodiments, when the oral pharmaceutical dosage form is in an expanded state, the size of the oral pharmaceutical dosage form is a size that inhibits and/or prevents the oral pharmaceutical dosage form from passing through the pyloric orifice formed by the pyloric sphincter. In some embodiments, when the oral pharmaceutical dosage form is in an expanded state, at least two perpendicular dimensions of the oral pharmaceutical dosage form each independently have a length of at least about 20 mm to about 70 mm, for example, a length of at least about 20 mm to about 50 mm, a length of about 30 mm to about 60 mm, or a length of about 40 mm to about 70 mm. In some embodiments, when the pharmaceutical dosage form is in an expanded state, at least two perpendicular dimensions of the pharmaceutical dosage form are each independently at least about 20 mm, for example, at least about 25 mm, 30 mm, 35 mm, 40 mm, 45 mm, 50 mm, 55 mm, 60 mm, 65 mm, or 70 mm in length. In some embodiments, when the oral pharmaceutical dosage form is in an expanded state, at least two perpendicular dimensions of the pharmaceutical dosage form are each independently about any one of 20 mm, 25 mm, 30 mm, 35 mm, 40 mm, 45 mm, 50 mm, 55 mm, 60 mm, 65 mm, or 70 mm in length. In some embodiments, when the oral pharmaceutical dosage form is in an expanded state, one of the at least two perpendicular dimensions is different from the other dimension. In some embodiments, when the pharmaceutical dosage form is in an expanded state, one of the at least two perpendicular dimensions is the same as the other dimension. It should be noted that subjects may have different anatomical characteristics and sizes (e.g., adults versus children), and this application includes oral

pharmaceutical dosage forms designed for these considerations to achieve desired gastric retention.

[0202] The oral pharmaceutical dosage forms described herein are configured to be retained in the stomach for a relatively long period of time, for example, compared to a pharmaceutical dosage form without gastric retention characteristics (e.g., the oral pharmaceutical dosage form naturally flows through the stomach according to the natural outflow of ingested substances from the stomach). In some embodiments, the oral pharmaceutical dosage form is configured to be retained in the stomach for about 6 hours to about 3 months, for example, about 6 hours to about 24 hours, about 6 hours to about 36 hours, about 8 hours to about 24 hours, about 8 hours to about 36 hours, about 18 hours to about 30 hours, about 20 hours to about 28 hours, about 12 hours to about 36 hours, about 1 day to about 3 days, about 3 days to about 7 days, about 6 hours to about 1 month, or about 6 hours to about 2 months. In some embodiments, the oral pharmaceutical dosage form is configured to be retained in the stomach for at least about 6 hours, for example, at least about 7 hours, about 8 hours, about 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, 18 hours, 19 hours, 20 hours, 21 hours, 22 hours, 23 hours, 24 hours, 25 hours, 26 hours, 27 hours, 28 hours, 29 hours, 30 hours, 31 hours, 32 hours, 33 hours, 34 hours, 35 hours, or 36 hours. In some embodiments, the oral pharmaceutical dosage form is configured to be retained in the stomach for at least about 1 day, for example, any of at least about 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 14 days, 21 days, 1 month, 1.5 months, 2 months, 2.5 months, or 3 months. In some embodiments, the oral pharmaceutical dosage form is configured to be retained in the stomach for no more than about 7 days, for example, any of no more than about 6 days, 5 days, 4 days, 3 days, 2 days, 36 hours, 30 hours, 24 hours, 18 hours, or 12 hours. In some embodiments, the oral pharmaceutical dosage form is configured to be retained in the stomach for no more than about 3 months, for example, any of no more than about 2.5 months, 2 months, 1.5 months, 1 month, 21 days, 14 days, or 7 days. In some embodiments, the oral pharmaceutical dosage form is configured to be retained in the stomach for about 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, 18 hours, 19 hours, 20 hours, 21 hours, 22 hours, 23 hours, 24 hours, 25 hours, 26 hours, 27 hours, 28 hours, 29 hours, 30 hours, 31 hours, 32 hours, 33 hours, 34 hours, 35 hours, 36 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 14 days, 21 days, 1 month, 1.5 months, 2 months, 2.5 months, or 3 months.

[0203] In some embodiments, the post-administration state of the oral pharmaceutical dosage form occurs within about 1 hour or less after the oral pharmaceutical dosage form is administered

to a subject. For example, in some embodiments, the oral pharmaceutical dosage form achieves a gastric retention state within about 1 hour or less, 50 minutes or less, 40 minutes or less, 30 minutes or less, 20 minutes or less, 10 minutes or less, or 5 minutes or less after administration to a subject.

[0204] In some embodiments, the oral pharmaceutical dosage form is configured such that the oral pharmaceutical dosage form or a portion thereof can pass through the pylorus to exit the stomach. For example, in some embodiments, one or more components of the oral pharmaceutical dosage form, such as one or more movable arms, erode and/or soften in the stomach, thereby allowing the components to exit the stomach in one or more portions. In some embodiments, the oral pharmaceutical dosage form softens after being retained in the stomach for a period of time and is configured to pass through the pylorus as a whole. In some embodiments, the erosion or dissolution of a component of the oral pharmaceutical dosage form or a portion thereof is due to prolonged exposure to gastrointestinal fluid in the stomach (e.g., due to prolonged exposure to low pH).

[0205] E. Characteristics of oral pharmaceutical dosage forms in a pre-administration state

[0206] The oral pharmaceutical dosage forms described herein can be formed in any quantity of shapes, sizes, weights, and appearances. As described herein, the oral pharmaceutical dosage forms of this application can take forms having different characteristics (e.g., size and shape) during the life cycle of the administered oral pharmaceutical dosage forms (e.g., in an administered state and in a post-administration gastric retention state).

[0207] In some embodiments, the oral pharmaceutical dosage forms described herein are suitable for oral administration to a human subject. Such oral pharmaceutical dosage forms of this application may be, for example, any size, shape, or weight suitable for oral administration to a specific human subject, such as children and adults. In some embodiments, the oral pharmaceutical dosage form is suitable for oral administration to a subject, where the size, shape, or weight of the pharmaceutical dosage form is selected based on one or more attributes of the subject, such as height, weight, age, or anatomical features, for example, those related to oral administration.

[0208] In some embodiments, a surface of the oral pharmaceutical dosage form, such as an outer surface, such as a body, has a capsule shape, a circular shape, an elliptical shape, a bullet shape, an arrow shape, a triangular shape, a rounded triangle shape, a square shape, a rounded square shape, a rectangular shape, a rounded rectangular shape, a rhombic shape, a pentagonal shape, a hexagonal shape, an octagonal shape, a half-moon shape, an almond shape, or a

combination thereof.

