

Description

Title of Invention: PHARMACEUTICAL DOSAGE FORMS AND PREPARATION METHODS THEREOF

[0001] CROSS-REFERENCE TO RELATED APPLICATIONS

[0002] This application claims priority benefit of International Patent Application No. PCT/CN2023/118043, filed September 11, 2023, the content of which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0003] This application relates to a pharmaceutical dosage form and a method for preparing it, such as a pharmaceutical dosage form prepared by a three-dimensional (3D) printing method. In one aspect, the present application relates to pharmaceutical dosage forms loaded with liquid or semi-solid materials. In one aspect, the present application relates to a pharmaceutical dosage form loaded with solid material.

BACKGROUND

[0004] Additive manufacturing, also known as three-dimensional printing ("3D printing"), is a rapid prototyping technology that involves the process of joining or curing materials to create three-dimensional objects. Specifically, based on a digital model, materials are usually added together layer by layer. The flow of material and the movement of the print nozzle is typically controlled by a computer until the desired shape is formed. Commonly used 3D printing technologies include material extrusion molding technology, adhesive jet molding technology, powder bed fusion molding technology and photopolymerization curing technology.

[0005] In recent years, there have been attempts to apply additive manufacturing technology to the manufacture of pharmaceutical dosage forms with high precision and high process requirements. However, for pharmaceutical dosage forms containing liquid or semi-solid drugs, excipients or adjuvants, it is still difficult to use additive manufacturing techniques to accurately print such pharmaceutical dosage forms. In addition, high temperatures can have a number of effects on material properties during additive manufacturing. Also, there is little focus on how compatibility of drugs and pharmaceutical excipients or adjuvants with printing materials can be improved during long-term storage.

[0006] BRIEF SUMMARY OF THE INVENTION

[0007] The application provides pharmaceutical dosage forms, preparation methods thereof, and printing devices. The pharmaceutical dosage form can be loaded with a liquid, a semi-solid, or a solid material.

- [0008] One aspect of the application provides a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, wherein the interior cover at least partially covers the opening of the compartment, and wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the fourth material is liquid or semi-liquid. In some embodiments, the fourth material is solid. In some embodiments, the pharmaceutically acceptable material is heat labile and/or incompatible with another component of the pharmaceutical dosage form (e.g., a component of the fifth material) .
- [0009] Another aspect of the application provides a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover covers the opening of the compartment; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the fourth material is liquid or semi-liquid. In some embodiments, the fourth material is solid. In some embodiments, the pharmaceutically acceptable material is heat labile and/or incompatible with another component of the pharmaceutical dosage form (e.g., a component of the fifth material) .
- [0010] Another aspect of the application provides a medical device, comprising: a bottom formed by a first material; a peripheral wall formed by a second material; wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and the interior cover at least partially covers the opening; a fourth material contained in the compartment; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the fourth material is liquid or semi-liquid. In

some embodiments, the fourth material is solid. In some embodiments, the fourth material comprises a pharmaceutically acceptable material. In some embodiments, the pharmaceutically acceptable material is heat labile and/or incompatible with another component of the medical device (e.g., a component of the fifth material) .

[0011] Another aspect of the application provides a method for preparing a pharmaceutical dosage form by three-dimensional printing, wherein the method comprises: printing a bottom of the pharmaceutical dosage form using a first material; printing a peripheral wall of the pharmaceutical dosage form using a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; printing an interior cover attached to the shell using a third material, wherein the interior cover at least partially covers the opening of the compartment, and wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell; delivering, after the printing of the interior cover, a fourth material to the compartment through the opening of the compartment; and printing an exterior cover attached to the interior cover and/or shell using a fifth material, such that the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the fourth material is liquid or semi-liquid. In some embodiments, the fourth material is solid. In some embodiments, the fourth material comprises a pharmaceutically acceptable material. In some embodiments, the pharmaceutically acceptable material is heat labile and/or incompatible with another component of the pharmaceutical dosage form (e.g., a component of the fifth material) .

[0012] Another aspect of the application provides a method for preparing a pharmaceutical dosage form, comprising: forming a first surface by a first material along a first preset path; forming a second surface by a second material along a second preset path, wherein the first surface and the second surface together form at least one compartment; forming a third surface by a third material along a third present path to partially enclose the compartment; delivering a fourth material to the compartment; forming a fourth surface by a fifth material along a fourth preset path to seal the compartment via covering any opening defined by the third surface.

[0013] Another aspect of the application provides a drug production apparatus, comprising: a first feeding unit, capable of providing a first printing material to a first printing unit; a second feeding unit, capable of providing a second printing material to a second printing unit; a carrying platform capable of moving relative to the first feeding unit and/or the second feeding unit; wherein the first printing unit comprises at least one nozzle, wherein each of the at least one nozzle comprises a feeding channel and a sealing structure, and the sealing structure moves in whole or in part to seal or open the feeding channel; the second printing unit comprises at least one discharging module,

a driving device, and a mounting frame, wherein the discharging module comprises a discharging barrel, wherein the driving device drives the discharging of the second printing material from the discharging barrel, and wherein the driving device and the discharging barrel are fixed with the mounting frame; and the first printed material and/or the second printed material comprises a pharmaceutically active material. In some embodiments, the pharmaceutically active material is heat labile.

- [0014] The above is an overview of the application and may be simplified, generalized and omitted in detail, so those skilled in the art should be aware that this part is only illustrative of examples and is not intended to limit the scope of the application in any way. This overview section is neither intended to identify the key or necessary features of the subject matter for which protection is claimed, nor is it intended to be used as an aid in determining the scope of the subject matter claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

- [0015] It is understood that these drawings only depict some embodiments of the contents of the present application and should not be considered as limiting the scope of the contents of the present application. By adopting the drawings, the contents of the present application will be described more clearly and in detail.
- [0016] FIG. 1A to FIG. 1D show the cross-sectional front view schematic diagrams of the pharmaceutical dosage form according to different embodiments of the present application.
- [0017] FIG. 2A and FIG. 2B show schematic diagrams of the surface tension of the pharmaceutically active materials in the pharmaceutical dosage forms according to different embodiments of the present application.
- [0018] FIG. 3A to FIG. 3C show perspective schematic diagrams of the pharmaceutical dosage form according to different embodiments of the present application.
- [0019] FIG. 4A to FIG. 4F show top view schematic diagrams of the interior cover of the pharmaceutical dosage form according to different embodiments of the present application.
- [0020] FIG. 5A and FIG. 5B show cross-sectional front view schematic diagram of the pharmaceutical dosage form according to different embodiments of the present application.
- [0021] FIG. 6A and FIG. 6B show cross-sectional front view schematic diagram of the pharmaceutical dosage form according to different embodiments of the present application.
- [0022] FIG. 7A and FIG. 7B show cross-sectional schematic diagrams of the pharmaceutical dosage form according to different embodiments of the present application.
- [0023] FIG. 8 shows a flowchart of a method for preparing pharmaceutical dosage forms by three-dimensional printing according to one embodiment of this application.

- [0024] FIG. 9 shows a flowchart of a method for preparing pharmaceutical dosage forms by three-dimensional printing according to one embodiment of this application.
- [0025] FIG. 10 shows a cross-sectional front view schematic diagram of a pharmaceutical dosage form according to one embodiment of this application.
- [0026] FIG. 11A to FIG. 11C show a method for preparing pharmaceutical dosage forms according to one embodiment of this application.
- [0027] FIG. 12A to FIG. 12C show schematic diagrams of different nozzle printing paths of the interior cover shown in FIG. 4E.
- [0028] FIG. 12D illustrates a schematic diagram of the nozzle printing path of the interior cover of a pharmaceutical dosage form according to one embodiment of this application.
- [0029] FIG. 13 shows a perspective view of a print head used for printing the pharmaceutical dosage forms of this application according to one embodiment of this application.
- [0030] FIG. 14A and FIG. 14B show perspective views of printing apparatus for printing pharmaceutical dosage forms according to different embodiments of this application.
- [0031] FIG. 15A and FIG. 15B show the front view and top view schematic diagrams of a printed pharmaceutical dosage form, respectively.
- [0032] FIG. 15C and FIG. 15D show front view and top view schematic diagrams of another printed pharmaceutical dosage form, respectively.
- [0033] FIG. 16A and FIG. 16B show the front view and top view schematic diagrams of a printed pharmaceutical dosage form, respectively.
- [0034] FIG. 16C and FIG. 16D show front view and top view schematic diagrams of another printed pharmaceutical dosage form, respectively.
- [0035] FIG. 17A to FIG. 17D show cross-sectional front view schematic diagrams of intermediates of pharmaceutical dosage forms according to different embodiments of this application.
- [0036] FIG. 18A and FIG. 18B show VHX imaging 3D diagrams of intermediates of pharmaceutical dosage forms according to different embodiments of this application.

DETAILED DESCRIPTION

- [0037] The subject application provides products (e.g., such as a pharmaceutical dosage form), and methods and system of making thereof, provided herein have distinct advantages providing improvement to what is available in the art. For example, in certain aspects, during the production process, the high-temperature exterior cover is isolated from the material in the compartment, such as that containing a heat labile pharmaceutically active material, to avoid the influence of high temperature. Thus, the resulting products, such as a pharmaceutical dosage form, may comprise

less degradation product (s) than would be present in a differently designed and/or produced product. In certain aspects, during the production process, the interior cover of the pharmaceutical dosage form can increase the loading amount of the pharmaceutically active material in the compartment, or reduce the surface tension of the pharmaceutically active material in the compartment, so that a higher dose (e.g., at least about 1%, 2%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, or more, higher) can be achieved within a fixed volume of pharmaceutical dosage form. Moreover, in certain aspects, during the storage process, the outer cover material (e.g., exterior cover) is isolated from the material (e.g., API-containing material) in the compartment to avoid the incompatibility between the exterior cover material and the material in the compartment thereby also reducing any issues resulting therefrom, e.g., increased degradation. Pharmaceutical dosage forms as well as preparation methods provided herein can also provide higher purity (e.g., at least about 1%, 2%, 4%, 5%, 10%, 20%, 50%, 70%, 90%, 1-fold, 2-fold, or more, higher) of the pharmaceutically active material.

- [0038] The illustrative embodiments described in the detailed description, drawings, and claims are not meant to be limiting. Other embodiments may be utilized, and other changes may be made, without departing from the spirit or scope of the subject matter of this application. Before providing a more detailed description of this application, it should be understood that this application is not limited to the specific embodiments described, and it is, of course, subject to change.
- [0039] All publications and patents cited in this specification are incorporated herein by reference as if each individual publication or patent were specifically and individually indicated to be incorporated by reference, and the same are incorporated herein by reference to disclose and describe the methods and/or materials related to the publications cited. All publications and patents cited in this specification are incorporated herein by reference as if each individual publication or patent were specifically and individually indicated to be incorporated by reference, and the same are incorporated herein by reference to disclose and describe the methods and/or materials related to the publications cited.
- [0040] Those skilled in the art will understand, upon reading this application, that the various embodiments described and explained herein have discrete components and features that can be easily separated or combined with features of any other embodiments without departing from the scope or spirit of this application. Any described methods can be performed in the order of events described or in any other logically possible order. Before providing a detailed description of the embodiments of this application, it should be understood that this application is not limited to specific materials, reagents, reactants, manufacturing processes, etc., and these can be varied.

It should also be understood that the terminology used in this application is for the purpose of describing particular embodiments only and is not intended to limit.

[0041] I. Definition

[0042] The terms “comprises”, “includes”, “contains” and “has” and other similar expressions as used herein shall have the same meanings, and the list or elements of the following words is not intended to be exhaustive or limited to one or more of the listed elements. For example, an item that “includes” components A, B, and C may consist of components A, B, and C (i.e., contain only), or may contain not only components A, B, and C, but also one or more other components. It is understood that embodiments described herein as “comprising” include “consisting of” and “consisting essentially of” embodiments.

[0043] It should be noted that, as used in this description and the accompanying claims, the singular forms “a”, “one” and “described” include plural objects, unless the context otherwise expresses. So, for example, “compound” includes multiple compounds.

[0044] The term “liquid” refers to an incompressible fluid material that flows freely and has a constant volume.

[0045] The term “semi-solid” refers to a viscous liquid that can flow under external forces (pressure, thrust, rotational force, gravity, etc.) or under process conditions (temperature, pressure, etc.).

[0046] The term “cover” or “covering” refers to the ability to prevent substances from flowing out of or spilling through the opening. In some embodiments, “covering” can be achieved by directly contacting the cover with the item to be covered. In some embodiments, “covering” can be achieved by putting the cover above the item to be covered, but not directly contacting them.

[0047] The term “pharmaceutical active material” refers to a biologically active material.

[0048] The term “pharmaceutically acceptable” refers to compounds, materials, compositions and/or dosage forms that are suitable for use in contact with human and animal tissues within the limits of sound medical judgment without excessive toxicity, irritation, allergic reactions, or other problems or complications, commensurate with a reasonable benefit/risk ratio.

[0049] The term “pharmaceutically acceptable salts” includes salts formed by alkali ions and free acids or salts formed by acid ions and free bases, for example, metal salts, ammonium salts, salts formed with organic bases, salts formed with inorganic acids, salts formed with organic acids, salts formed with alkaline or acidic amino acids, etc.

[0050] The term “stereoisomer” refers to isomers resulting from different spatial arrangements of atoms in a molecule, including cis-isomers, trans isomers, enantiomers, and diastereomers.

- [0051] The term “peptide” as used in this article refers to polymers containing amino acid residues linked by peptide bonds. In some embodiments, peptides contain 2 to 100 amino acid residues, including 2 to 50 amino acid residues or 2 to 40 amino acid residues. Such polymers can contain natural or unnatural amino acid residues, or a combination thereof. In some embodiments, peptides can be monomers. In some embodiments, peptides can be dimers, trimers, or multimers, including subunits with covalently linked subunits linked by non-peptide bonds, such as disulfide bonds, such as human insulin. The term also includes the kind of its modifications, e.g., post-translational modifications of one or more residues, e.g., methylation, phosphorylation, glycosylation, sialylation, or acetylation.
- [0052] References to values or parameters preceded by “about” or “approximate” are to be understood as describing variations of the stated value or parameter. For example, a description referring to “about X” includes a description of “X”.
- [0053] When providing numerical ranges, it should be understood that each intervening value between the upper and lower limits of that range, and any other stated or intervening value within that stated range, is encompassed within the scope of this application, unless the context clearly dictates otherwise. The upper and lower limits of ranges provided herein also encompass a $\pm 10\%$ variation of the specified limits. For example, for a range 10% to 20%, the low limit could vary from 9% to 11%, and the upper limit could vary from 18% to 22%, and this range covers 9% to 22%, 9% to 20%, 10% to 20%, and 10% to 22%. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges and are also encompassed within the scope of this application, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also within the scope of this application.
- [0054] The terms “first material”, “second material”, “third material”, “fourth material”, “fifth material” refer to a material that contains only one component, or a mixture of multiple components.
- [0055] II. Pharmaceutical dosage forms
- [0056] In one aspect, provided herein is a pharmaceutical dosage form comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming (or defining) a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, wherein the interior cover at least partially covers the opening of the compartment, and wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material,

wherein the exterior cover is attached to the interior cover and/or the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the exterior cover is configured to fully cover the interior cover. In some embodiments, the exterior cover is configured to fully cover each opening of the one or more openings of the interior cover. In some embodiments, the exterior cover is configured to fully cover each (or all of) opening of the one or more openings of the interior cover, but does not fully cover the interior cover. In some embodiments, the exterior cover is attached to the interior cover but not the shell. In some embodiments, the exterior cover is attached to both the interior cover and the shell. In some embodiments, the exterior cover is attached to the shell.