[0209] In some embodiments, the maximum cross dimension of the oral pharmaceutical dosage form is about 5 mm to about 26 mm, for example, about 5 mm to about 15 mm, about 6 mm to about 13 mm, or about 7 mm to about 11 mm. In some embodiments, the maximum cross dimension of the oral pharmaceutical dosage form is at least about 5 mm, for example, at least about 6 mm, 7 mm, 8 mm, 9 mm, 10 mm, 11 mm, 12 mm, 13 mm, 14 mm, 15 mm, 16 mm, 17 mm, 18 mm, 19 mm, 20 mm, 21 mm, 22 mm, 23 mm, or 24 mm. In some embodiments, the maximum cross dimension of the pharmaceutical dosage form is less than about 26 mm, for example, less than about 25 mm, 24 mm, 23 mm, 22 mm, 21 mm, 20 mm, 19 mm, 18 mm, 17 mm, 16 mm, 15 mm, 14 mm, 13 mm, 12 mm, 11 mm, 10 mm, 9 mm, 8 mm, 7 mm, 6 mm, or 5 mm. In some embodiments, the maximum cross dimension of the pharmaceutical dosage form is about 5 mm, 6 mm, 7 mm, 8 mm, 9 mm, 10 mm, 11 mm, 12 mm, 13 mm, 14 mm, 15 mm, 16 mm, 17 mm, 18 mm, 19 mm, 20 mm, 20.5 mm, 21 mm, 21.5 mm, 22 mm, 22.5 mm, 23 mm, 23.5 mm, or 24 mm. In some embodiments, the maximum cross dimension is measured on the surface of the pharmaceutical dosage form, for example, the outer surface (e.g., represented by the length or width of the oral pharmaceutical dosage form). In some embodiments, the measured maximum cross dimension extends through or diagonally through the oral pharmaceutical dosage form.

[0210] In some embodiments, a cross dimension of the oral pharmaceutical dosage form perpendicular to the maximum cross dimension is about 5 mm to about 20 mm, for example, any one of about 5 mm to about 15 mm, about 6 mm to about 13 mm, or about 7 to about 11 mm. In some embodiments, the cross dimension of the oral pharmaceutical dosage form perpendicular to the maximum cross dimension is at least about 5 mm, for example, at least about 6 mm, 7 mm, 8 mm, 9 mm, 10 mm, 11 mm, 12 mm, 13 mm, 14 mm, 15 mm, 16 mm, 17 mm, 18 mm, 19 mm, or 20 mm. In some embodiments, the cross dimension of the oral pharmaceutical dosage form perpendicular to the maximum cross dimension is less than about 20 mm, for example, less than about 19 mm, 18 mm, 17 mm, 16 mm, 15 mm, 14 mm, 13 mm, 12 mm, 11 mm, 10 mm, 9 mm, 8 mm, 7 mm, 6 mm, or 5 mm. In some embodiments, a cross dimension of the oral pharmaceutical dosage form perpendicular to the maximum cross dimension is about 5 mm, 6 mm, 7 mm, 8 mm, 9 mm, 10 mm, 11 mm, 12 mm, 13 mm, 14 mm, 15 mm, 16 mm, 17 mm, 18 mm, 19 mm, or 20 mm. In some embodiments, the cross dimension perpendicular to the maximum cross dimension is measured on the surface of the oral pharmaceutical dosage form. In some embodiments, the

cross dimension perpendicular to the maximum cross dimension is measured through or diagonally through the oral pharmaceutical dosage form.

[0211] In some embodiments, the thickness of the oral pharmaceutical dosage form is about 5 mm to about 20 mm, for example, any one of about 5 mm to about 15 mm, about 6 mm to about 13 mm, or about 7 mm to about 11 mm. In some embodiments, the oral pharmaceutical dosage form has a thickness of at least about 5 mm, for example, at least about 6 mm, 7 mm, 8 mm, 9 mm, 10 mm, 11 mm, 12 mm, 13 mm, 14 mm, 15 mm, 16 mm, 17 mm, 18 mm, 19 mm, or 20 mm. In some embodiments, the thickness of the oral pharmaceutical dosage form is less than about 20 mm, for example, any one of less than about 19 mm, 18 mm, 17 mm, 16 mm, 15 mm, 14 mm, 13 mm, 12 mm, 11 mm, 10 mm, 9 mm, 8 mm, 7 mm, 6 mm, or 5 mm. In some embodiments, the thickness of the oral pharmaceutical dosage form is any one of about 5 mm, 6 mm, 7 mm, 8 mm, 9 mm, 10 mm, 11 mm, 12 mm, 13 mm, 14 mm, 15 mm, 16 mm, 17 mm, 18 mm, 19 mm, or 20 mm.

[0212] In some embodiments, the total weight of the oral pharmaceutical dosage form is about 50 mg to about 1,000 mg, for example, about 50 mg to about 100 mg, about 100 mg to about 200 mg, about 200 mg to about 300 mg, about 300 mg to about 400 mg, about 400 mg to about 500 mg, about 500 mg to about 600 mg, about 600 mg to about 700 mg, about 700 mg to about 800 mg, about 800 mg to about 900 mg, or about 900 mg to about 1,000 mg. In some embodiments, the total weight of the oral pharmaceutical dosage form is at least about 50 mg, for example, at least about 75 mg, 100 mg, 125 mg, 150 mg, 175 mg, 200 mg, 225 mg, 250 mg, 275 mg, 300 mg, 325 mg, 350 mg, 375 mg, 400 mg, 425 mg, 450 mg, 475 mg, 500 mg, 550 mg, 600 mg, 650 mg, 700 mg, 750 mg, 800 mg, 850 mg, 900 mg, 950 mg, or 1,000 mg. In some embodiments, the total weight of the oral pharmaceutical dosage form is less than about 1,000 mg, for example, less than about 950 mg, 900 mg, 850 mg, 800 mg, 750 mg, 700 mg, 650 mg, 600 mg, 550 mg, 500 mg, 475 mg, 450 mg, 425 mg, 400 mg, 375 mg, 350 mg, 325 mg, 300 mg, 275 mg, 250 mg, 225 mg, 200 mg, 175 mg, 150 mg, 125 mg, 100 mg, 75 mg, or 50 mg. In some embodiments, the total weight of the oral pharmaceutical dosage form is about 50 mg, 75 mg, 100 mg, 125 mg, 150 mg, 175 mg, 200 mg, 225 mg, 250 mg, 275 mg, 300 mg, 325 mg, 350 mg, 375 mg, 400 mg, 425 mg, 450 mg, 475 mg, 500 mg, 550 mg, 600 mg, 650 mg, 700 mg, 750 mg, 800 mg, 850 mg, 900 mg, 950 mg, or 1,000 mg.

[0213] F. Additional features of pharmaceutical dosage forms

[0214] In some embodiments, an oral pharmaceutical dosage form includes a gas-filled

compartment, for example, to provide buoyancy to the oral pharmaceutical dosage form. In some embodiments, the gas-filled compartment is embedded in a component of the oral pharmaceutical dosage form, such as the body or one or more movable arms. In some embodiments, the gas-filled compartment has an eruptible plug, where the eruptible plug is configured to open the gas-filled compartment at a point after the oral pharmaceutical dosage form is administered to a subject.

[0215] In some embodiments, the oral pharmaceutical dosage form includes additional features, such as an outer coating, an outer layer (e.g., a capsule shell), or external markings. In some specific implementations, the outer coating or coating includes or is a flavor coating. In some specific implementations, the outer coating or layer includes or is a sugar coating. In some specific implementations, the outer coating or coating includes or is a cosmetic coating. In some specific implementations, the outer coating or layer includes or is a colored coating. In some specific implementations, the outer coating or layer is a film coating. In some specific implementations, the outer coating or layer is a polymer coating. In some embodiments, the outer coating completely surrounds the pharmaceutical dosage form. In some embodiments, the outer layer forms part of an exterior of the oral pharmaceutical dosage form. In some embodiments, an additional component is a label, such as a drug identifier, a company name or abbreviation, a graphic, a drug label, a chemical name or abbreviation of a drug, drug instructions, an identification barcode, or a combination thereof.

[0216] G. Exemplary medical devices

[0217] The above inventive concept can be applied to medical devices. In some embodiments, a medical device is provided. The medical device includes: a body structure, where the body structure forms a swellable material chamber, and the swellable material chamber includes a swellable material; and an arm, where the arm is operably connected to the body, and the arm rotates around the body of the medical device by force provided by the swellable material. The medical device is configured to have a compact state, and an expanded state in which the arm is driven by the expansion of the swellable material in the presence of a liquid.

[0218] H. Exemplary oral pharmaceutical dosage forms

[0219] An oral pharmaceutical dosage form for gastric retention is provided. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms a swellable material chamber, and the swellable material chamber includes a swellable material and a movable member structure, where the body structure includes a base and a cover, and the base is composed

of a semipermeable membrane; arms including a first arm, a second arm, a third arm, and a fourth arm. The arms are operably connected to the body. The swellable material absorbs a liquid and expands, and a provided force pushes the movable member to move in the directional channel closer to a top portion of the cover. The first arm, the second arm, the third arm, and the fourth arm are configured such that each of the arms rotates around a body axis through pushing by the movable member. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention. The expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the swellable material in the presence of gastrointestinal fluid.

[0220] I. Pharmaceutical dosage forms configured for other body cavities

[0221] The concept of the pharmaceutical dosage form or medical device of the present invention can be applied not only to oral administration, but also to other parts of the human body, such as the large intestine, small intestine, rectum, cecum, colon, and vagina, and the pharmaceutical dosage form or medical device of the present invention is also applicable. A person of ordinary skill in the art will readily appreciate that these other body cavities may have anatomical features that guide the pharmaceutical dosage forms described herein. For example, the anatomical size of the rectum may guide the size of a pre-administration pharmaceutical dosage form for such use, and, in some embodiments, may be different from the size of the oral pharmaceutical dosage form. That being said, the mechanisms of retention in a subject taught herein are still applicable.

[0222] **III. Commercial batches**

[0223] In some aspects, oral pharmaceutical dosage forms of commercial batches as described herein are provided herein. In some embodiments, a commercial batch includes at least any one of 100, 150, 200, 250, 500, 750, 1,000, 2,500, 5,000, 7,500, 10,000, 20,000, 30,000, 40,000, 50,000, 60,000, 70,000, 80,000, 90,000 or 100,000 oral pharmaceutical dosage forms as described herein. In some embodiments, each oral pharmaceutical dosage form of a commercial batch is produced using the same technology, for example, involving producing one or more components of the oral pharmaceutical dosage form by three-dimensional (3D) printing, injection molding, ultrasonic welding, or any combination thereof.

[0224] In some embodiments, for one or more of the following, the standard deviation of a

commercial batch is about 0.1 or less, such as 0.05 or less: drug amount in an oral pharmaceutical dosage form; the weight of the oral pharmaceutical dosage form; the dimension of the oral pharmaceutical dosage form (e.g., in a pre-administration state and/or a post-administration state); and gastric retention time of the oral pharmaceutical dosage form. In some embodiments, the dimension of the oral pharmaceutical dosage form is the maximum cross dimension of the oral pharmaceutical dosage form in a pre-administration state. In some embodiments, the dimension of the oral pharmaceutical dosage form is the cross dimension perpendicular to the maximum cross dimension of the oral pharmaceutical dosage form in a pre-administration state. In some embodiments, the dimension of the oral pharmaceutical dosage form is the maximum cross dimension of the oral pharmaceutical dosage form after the swellable material has swollen (e.g., in a post-administration state in the stomach, where the swellable material has reached a substantially completely expanded state). In some embodiments, the dimension of the oral pharmaceutical dosage form is a dimension perpendicular to the maximum cross dimension of the oral pharmaceutical dosage form after the swellable material has swollen (e.g., in a post-administration state in the stomach, where the swellable material has reached a substantially completely swollen state).

[0225] IV. Preparation method

[0226] In some aspects, a preparation method for the oral pharmaceutical dosage form described herein is provided herein. In some embodiments, a manufacturing method includes a three-dimensional (3D) printing technology to form at least one component of the pharmaceutical dosage forms described herein or a portion thereof. In some specific implementations, the manufacturing method includes using 3D printing, injection molding, ultrasonic welding, or any combination thereof. In some embodiments, components of the oral pharmaceutical dosage form taught herein are produced separately and then assembled by a machine and/or manually.

[0227] As used herein, "printing", "three-dimensional printing", "3D printing", "additive manufacturing", or an equivalent thereof, refers to the process of producing three-dimensional objects layer by layer using a digital design, such as delayed-sustained-release oral pharmaceutical dosage forms. Basic processes of three-dimensional printing are described in U.S. Patent Nos. 5,204,055; 5,260,009; 5,340,656; 5,387,380; 5,503,785; and 5,633,021. Other U.S. patents and patent applications related to three-dimensional printing include: U.S. Patent Nos. 5,490,962; 5,518,690; 5,869,170; 6,530,958; 6,280,771; 6,514,518; 6,471,992; 8,828,411; U.S. Patent

Publication Nos. 2002/0015728; 2002/0106412; 2003/0143268; 2003/0198677; 2004/0005360. The contents of the aforementioned U.S. patents and patent applications are hereby incorporated herein by reference in their entireties. In some embodiments, additive manufacturing techniques are used to produce the oral pharmaceutical dosage forms or components thereof as described herein. In some embodiments, a layer-by-layer technique is used to produce the oral pharmaceutical dosage forms or components thereof as described herein. For example, in some embodiments, the layer-by-layer technique includes printing one or more materials for an entire first layer of oral pharmaceutical dosage form or a component thereof, and then continuing to print one or more materials for an entire second layer of oral pharmaceutical dosage form or a component thereof. In some embodiments, the layer, such as the first layer or the second layer, is a cross-section of the oral pharmaceutical dosage form or the component thereof. Because 3D printing can handle a range of pharmaceutical materials and locally control a composition and structure, 3D printing is well-suited for manufacturing a pharmaceutical dosage form with a complex geometry and a composition according to the present invention.

[0228] In some embodiments, when used to refer to a component of a pharmaceutical dosage form, such as a swellable material, a layer refers to a configuration of the component of the oral pharmaceutical dosage form and may include a plurality of printed layers of the same material. In some specific implementations, the layer has a predetermined fill density, such as a three-dimensional printing fill density. In some embodiments, the layer includes about 5 printed layers to about 2,500 printed layers among the plurality of printed layers, for example, about 10 printed layers to about 2,500 printed layers, about 25 printed layers to about 100 printed layers, about 50 printed layers to about 200 printed layers, about 100 printed layers to about 200 printed layers, about 150 printed layers to about 250 printed layers, about 200 printed layers to about 250 printed layers, about 500 printed layers to about 1,000 printed layers, or about 2,000 printed layers to about 2,400 printed layers. In some specific implementations, the thickness of the printed layer is no more than about 5 mm, for example, no more than about 4 mm, 3 mm, 2 mm, 1 mm, 0.9 mm, 0.8 mm, 0.7 mm, 0.6 mm, 0.5 mm, 0.4 mm, 0.3 mm, 0.2 mm, 0.1 mm, 0.09 mm, 0.08 mm, 0.07 mm, 0.06 mm, 0.05 mm, 0.04 mm, 0.03 mm, 0.02 mm, or 0.01 mm. In some implementations, the thickness of the printed layer is about 5 mm, 4 mm, 3 mm, 2 mm, 1 mm, 0.9 mm, 0.8 mm, 0.7 mm, 0.6 mm, 0.5 mm, 0.4 mm, 0.3 mm, 0.2 mm, 0.1 mm, 0.09 mm, 0.08 mm, 0.07 mm, 0.06 mm, 0.05 mm, 0.04 mm, 0.03 mm, or 0.01 mm.