[0057] In some aspects of the description provided herein, numerical descriptors are provided to identify openings of aspects of the pharmaceutical dosage forms described herein. For example, in some embodiments, the opening of a compartment formed by a shell is described as a first opening. In some embodiments, the one or more openings of an interior cover are described as one or more second openings, or second opening, third opening, and so forth. In some embodiments, the two or more openings of the interior cover are in communication with the same compartment formed by the shell. In some embodiments, at least one of the two or more openings of the interior cover is in communication with a different compartment formed by the shell.

[0058] In some embodiments, the pharmaceutical dosage forms provided herein comprise a shell forming one or more compartments, such as a compartment containing a pharmaceutically active material, an excipient, and/or an adjuvant. In some embodiments, the shell comprises a bottom formed by a first material and a peripheral wall formed by a second material. In some embodiments, the first material and the second material are the same. In some embodiments, the boundary between a bottom and a peripheral wall of a shell may be arbitrarily defined, such as when the material of the bottom and the material of the peripheral wall are the same.

[0059] The pharmaceutical dosage forms provided herein comprise one or more pharmaceutically acceptable materials, such as a pharmaceutically active material, excipient, or an adjuvant. In some embodiments, wherein the pharmaceutical dosage form comprises more than one pharmaceutically acceptable material, at least one pharmaceutically acceptable material is contained in a compartment formed by a shell, wherein the compartment comprises an opening, wherein an interior cover at least partially covers the opening of the compartment, and wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell.

- [0060] In some embodiments, the pharmaceutical dosage form comprises a volume of gas contained in the area delimited by the shell, interior cover, and, optionally, the exterior cover (e.g., when the interior cover comprises one or more openings). In some embodiments, the volume of gas is based on the volume of the fourth material in the compartment and the volume of the pharmaceutical dosage form delimited by the bottom, peripheral wall, interior cover, and, optionally, exterior cover (e.g., when the interior cover comprises one or more openings). In some embodiments, the gas is air, oxygen, or nitrogen. In some embodiments, the gas is air. In some embodiments, the pharmaceutical dosage form does not comprise a volume of gas.
- [0061] In some embodiments, the ratio of the area of an opening of the one or more openings (e.g., all of the one or more openings) of the interior cover to the area of the opening of the compartment formed by the shell is less than 95%, such as less than any of 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10%, 5%, 1%, or less. In some embodiments, the ratio of the area of an opening of the one or more openings (e.g., all of the one or more openings) of the interior cover to the area of the opening of the compartment formed by the shell is between about 5% to about 90%, such as any of between about 10% to about 90%, between about 10% to about 80%, between about 20% to about 70%, between about 20% to about 60%, between about 20% to about 50%, between about 15% to about 70%, between about 15% to about 60%, between about 15% to about 50%, between about 15% to about 30%, between about 15% to about 20%, or between about 20% to about 30%.
- [0062] In some embodiments, the third material of the interior cover and the second material of the peripheral wall are monolithic. In some embodiments, the first material of the bottom and the second material of the peripheral wall are monolithic. In some embodiments, the third material of the interior cover, the second material of the peripheral wall, and the first material of the bottom are monolithic.
- [0063] In some embodiments, the shell forms one or more additional compartments. In some embodiments, each of the one or more additional compartments comprises an opening. The opening of the one or more additional compartments can be the same or different from the opening of the compartment, such as varying in shape and/or size. The one or more additional compartments can contain the same or different material from the fourth material (e.g., the additional compartment contains adjuvant (s) and the fourth material comprises API), and/or can contain the same or different amount of the fourth material. In some embodiments, at least one of the one or more additional compartments is empty, i.e., not loaded with a material. In some embodiments, the interior cover at least partially covers at least one opening of the one or more additional compartments. In some embodiments, the interior cover fully covers at least one opening of the one or more additional compartments. In some embodiments, at least one opening

of the one or more openings of the interior cover is in communication with the at least one opening of the one or more additional compartments. In some embodiments, the pharmaceutical dosage form further comprises a second interior cover that at least partially covers at least one opening of the one or more additional compartments. In some embodiments, the second interior cover comprises one or more openings in communication with the at least one opening of the one or more additional compartments. The interior cover and the second interior cover: (i) can comprise the same or different materials, (ii) can have the same or different sizes, (iii) can have the same or different shapes, and/or (iv) can have the same or different numbers of openings.

[0064] In some embodiments, the exterior cover is attached to the shell. In some embodiments, the exterior cover is attached to the interior cover. In some embodiments, the exterior cover is attached to both the shell and the interior cover.

[0065] In some embodiments, the shape of the pharmaceutical dosage form is a cylinder. In some embodiments, when the ratio of the maximum length of any two points on the bottom edge (e.g., diameter) of the cylinder to the height of the cylinder is less than 1 (e.g., less than about any of 0.9, 0.8, 0.5, 0.2, 0.1, 0.05, or less), the ratio of the area of all openings of the one or more openings of the interior cover and the area of the opening of the compartment formed by the shell is less than 90% (e.g., less than about any of 80%, 70%, 60%, 50%, 40%, 30%, 20%, 15%, 10%, 5%, 1%, or less), such as any of between about 10% to about 30%, between about 15% to about 30%, between about 15% to about 20%, or between about 20% to about 30%. In some embodiments, when the ratio of the maximum length of any two points on the bottom edge (e.g., diameter) of the cylinder to the height of the cylinder is between 1 and 5.5 (e.g., about any of 1, 2, 3, 4, 5, 5.5, or any values in between), the ratio of the area of all openings of the one or more openings of the interior cover and the opening of the compartment formed by the shell is less than 90% (e.g., less than about any of 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10%, 5%, 1%, or less), such as any of between about 10% to about 30%, between about 15% to about 30%, between about 15% to about 20%, or between about 20% to about 30%. In some embodiments, when the ratio of the maximum length of any two points on the bottom edge (e.g., diameter) of the cylinder to the height of the cylinder is more than 5.5 (e.g., more than about any of 6, 7, 8, 10, 15, or more), the ratio of all openings of the one or more openings of the interior cover and the opening of the compartment formed by the shell is less than 90% (e.g., less than about any of 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10%, 5%, 1%, or less), such as any of between about 10% to about 30%, between about 15% to about 30%, between about 15% to about 20%, or between about 20% to about 30%.

[0066] In another aspect, provided herein is a pharmaceutical dosage form comprising: a bottom formed by a first material; a peripheral wall formed by a second material,

wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover covers the opening of the compartment; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the fifth material comprises a component that is incompatible with a component (e.g., API) of the fourth material. In some embodiments, the pharmaceutically acceptable material comprises a heat labile component. In some embodiments, the third material of the interior cover is an erodible material. In some embodiments, the interior cover comprises a mesh. In some embodiments, the exterior cover is configured to fully cover the interior cover. In some embodiments, the exterior cover is attached to the interior cover but not the shell. In some embodiments, the exterior cover is attached to both the interior cover and the shell. In some embodiments, the exterior cover is attached to the shell. In some embodiments, the first material of the bottom and the second material of the peripheral wall are monolithic. In some embodiments, the shell forms one or more additional compartments. In some embodiments, each of the one or more additional compartments comprises an opening. The opening of the one or more additional compartments can be the same or different from the opening of the compartment, such as varying in shape and/or size. The one or more additional compartments can contain the same or different material from the fourth material (e.g., the additional compartment contains excipient (s) and the fourth material comprises API), and/or can contain the same or different amount of the fourth material. In some embodiments, at least one of the one or more additional compartments is empty, i.e., not loaded with a material. In some embodiments, the interior cover also covers all openings of the one or more additional compartments. In some embodiments, the pharmaceutical dosage form further comprises a second interior cover that covers all openings of the one or more additional compartments. The interior cover and the second interior cover: (i) can comprise the same or different materials, (ii) can have the same or different sizes, and/or (iii) can have the same or different shapes. In some embodiments, the material of the second interior cover is an erodible material. In some embodiments, the second interior cover comprises a mesh.

[0067] In some embodiments, the first material is different from the second material. In some embodiments, the first material and the second material are the same. In some embodiments, the second material is different from the third material. In some embodiments, the second material and the third material are the same. In some em-

bodiments, the first material is the same as the third material. In some embodiments, the first material is different from the third material. In some embodiments, the first, second, and third materials are all the same. In some embodiments, the first and second materials are the same, which are different from the third material. In some embodiments, the third material is different from the fifth material. In some embodiments, the dissolution rate (such as in body fluid) of the third material is different from (can be faster or slower) that of the fifth material. In some embodiments, the third material has a higher rate of dissolution. In some embodiments, the fifth material has a higher rate of dissolution. In some embodiments, the fifth material is different from all of the first, second, and third materials. In some embodiments, the third material and the fifth material are the same. In some embodiments, the third material and the fifth material have the same dissolution rate. In some embodiments, the third and fifth material have different melting temperature or printing temperature. In some embodiments, the fifth material has a higher melting temperature or printing temperature than the third material. In some embodiments, the third and fifth material have different mechanical strength. In some embodiments, the fifth material has a higher mechanical strength than the third material. In some embodiments, the third material (e.g., material used in the interior cover) has a higher compatibility with the pharmaceutical active material in the compartment compared to the fifth material (e.g., material used in the exterior cover) .

- [0068] In some embodiments, the shape of the pharmaceutical dosage form is a cylinder, a runway-shaped cylinder, an elliptical cylinder, a cube, a cuboid, a capsule, or a circular truncated cone.
- [0069] In some embodiments, the first, second, third, and/or fifth material is each independently selected from the materials provided herein.
- [0070] In some embodiments, the first, second, third, and/or fifth material independently comprises thermoplastic materials. In some embodiments, the thermoplastic material is a dissolvable material (e.g., dissolvable in body fluid, such as in gastrointestinal tract) . In some embodiments, the thermoplastic material is edible (i.e., suitable for individual digestion and absorption) . Any thermoplastic materials suitable for making pharmaceutical dosage forms can be used herein, such as selected from of the group consisting of hydrophilic polymers, hydrophobic polymers, swollen polymers, non-swelling polymers, porous polymers, non-porous polymers, dissolved polymers (e.g., soluble polymers) , pH-sensitive polymers, natural polymers, waxy materials, and combinations thereof. In some embodiments, the thermoplastic material is cellulose ether, cellulose ester, acrylic resin, ethylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxymethylcellulose, mono-or diglyceride of C12-C30 fatty acids, C12-C30 fatty alcohols, wax, poly (meth) acrylic acid, polyvinyl-

caprolactam-polyvinyl acetate-polyethylene glycol graft copolymer, vinylpyrrolidone-vinyl acetate copolymer (PVP-VA), polyvinylpyrrolidone (PVP), vinylpyrrolidone-vinyl acetate copolymer, polyvinyl alcohol-polyethylene glycol graft copolymer, polyvinyl alcohol (PVA), poly (vinyl acetate) (PVAc), butyl methacrylate- (2-dimethylaminoethyl) methacrylate-methyl methacrylate copolymer, dimethylaminoethyl methacrylate-methacrylate copolymer, ethyl acrylate-methyl methacrylate-trimethylammonium ethyl methacrylate chloride copolymer, methyl methacrylate-methyl methacrylate-methacrylic acid copolymer, methyl methacrylate-methyl methacrylate copolymer, ethyl methacrylate-acrylate copolymer, polyethylene oxide (PEO), polyethylene glycol (PEG), hyperbranched polyesteramide, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose (HMPC), hypromellose acetate succinate (HPMCAS), lactide glycolide copolymer (PLGA), carbomer, Ethylene-vinyl acetate copolymer, polyethylene (PE), polycaprolactone (PCL), hydroxypropyl cellulose (HPC), polyoxyethylene 40 hydrogenated castor oil, methylcellulose (MC), ethylcellulose (EC), poloxamer, hydroxypropyl methylcellulose phthalate (HPMCP), hydrogenated castor oil, hydrogenated soybean oil, glyceryl palmitic acid stearate, polylactic acid (PLA), polyglycolic acid (PGA), cellulose acetate butyrate (CAB), Polyvinyl acetate phthalate (PVAP), hydrogel, gelatin, hydrogenated vegetable oil, polyvinyl acetaldehyde aminolactate (AEA), shellac, sodium alginate, cellulose acetate phthalate (CAP), gum arabic, xanthan gum, glyceryl monostearate, octadecanoic acid, thermoplastic starch and their derivatives such as their salts, amides, halogenates or esters. In some embodiments, the wax may be selected from one or a more of beeswax, paraffin, Brazil carnauba wax, and any combination thereof.

- [0071] In some embodiments, the first, second, third, and/or fifth material independently comprises a non-thermoplastic material. Any non-thermoplastic materials suitable for making pharmaceutical dosage forms can be used herein, such as selected from the group consisting of non-thermoplastic starch, sodium starch glycolate (CMS-Na), sucrose, dextrin, lactose, microcrystalline cellulose (MCC), mannitol, magnesium stearate, silica gel, glycerin, syrup, lecithin, soybean oil, camellia oil, ethanol, propylene glycol, Tween, animal fat, silicone oil, cocoa butter, fatty acid glycerides, petrolatum, chitosan, cetyl alcohol, stearyl alcohol, polymethacrylate, non-toxic polyvinyl chloride, and silicone rubber, or any combination thereof.
- [0072] First material of the bottom
- [0073] In some embodiments, the first material comprises HPC SSL and TEC. In some embodiments, the weight ratio of HPC SSL and TEC in the first material is about 1: 1 to about 15: 1, such as any of about 5: 1 to about 10: 1, or about 9: 1.
- [0074] Second material of the peripheral wall

- [0075] In some embodiments, the second material comprises HPC SSL and TEC. In some embodiments, the weight ratio of HPC SSL and TEC in the second material is about 1: 1 to about 15: 1, such as any of about 5: 1 to about 10: 1, or about 9: 1.
- [0076] Third material of the interior cover
- [0077] In some embodiments, the third material of the interior cover is an erodible material.
- [0078] In some embodiments, the third material comprises HPC SSL and TEC. In some embodiments, the weight ratio of HPC SSL and TEC in the third material is about 1: 1 to about 15: 1, such as any of about 5: 1 to about 10: 1, or about 9: 1.
- [0079] Fourth material in the compartment
- [0080] In some embodiments, the fourth material comprises a pharmaceutically acceptable material. The fourth material can be a liquid, semi-solid, or solid material. In some embodiments, the fourth material is liquid or semi-solid.
- [0081] In some embodiments, the pharmaceutically acceptable material is heat labile, i.e., can be partially or fully damaged and/or inactivated when exposed to high temperatures (e.g., above 50 degrees Celsius, such as at least above any of 60, 75, 80, 90, 100, or higher degrees Celsius) or moderate heat (e.g., above 30°C) . In some embodiments, the pharmaceutically acceptable material, such as that of a fourth material in a compartment of a pharmaceutical dosage form described herein, is heat labile such that degradation of the pharmaceutically acceptable material (e.g., degradation of at least about 1%) is observed when the pharmaceutically acceptable material is subject to elevated temperatures (e.g., at least about 30°C for any period of time including for short periods of time, such as 5 seconds or more, during manufacturing) .
- [0082] In some embodiments, the pharmaceutically acceptable material is incompatible with another component of the pharmaceutical dosage form, such as one or more components of the fifth material of the exterior cover. In some embodiments, the pharmaceutically acceptable material is incompatible with another component of the pharmaceutical dosage form, e.g., the pharmaceutically acceptable material degrades (e.g., degradation of at least about 1%) in the presence of the other component, such as via contact of the pharmaceutically acceptable material and the other component. The incompatibility of the pharmaceutically acceptable material and another component of the pharmaceutical dosage form may result in one or more of the following: (i) the biological, chemical and/or physical properties of the pharmaceutically acceptable material may change, such as reducing in activity and/or stability, or increasing in activity (e.g., undesired overactivity) ; and/or (ii) the stability, diffusion, and/or dissolution properties of the another component of the pharmaceutical dosage form may change.
- [0083] In some embodiments, the pharmaceutically acceptable material is a pharmaceutically active material, excipient, or an adjuvant.

- [0084] In some embodiments, the pharmaceutically acceptable material is a pharmaceutically active material. In some embodiments, the pharmaceutically active material selected from one or more of a small molecule compound, polypeptide, protein (e.g., antibody or antigen-binding fragment thereof), nucleic acid, cell-containing hydrogel, probiotic, antibody-drug conjugate (ADC), and microbiome, or a combination thereof. In some embodiments, the pharmaceutical active material is selected from the group consisting of small molecule compounds, peptides, and proteins, and any combination thereof.
- [0085] In some embodiments, the pharmaceutically active material is a small molecule compound, such as selected from the group consisting of 11-deoxypietol-17 α -ethylenepropionate, 16-dehydropregnenolone, 3-carboxamide-4-hydroxypromethoxymorphone, 3-formamide-4-hydroxypromethoxymorphone, 5-fluoro-2-deoxycytidine, 6-mercaptopurine, 6-Methampisone, 6-methylhydroprednisone, abacavir, abeckacin, abekavacin, abiraterone, acamprosic acid, acarbose, acatadine, aceclofenac, acemadolin, acetalaminate, acetaminophen, acetonularic acid, acetylcysteine, acetyl-L-carnitine, acetylsalicylic acid, Acridinium bromide, acobifene, acotalide, acotinide, Actaride, acyclovir, adapalene, adefovir disoproxil, Adefovir disoxilate, adenosylcobalamin, Adipine, afatinib, aglilimus, Agmatimus, Agomelatine, Alamolin, alamorin, alapaglitin, alatrofloxacin, Albendazole, albuterol, Albuterol Sulfate, alpine, alendronic acid, alfacalciferol, alfasalon, Alfassalon, Alfentanil, Alfuzosin, alibritin, Aliretinoin, alisartan cil, Alisartan Ester, aliskiren, Allogestrolone, Allopurinol, Alogliptin, Alogli, Alosetron, Alpha Lipoic Acid, Alphaketoglutarate, alprazolam, Alprostadil, Aluminum Sulfate, Amampridine, Amantadine, Ambersentan, ambrisentan, Ambroxol, Amethiourea, Amfostine, amienylthiourea, amifostine, Amikacin, amiloride, Aminnon, aminoacetyl, aminopiridine, aminopterin, aminopyridine, amiodarone, Amiopterin, Amipidine, amipridine, amipyridine, amirexen, amirinone, amisulpride, Amitriptyline, Amitrometin, amlefunol, Amlefunol, amlezhanol, Amlodipine, Ammonium Lactate, amodiaquine, amorolfine, amotometin, Amotriptan, Amoxicillin, amoxicillin amphetamine, amphetamine, amphetamine sulfonated divinylbenzene, Ampicillin, ampixiclam, amrubicin, Amisulpride, Anagrelide, Analgin, anandamide, anaprevir, Anastrozole, Anclo, andrographolide, androquinol, anekostat, anekota, anidulafungin, aniplase, aniracetam, anlotinib, ansulone, anthralcinol, Anthraltriol, antomine, apatinib, Aperine, apixaban, aplite, apomorphine, apremilast, aprepitant, arolmorphine, aradidipine, Araglipitin, Aratrafloxacin, Arcatadine, aredipine, arformoterol, argatroban, aricitabine, aripiprazole, armodafinil, arsenite, artemether, artemisinin, artesunate, asenapine, astragaloside, atazanavir, atazoline, Atenolol, atomoxetine, atorvastatin, atovaquone, atracuramide, atrasentan, atropine, auranofin, avanafil, Avastine, avibactam,

Avimopan, axilimus, axitinib, azacitidine, azadast, azadlast, azasetron, azelaic acid, azelastine, azeldipine, azelide, azilsartan, aztreonam, azvudine, baclofen, baflutinib, baicalin, balfloxacin, baloxacin, balsalazide, bambutrol, banbuterol, barflutinib, baricitinib, baridipine, bazedoxifene, becifovir, Becipyridine, beclomethasone dipropionate, beclomethasone propionate, bedoladryne, bedolaridene, belacontan, Bellacontan, belotecan, Bemian, benazepril, bendamustine, Benet-hazazide, Benidazole, benidipine, Benzafibrate, benzalkonium chloride, benzethazide, benznidazole, benzocaine, Benzocaine Peroxide, Benzodamine, benzoic acid, benzoyl peroxide, benzycircular quintamium bromide, benzydamine, beprost, besalrodin, besifloxacin, Besifovir, besipridine, betahistine, betaine, Betalastine, betalol, betamethasone, betamilon, Betamilone, Betarol, betaspiramycin, Betasten, betastine, Betraziban, betrazibane, bevacizumab, bezafibrate, biapenem, bicalutamide, bilastine, Bilit, Bimatoprost, Bismuth Galalate, bismuth gallate, bisoprolol, Bleomycin, blonanserine, Bluvudine, Boceprevir, bofexan, Bortezomib, Bosentan, bosutinib, Bradesin, bradisin, Brepiprazole, Brimonidine, bripiprazole, Briracetam, brivaracetam, brixafor, Bromfenac, Bromocriptine, bromovudine, Bromtizolam, Bromzepam, brorazepam, brotezolam, Bubisbenzidine, bucillamine, Budesonide, bufludil, Bufludil, Bunanserine, Bunazosin, Bupivacaine, buprenorphine, bupropion, Bupropionone, Buserelin, Buspirone, Busulfan, Butenafine, butinafine, butipipridine, butorphanol, Butrimalide, butylphthalide, Buxinol, cabazitaxel, cabergoline, cabozantinib, caditrel, cadoltril, cadtrafloxacin, caffeine, caglutamic acid, calcipotriol, calcitriol, calcium-manganese formepipi, calfatan, calmanganese fedipid, campothecin, canagliflozin, candesartan, cangrelo, cangrelor, capecitabine, captopril, carbamazepine, Carbamoylmethacholine, carbecrose, carbegolin, carbidopa, carbitosin, carbixamine, carbocisteine, carboplatin, carfiramib, carfirumibu, carlira, carmustat, carmustine, carpixamine, carumonan, Carvedilol, carvidilol, caspofungin, cadtrafloxacin, catechin, catechins, catemolol, catevolol, cecidianb, Cediranib, cefaclor, cefadroxime, cefazolan, cefcarpine, cefdinir, cefdroline, cefepime, cefminol, cefoperazone, cefotaxime, cefpiro, cefpodoxime, cefprofene, cefproplene, cef-tametaxim, ceftazidime, cefthiamidine, ceftiam, ceftiamidine, ceftiolite, ceftioride, ceftobutene, ceftolenpilate, ceftolerimpilate, ceftorolate, ceftotrolate, ceftriaxone, cefuroxime, celecoxib, celilol, ceritinib, certramilast, cetiristat, cetiristostat, Cetirizine, cetramilast, cetrimonin, cetromate, cevelis, cevimelin, cevimeline, chenodeoxycholic acid, Chermilofiban, chlorabinazole acid, chlorabthenazole acid, Chlorbenzindole, chlorgestrol, chloridamine, chlorobestrel, chlorogenic acid, chlorpheniramine, chlorthalidone, cholecalciferol, cholic acid, choline fenofibrate, choline glycophosphate, choline glycophosphatecholine, chuanbuterol, ciclesonide, ciclopirox olamine, cidofovir, cidoxepin, cilapril, cilastatin, cilostazol, cimeprevir,

cimetidine, cimiprevir, cinacalcet, cinapazide, cinepazide, cinidipine, ciprofibrate, ciprofloxacin, cisofiran, cisophane, cisplatin, citalopram, citicoline, citrulline, cizolan, cizoline, cizonose, cizoran, cladribine, clarithromycin, clasentan, Clavulanate, clavulanic acid, clavidine, clevidipine, climod, clizotinib, clobazam, clobenzindole, clobetasol, clocyclazine, clofazimine, cloiodohydroxyquine, clomexib, clomipramine, clonazepam, clonidine, clopidogrel, clotrimazole, clozapine, cobitate, codeine, cofosel, cofoser, colchicine, colesevelen, colestilane, colestine, colestinol, conivatan, crizotinib, cromolyn, cyanocobalamin, cyclic lactic acid, cyclobenzaprine, cyclophosphamide, cyclosporine, cymonolactic acid, cyproterone, cytarabine, cytidine, dabavavancin, Dabigatran etexilate, dabrafenib, dacetil, daclatasvir, dacotinib, dafinacin, dafoxipidine, daformbutin, danazol, dantrolene, dapirazole, dapiverine, dapizole, dapoxetine, dapsone, darbavancin, darfinacin, darunavir, darusethatib, darussertinib, dasabvir, dasatinib, dasetripi, daunorubicin, daviverine, decitabine, defadidine, defamadi, defukotide, Dekeodermin B, delafloracin, delapril, delaviridine, denibulin, deoxyfluorouridine, Deoxygestrel, desandrographolide, desflurane, desipramine, desmopressin, desogestrel, desonide, desoxyandrographolide, Desufenone, desufenton, dexamethasone, dexamethasone perate, dexamethasone peretate, dexammineol, dexamminol, dexketoprofen, dextansoprazole, dexmedetomidine, dexsurose, dextroamphetamine, dextromethorphan, dextrophenylisopropetamine, dextropropoxyphene, dextropropylimide, dextrosucrose, dexzopiclone, diacemorphine, diacerein, diacetylmorphine, diazazine choline, diazepam, Dichlorofenamide, diclofenac, diclofenamide, Dicopipam, dicyclic alcohol, Dicycline, dicycloplatin, Didanol, Didarol, Difluorprednidate, digoxin, Dihydroergotamine, Dihydroergotten, Dikeglucarben B, Dileiracetam, Diltiazem, dimease, dimethyl fumarate, Dimex, Dinoprostone, Diphenylcyclopropaphenone, diphenylcyclopropenone, Dipyrindamole, diquinopamine, diquinoperane, diracetam, disulfiram, Disulfulam, dlansoprazole, Docarbamine, docuconium chloride, docuronium, Doenetaxel, Dofetilide, dolasetron, dolopenem, dolutegravir, domperidone, Donepezil, Dopamine, Doperidone, Dorasetron, Doripenem, Dosaxyl ester, dosimamate, Doxazosin, Doxepin hydrochloride, doxofylline, doxorubicin, Doxycycline, Doxylamine Succinate, dozolamide, drocannabinol, Dronedarone, Dronolol, drospirenone, Droxidopa, Droxylendone, D-tagatose, D-Tagose, Ducalciferol, duloxetine, Durutegravir, dutasteride, Ebaseride, ebastine, eberconazole, eboptan, ebselen, Ebuselen, Ecarbet, ecopipam, edaravone, Edinafil, edoxaban, Efaviren, efavirenz, Efinaconazole, efodipine, Eguanidanone, eicosapentaenoic acid, Elodotan, eltrombopag, emestine, Emitasvir, emtricitabine, enacarbi, enalapril, enclomiphene, Enecalciferol, enlicassen, enlikasen, enoxoxacin, enprost, entacapone, entecavir, entenolutamide, entenot, enzalutamide, epagliflozin, epalastat, ephedrine, epifitinib, epimedium, Epimedium Weed, ep-