[0229] Different 3D printing methods have been developed for manufacturing in terms of raw materials, equipment, and curing. These 3D printing methods include binder deposition (see Gibson *et al.*, Additive Manufacturing Technologies: 3D Printing, Rapid Prototyping, and Direct Digital Manufacturing., 2 ed. Springer, New York, 2015; Katstra *et al.*, Oral dosage forms fabricated by three dimensional printing, *J Control Release*, 66, 2000; Katstra *et al.*, Fabrication of complex oral delivery forms by three dimensional printing, Dissertation in Materials Science and Engineering, Massachusetts Institute of Technology, 2001; Lipson *et al.*, Fabricated: The New World of 3D printing, John Wiley & Sons, Inc., 2013; Jonathan, Karim 3D printing in pharmaceutics: a new tool for designing customized drug delivery systems, *Int J Pharm*, 499, 2016), material jetting (see Jonathan, Karim, 3D printing in pharmaceutics: a new tool for designing customized drug delivery systems, Int J Pharm, 499, 2016), extrusion (see Gibson et al., Additive Manufacturing Technologies: 3D Printing, Rapid Prototyping, and Direct Digital Manufacturing. 2 ed. Springer, New York, 2015), and photopolymerization (see Melchels *et al.*, A review on stereolithography and its application in biomedical engineering. Biomaterials, 31, 2010).

[0230] In some embodiments, the oral pharmaceutical dosage forms described herein are produced by injection molding. Different raw materials for different components are loaded into an injection molding machine and are shaped according to a mold shape, and then shaped components are assembled.

[0231] In some embodiments, the oral pharmaceutical dosage forms described herein are 3D printed using an extrusion method. In some implementations, the 3D printing method includes using a twin-screw extrusion method. During extrusion, a material is extruded through a printing nozzle from a robot-driven print head. Unlike binder deposition, which requires a powder bed, extrusion methods can achieve printing on any substrate. A variety of materials can be extruded for three-dimensional printing, including the thermoplastic materials, pastes and colloidal suspensions, silicones, and other semi-solids disclosed herein. One extrusion printing method is melt extrusion deposition (MED), which uses extruded material from the print head to print material layers to form a component of an oral pharmaceutical dosage form or a portion thereof. Another common type of extrusion printing is fused deposition modeling, which uses solid polymer filaments for printing. In fused deposition modeling, a gear system drives the filament into a heated nozzle assembly for extrusion (see Gibson et al., Additive Manufacturing Technologies: 3D Printing, Rapid Prototyping, and Direct Digital Manufacturing, 2nd ed., Springer,

New York, 2015).

[0232] In some specific implementations, 3D printing is performed by melt extrusion deposition (MED). In some specific implementations, the melt extrusion deposition technique includes preparing a material to be printed, for example, preparing powders in a hot melt extruder, and then feeding the material into an MED print head. Then, the MED print head prints (deposits layer by layer) the material in an additive manner to form an oral pharmaceutical dosage form or a component thereof. In some embodiments, materials or components of the oral pharmaceutical dosage form are printed from different MED print heads. In some embodiments, the MED print head prints the material according to instructions in one or more G-code files. For example, Patent Applications Nos. WO2019/137333 and WO2018137686, and U.S. Patent No. 10,201,503 disclose exemplary MED techniques, each of which is incorporated herein by reference in its entirety.

[0233] In some specific implementations, 3D printing is performed by fused deposition modeling (FDM). In some specific implementations, three-dimensional printing is performed by melt extrusion deposition or a combination of hot melt extrusion and three-dimensional printing technology (e.g., FDM). In some embodiments, 3D printing is performed by non-filament FDM. In some embodiments, 3D printing is performed by inkjet printing. In some specific implementations, 3D printing is performed by selective laser sintering (SLS). In some embodiments, 3D printing is performed by stereolithography (SLA or SL). In some embodiments, 3D printing is performed by PolyJet, a MultiJet Printing (MJP) system, Perfactory, a solid object ultraviolet laser printer, a bioplotter, 3D bioprinting, rapid freeze prototyping, a desktop system, selective deposition lamination (SDL), laminated object manufacturing (LOM), ultrasonic consolidation, ColorJet Printing (CJP), an EOSINT system, laser engineered net shaping (LENS), an aerosol jet system, electron beam melting (EBM), LaserCUSING®, selective laser melting (SLM), Phenix PX™ series, micro-sintering, digital part materialization (DPM), or a VX system.

[0234] In some implementations, the 3D printing method described herein includes a continuous production method. In some embodiments, the 3D printing method described herein includes a batch production method.

[0235] In some embodiments, a method for producing a pharmaceutical dosage form described herein includes a 3D printing technology, such as a combination of 3D printing and another method, for example, a combination of injection molding and 3D printing. In some specific

implementations, the method for production further includes an injection molding technology. In some specific implementations, the method for production further includes an ultrasonic welding method. In some implementations, the 3D printing technology, the injection molding technology, and ultrasonic welding methods may be used alone or in any combination.

[0236] The specification of a method for 3D printing of a pharmaceutical dosage form as disclosed herein can be generated in a variety of ways, including direct encoding, derivation from a solid CAD model, or other means specific to computer interfaces and application software of a 3D printer. These instructions may include information regarding the number and spatial location of droplets, as well as information on general 3D printing parameters, such as droplet spacing in each linear dimension (X, Y, Z) and the volume or mass of each droplet. For a given set of materials, these parameters can be adjusted to refine the quality of the created structure. The overall resolution of the created structure is a function of powder particle size, droplet size, printing parameters, and material characteristics.

[0237] In some embodiments, one or more components of an oral pharmaceutical dosage form are created separately, for example, printed separately, and then assembled to form the oral pharmaceutical dosage form. In some embodiments, all components of the oral pharmaceutical dosage form are created in a single method, for example, printed in a single method, without the need for subsequent assembly.

[0238] The oral pharmaceutical dosage forms and components thereof described in this application may be printed at a commercial scale. For example, in some embodiments, the methods disclosed herein can be used to 3D print 1,000 to 100,000 units of oral pharmaceutical dosage forms per hour, including printing components thereof for subsequent assembly.

[0239] In some embodiments, materials used to print the oral pharmaceutical dosage forms or components thereof are printed by different print heads, respectively. The 3D printing methods described herein each include printing materials in any order to allow for the production of oral pharmaceutical dosage forms or components thereof.

[0240] In some embodiments, the 3D printing method includes designing all or part of the oral pharmaceutical dosage forms or components thereof on a computer system. In some embodiments, the method includes inputting parameters of desired gastric retention, a drug release profile, and/or an oral pharmaceutical dosage form and/or a component thereof into a computer system. In some specific implementations, the method includes providing one or more parameters to be printed, for

example, layer surface area, thickness, drug mass fraction, and erosion rate. In some embodiments, the method includes providing a desired drug release profile. In some embodiments, the method includes creating a virtual image of an item to be printed. In some embodiments, the method includes creating a computer model that includes predetermined parameters. In some implementations, the method includes feeding predetermined parameters to a 3D printer and printing an item according to the predetermined parameters. In some embodiments, the method includes creating a 3D drawing of an item to be printed based on predetermined parameters, where the 3D drawing is created on a computer system. In some embodiments, the method includes converting a 3D drawing, such as a slice, into 3D printing code, such as G-code. In some embodiments, the method includes using a computer system to execute 3D printing code to print according to the methods described herein.