inephrine, epipitinib, epirubicin, epistasine, epistine, Epixicam, eplastat, eplatin, eplerenone, eplodesade, epoprostenol, epoxylactol, eprepretinide, epsaltan, epsartan, Erdosteine, Erecoxib, ergobenzyl ester, eribulin, eritriptan, erlotinib, ertapenem, erythromycin, escholesaponin, escitalopram, escloside, esketamine, eslicarbazepine, esmolol, Esoladine, esomeprazole, estidine, estradiol, etagvir, ethambutol, ethane-selenoline, ethidine, ethinyl estradiol, ethinylestradiol, ethperisone, ethyl 11-deuterated linoleate, Ethyl Eicosapentaenoic Acid, ethyl-11-di-deuterated linoleate, ethyleicosapentaenoic acid, ethylfumaric acid, etidronic acid, etigvir, etimicin, etizolam, etocoxib, etodolacin, etogestrel, etoposide, etrovirine, etymicin, eudenafile, everolimus, exemestane, ezetimibe, famciclovir, Famotidine, Faropenem, Farragolil, fartrozole, faszacetam, fasudil, fatrozole, favipiravir, faxisidazole, febabamate, febuxostat, felodipine, femarsartan, fenclofenac, Fencrozone, fenfluramine, Fenodora-zam, fenofibrate, fenoldopam, Fenoteramide, fenoterol, fenretinoamide, Fenretinoramide, Fentanyl, Fenticonazole, Ferric Citrate, Ferric Maltol, fesolo, Fexinidazole, fexofenadine, fidamycin, finafloxacin, Finasteride, Fingolimod, Flecainide, fleroxacin, Flubanserin, fluconazole, Fludarabine, Flumazenil, flunison, fluocinol, fluocinolone, fluoerycin, fluoerythromycin, fluorosynchale, fluorouracil, fluorourididine, Fluorouridine, fluosynchamine, fluoxetine, Fluoxycyclase, flupiridene, flupiridetin, flurbiprofen, fluticasone, flutramazole, fluvastatin, fluvoxamine, fodoxone, folic acid, folinic acid, formate, formetan, formustine, formomustine, formoterol, fosapitem, fosapitan, fosfomycin, fosinopril, fosinoprim, fosmetrin, fosphenytoin, fospofol, Frol-floxacin, frotriptan, fruquintinib, fulvestrant, Furfluridine, furlodesine, furosemide, fushanavir, fusidic acid, fusanavir, Fydamicin, gabapentin, Gabapentin enacarbi, Gaberate, Gadolin, Gadolinium-Forsamine, Gadolinol, Galantamine, Galefloxacin, Galinium-Forsamine, Gallium Nitrate, Ganaxolone, Ganesoxone, Ganirelix, Garcinic Acid, Garenoxacin, Gargimic Acid, Gatifloxacin, Gefibrozil, Gefitinib, Gemcitabine, Gemifloxacin, Gemmyfloxacin, Gemperone, Geniopicrin, Gentamicin, Gilperone, Glatiram, Glibouramide, Glibourclamide, Glimeclazide, Glimepiride, Glipazide, Glus-cohamide, Glucosphamide, Glutamine, glycabizole, glyceryl eicosapentaenoate, Glyc-erylbenzene, glycinobidazole, glycol, Glycolate, Glycopyrrolate, Glycylene Glycol, Glycyrrhizic Acid, Glycyrrhizin, Gogilipitin, Golomod, Gotgliptin, granisetron, Grendienone, Grentrienone, Guaifenesin, guanaboline, guanadibenzin, Guanfacin, guanfacine, Guanimisaxil, guanimsapine, Halobetasol, Halofantrine, halomethasone, Hexamethylmelamine, hexammelamine, hyaluronic acid, hydrochlorothiazide, hy-drocobalamin, Hydrocodone, Hydrocortisone, hydromorphone, hydroxychloroquine, hydroxyprogesterone caproate, hydroxyurea, Hypericin, ibandronic acid, Ibrutinib, Ibuprofen, ibuprofen, ibutilate, ibutilide, Icabat, Iconazole, icotinib, Idebenone, idebenquinone, Idecalfiferol, Ifetroban, ifetroban, Iladipine, Ilapliflozin, Ilaprazole,

ilaprin, ilismo, ilodesed, ilodisece, Ilofen, Ilonisad, ilonised, Iloperidone, Iloprost, Imatinib, imidazorbine, Imipenem, Imiquimod, Incapronate, Incapronic Acid, Indacaterol, Indapamide, Indidomethacin, Indinavir, Indistra, Indistravir, Indolamine, Indomethacin, Indoxigen, Indulozin, Iodoseronin, Iodoside, Iodoxronin, Ipratropium, Ipuride, Iramod, irattimod, Irbesartan, Irinotecan, Irinotecan Thiosarose, Irisimo, iron dextran, Ishabelon, Ishabelong, isoconazole, Isoflurane, Isoniazazide, Isonizid, Isorbate, Isotolivia, Isotoretin, Isotorivia, Isotretinoin, isozelaflax, isozelanflavin, Itopride, Itraconazole, Itraculine, Ivabradine, Juchlorothiol, kaglutamic acid, Ketamine, Ketoconazole, Ketolac, Ketoprofen, Ketotifen, L-18-Methylnorethindrone, L-18-Methylnorethindrone Butyrate, Lactitol, ladotinib, Laflulimus, Lafurtidine, L-Albuterol, lamfluridine, Lamivudine, Lamotrigine, Landelol, Lanoconazole, Lansoprazole, Lanthanum Carbonate, Lapatinib, Laquinimod, laro, Iaroroxiro, Lasidipine, Lasoxifene, Latanoprost, Latanprost, Laxamide, Lecardipine, Leflunomide, Lenalidomide, Lenatinib, Lentinan Mushroom, Leprinine, Letrozole, Leucine, leucovorin, Leuprolide, Levamisole, Levamlodipine, Levetiracetam, Levobativaine, Levobupivacaine, Levocarbistine, Levocarnitine, Levocetirizine, levodopa, Levofenopril, Levofloxacin, levonidazole, Levoornidazole, levopraziquantel, Levopril, Levosnostrestrel, levulin, L-Glutamine, Lidocaine, Ligustrazine Hydrochloride, Limaprost, Linezolid, linolenic acid, lipoic acid, Liralipin, Liraliptin, Liranadipate, Lisinopril, lofexidine, lomefloxacin, lomerizine, lopinavir, loratadine, Loratlox, lorazepam, lorinamine, loritrex, loroxicam, losartan, losartan potassium, lotepnol, loteprenol, lovastatin, loxoprofen, L-Phencyclanide Hydrochloride, L-Phencycline Hydrochloride, L-Salbuterol, lubitécan, lubittican, luminol, lupatadine, magnesium isoglycyrrhizate, maindole, manganese formipidine, manganese formipira, manidipine, mannitol, maraviro, maribavir, masitinib, mebendazole, megestrol, meloxicam, memantine and menaquinone, memantine mantine, menaquinone, mepirazole, Mepyrpyramidone, mepyrpyramidone, Mercaptoethylene, mercaptothylamine, Mercaptopurine, meropenem, mesalazine, mesulfonilast, Metadoxin, metadoxine, Metaxadone, metaxavir, metformin, methadone, Methazolamide, methonlast, methopyrazine, methotrexate, Methoxyflurane, methoxypyrazine, methylcobalamin, methylene blue, methylphenidate, methylprednisolone acetate, metoclopramide, metoprolol, metoxyflurane, metronidazole, metyrosine, mezazolam, mibeladil, Mibelaxidil, miceglinide, Miconazole, midadoline, Midanasin, Midapril, midazolam, midazolestine, midodrine, mifepristone, Miglitol, Milnacipran, milnaplin, Milofiban, Milrinone, miltefosin, minocycline, minodronic acid, minoxidil, mirabegron, Mirabelon, Mironafil, Mirtazapine, Misoprostol, Mitifosin, Mitiglinide, Mitoxantrone, mivotilate, Mivotine, Mizolastine, Mizoribine, moclobemide, modafinil, modipafene, Modipapan, Mofenolid, mofenzolic acid, Mometasone Furoate, Monobenzene, Monoterpene

Perillatol, Montelukast, morexizine, Morolidone, Morolinolinidazole, Morolinonirazole, morphine, Morphine glucuronic acid, morpholidone, morpholinoline, mosapride, mosonidine, mosononidine, moxidectin, Moxidepril, moxifloxacin, moxipril, mozavaptan, mupirocin, mycophenolate, mycophenolate mofetil, Mypakeline, mypaklin, myristicol nicotinate, nabumetone, N-acetylcysteine, nadolol, nafloxacin, nafperidil, naftifene, naglitinide, nalbuphine, naldolol, nalfuraphine, nalmefene, naloxan ether, naloxifene, naloxone, naltrexone, naltrexone methyl, nandrolone caprate, nandrolone decanoate, Naninamivir, naphazoline, naphtholaquine, naphtholquine, naproxen, naratriptan, nasaprose, nasfetifen, nebivolol, nedaplatin, nedoromi, nedoromide, nelarabine, Nelfinavir, nemopride, Nenofofloxacin, neostigmine, nepafenamide, Nepatante, nepatitante, nepilastat, neridronic acid, netilamicin, Netirmicin, netupitant, nevirapine, niacin, nicardipine, nicergoline, Niclolimin, Nicloside, nicomycin, nicorandil, Nicotin, nicotine, Niergoline, Nifecalan, nifedipine, Nifeviviro, nifurazide, Nifurilimus, Nifurozid, nilotinib, Nilutamide, Nimesulide, nimodipine, Nisodipine, nisoldipine, nitazoxanide, nitisinone, Nitrandipine, nitrogen mustard, nitroglycerin, nitrosalimide, Nivadipine, Nizatidine, Nizazonit, Nor-epinephrine, norestrolpine, Norethindrone, Norfloxacin, norgest, norgestrogel, Normestrogel, Nororgestrel, Norprgingroxymine, norvenlafaxine, Obeticholic Acid, offendazole, Ofloxacin, Olanzapine, Olaparib, Olisoxi, olisoxib, Olmesartan, Olodaterol, Olopatadine, olsen-leset, omeprazole, Omoconazole, Onariskone, onastrone, Ondansedone, onoprost, Opipe, opipepera, oprinon, Oprinone, Oritaxin, oritvancin, Orlistat, ornithine phenylacetic acid, osalazine, oseltamivir, ospipifene, ospipimidhene, Otepla, oteprazine, Otinidine, Otriglipitin, oxaliplatin, oxaloacetate, oxazepam, oxcarbazepine, Oxenate, oxendazole, Oxenecide, oxiracetam, Oxybutyric acid, oxycodone, oxymetazoline, oxymorphone, oxytocin, ozagrel, ozelfloxacin, palclitaxel, pajufloxacin, Paladefovir, Palichlor, paliperidone, paliperizone, paliprevir, palnatinib, palonosetron, pamiol, Pamomomycin, Panatitinib, pandecrenone, panipenem, pantoprazole, papupirone, parbilastat, parbistat, parecoxib, paricalcitol, parivatin, parogliglita, Paroglil, paromomycin, paroxetine, pazopanib, Pebiprufen, pefican, Pemetrexed, Penciclovir, pendarubicin, pentamidine, Pentenoic Acid, penteric acid, pentiacid, pentostatin, pentoxifylline, peramivir, perampanel, Perfluorooctane, perfluorooctanium bromide, perfluorooopentane, Perfluoropentane, Pergolide, perifofacine, Perifosine, perindopril, Phenafloxacin, phencycline quineclidine, phenobenzamine hydrochloride, phenoredenozin, phenorezin, Phentermine, Phentolamine, phenylacetic acid, Phenylbenzamine Hydrochloride, phenylbutyric acid, Phenytoin, piccicarib, Picuronium, pidotimod, Pimasaserin, pimecrolimus, Pimenol, pimobendone, Pimobenzene, pineone benzmustard, pioglitazone, pipercuronium, pipemaserin, Pipepipene, piperacillin, piperazine, piperidone, piperobirone,

piracetam, Pirarubicin, Pirfenidone, Piroberon, Pirotinib, piroxicam, pishanqiong, Pisicanide, Pitavastatin, Pitaxon, Plecone, plerixafor, pliraconi, plucloxacillin, plucloxacillin, pluka, p-Methoxyphenol, p-methoxyphenol, podofilol, Pomalidomide, poracoli, Porphim, porphum, Posaconazole, Posutinib, potassium oxazinate, pradefovir, pramipexole, pramiracetam, praquintinib, prasugrel, Pratestosterone, pravastatin, prazosin, Prdefovir, pre-Bahrain, prednisolone, prednisone, prepre Bahrain mean, prepresone, prilocaine, procaterol, prochlorperazine, progesterone, progestogen deenogest, progestogen dienogest, proguanil, promethazine, Promicetam, propafenone, propagermanium, Propanalidom, propazine, propofol, propranol, propylol, prosolol, proxolol, prukast, prussian blue, pseudoephedrine, Pudaofilol, puerarin, pyrazinamide, pyridine, pyridoxine, Pyrimilast, pyrimilast potassium, pyrimimine, pyronadidine, pyronadipine, pyroside, pyruvate, quadrazepam, qualunic acid, quarumic acid, quetiapine, quezatinib, quinapril, quinazepam, quinidine, Quinine, quintiapine, quizatinib, rabeprazole, Radipavir, ralitrexed, rallosifene, raloxifene, raloxifene, raltegravir, ramatroban, ramelton, ramipril, ramosetron, ramustron, ranitidine, ranolazine, rasagiline, rebamipide, reboxetine, reelin acetate, refegabine, regigabine, regorafenib, Relin Acetate, rematroban, rebamipide, remifentanil, remitamolin, remitamorelin, remitaparen, remtegabine, remtigabin, repaglinide, repaglinide, resimod, resimotide, retaparaline, rhebin acid, ribavirin, rifabutin, rifampicin, rifamycin, rifapentine, rifaximin, rilapatinide, rilpivirine, rilpivirine hydrochloride, rilurazole, riluzole, rimexolone, riociguat, ripilast, ripimilast, risedronate, risedronic acid, risguarate, risiguater, risperidone, ritonavir, rivarazan, riva-roxaban, rivastigmine, rizatriptan, roddenafile, roflumilast, rolapedem, rolapetan, ropinirole, ropivacaine, rosiglitazone, rotamycin, rotigotine, roxithromycin, rufinamide, rufloxacin, rusovavastatin, russell vastatin, ruxolitinib, sacubitril, safinamide, sagretatransate, sagretilate, salicylic acid, salmeterol, salvesin, salicine, Saperine, sapropterine, sapropterine, saquinavir, saxagliptin, saxagliptinin, scopolamine, secalatinib, secatinib, secenidazole, secnidazole, selegiline, selumetinib, selyllol, semeltinib, sertaconazole, sertaconitrate, sertanitic acid, sertraline, sesquiterpene, sevelamer, sevoflurane, sevotican, Shiitan Phytosanide, sibutramine, sigosvir, siladas, sildenafil, silodosin, simiponimod, simotinib, simpomodide, simvastatin, sinidipine, sipride, sirolimus, sitafloxacin, sitagliptin, sofosbuvir, solifenacin, sorafenib, sorbitol, sorbusosen, sorbusosen, soscopolamine, sotalol, sparfloxacin, spirapril, stavudine, stipentanol, stironine, stitopentol, stronine, strontium ranelate, Succinoclacon, succinyloctahydroacridine, sugammadex, sulbactam, sulfamiam, sulfamimilone, sulfan, sulfasalazine, sulindine, sulxindine, sumatriptan, sunitinib, suramine sodium, surufatinib, tacacisol, taccacisol, Tacitabine, tacrine, tacrolimus, tadalafil, tafenoquine, talapofen, Talapofine, Talinacin, talineacin, Talixole, talixor, talodipine, tamibarotene,