[0241] V. Methods for delivering a drug to a subject

[0242] In some aspects, a method for delivering an oral pharmaceutical dosage form to a subject is provided, such that the oral pharmaceutical dosage form is retained in the stomach of the subject for a relatively long period of time. The method includes orally administering to the subject any of the oral pharmaceutical dosage forms described herein. In some aspects, a method for delivering a drug to the stomach and/or the upper gastrointestinal tract of a subject is provided. The method includes orally administering to the subject any of the oral pharmaceutical dosage forms described herein, where the oral pharmaceutical dosage form includes a drug. In some embodiments, the drug is released from the oral pharmaceutical dosage form (including an immediate-release dosage form, a sustained-release dosage form, a pulsatile-release dosage form, or any combination thereof) into the stomach and/or the upper gastrointestinal tract over a relatively long period of time. In some embodiments, the oral pharmaceutical dosage form is configured to be retained in the stomach of the subject for a relatively long period of time (e.g., at least about 6 hours to about 3 months). In some embodiments, a drug in the oral pharmaceutical dosage form can be released from the oral pharmaceutical dosage form at a predetermined time after the oral pharmaceutical dosage form is administered to the subject. For example, in some embodiments, the drug or at least a portion thereof is released in the stomach of the subject as or after the oral pharmaceutical dosage form reaches a post-administration state designed for gastric retention. In some embodiments, the drug or at least a portion thereof is released in the stomach of the subject for at least about 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, 12 hours, 14 hours, 16

hours, 18 hours, 20 hours, 22 hours, 24 hours, 26 hours, 28 hours, 30 hours, 32 hours, 34 hours, or 36 hours after the pharmaceutical dosage form is administered to the subject. In some embodiments, the pharmaceutical dosage form is retained in the stomach for at least about 72 hours, 80 hours, 88 hours, 96 hours, 104 hours, 112 hours, 120 hours, 128 hours, 136 hours, 144 hours, 152 hours, 160 hours, or 168 hours.

[0243] In some aspects, a method for delivering an oral pharmaceutical dosage form to a subject is provided, where after the subject takes the pharmaceutical dosage form, the pharmaceutical dosage form completely undergoes three stages: retention initiation, retention time control, and retention termination. The retention initiation includes, after the pharmaceutical dosage form enters a gastric space, an expandable material within a body of the pharmaceutical dosage form absorbs water and expands, and a movable arm begins to rotate as the volume of the expandable material increases. The retention initiation further includes that, before the expandable material absorbs water and expands, a restraining member releases inhibition on the movable arm. The retention time control can be controlled by selection of a material and a dimension of each component. The gastric retention termination may also be achieved through dissolution, decomposition, or degradation of a component. For example, an expandable material undergoes dissolution, decomposition, or degradation, a movable member returns to a first compartment, and the movable arm is folded; or a connecting end between the movable arm and the body undergoes partial or complete dissolution, decomposition, or degradation, and the movable arm disengages from the body; or the pharmaceutical dosage form undergoes overall softening or the movable arm softens, so that the mechanical strength of the pharmaceutical dosage form is weakened, and the pharmaceutical dosage form is deformed and then leaves an original retention position.

[0244] A person skilled in the art will recognize that several embodiments can be implemented within the scope and spirit disclosed in this application. The following examples further illustrate the disclosure, and these examples should not be construed as limiting the scope or spirit of the disclosure to the specific procedures described therein.

[0245] A person skilled in the art will recognize that, within the scope and spirit disclosed in this application, the assemblies, components, structures, and materials disclosed in this application can be arranged and combined according to the objectives or technical effects that the pharmaceutical dosage form needs to achieve, and all such arrangements and combinations should fall within the protection scope of the present invention.

Examples

[0246] Example 1

[0247] This example illustrates a design, production, and testing of the oral pharmaceutical dosage form described herein. **FIG. 9a** is a schematic diagram of an oral pharmaceutical dosage form in an expanded state. The component composition of the prepared dosage form is shown in **Table 1.** The oral pharmaceutical dosage form includes: a body structure, where the body structure forms an expandable material chamber, the body structure is composed of a cover and a base, the base is a semipermeable membrane, the expandable material chamber includes a swelling block and a pushing post, and the swelling block contains an expandable material; and four arms, where the four arms are operably connected to the body, and the arms rotate around the body of the oral pharmaceutical dosage form by force provided by the expandable material. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the expandable material in the presence of gastrointestinal fluid.

Table 1 Component composition of the oral pharmaceutical dosage form

Component	Composition (where a ratio is a mass ratio)
Semipermeable membrane	Cellulose acetate: copovidone: triacetin = 50:25:25
Cover	Cellulose acetate: diethyl phthalate = 70:30
Swelling block	Crospovidone
Pushing post	Cellulose acetate: diethyl phthalate = 70:30
Arm	Cellulose acetate: diethyl phthalate = 70:30

[0248] A preparation method for the oral pharmaceutical dosage form described herein was as follows: (1) Preparation of a swelling block: A prescribed amount of crospovidone was accurately weighed, and was pressed into a cylindrical swelling block by a tablet press. (2) Model assembly: The swelling block, the pushing post, and the cover were sequentially loaded into the semipermeable membrane, four arms were assembled on the cover, and the components were connected by glue, and were placed into a No. 1 hard gelatin capsule shell to obtain a capsule of the oral pharmaceutical dosage form described herein.

[0249] Six capsules of the oral pharmaceutical dosage form described herein were subjected to an expansion test, and the test method was as follows: Six capsules of the oral pharmaceutical dosage form described herein were freely placed into a hydrochloric acid medium with a pH of about 1.2. A rotational speed of a dissolution tester was set to 100 rpm. The capsules were observed from an initial state to a final fully expanded state, and the time was recorded. Test results are shown in **FIG. 12**, indicating that the oral pharmaceutical dosage form described herein fully expanded in about 1 hour, thereby meeting the requirements for swelling and expansion.

[0250] **Example 2**

[0251] This example illustrates a design, production, and testing of arms of the oral pharmaceutical dosage form described herein. Two types of arms were prepared, as shown in **FIG. 13a** and **FIG. 13b**. Side wing reinforcing ribs are arranged on both sides of a connecting end of the arm in **FIG. 13b**. A material composition ratio (mass ratio) of each of the two types of arms was: Eudragit / polyacrylic resin: triacetin = 8:2, with consistent design dimensions.

[0252] Mechanical properties of the arms in **FIG. 13a** and **FIG. 13b** were tested separately. A test method was as follows: (1) Mounting of compression fixtures: Four arms of **FIG. 13a** and four arms of **FIG. 13b** were placed into cyclic compression fixtures respectively, the cyclic compression fixtures were secured on a tensile machine, and an immersion medium (hydrochloric acid at pH 1.2) was added to immerse the arms. (2) Cyclic compression: Cyclic compression was performed according to the following parameters: ① compression speed: 1 mm/min, ② Maximum trigger force: 3.2 N (when downward pressing was performed to reach this pressure, upward movement was performed) and minimum trigger force: 0.1 N (when upward movement was performed to reach this pressure, downward pressing was performed); and ③ total number of cycles: 100. (3) Bending observation: The arms subjected to bending were placed under a digital microscope for observation, and bending angles were measured. Test results are shown in Table 2.