Tamoxifen, Tamsulosin, Tapentadol, Taquinimod, Tasematron, Tatirelin, Tazarotene, tazobactam, Tebipenamate, tebipenemate, Tebivudine, tecovir, Tecovirib, tedesamide, Tedizolid, Teergothiolare, tegasero, Tegaserol, teicoplanin, telaprevir, Telazosin, telbivudine, Telliputin, Telly, telmisartan, temoporfen, Temoporfin, Temoporphene, temoporphine, temopril, temozolomide, tenofovir, Tenoxicam, tepedine, tepifanib, Tepredone, terazosin, terbinafine, tercoco, terergocartium, teriflunomide, terisofenxine, terlilitin, tesofensine, tetracycline, tetrahydroazoleline, tetrahydronaphthazolin, tetrahydronazolin, tetrathiomolybdate, thalidomide, thienophine, thiiconazole, thioteipa, thiotepa, ticagrel, ticagrene, ticalopidine, Tidesamide, tigecycline, Tilatinib, tiludronic acid, Timolol, timolol maleate, tinidazole, tiotropium, tipedine, Tipepidine, tiprafarib, tiprapidine, tipropronin, tiranavir, tirazamine, tirazate, tirobanidine, tirofiban, tizanidine, tobramycin, tobuterol, tocosolam, tofacitinib, Tofaptan, tolcapone, tolimidone, tolterodine, tolvaptan, tonabosa, tonin, topagliflozin, toperone, topiramate, topostat, topotecan, topperidone, toppistat, torremifhene, torsemide, tosedoride, toshedote, tosulfoxacin, totremifene, trabectedin, tramadol, trametinib, trandopril, tranexamic acid, travafloxacin, trazodone, tretinoin, tretinolin, triamcinolone acetonide, triazolam, trichlorothiazide, triclitabine, triclazazole, triclazendazole, tricloctan, trientine, trimebutin, trimegestrel, trimethoprim, trinitilast, trioxirilbine, troglitriptin, trolostetam, trolostine, tromethamine, tropisetron, trospikonium chloride, trosponium chloride, trotagliptin, trotanasetron, trovafloxacin, troxipit, troxipiter, tylo-dipine, ubenmex, ubetasol, ubidecenenone, ubomex, Uclafil, Uclonafil, udenafil, uderafil, ulinafil, ulinastat, ulipristal, Unoprostone Isopropyl, Uracholine, urapidil, uroxycholine, valacyclovir, valdecoxib, Valeric Acid, valganciclovir, valsartan, vandetan, vandetanib, vanoserin, vanoxeline, vardenafil, varencicline, vemurafenib, venacalan, Venalidone, venlafaxine, Venolidone, verapamil, Verazolone, Vesnaridone, vesrinone, Vesserinone, veteporfin, Vicagrel, Vigabatin, Vilanterol, Vildagliptin, vistruffeg, Viteporfin, vitrotripla, Voriconazole, Vorinostat, Vortioxetine, xinotecan, Zacitabine, Zafirlukast, Zaleplon, Zalulukast, Zanamivir, Zatoprofen, Zhucaixine, Zhucasaisin, Zhuchlorothiol, Zidovudine, zinc sultalan, Ziprasidone, Zoledronic Acid, Zolmitriptan, Zolpidem, Zolpisamine, Zolpitratan, Zonisamide, Zopiclone, Zotepin, β -elemene, β -olivene, 3, 5-diiodothyroic acid, their pharmacologically acceptable salts, esters, prodrugs, hydrates, deuterated compounds, stereoisomers, and any combination thereof.

- [0086] In some embodiments, the pharmaceutically active material is a polypeptide, such as selected from the group consisting of an insulin, antidiuretic hormone, calcitonin, calcitonin gene-related peptide, parathyroid hormone, luteinizing hormone, erythropoietin, tissue plasminogen activator, growth hormone, adrenocorticotrophic hormone, interleukin, enkephalin, epinephrine, glucagon-like peptide-1 (GLP-1)

receptor agonist, semaglutide, liraglutide, dulaglutide, exenatide, octreotide, teriparatide, vancomycin, linacotide, pukanatide, vorcyclyde, vorcyclyne, taltirelin, taltirelin, acetylaminopressin, acetaminopressin, marsimorelin, and GLP-2 analogue. In some embodiments, the pharmaceutically active material is a GLP-1 receptor agonist, such as semaglutide. In some embodiments, the pharmaceutically active material is GLP-2 analog, such as teduglutide, apraglutide, elsiglutide, dapiglutide, or glepaglutide.

[0087] In some embodiments, the pharmaceutically active material is a protein, such as those used in the field of medicine, agriculture, scientific research, and other industrial fields. In some embodiments, the protein is selected from the group consisting of a blood factor, colony-stimulating factor (CSF), interleukin, growth factor, tumor necrosis factor (TNF), and enzyme. In some embodiments, the protein is selected from the group consisting of an asparaginase, glutaminase, arginase, arginine deaminase, adenosine deaminase ribonuclease, cytosine deaminase, trypsin, chymotrypsin, papain, epidermal growth factor (EGF), insulin-like growth factor (IGF), transforming growth factor (TGF), nerve growth factor (NGF), platelet-derived growth factor (PDGF), bone morphogenetic protein (BMP), fibroblast growth factor, somatostatin, somatostatin, CSF, coagulation factor, tumor necrosis factor, interferon, gastrointestinal peptide, vasoactive intestinal peptide (VIP), incretin (CCK), gastrin, secretin, hormone, pancreatic enzymes, superoxide dismutase, thyrotropin-releasing hormone (TRH), thyroid-stimulating hormone, luteinizing hormone, luteinizing hormone-releasing hormone (LHRH), tissue plasminogen activator, receptor antagonist (IL-1RA), leptin, auxin, granulocyte-macrophage colony-stimulating factor (GM-CSF), adenosine deaminase, uricase, chorionic gonadotropin, heparin, atrial natriuretic peptide, hemoglobin, relaxin, cyclosporine, oxytocin, ankyrin repeat protein, and avidin, or any combination thereof.

[0088] In some embodiments, the protein is an antibody or antigen-binding fragment thereof (e.g., scFv, Fab, sdAb), such as selected from the group consisting of abagovomab, abciximab, actoxumab, adalimumab, adecatumumab, aducanumab, afelimumab, afimimab, Afutuzumab, ajuzumab (Alacizumab pegol), ALD518, Alemtuzumab, Alirocumab, altumomabpentetate, amtusimab, Amuximab, Anatumomabmafenatox, Anifrolumab, Anifrolumab (Anrukizumab), Apolizumab, Arcitumomab, Aselizumab, atemomab (Telimomabaritox), Atinumab, atodomimab (Dorlimomabaritox), Atorolimumab, avtuzumab, azolimab aritox, azolimomab (Zolimomab aritox), Bapineuzumab, Basiliximab, Batuximab (Bavituximab), Bectumomab, Belimumab, Benralizumab, Bertilimumab, Besilesomab, Bevacizumab, bevacizumab (Briakinumab), Bezlotoxumab, Biciromab, Bimagrumab (Bimagrumab), bivatuzumab mertansine, brentuximabvedotin, bruzozonzumab

(Bloszumab) , Buda lumab (Brodalumab) , canakinumab, Cantuzumabravtansine, caplacizumab, capromabpendetide, carlumab, Catumaxomab, cBR96-doxorubicin immunoconjugate, cedelizumab, certizumabpegol, cetuximab, citatuzumab bogatox, cixutumumab, Clazakizumab, Clivatuzumabtetraxetan, Conatumumab, Concizumab, Crenezumab, D alotuzumab, Dacetuzumab, Daclizumab, Dalatuzumab (Daratumumab) , Dalotuzumab, Darotuzumab, demomomizomab (Dencizumab) , Denosumab, detumomab (Detumomab) , Dorlimomabaritox, Drozitumab, Duligotumab, Dupilumab, Dusigitumab, eculcumab (Icrucumab) , Eculizumab, Edobacomab, Edrecolomab, Efalizumab, Efungumab, Eldelumab, Elotuzumab, El-silimomab, Enavatuzumab, Enlimomab pegol, Enokizumab, Enoticumab, Ensituximab, Epitumomabcituxetan, Epratuzumab, Erlizumab, Ermamab (Ertumaxomab) , Etaracizumab, Etrolizumab, EvimumabEnavatuzumab, Evolocumab, Exbivirumab, Ex-emeximab (Ecromeximab) , Fanolesomab, Faralimomab, Farletuzumab, Fasinumab, FBTA05, Felvizumab, fezakinumab, Fezakinumab Greece, Ficlaturumab, Fig- itumumab, fintutumab, Flanvotumab, Fontolizumab, Foralumab, Foravirumab, Fulranumab, fusumumab (Fresolimumab) , Futuximab, Galiximab, Ganitumab, Gan- tenerumab, Gavilimomab, Gemtuzumab, Gemtuzumab ozogamicin, Gemtuzumab Ozomicin, Gemtuzumabozogamicin (Gemtuzumab) , Gevokizumab, Girentuximab, Glembatumumabvedotin, Golimumab, Gomiliximab, Greece ficlaturumab, Guselkumab, Ibalizumab, Igovomab, IMAB362, imciromab, imgatuzumab, Indatux- imabravtansine, infriximab (Infliximab) , ingramumab (Inclacumab) , Inolimomab, Inotuzumab ozogamicin, Intetumumab, Ipilimumab, Iratumumab, Itolizumab, Ix- ekizumab, keliximab, kriximab (Clenoliximab) , Labegizumab Labetuzumab) , la- betuzumab, Lambrolizumab, Lampalizumab, Lebrikizumab, ledelimumab, lemasomab, Lerdelimumab, Lexatumumab, Libivirumab, Ligelizumab, Lintuzumab, Lirilumab, Lodelcizumab, Lorvotuzumabmertansine, Lucatumumab, Lumiliximab, Map- atumumab, Margetuximab, Maslimomab, Matuzumab, Mavrilimumab, mecan- clizumab (Cantuzumab mertansine) , Mepolizumab, Metelimumab, Milatuzumab, Minretumomab, Mitumomab, Mogummimab (Mogamulizumab) , Morolimumab, Motavizumab, Moxetumomabpasudotox, Muromonab-CD3, Nacolumabtafenatox, Namilumab, Naptumomabestafenatox, Narnatumab, Natalizumab, Nebacumab, Necitumumab, Nerelimomab, nerolimomab, nesvacumab, Nimotuzumab, nivelumab (Nivolumab) , Nofetumomabmerpentan, Ocaratuzumab, Ocilusumab Oxelumab, ocrelizumab, Odulimab, Ofatumumab, Olaratumab, Olokizumab, Omalizumab, Onartuzumab, Ontuxizumab, Oportuzumabmonatox, Oregovomab, Orticumab, Otelixizumab, Otlertuzumab, Oxelumab, Ozanezumab, Ozoralizumab, Pacolizumab, Pagibaximab, Palivizumab, Panitumumab, Pankomab, Panobacumab, Parsatuzumab, Pascolizumab, Patamomumab (Taplutumomabpaptox) , Pateclizumab, Patritumab,

pembrolizumab, Pemtumomab, Perakizumab, Pertuzumab, Pexelizumab, Piedilizumab (Pidilizumab), Pinatuzumabvedotin, Pintumomab, Placulumab, Polatuzumabvedotin, ponezumab, prilimumab (Pritumumab), priliximab, Pritoxaximab, PRO140, Quilizumab, Racotumomab, Radretumab, Rafivirumab, Ramucirumab, Ranibizumab, Ranibizumab, rantumomab (Blinatumomab), raxibacumab, regavirumab, Regavirumab, Reslizumab, rilotumumab, rituximab, Rlinatumomab, robatumumab, Roledumab, Romosozumab, Rontalizumab, Rovelizumab, Ruplizumab, Samalizumab, Sarilumab, Satumomabpendetide, Secukinumab, Seribantumab, Setoxaximab, sevirumab, SGN-CD19A, SGN-CD33A, sifalimumab, siltuximab, simtuzumab, siplizumab, Sirozozumab (Sibrotuzumab), Sirukumab, Solanezumab, Solitomab, Sonepcizumab, Sontuzumab, Stamulumab, Sulesomab, Suvizumab, Tabalumab, Tacatuzumabtetraxetan, Tadocizumab, Talizumab, Tanezumab, tatumomabestafenatox, Teeliximab, tefibulizumab (Tefibazumab), Teimumab (Ibritumomab tiuxetan), teneliximab, Teneximab, teplizumab, teprotumumab, tesimumab (Ticilimumab), tetumomab (Tenatumomab), TGN1412, Tigatuzumab, tildrakizumab, TNX-650, tocilizumab (atlizumab), Toralizumab, tositumomab, tovetumab, tralocymumab (Tralokinumab), trastuzumab, TRBS07, Tregalizumab, tremelimumab, Tucotuzumabcelmoleukin, Tuvirumab, Ublituximab, Urelumab, Urttoxazumab, Ustekinumab, Vantictumab, Vapaliximab, Vatelizumab, Vedolizumab, Veltuzumab, Vepalimomab, Vesencumab, Vesicuxumab (Vesencumab), Visilizumab, Volociximab, Vorsetuzumabmafodotin, Votumumab, Zalutumumab, Zanolimumab, Zatuximab, Zilalimumab (Ziralimumab), or a fragment thereof, and any combination thereof.

[0089] In some embodiments, the pharmaceutically active material is a nucleic acid. In some embodiments, the nucleic acid comprises oligomers or polymers of at least two linked nucleotides or nucleotide derivatives, a DNA and an RNA linked together by phosphodiester bonds, a DNA, a cDNA, or an RNA. In some embodiments, the nucleic acid comprises a DNA molecule and an RNA molecule. The nucleic acid can be single-stranded or double-stranded. In some embodiments, the nucleic acid is cDNA. In some embodiments, the nucleic acid is selected from the group consisting of an antisense nucleic acid, messenger RNA (mRNA), transfer RNA (tRNA), small interfering RNA (siRNA), short hairpin RNA (shRNA), guide RNA (gRNA), small RNA (sRNA), microRNA (miRNA), circular RNA (circRNA), trans-amplifying RNA (taRNA), small activating RNA (saRNA), complementary RNA (cRNA), non-coding RNA, and long RNA, or any combination thereof.

[0090] In some embodiments, the pharmaceutically active material is a probiotic, such as selected from the group consisting of *Bifidobacterium* spp., *Bifidobacterium brevis*, *Bifidobacterium animalis*, *Bifidobacterium lactis*, *Bifidobacterium longum*, Bifi-

dobacterium bifidum, Lactococcus lactis, Streptococcus lactis, Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus kefir, Lactobacillus bifidus, Lactobacillus brevis, Lactobacillus Switzerland, Lactobacillus paracasei, Lactobacillus rhamnosus, Lactobacillus salivarius, Lactobacillus campylobacter, Lactobacillus Bulgaria, Lactobacillus sake, Lactobacillus reuteri, Lactobacillus lactis, Lactobacillus del Brückella, Lactobacillus plantarum, Lactobacillus johnsonii, and Streptococcus thermophilus, or any combination thereof.

- [0091] In some embodiments, the pharmaceutically acceptable material is an excipient or an adjuvant, such as selected from the group consisting of a wetting agent, permeation enhancer, plasticizer, adhesive, developer, filler, and pH adjuster, or any combination thereof. Any suitable excipient can be used herein, such as any one or more of span 80 (can stabilize aqueous formulations), salcaprozate sodium (SNAC; can enhance the oral absorption of macromolecules, proteins, and peptides), and sodium caprate or sodium decanoate (can improve drug absorption and stability).
- [0092] In some embodiments, the fourth material comprises a liquid excipient. The liquid excipient may comprise water, triacetate, triethyl citrate, tributyl O-acetylcitrate, ethylene glycol, glycerin, 1, 2-Propanediol, tetraethylene glycol, diethyl phthalate, castor oil, castor oil ethoxylate, caprylic capric acid polyethylene glycol glycerol, medium chain triglycerides, ethyl oleate, Tween, span, propylene glycol monolaurate, propylene glycol monocaprylate, propylene glycol dicaprylate caprate, oleoyl polyoxyethylene glycerides, linoleoyl polyoxyethylene-6 glycerides, polyglyceryl oleate, soybean oil mixed fatty acid glycerides, monolinoleic glycerides, or any combination thereof.
- [0093] In some embodiments, the fourth material comprises a semi-solid excipient. The semi-solid excipient may comprise vitamin E polyethylene glycol succinate, polyethylene glycol stearate, behenyl esters, mono and diglyceryl stearate, lauroyl polyoxyethylene 32 glycerides, polyethylene glycol, stearoyl ethoxyethylene glycerides, ceteth-20/polyoxytol 1000, glyceryl distearate, poloxamer, polyoxyethylene (10) stearyl ether, or any combination thereof.
- [0094] In some embodiments, the fourth material comprises a solid excipient. The solid excipient may comprise solid plasticizers, fillers, adhesives, lubricants, flow aids, disintegrants, or any combination thereof.
- [0095] In some embodiments, the viscosity of the fourth material is about 10 Pa to about 3000 Pa, such as any of about 100 Pa to about 3000 Pa, about 100 Pa to about 2000 Pa, about 500 Pa to about 2000 Pa, or about 500 Pa to about 1000 Pa. In some embodiments, the viscosity is measured under a temperature of about 0 °C to about 50 °C, such as any of about 10 °C to about 40 °C, about 20 °C to about 30 °C, or about room temperature (e.g., about 25°C).

- [0096] In some embodiments, the fourth material is in liquid form. The fourth material can be a homogeneous liquid or a heterogeneous liquid. In some embodiments, the fourth material is a small molecule solution or a polymer solution. In some embodiments, the fourth material is a sol, emulsion, or suspension. In some embodiments, the fourth material is semi-solid. In some embodiments, the fourth material is a suppository, gel, or cream.
- [0097] In some embodiments, the fourth material is a liquid at about ambient room temperature (about 20 °C) and about 101.3 kPa pressure. In some embodiments, the fourth material is a liquid during at least a part of the manufacturing process, such as during MED three-dimensional printing. In some embodiments, the fourth material is a semi-solid at about ambient room temperature (about 20°C) and about 101.3 kPa pressure. In some embodiments, the fourth material is a semi-solid during at least a part of the manufacturing process, such as during MED three-dimensional printing.
- [0098] In some embodiments, the fourth material is solid. In some embodiments, the fourth material is semi-solid or liquid before entering the compartment and transforms into a solid state after entering the compartment. In some embodiments, the manner in which the fourth material is converted from a semi-solid or liquid state to a solid state includes but is not limited to, drying, freezing, low temperature drying, or setting aside.
- [0099] In some embodiments, the fourth material comprises an antidiabetic API and/or an anti-obesity API, such as semaglutide, or GLP-1 or a derivative thereof. In some embodiments, the antidiabetic API is for treating type 1 and/or type 2 diabetes. In some embodiments, the fourth material further comprises one or more excipients, such as any one or more of span 80, SNAC, and sodium caprate.
- [0100] In some embodiments, the fourth material comprises semaglutide and an excipient (e.g., span 80, or a combination of span 80, SNAC, and sodium caprate) . In some embodiments, the weight ratio of semaglutide and excipient (e.g., span 80, or a combination of span 80, SNAC, and sodium caprate) in the fourth material is about 1: 1 to about 1: 200, such as any of about 1: 120 to about 1: 180, or about 1: 160. In some embodiments, the weight ratio of semaglutide, sodium caprate, span 80, and SNAC in the fourth material is about 1: 10: 50: 100.
- [0101] Fifth material of the exterior cover
- [0102] In some embodiments, the fifth material comprises HPC SSL and TEC. In some embodiments, the weight ratio of HPC SSL and TEC in the fifth material is about 1: 1 to about 15: 1, such as any of about 5: 1 to about 10: 1, or about 9: 1.
- [0103] In some embodiments, the fifth material comprises HPC SSL and glycerol. In some embodiments, the weight ratio of HPC SSL and glycerol in the fifth material is about 1: 1 to about 15: 1, such as any of about 1: 1 to about 10: 1, about 1: 1 to about 5: 1, or about 4: 1.

- [0104] Interior cover
- [0105] The interior cover described herein can provide one or more following beneficial effects: (i) reducing (e.g., reducing at least about 10%, such as any of 20%, 30%, 50%, 70%, 90%, 95%, or more) and/or preventing the fourth material in the compartment (e.g., a heat labile API) from directly contacting the high-temperature exterior cover during the production process which might destroy or reduce the potency of the fourth material; (ii) reducing (e.g., reducing at least about 10%, such as any of 20%, 30%, 50%, 70%, 90%, 95%, or more) and/or preventing the incompatibility between the exterior cover material and the fourth material in the compartment (e.g., API), which might destroy or reduce the potency of the fourth material; and/or (iii) increasing (e.g., increasing at least about 10%, such as any of 20%, 30%, 50%, 70%, 90%, 1-fold, or more) the loading amount of the fourth material in the compartment, or reducing (e.g., reducing at least about 10%, such as any of 20%, 30%, 50%, 70%, 90%, 95%, or more) the surface tension of the fourth material in the compartment (compare, e.g., FIG. 2A and FIG. 2B).
- [0106] In some embodiments, the interior cover is an elongated structure extending roughly along a first axis, and each opening of the one or more openings of the interior cover is an elongated opening extending roughly along a second axis. In some embodiments, the angle between the first axis and the second axis is 0° - 90° , such as about any of 0° , 10° , 20° , 30° , 40° , 45° , 50° , 60° , 70° , 80° , 90° , or any values in between. In some embodiments, the angle between the first axis and the second axis is from about 5° to less than 90° , such as any of from about 10° to less than 90° , from about 10° to about 80° , from about 20° to about 80° , from about 20° to about 70° , from about 30° to about 70° , from about 30° to about 60° , from about 40° to about 60° , from about 40° to about 50° , from about 40° to about 45° , from about 45° to about 50° , or from about 5° to about 30° .
- [0107] In some embodiments, the interior cover only comprises one opening. In some embodiments, the one or more openings of the interior cover comprises two openings, wherein each of the two openings are formed along an independent axis. Each independent axis can be parallel with the other or not parallel with the other. In some embodiments, each independent axis is parallel with the other.
- [0108] In some embodiments, the opening of the interior cover is in parallel to the opening of the compartment formed by the shell.
- [0109] In some embodiments, the shape of each opening of the one or more openings of the interior cover is independently selected from the group consisting of circle, square, rectangle, parallelogram, rhomboid, runway-shape, or irregular shape, or a combination thereof. Each opening of the one or more openings of the interior cover can have the same shape or different shapes. In some embodiments, each opening of the

one or more openings of the interior cover is a circle. In some embodiments, each opening of the one or more openings of the interior cover is a runway-shape. In some embodiments, each opening of the one or more openings of the interior cover is an irregular shape.

- [0110] In some embodiments, each opening of the one or more openings of the interior cover does not comprise a plug. In some embodiments, some or all of the one or more openings of the interior cover comprise a plug. The plug can be the same or different from each other, such as varying in material and/or dimension. In some embodiments, the plug comprises a dissolvable material (e.g., in gastrointestinal tract environment, such as stomach, small intestine, or large intestine) . In some embodiments, the plug comprises a thermoplastic material (e.g., any of the thermoplastic material described herein) . In some embodiments, the material of the plug is compatible with the fourth material with the component, such as during long-term storage (e.g., 1, 3, 6, 12 months, or longer) . In some embodiments, the material of the plug does not affect, or reduces at most about 20% (e.g., at most about any of 15%, 10%, 5%, 1%, or less) of, the biological and/or chemical activity of the pharmaceutically acceptable material of the fourth material. In some embodiments, the plug is prepared (e.g., 3D-printed) separately (preferably letting cool down) and inserted into the one or more openings of the interior cover after the fourth material is loaded into the compartment formed by the shell.
- [0111] In some embodiments, the interior cover is prepared (e.g., 3D-printed) separately (preferably letting cool down) and covers, at least partially, the opening of the compartment formed by the shell after the fourth material is loaded into the compartment.
- [0112] In some embodiments, the interior cover has a surface area of about 1 mm² to about 300 mm², such as any of about 1 mm² to about 50 mm², about 50 mm² to about 100 mm², about 100 mm² to about 300 mm², about 100 mm² to about 200 mm², about 100 mm² to about 150 mm², about 20 mm² to about 150 mm², about 200 mm² to about 300 mm², or about 50 mm² to about 200 mm².
- [0113] In some embodiments, the interior cover has a thickness of about 0.01 mm to about 2 mm, such as any of about 0.01 mm to about 0.1 mm, about 0.01 mm to about 0.05 mm, about 0.05 mm to about 0.5 mm, about 0.1 mm to about 1 mm, about 0.1 mm to about 0.5 mm, about 0.5 mm to about 1.5 mm, or about 1 mm to about 2 mm. In some embodiments, the interior cover has a thickness of about 0.4 mm.
- [0114] In some embodiments, the interior cover does not have any opening. In some embodiments, the interior cover comprises or is a mesh. For example, in some embodiments, the third material forming the interior cover is a mesh. In some embodiments, the mesh is a porous material, e.g., comprising pores configured to allow

a fluid to enter a compartment and/or comprising pores configured to allow the fourth material or a component thereof, such as a pharmaceutically acceptable material, to pass therethrough.

- [0115] In some embodiments, the interior cover is parallel to the bottom of the pharmaceutical dosage form. In some embodiments, the interior cover and the bottom forms an angle between 0° and 90° . In some embodiments, the interior cover is an elongated structure extending roughly along a first axis, and the bottom is extending roughly along a second axis, and the angle between the first axis and the second axis is equal to or more than 0° and less than 90° , such as any of 0° , 10° , 20° , 30° , 40° , 50° , 60° , 70° , 80° , 89° , or any values in between. The angle between the first axis and the second axis can be any suitable value as long as the fourth material can be contained in the compartment defined by the shell and the interior cover, and that the exterior cover can fully cover the one or more openings (if present) of the interior cover. In some embodiments, the interior cover is flat. In some embodiments, the interior cover is not flat, such as in a dome shape.
- [0116] In some embodiments, the interior cover is attached to each side of the peripheral wall. In some embodiments, the interior cover is not attached to all sides of the peripheral wall. For example, when the pharmaceutical dosage form has 4 sides of peripheral walls (e.g., a cuboid or a runway-shaped cylinder), the interior cover can be attached to opposing sides of the peripheral walls. Different attachment configurations of the interior cover to the peripheral wall can apply (e.g., see FIGs. 4A-4F), as long as the interior cover can form one or more openings for loading the fourth material, and/or the interior cover can prevent the fourth material from directly contacting the exterior cover.
- [0117] Exterior cover
- [0118] In some embodiments, the exterior cover is parallel to the bottom of the pharmaceutical dosage form. In some embodiments, the exterior cover and the bottom forms an angle between 0° and 90° . In some embodiments, the exterior cover is an elongated structure extending roughly along a first axis, and the bottom is extending roughly along a second axis, and the angle between the first axis and the second axis is equal to or more than 0° and less than 90° , such as any of 0° , 10° , 20° , 30° , 40° , 50° , 60° , 70° , 80° , 89° , or any values in between. The angle between the first axis and the second axis can be any suitable value as long as the fourth material can be contained in the compartment defined by the shell and the interior cover, and that the exterior cover can fully cover the one or more openings (if present) of the interior cover and/or that the exterior cover can at least partially cover the interior cover. In some embodiments, the exterior cover is flat. In some embodiments, the exterior cover is not flat, such as in a dome shape.