Table 2 Mechanical property test results

Arm	Bending angle (°)					**Number of cycles to failure**
	Sample 1	Sample 2	Sample 3	Sample 4	Mean	
Arm with no reinforcing	5.73	7.97	5.45	9.59	7.19	100 times

Arm	Bending angle (°)					**Number of cycles to failure**
	Sample 1	Sample 2	Sample 3	Sample 4	Mean	
rib						
Arm with a reinforcing rib	0.03	0.16	0.79	0.215	0.30	100 times

[0253] It can be seen from Table 2 that the arms of the oral pharmaceutical dosage form described herein all had high resistance to lateral bending. Arms with a reinforcing rib had better bending resistance.

[0254] Example 3

[0255] This example illustrates a design, production, and testing of the oral pharmaceutical dosage form described herein. **FIG. 9a** is a schematic diagram of an oral pharmaceutical dosage form. The component composition of the prepared dosage form is shown in **Table 3**. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms an expandable material chamber, the body structure is composed of a cover and a base, the base is provided with a water inlet shown in FIG. 8, the expandable material chamber includes a swelling block and a pushing post, and the swelling block contains an expandable material; and four arms, where the four arms are operably connected to the body, and the arms rotate around the body of the oral pharmaceutical dosage form by force provided by the expandable material. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the expandable material in the presence of gastrointestinal fluid.

Table 3 Component composition of the oral pharmaceutical dosage form

Component	Composition (where a ratio is a mass ratio)
Base	Hypromellose acetate succinate: stearic acid: hydroxypropyl cellulose = 76.5:8.5:15
Cover	Hypromellose acetate succinate: stearic acid:

Component	Composition (where a ratio is a mass ratio)
	hydroxypropyl cellulose = 76.5:8.5:15
Swelling block	Hydroxypropyl methylcellulose: hydroxypropyl cellulose: croscarmellose sodium: barium sulfate = 15:10:60:15
Pushing post	Hypromellose acetate succinate: stearic acid: hydroxypropyl cellulose = 76.5:8.5:15
Arm	Hypromellose acetate succinate: stearic acid: hydroxypropyl cellulose = 76.5:8.5:15

[0256] A preparation method for the oral pharmaceutical dosage form described herein was as follows: (1) Preparation of a swelling block: A prescribed amount of each component was accurately weighed, and was pressed into a cylindrical swelling block by a tablet press. (2) Model assembly: The swelling block, the pushing post, and the cover were sequentially loaded into the base, four arms were assembled on the cover, and the components were connected by glue, and were placed into a No. 0 hard gelatin capsule shell to obtain a capsule of the oral pharmaceutical dosage form described herein.

[0257] Four capsules of the oral pharmaceutical dosage form described herein were subjected to an expansion test, and the test method was as follows: (1) Medium preparation: Sodium chloride was dissolved in purified water, the pH was adjusted to 1.6 with hydrochloric acid, FaSSGF powder was added, the solution was stirred evenly, and 900 mL of solution was measured and poured into a dissolution tester. (2) The four capsules of the oral pharmaceutical dosage form described herein were mounted onto an expansion fixture, the fixture was fixed onto a basket shaft of the dissolution tester, the rotational speed was set to 100 rpm, the capsules were immersed in the medium, and expansion times of the capsules were observed and recorded. The test results are shown in **Table 4**, and the expanded state is shown in FIG. 14.

Table 4 Test results

Sample No.	Expansion time (min)	Mean and range (min)
1	60	67.5(30-90)

Sample No.	Expansion time (min)	Mean and range (min)
2	90	
3	90	
4	30	

[0258] Test results in **Table 4** indicate that the oral pharmaceutical dosage form described herein was fully expanded in about 1 hour, thereby meeting the requirements for swelling and expansion.

[0259] **Example 4**

[0260] This example illustrates a design, production, and testing of the oral pharmaceutical dosage form described herein. **FIG. 9a** is a schematic diagram of an oral pharmaceutical dosage form. The component composition of the prepared dosage form is shown in **Table 6**. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms an expandable material chamber, the body structure is composed of a cover and a base, the base includes a water inlet, the expandable material chamber includes a swelling block and a pushing post, and the swelling block contains an expandable material; and four arms, where the four arms are operably connected to the body. The drug-carrying grooves are located in internal spaces of the four arms, and a bottom portion of each of the drug-carrying grooves includes an imaging layer. The arms rotate around the body of the oral pharmaceutical dosage form by force provided by the expandable material. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the expandable material in the presence of gastrointestinal fluid.

Table 6 Component composition of the oral pharmaceutical dosage form

Component	Composition (where a ratio is a mass ratio)
Base	Cellulose acetate: triacetin = 8:2
Cover	Cellulose acetate: triacetin = 8:2
Swelling block	Crospovidone

Component	Composition (where a ratio is a mass ratio)
Pushing post	Cellulose acetate: triacetin = 8:2
Arm	Cellulose acetate: triacetin = 8:2
Imaging layer	Ethyl cellulose: acetyl tributyl citrate: barium sulfate = 15:10:75

[0261] A preparation method for the oral pharmaceutical dosage form described herein was as follows: (1) Preparation of a swelling block: A prescribed amount of each component was accurately weighed, and was pressed into a cylindrical swelling block by a tablet press. (2) Model assembly: The swelling block, the pushing post, and the cover were sequentially loaded into the base, four arms were assembled on the cover, and the components were connected by glue, and were transferred into a No. 0 hard gelatin capsule shell to obtain a capsule of the oral pharmaceutical dosage form described herein.

[0262] A canine test was performed on the oral pharmaceutical dosage form described herein, with the details as follows: Male Beagle dogs weighing 8-12 kg were selected. The Beagle dogs were fasted for at least 14 h before administration of the oral pharmaceutical dosage form and had free access to drinking water. On the day of the experiment, each Beagle dog was first administered approximately 120 mL of a liquid special diet (canine maintenance feed: water = 1:3 (w/w)) by gavage into the pharynx. Ten minutes after feeding, one capsule was orally administered, followed by gavage of 50 mL of water to ensure the capsule entered the stomach. The animals were allowed free access to drinking water after the administration was completed. At 5.83 h and 11.83 h after administration (i.e., 10 min before the 6 h and 12 h sampling time points), 120 mL of diet was administered in the same manner. In order to evaluate the retention time and state of the preparation, X-ray images of the canine front view and side view were taken before administration and at 0.5 hours, 1 hour, 10 hours, 24 hours, and 36 hours after administration to observe the position and state of the preparation in the dog's body. The X-ray images are shown in FIG. 15. It can be seen from FIG. 15 that the oral pharmaceutical dosage form described herein can be retained in the stomach for 24 hours or more and can disintegrate in vivo, avoiding the potential risk of intestinal obstruction.

[0263] **Example 5**

[0264] This example illustrates a design, production, and testing of the oral pharmaceutical

dosage form described herein. **FIG. 9a** is a schematic diagram of an oral pharmaceutical dosage form. The component composition of the prepared dosage form is shown in **Table 7**. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms an expandable material chamber, the body structure is composed of a cover and a base, the base includes a water inlet, and the expandable material chamber is configured to accommodate a swelling block and a pushing post; and four arms, where the four arms are operably connected to the body, and the arms rotate around the body of the oral pharmaceutical dosage form by force provided by the expandable material. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the expandable material in the presence of gastrointestinal fluid. The expandable material chamber of the oral pharmaceutical dosage form in this embodiment does not accommodate a swelling block and a pushing post.