- [0119] In some embodiments, the exterior cover is prepared (e.g., 3D-printed) separately (preferably letting cool down) before assembling into the pharmaceutical dosage form.
- [0120] In some embodiments, the exterior cover has a thickness of about 0.01 mm to about 2 mm, such as any of about 0.01 mm to about 0.1 mm, about 0.01 mm to about 0.05 mm, about 0.05 mm to about 0.5 mm, about 0.1 mm to about 1 mm, about 0.1 mm to about 0.5 mm, about 0.5 mm to about 1.5 mm, or about 1 mm to about 2 mm. In some embodiments, the exterior cover has a thickness of about 0.4 mm.
- [0121] Pharmaceutical dosage form I
- [0122] In some embodiments, there is provided a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover at least partially covers the opening of the compartment, wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell, and wherein the interior cover is attached to the shell via placement on top of the peripheral wall; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the bottom is a layer of the first material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the second material forming the peripheral wall is positioned on top of the bottom (e.g., wherein the bottom is a layer of material of the first material, the peripheral wall is positioned on top of the layer forming the bottom). In some embodiments, the first material and the second material are the same material. In some embodiments, the interior cover comprises any of 1, 2, 3, 4, or 5 openings. In some embodiments, the interior cover is a layer of the third material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the fourth material is a liquid or a semi-solid. In some embodiments, the pharmaceutically acceptable material of the fourth material is a pharmaceutically active material. In some embodiments, the pharmaceutically acceptable material of the fourth material is an excipient or an adjuvant. In some embodiments, the fourth material comprises a component that is heat labile, such as a heat labile pharmaceutically acceptable material. In some embodiments, the fourth material comprises a component that is not compatible with another component of the pharmaceutical dosage form, such as a pharmaceutically acceptable material that may degrade upon contact (including upon extended contact) with a component of the exterior cover. In some embodiments, the exterior cover is configured to cover, at least partially, the

interior cover including the one or more openings of the interior cover. In some embodiments, the exterior cover is not in direct contact with the peripheral wall. FIGs. 1A and 1C show an exemplary pharmaceutical dosage form described herein.

[0123] In some embodiments, there is provided a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover at least partially covers the opening of the compartment, wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell, and wherein the interior cover is attached to the shell via at least partial placement on an internally facing (i.e., towards the inside of the compartment) portion of the peripheral wall; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the bottom is a layer of the first material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the second material forming the peripheral wall is positioned on top of the bottom (e.g., wherein the bottom is a layer of material of the first material, the peripheral wall is positioned on top of the layer forming the bottom). In some embodiments, the first material and the second material are the same material. In some embodiments, the interior cover comprises any of 1, 2, 3, 4, or 5 openings. In some embodiments, the interior cover is a layer of the third material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the fourth material is a liquid or a semi-solid. In some embodiments, the pharmaceutically acceptable material of the fourth material is a pharmaceutically active material. In some embodiments, the pharmaceutically acceptable material of the fourth material is an excipient. In some embodiments, the fourth material comprises a component that is heat labile, such as a heat labile pharmaceutically acceptable material. In some embodiments, the fourth material comprises a component that is not compatible with another component of the pharmaceutical dosage form, such as a pharmaceutically acceptable material that may degrade upon contact (including upon extended contact) with a component of the exterior cover. In some embodiments, the exterior cover is configured to cover, at least partially, the interior cover including the one or more openings of the interior cover. In some embodiments, the exterior cover is in direct contact with the peripheral wall. FIGs. 1B and 1D show an exemplary pharmaceutical dosage form described herein.

- [0124] FIG. 1A to FIG. 1D show a cross-sectional front view schematic diagram of a pharmaceutical dosage form prepared according to a three-dimensional printing of one embodiment of the present application.
- [0125] FIG. 1A shows a cross-sectional front view schematic diagram of an exemplary pharmaceutical dosage form 100 prepared according to a three-dimensional printing of one embodiment of the present application. As shown in FIG. 1A, the pharmaceutical dosage form 100 comprises a shell (not numbered in the figure), an interior cover 102 attached to the shell, and an exterior cover 103 attached to the interior cover 102. As shown in FIG. 1A, the shell comprises a bottom 113 and a peripheral wall 114, and the two together form a compartment 112 comprising a first opening 111. The peripheral wall 114 can be stacked layer by layer in the form of 3D printing with the bottom 113 as the base. The peripheral wall 114 can also surround the bottom 113 from the side. The interior cover 102 has one or more second opening 121, and the interior cover 102 is arranged to at least partially cover the first opening 111 and let the second opening 121 becomes an opening in communication with the compartment 112. The compartment 112 is loaded with liquid or semi-solid material, such as pharmaceutical material comprising active pharmaceutical ingredient and/or pharmaceutical preparation excipients, etc. The exterior cover 103 is attached to the interior cover 102 and is configured to cover the second opening 121.
- [0126] FIG. 1B shows a cross-sectional front view schematic diagram of an exemplary pharmaceutical dosage form 200 prepared according to an embodiment of the present application. As shown in FIG. 1B, the pharmaceutical dosage form 200 comprises a shell (not numbered in the figure), an interior cover 202 attached to the shell, and an exterior cover 203 attached to the shell. As shown in FIG. 1B, the shell comprises a bottom 213 and a peripheral wall 214, and the two together define a compartment 212 comprising an opening 211. The interior cover 202 has a second opening 221, and the interior cover 202 is configured to at least partially cover the opening 211. The second opening 221 can be in communication with the compartment 212, such that a substance (e.g., a liquid, semi-solid, or solid) can enter the compartment through the second opening. The compartment 212 can be filled with liquid or semi-solid materials, such as pharmaceutical materials and/or pharmaceutical preparation excipients including active pharmaceutical ingredients. The exterior cover 203 is attached to the peripheral wall 214 and is configured to cover the second opening 221. The exterior cover 203 is attached to the peripheral wall 214, which can increase the sealing property of the pharmaceutical dosage form 200, and also can avoid the dissolution of the interior cover 202 to be in contact with the body fluid when the pharmaceutical dosage form is administered to the individual, so that the pharmaceutical dosage form can release the material in the compartment at a desired location.

- [0127] In the pharmaceutical dosage forms shown in FIG. 1A and FIG. 1B, the bottom can be formed by a first material, the peripheral wall can be formed by a second material, the interior cover can be formed by a third material, the compartment can be loaded with a fourth material that is liquid or semi-solid, and the exterior cover is formed by a fifth material.
- [0128] By adopting the interior cover structure with a second opening as shown in FIG. 1A and FIG. 1B, the liquid material in the compartment of the pharmaceutical dosage form can effectively overcome the influence of its own surface tension and the interaction force with the shell during the three-dimensional printing process, so as to achieve a relatively high filling rate of the liquid or semi-solid material in the compartment. Taking FIG. 1A as an example, if there is no interior cover with the second opening, when injecting the liquid material into the compartment, the liquid material may climb upward along the periphery wall of the shell due to the difference in surface tension and the interaction force between the injected material and the shell, so that a non-flat liquid surface is formed in the compartment, and finally the overall filling rate of the liquid or semi-solid material is lower (see, e.g., FIG. 2A) . When the interior cover partially covers the opening on the compartment, the upper part of the compartment can be filled with the liquid or semi-solid material (see, e.g., FIG. 2B) . When the liquid material is injected into the compartment, the interior cover can effectively reduce the influence of the difference between the surface tension and the interfacial tension of the liquid material, counteracting the tendency of the liquid to climb upward along the edge of the shell, effectively increasing the filling of the liquid material in the compartment, decreasing the size necessary for the pharmaceutical dosage form, increasing the convenience for patient, and improving consistency and controllability of the liquid material loading. FIG. 2A and FIG. 2B show a schematic diagram of the surface tension of the dosage form structure according to FIG. 1A of the present application, with and without interior cover, respectively.
- [0129] By adopting the interior cover structure with a second opening as shown in FIG. 1A and FIG. 1B, the liquid or semi-solid material compartment of the pharmaceutical dosage form can reduce the direct contact with the high-temperature exterior cover as much as possible in the three-dimensional printing process, ensuring the physical and/or chemical stability of the liquid or semi-solid drug or excipient, and also increasing the speed of cooling and forming of the exterior cover during the printing process. Further, the liquid or semi-solid material in the compartment can be separated from the exterior cover material, and this design could reduce the material incompatibility between the material in the compartment and the exterior cover material, thereby improve the stability of the material in the compartment (e.g., stability of a drug) .

- [0130] FIG. 1C shows a cross-sectional front view schematic diagram of an exemplary pharmaceutical dosage form 300 prepared according to a three-dimensional printing of an embodiment of the present application. As shown in FIG. 1C, the pharmaceutical dosage form 300 comprises a shell (not numbered in the figure), an interior cover 302 attached to the shell, and an exterior cover 303 attached to the interior cover 302. The shell comprises a bottom 313 and a peripheral wall 314, and the two jointly define a compartment 312 comprising an (e.g., one or more) opening 311. The peripheral wall 314 can be formed with the bottom 313 as the base or formed around the bottom 313. The interior cover 302 has a second opening 321, and the interior cover 302 is arranged to at least partially cover the opening 311 and in communication with the compartment (e.g., solid material can enter the compartment 312 via the second opening 321). The compartment 312 can be loaded with solid materials, such as pharmaceutical materials and/or excipients for pharmaceutical preparations comprising active pharmaceutical ingredients. The exterior cover 303 is attached to the interior cover 302 and is configured to cover the second opening 321.
- [0131] FIG. 1D shows a cross-sectional front view schematic diagram of an exemplary pharmaceutical dosage form 400 prepared according to a three-dimensional printing of one embodiment of the present application. As shown in FIG. 1D, the pharmaceutical dosage form 400 comprises a shell (not numbered in the figure), an interior cover 402 attached to the shell, and an exterior cover 403 attached to the shell. The shell comprises a bottom 413 and a peripheral wall 414, and the two jointly form a compartment 412 comprising an opening 411. The interior cover 402 has a second opening 421, and the interior cover 402 is configured to at least partially cover the opening 411. The second opening 421 is in communication with the compartment 412, such that a solid can enter the compartment 412 through the second opening 421. The compartment 412 is loaded with solid materials, such as pharmaceutical materials and/or excipients for pharmaceutical preparations comprising active pharmaceutical ingredients. The exterior cover 403 is attached to the peripheral wall 414 and is set to cover the second opening 421. The exterior cover 403 is attached to the peripheral wall 414, which can increase the sealing property of the pharmaceutical dosage form 400, and can also avoid the dissolution of the interior cover 402 in contact with the body fluid when the pharmaceutical dosage form is administered to the individual, so that the pharmaceutical dosage form can release the material in the compartment at the required position.
- [0132] In the exemplary pharmaceutical dosage forms shown in FIG. 1C and FIG. 1D, the bottom is formed by the first material, the peripheral wall is formed by the second material, the interior cover is formed by the third material, the fourth material loaded with solids in the compartment, and the exterior cover is formed by the fifth material.

- [0133] By adopting the interior cover structure as shown in FIG. 1C and FIG. 1D, the solid material in the compartment of the pharmaceutical dosage form can reduce the direct contact with the high-temperature exterior cover as much as possible during the three-dimensional printing process, so as to ensure the structural stability of the drug or excipients.
- [0134] By adopting the interior cover structure as shown in FIG. 1C and FIG. 1D, the solid material in the compartment can be separated from the exterior cover material, and this design could reduce the material incompatibility between the solid material in the compartment and the exterior cover material, thereby improve the stability of the material in the compartment (e.g., stability of a drug) .
- [0135] In some embodiments, the area ratio of the opening (e.g., 111 in FIG. 1A) of the compartment formed by the shell and the opening of the interior cover (e.g., second opening 121 in FIG. 1A) is configured to a certain range to achieve better drug loading effect. In some embodiments, the ratio of the area of the opening of the interior cover to the opening of the compartment formed by the shell is less than about 95%, such as any of about 10%-80%, about 20%-70%, about 20%-60%, about 20%-50%, about 15%-70%, about 15%-60%, about 15%-50%, about 15%-30%, about 15%-20%, or about 20%-30%.
- [0136] In some embodiments, the area ratio of the opening of the interior cover (e.g., second opening) and the opening of the compartment formed by the shell may be designed based on the height of the pharmaceutical dosage form and the maximum length of any two points on the bottom edge of the pharmaceutical dosage form (e.g., diameter in a cylinder dosage form) . FIG. 3A to FIG. 3C show perspective schematic diagrams of exemplary pharmaceutical dosage forms according to different embodiments of the present application.
- [0137] As shown in FIG. 3A, when the ratio of the maximum length 106 of any two points on the bottom edge of the cylinder (e.g., diameter of the cylinder) to the height of the cylinder 107 is 1 or less than 1, the ratio of the area of the opening of the interior cover (e.g., second opening) 108 and the opening of the compartment formed by the shell (not shown in the figure) is less than about 90%, such as less than about any of 80%, 70%, 60%, 50%, 40%, 30%, or 20%. In some embodiments, the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the maximum length of any two points on the bottom edge of the cylinder (e.g., diameter of the cylinder) to the height of the cylinder is less than 1, the ratio of the area of the opening of the interior cover (e.g., second opening) 108 and the opening of the compartment formed by the shell is about 15%to about 30%, about 15%to about 20%, about 20%to about 30%, about 20%to about 25%, or about 25%to about 30%.

- [0138] As shown in FIG. 3B, when the ratio of the maximum length 206 of any two points on the bottom edge of the cylinder (e.g., diameter of the cylinder) to the height of the cylinder 207 is 1 to 5.5, the ratio of the area of the opening of the interior cover (e.g., second opening) 208 and the opening of the compartment formed by the shell (not shown in the figure) is below 90%, such as below about any of 80%, 70%, 60%, 50%, 40%, 30%, or 20%. In some embodiments, the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the maximum length of any two points on the bottom edge of the cylinder (e.g., diameter of the cylinder) to the height of the cylinder is more than 1 and less than 5.5, the ratio of the area of the opening of the interior cover (e.g., second opening) 208 and the opening of the compartment formed by the shell is about 15% to 30%, about 15% to about 20%, about 20% to about 30%, about 20% to about 25%, or about 25% to about 30%.
- [0139] As shown in FIG. 3C, when the ratio of the maximum length 306 of any two points on the bottom edge of the cylinder (e.g., diameter of the cylinder) to the height of the cylinder 307 is more than 5.5, the ratio of the area of the opening of the interior cover (e.g., second opening) 308 and the opening formed by the shell (not shown in the figure) is less than 90%, such as less than about any of 80%, 70%, 60%, 50%, 40%, 30%, or 20%. In some embodiments, the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the maximum length of any two points on the bottom edge of the cylinder (e.g., diameter of the cylinder) to the height of the cylinder is more than 5.5, the ratio of the area of the opening of the interior cover (e.g., second opening) 308 and the opening of the compartment formed by the shell is about 15% to about 30%, about 15% to about 20%, about 20% to about 30%, about 20% to about 25%, or about 25% to about 30%.
- [0140] It should be noted that although the shape of the exemplary pharmaceutical dosage forms shown in FIG. 3A to FIG. 3C is cylindrical, the above-mentioned relationship between the area ratio of the second opening (the opening of the interior cover) and the opening of the compartment formed by the shell and the ratio range of the maximum length to height of any two points on the bottom edge is also applicable to other cylinders or structures close to the cylinder, such as run-way shaped cylinders, elliptical cylinders, cuboids, capsules, or frustum of cones.
- [0141] FIG. 4A to FIG. 4F respectively show a top view schematic diagram of exemplary interior covers of the pharmaceutical dosage forms according to the different embodiments of the present application. The exemplary interior covers shown in FIG. 4A to FIG. 4F are elongated structures (e.g., runway and elliptical) extending along the direction of a first axis (solid axis in the figure) as shown in the figures, while the second opening (the opening of the interior cover) on it is an elongated opening (e.g., elongated, elliptical, S-shaped, and parallelogram) that is configured to extend roughly

along a second axis (the dashed axis in the figure) . In some embodiments, as shown in FIG. 4A and FIG. 4C, the angle between the first axis and the second axis is 90° . In other embodiments, as shown in FIG. 4D and FIG. 4E, the first axis and the second axis are less than 90° . In some embodiments, as shown in FIG. 4B and FIG. 4F, the first axis is roughly parallel to the second axis (e.g., angle is less than 10° , 5° , 3° , 2° , or 1° , or is 0°) . As shown in FIG. 4C, the interior cover can further comprise a third opening. In some embodiments, when an interior cover is attached to a shell, the third opening may be used as an opening to be in communication with the compartment. In other embodiments, the pharmaceutical dosage form may comprise two compartments, and the third opening may be used as an opening to be in communication with a second compartment that is different from the compartment formed by the shell (i.e., the first compartment) . In some embodiments, the two compartments and/or separate openings on the interior cover allow for injecting different liquid, semi-solid, or solid materials separately from each other.