Table 7 Component composition of the oral pharmaceutical dosage form

Component	Composition (where a ratio is a mass ratio)
Base	Hypromellose acetate succinate: stearic acid: hydroxypropyl cellulose = 76.5:8.5:15
Cover	Hypromellose acetate succinate: stearic acid: hydroxypropyl cellulose = 76.5:8.5:15
Arm	Hypromellose acetate succinate: stearic acid: hydroxypropyl cellulose = 76.5:8.5:15

[0265] A preparation method for the oral pharmaceutical dosage form described herein was as follows: Four arms were assembled onto the cover, the base was assembled to the cover, and the components were connected by glue, and were placed into a No. 0 hard gelatin capsule shell to obtain a capsule of the oral pharmaceutical dosage form described herein.

[0266] The oral pharmaceutical dosage form described herein was subjected to an immersion test, specifically as follows: (1) Immersion medium preparation: 5 L of degassed pure water was taken, with the pH adjusted to about 1.2 with hydrochloric acid; and 900 mL of solution was measured and poured into a dissolution tester. (2) Immersion test: 6 capsules of the oral

pharmaceutical dosage form described herein were placed into the medium for immersion, with 3 capsules removed after 10 hours, and the other 3 capsules removed after 24 h, and reverse compressive strength tests were performed separately. (3) Reverse compression test: 3 unimmersed capsules of the oral pharmaceutical dosage form described herein, 3 capsules of the oral pharmaceutical dosage form described herein that had been immersed for 10 hours, and 3 capsules of the oral pharmaceutical dosage form described herein that had been immersed for 24 hours were inverted on a fixture, and the fixture was fixed on a tensile machine to perform reverse compression at a compression speed of 4 mm/min, and the maximum compressive strength was recorded. Test results are shown in **Table 8**.

Table 8 Immersion test results

Immersion time	**Test direction**	**Test No.**	**Compressive strength (N)**	**Mean**
Unimmersed	Reverse compression	1	8.07	8.20±0.12
		2	8.24	
		3	8.29	
Immersed for 10 hours	Reverse compression	1	3.73	3.71±0.27
		2	3.43	
		3	3.96	
Immersed for 24 hours	Reverse compression	1	3.79	3.69±0.31
		2	3.94	
		3	3.35	

[0267] It can be seen from **Table 8** that the oral pharmaceutical dosage form described herein has good mechanical strength, and as the immersion time increases, the mechanical strength of the structure can gradually decrease. This is conducive to the disintegration of the preparation structure and exit from the pylorus, reducing safety risks during administration.

[0268] **Example 6**

[0269] This example illustrates a design, production, and testing of the oral pharmaceutical

dosage form described herein. **FIG. 16** is a schematic diagram of an oral pharmaceutical dosage form. The component composition of the prepared dosage form is shown in **Table 9**. The oral pharmaceutical dosage form includes: a body structure, where the body structure forms an expandable material chamber, the body structure is composed of a cover and a base, the base includes a water inlet, and the expandable material chamber is configured to accommodate a swelling block and a pushing plunger; and five arms, where the five arms are operably connected to the body, and the arms rotate around the body of the oral pharmaceutical dosage form by force provided by the expandable material. The oral pharmaceutical dosage form is configured to have a pre-administration state in a compact form and a post-administration state in an expanded form that provides gastric retention, and the expanded form of the post-administration state of the oral pharmaceutical dosage form is, at least in part, due to expansion of the expandable material in the presence of gastrointestinal fluid. The expandable material chamber of the oral pharmaceutical dosage form in this embodiment does not accommodate a swelling block and a pushing post.

Table 9 Component composition of the oral pharmaceutical dosage form

Component	Composition (where a ratio is a mass ratio)
Base	Cellulose acetate: diethyl phthalate = 85:15
Cover	Cellulose acetate: diethyl phthalate = 85:15
Pushing post	Cellulose acetate: diethyl phthalate = 85:15
Arm	Cellulose acetate: diethyl phthalate: hydroxypropyl cellulose = 80:15:5

[0270] A preparation method for the oral pharmaceutical dosage form described herein was as follows: Five arms were assembled onto the cover, the base was assembled to the cover, and the components were connected by glue, and were placed into a No. 0 hard gelatin capsule shell to obtain a capsule of the oral pharmaceutical dosage form described herein.

[0271] The oral pharmaceutical dosage form described herein was subjected to an immersion test, specifically as follows: (1) Immersion medium preparation: 5 L of degassed pure water was taken, with the pH adjusted to about 1.2 with hydrochloric acid; and 900 mL of solution was measured and poured into a dissolution tester. (2) Immersion test: 6 capsules of the oral pharmaceutical dosage form described herein were placed into the medium for immersion, with 3

capsules removed after 10 hours, and the other 3 capsules removed after 24 h, and reverse compressive strength tests were performed separately. (3) Reverse compression test: 3 unimmersed capsules of the oral pharmaceutical dosage form described herein, 3 capsules of the oral pharmaceutical dosage form described herein that had been immersed for 10 hours, and 3 capsules of the oral pharmaceutical dosage form described herein that had been immersed for 24 hours were inverted on a fixture, and the fixture was fixed on a tensile machine to perform reverse compression at a compression speed of 4 mm/min, and the maximum compressive strength was recorded. Test results are shown in **Table 10**.

Table 10 Immersion test results

Immersion time	**Test direction**	**Test No.**	**Compressive strength (N)**	**Mean**
Unimmersed	Reverse compression	1	20.23	20.33±0.17
		2	20.53	
		3	20.23	
Immersed for 10 hours	Reverse compression	1	11.41	11.29±0.12
		2	11.28	
		3	11.18	
Immersed for 24 hours	Reverse compression	1	11.70	11.50±0.21
		2	11.52	
		3	11.29	

[0272] It can be seen from **Table 10** that after the oral pharmaceutical dosage form described herein was immersed for 24 hours, the reverse compressive strength was still at least 45% of the strength of the unimmersed one, and the mechanical properties of the oral pharmaceutical dosage form described herein are still good. For oral pharmaceutical dosage forms of identical dimensions, the mechanical strength of the five-arm oral pharmaceutical dosage form is greater than that of the four-arm oral pharmaceutical dosage form.

CLAIMS

1. A pharmaceutical dosage form, configured to have a pre-administration state in a compact form and a post-administration state in an expanded form, the pharmaceutical dosage form comprising:

an arm and a body connected to the arm, wherein

the body comprises: a first compartment configured to accommodate an expandable member; a second compartment, wherein the first compartment is in communication with the second compartment through an orifice; a movable member movable from the first compartment to the second compartment; and a fluid inlet connected to the first compartment and/or the second compartment, wherein force provided by the expandable member extends to the movable member, enabling at least a portion of the movable member to be accommodated in the second compartment and pushing the arm to extend beyond the body or rotate around the body; and

a drug, wherein the drug is carried on the arm and/or the body.

2. The pharmaceutical dosage form according to claim 1, wherein the expandable member comprises a swellable material.

3. The pharmaceutical dosage form according to claim 2, wherein the pharmaceutical dosage form is an oral pharmaceutical dosage form, and an expanded form of the post-administration state of the oral pharmaceutical dosage form is at least partially due to expansion of the swellable material in the presence of gastrointestinal fluid.

4. The pharmaceutical dosage form according to any one of claims 1 to 3, wherein a gastric retention time of the oral pharmaceutical dosage form is about 6 hours to about 3 months.

5. The pharmaceutical dosage form according to any one of claims 1 to 4, wherein the swellable material expands by at least about 1.2 times in volume upon exposure to the gastrointestinal fluid.

6. The pharmaceutical dosage form according to any one of claims 1 to 5, wherein an amount of the swellable material in the first compartment is at least about 5 mg.

7. The pharmaceutical dosage form according to any one of claims 1 to 6, wherein the arm, the first compartment, the second compartment, the movable member, and the expandable member are all made of a pharmaceutically acceptable material.

8. The pharmaceutical dosage form according to any one of claims 1 to 7, wherein a quantity

of arms is 2 to 6.

9. The pharmaceutical dosage form according to any one of claims 1 to 8, wherein in the post-administration state, angles between two adjacent arms are equal and range from 60° to 120°.

10. The pharmaceutical dosage form according to any one of claims 1 to 9, wherein the body comprises an opening, the arm passes through the opening, and at least a portion of the arm is accommodated in the second compartment.

11. The pharmaceutical dosage form according to any one of claims 1 to 10, wherein the first compartment is formed by a base, and the second compartment is formed by a cover.

12. The pharmaceutical dosage form according to claim 11, wherein the arm comprises a connecting end accommodated in the second compartment, an extension section connected to the connecting end, and a distal end opposite in position to the connecting end.

13. The pharmaceutical dosage form according to claim 12, wherein the connecting end of the arm comprises a pivot and a pushing member, and the pivot is connected to the cover; and the pushing member abuts against the movable member.

14. The pharmaceutical dosage form according to claim 13, wherein the connecting end of the arm further comprises a neck connected to the pivot and a transition section.

15. The pharmaceutical dosage form according to claim 14, wherein a ratio of a width of the extension section to a width of the neck ranges from 5:1 to 1:1.

16. The pharmaceutical dosage form according to claim 13, wherein the pushing member comprises four side surfaces, and a shape of the four side surfaces is selected from a trapezoid, a triangle, or a combination thereof.

17. The pharmaceutical dosage form according to any one of claims 12 to 16, wherein the distal end of each of the arms comprises a protrusion, and in the pre-administration state, the protrusions of the distal ends of adjacent arms abut against each other.

18. The pharmaceutical dosage form according to claim 1, wherein in the pre-administration state, the arm forms a relatively independent accommodating space, and the drug is located in the accommodating space.

19. The pharmaceutical dosage form according to any one of claims 1 to 18, wherein the body further comprises a central post, and in the pre-administration state, an axial length of the central post does not exceed an axial length of the arm.

20. The pharmaceutical dosage form according to claim 19, wherein the central post carries

the drug.

21. The pharmaceutical dosage form according to claim 1, wherein the movable member comprises a bottom portion and a protruding portion connected to the bottom portion, and the protruding portion abuts against a pushing member.

22. The pharmaceutical dosage form according to claim 21, wherein a bottom surface of the bottom portion is circular or annular.

23. The pharmaceutical dosage form according to claim 21 or 22, wherein the bottom portion is in smooth transition with the protruding portion, or the bottom portion and the protruding portion have a chamfer therebetween.

24. The pharmaceutical dosage form according to any one of claims 21 to 23, wherein the protruding portion has an arcuate top or a flat top.

25. The pharmaceutical dosage form according to any one of claims 21 to 24, wherein an outer surface of the movable member matches an outer side surface and a bottom surface of the connecting end of the arm, and in the post-administration state, the outer side surface of the connecting end of the arm abuts against the bottom portion of the movable member, and the bottom surface of the connecting end abuts against an outer side surface of the protruding portion of the movable member.

26. The pharmaceutical dosage form according to any one of claims 1 to 25, wherein an engagement feature is configured on the movable member, and in the post-administration state, the engagement feature on the movable member engages with engagement features on the arm and/or the cover and/or the base and/or the expandable member.

27. The pharmaceutical dosage form according to claim 26, wherein the engagement feature is a form-fit surface or a mechanical snap-fit assembly or a binder.

28. The pharmaceutical dosage form according to any one of claims 1 to 27, wherein the opening comprises a first width at a position close to a central axis and a second width at a position away from the central axis.

29. The pharmaceutical dosage form according to claim 28, wherein the second width is greater than the first width.

30. The pharmaceutical dosage form according to any one of claims 1 to 29, wherein a reinforcing rib is provided on the cover and/or the arm.

31. The pharmaceutical dosage form according to claim 30, wherein the reinforcing rib is

located at the neck of the arm.

32. The pharmaceutical dosage form according to claim 30 or 31, wherein in the post-administration state, the reinforcing rib abuts against the body.

33. The pharmaceutical dosage form according to any one of claims 1 to 32, wherein the base is provided with at least one water inlet.

34. The pharmaceutical dosage form according to any one of claims 1 to 32, wherein the base is formed by a semipermeable membrane.

35. The pharmaceutical dosage form according to any one of claims 1 to 34, further comprising a restraining member configured to inhibit extension of the arm.

36. The pharmaceutical dosage form according to claim 35, wherein the restraining member is prepared from an erodible material, and the restraining member releases the inhibition of extension of the arm within about 30 minutes after administration to a subject.

37. A pharmaceutical dosage form, comprising:

a body extending in a Z axis direction, wherein the body comprises an internal chamber and an expandable structure accommodated in the internal chamber, and the internal chamber comprises a fluid inlet;

an arm, wherein the arm is rotatable around the body; and

a drug, wherein

the pharmaceutical dosage form is configured to have a first state in which the pharmaceutical dosage form extends in the Z axis direction, and a second state in which the pharmaceutical dosage form extends in directions of XY axes and the Z axis direction simultaneously; the second state arises at least in part from expansion of the expandable structure; and the extension in the directions of the XY axes results from rotation of the arm about the body.

38. The pharmaceutical dosage form according to claim 37, wherein a quantity of arms is 2 to 6.

39. The pharmaceutical dosage form according to claim 38, wherein in the second state, the arms are parallel to or coincide with a plane in which the XY axes are located, or intersect with a plane in which the XY axes are located.

40. The pharmaceutical dosage form according to claim 38, wherein in the second state, projections of the arms on a Z axis are at a same height or different heights.

41. A pharmaceutical dosage form, configured to have a pre-administration state in a compact

form and a post-administration state in an expanded form, the pharmaceutical dosage form comprising:

an arm and a body connected to the arm, wherein the arm is rotatable around the body, the body comprises a pushing device, the pushing device is triggered by an external condition and pushes the arm to rotate around the body to form a post-administration state in an expanded form, wherein

the pharmaceutical dosage form, when configured to have the pre-administration state in a compact form, comprises an outer surface and an interior opposite to the outer surface; and

a drug component, wherein the drug component is carried in the interior of the pharmaceutical dosage form, and when the pharmaceutical dosage form is in the post-administration state in an expanded form, the drug is at least partially exposed.

42. The pharmaceutical dosage form according to claim 41, wherein the pushing device comprises an expandable material.

43. The pharmaceutical dosage form according to claim 41 or 42, wherein the pushing device further comprises a movable member.

44. The pharmaceutical dosage form according to any one of claims 41 to 43, wherein the drug component is carried on the arm and/or the body.

45. The pharmaceutical dosage form according to any one of claims 41 to 44, wherein when the pharmaceutical dosage form is in the pre-administration state in a compact form, no drug is exposed on a surface of the pharmaceutical dosage form.