[0142] It should be noted that the illustration of the shape and position relationship between the interior cover and the second opening (the opening of the interior cover) in FIG. 4A to FIG. 4F is only an illustrative demonstration. The interior cover and its second opening may be selected in any other shape and positional relationship. In some embodiments, in order to improve the three-dimensional printing efficiency of the interior cover structure and the stability of the printed structure, when the interior cover has an elongated shape extending along a first axis, and the opening also has an elongated shape extending along a second axis, the angle between the first axis and the second axis is 0° - 90° (including 0° and 90°) , such as about any of 10° - 90° , 10° - 80° , 20° - 80° , 20° - 70° , 30° - 70° , 30° - 60° , 40° - 60° , 40° - 50° , 40° - 45° , or 45° - 50° . In some embodiments, the angle between the first axis and the second axis is about 45° .

[0143] Pharmaceutical dosage form II

[0144] In some embodiments, there is provided a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover at least partially covers the opening of the compartment, wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell, wherein the interior cover comprises a mesh or a sieve (e.g., a material having pores therethrough such that one or more opening in communication with the compartment are present) , and wherein the interior cover is attached to the shell via placement on top of the peripheral wall; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover

formed by a fifth material, wherein the exterior cover is attached to the interior cover, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the bottom is a layer of the first material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the second material forming the peripheral wall is positioned on top of the bottom (e.g., wherein the bottom is a layer of material of the first material, the peripheral wall is positioned on top of the layer forming the bottom). In some embodiments, the first material and the second material are the same material. In some embodiments, the interior cover comprises at least about 100 openings (e.g., pores). In some embodiments, the interior cover is a layer of the third material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the fourth material is a liquid or a semi-solid. In some embodiments, the pharmaceutically acceptable material of the fourth material is a pharmaceutically active material. In some embodiments, the pharmaceutically acceptable material of the fourth material is an excipient. In some embodiments, the fourth material comprises a component that is heat labile, such as a heat labile pharmaceutically acceptable material. In some embodiments, the fourth material comprises a component that is not compatible with another component of the pharmaceutical dosage form, such as a pharmaceutically acceptable material that may degrade upon contact (including upon extended contact) with a component of the exterior cover. In some embodiments, the exterior cover is configured to cover, at least partially, the interior cover including the one or more openings of the interior cover. In some embodiments, the exterior cover is not in direct contact with the peripheral wall. FIG. 5A shows an exemplary pharmaceutical dosage form described herein.

[0145] In some embodiments, there is provided a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover at least partially covers the opening of the compartment, wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell, wherein the interior cover comprises a mesh or a sieve (e.g., a material having pores therethrough such that one or more opening in communication with the compartment are present), and wherein the interior cover is attached to the shell via at least partial placement on an internally facing (i.e., towards the inside of the compartment) portion of the peripheral wall; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and the shell, and wherein the exterior cover is configured to cover, at least partially,

the interior cover. In some embodiments, the bottom is a layer of the first material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the second material forming the peripheral wall is positioned on top of the bottom (e.g., wherein the bottom is a layer of material of the first material, the peripheral wall is positioned on top of the layer forming the bottom). In some embodiments, the first material and the second material are the same material. In some embodiments, the interior cover comprises at least about 100 openings (e.g., pores). In some embodiments, the interior cover is a layer of the third material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the fourth material is a liquid or a semi-solid. In some embodiments, the pharmaceutically acceptable material of the fourth material is a pharmaceutically active material. In some embodiments, the pharmaceutically acceptable material of the fourth material is an excipient. In some embodiments, the fourth material comprises a component that is heat labile, such as a heat labile pharmaceutically acceptable material. In some embodiments, the fourth material comprises a component that is not compatible with another component of the pharmaceutical dosage form, such as a pharmaceutically acceptable material that may degrade upon contact (including upon extended contact) with a component of the exterior cover. In some embodiments, the exterior cover is configured to cover, at least partially, the interior cover including the one or more openings of the interior cover. In some embodiments, the exterior cover is in direct contact with the peripheral wall. FIG. 5B shows an exemplary pharmaceutical dosage form described herein.

- [0146] FIG. 5A and FIG. 5B show cross-sectional front view schematic diagram of exemplary pharmaceutical dosage forms according to different embodiments of the present application. The interior cover of the present application may contain a plurality of second openings. In some embodiments, the interior cover comprises a mesh or a sieve. In some embodiments, the interior cover is sieve-like. In some embodiments, the interior cover has a porosity between about 5% and about 95%, such as about any of 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or any values in between.
- [0147] As shown in FIG. 5A, the exemplary pharmaceutical dosage form 500 comprises a shell (not numbered in the figure), an interior cover 502 attached to the shell, and an exterior cover 503 attached to the interior cover 502. The shell comprises a bottom 513 and a peripheral wall 514, and the two jointly form a compartment 512 comprising an opening 511. The interior cover 502 is a sieve-like structure containing a plurality of second openings 521 (the opening of the interior cover), and the interior cover 502 is configured to cover the first opening 511 (the opening of the compartment formed by the shell), and the second openings 521 are in communication with the compartment

512. The exterior cover 503 is attached to the interior cover 502 and is configured to cover all second openings.

[0148] FIG. 5B shows a cross-sectional front view schematic diagram of an exemplary pharmaceutical dosage form 600 prepared according to a three-dimensional printing of one embodiment of the present application. As shown in FIG. 5B, the pharmaceutical dosage form 600 comprises a shell (not numbered in the figure), an interior cover 602 attached to the shell, and an exterior cover 603 attached to the shell. The shell comprises a bottom 613 and a peripheral wall 614, which together form a compartment 612 comprising an opening 611. The interior cover 602 is a sieve-like structure containing a plurality of second openings 621 (the opening of the interior cover), and the interior cover 602 is configured to cover the opening 611, and the second openings 621 are in communication with the compartment 612. The exterior cover 603 is attached to the peripheral wall 614 and is set to cover all second openings 621. The exterior cover 603 is attached to the peripheral wall 614, which can increase the sealing property of the pharmaceutical dosage form 600, and can also avoid the dissolution of the interior cover 602 in contact with the body fluid when the pharmaceutical dosage form is administered to the individual, so that the pharmaceutical dosage form can release the material in the compartment at a desired location.

[0149] In some embodiments, the compartment is loaded with a liquid or semi-solid material, or a solid material, such as a pharmaceutical material including an active pharmaceutical ingredient and/or pharmaceutical preparation excipients. By adopting the interior cover structure as shown in FIG. 5A and FIG. 5B, the material in the compartment of the pharmaceutical dosage form can reduce the direct contact with the high-temperature exterior cover as much as possible in the three-dimensional printing process, which improves the stability of the drug or excipient in the compartment, and also increase the speed of cooling and forming of the exterior cover during the printing process. Further, the material in the compartment can be separated from the exterior cover material, and this design could reduce the material incompatibility between the material in the compartment and the exterior cover material, thereby improving the stability of the material in the compartment (e.g., stability of a drug).

[0150] In some embodiments, the size of the openings of the sieve-like interior cover is 0.05mm-1.2mm, 0.1mm-1mm, or 0.2mm-0.8mm.

[0151] Pharmaceutical dosage form III

[0152] In some embodiments, there is provided a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover at

least partially covers the opening of the compartment, wherein the interior cover comprises does not comprise one or more openings in communication with the compartment formed by the shell, and wherein the interior cover is attached to the shell via placement on top of the peripheral wall; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the bottom is a layer of the first material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the second material forming the peripheral wall is positioned on top of the bottom (e.g., wherein the bottom is a layer of material of the first material, the peripheral wall is position on top of the layer forming the bottom) . In some embodiments, the first material and the second material are the same material. In some embodiments, the interior cover is a layer of the third material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the third material of the interior cover is erodible. In some embodiments, the fourth material is a liquid or a semi-solid. In some embodiments, the pharmaceutically acceptable material of the fourth material is a pharmaceutically active material. In some embodiments, the pharmaceutically acceptable material of the fourth material is an excipient. In some embodiments, the fourth material comprises a component that is heat labile, such as a heat labile pharmaceutically acceptable material. In some embodiments, the fourth material comprises a component that is not compatible with another component of the pharmaceutical dosage form, such as a pharmaceutically acceptable material that may degrade upon contact (including upon extended contact) with a component of the exterior cover. In some embodiments, the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the exterior cover is not in direct contact with the peripheral wall. FIG. 6A shows an exemplary pharmaceutical dosage form described herein.

[0153] In some embodiments, there is provided a pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover at least partially covers the opening of the compartment, wherein the interior cover does not comprise one or more openings in communication with the compartment formed by the shell, and wherein the interior cover is attached to the shell via at least partial placement on an internally facing (i.e., towards the inside of the compartment) portion of the peripheral wall; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover

formed by a fifth material, wherein the exterior cover is attached to the interior cover and the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the bottom is a layer of the first material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the second material forming the peripheral wall is positioned on top of the bottom (e.g., wherein the bottom is a layer of material of the first material, the peripheral wall is positioned on top of the layer forming the bottom). In some embodiments, the first material and the second material are the same material. In some embodiments, the third material of the interior cover is erodible. In some embodiments, the interior cover is a layer of the third material, such as a layer having a thickness of at least about 0.1 mm. In some embodiments, the fourth material is a liquid or a semi-solid. In some embodiments, the pharmaceutically acceptable material of the fourth material is a pharmaceutically active material. In some embodiments, the pharmaceutically acceptable material of the fourth material is an excipient. In some embodiments, the fourth material comprises a component that is heat labile, such as a heat labile pharmaceutically acceptable material. In some embodiments, the fourth material comprises a component that is not compatible with another component of the pharmaceutical dosage form, such as a pharmaceutically acceptable material that may degrade upon contact (including upon extended contact) with a component of the exterior cover. In some embodiments, the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the exterior cover is in direct contact with the peripheral wall. FIG. 6B shows an exemplary pharmaceutical dosage form described herein.

- [0154] FIG. 6A and FIG. 6B show cross-sectional front view schematic diagram of an exemplary pharmaceutical dosage form according to different embodiments of the present application. The interior cover of the dosage form of the present application may not contain an opening.
- [0155] As shown in FIG. 6A, the pharmaceutical dosage form 700 comprises a shell (not numbered in the figure), an interior cover 702 attached to the shell, and an exterior cover 703 attached to the interior cover 702. The shell comprises a bottom 713 and a peripheral wall 714, which together form a compartment 712 comprising an opening 711. The interior cover 702 is configured to cover the opening 711, and the exterior cover 703 is attached to the interior cover 702 and is configured to at least partially cover the interior cover 702.
- [0156] FIG. 6B shows a cross-sectional front view schematic diagram of an exemplary pharmaceutical dosage form 800 prepared according to a three-dimensional printing of one embodiment of the present application. As shown in FIG. 6B, the pharmaceutical dosage form 800 comprises a shell (not numbered in the figure), an interior cover 802

attached to the shell, and an exterior cover 803 attached to the shell. The shell 801 comprises a bottom 813 and a peripheral wall 814, and the two together form a compartment 812 comprising an opening 811. The interior cover 802 is configured to cover an opening 811, the exterior cover 803 is attached to the peripheral wall 814, and is configured to at least partially cover the interior cover 802. The exterior cover 803 is attached to the peripheral wall 814, which can increase the sealing property of the pharmaceutical preparation 800, and can also avoid the dissolution of the interior cover 802 in contact with the body fluid when it is administered to the individual, so that the pharmaceutical dosage form can release the material in the compartment at a desired location.

[0157] In some embodiments, the compartment is loaded with a liquid, semi-solid or solid material, such as a pharmaceutical material comprising an active pharmaceutical ingredient, excipients, and/or adjuvants. By adopting the interior cover as shown in FIG. 6A and FIG. 6B, the material in the compartment of the pharmaceutical dosage form can reduce the direct contact with the high-temperature exterior cover as much as possible during the 3D printing process, so as to ensure the physical and/or chemical stability of the drug or excipients. And the material in the compartment can also be separated from the exterior cover material, and this design could reduce the material incompatibility between the liquid, semi-solid or solid material in the compartment and the exterior cover material, thereby improve the stability liquid, semi-solid or solid material in the compartment (e.g., stability of a drug) .

[0158] It should be noted that the shapes and structures of the pharmaceutical dosage forms shown in the figures described above are schematic displays, and the pharmaceutical dosage forms of the present application may include any feasible shape and structure of the shell, interior cover and exterior cover part as defined. For example, in some embodiments, the exterior cover can be attached directly to the shell. In some embodiments, the exterior cover can be directly attached to the interior cover. In some embodiments, the peripheral wall is formed above the bottom with the bottom as the base. In some embodiments, the peripheral wall is stacked layer upon layer around the bottom. In some embodiments, the exterior cover is in direct contact with the second opening on the interior cover and covers the second opening. In some embodiments, the exterior cover does not come into direct contact with the second opening on the interior cover, but covers the second opening by preventing the material in the compartment from flowing out or overflowing. In some embodiments, the shape of the pharmaceutical dosage form can also be a runway-shaped cylinder, an elliptical cylinder, a cube, a capsule, a round table, a prism and other shapes.

[0159] Pharmaceutical dosage form IV

- [0160] In certain aspects, the pharmaceutical dosage forms described herein comprise more than one compartment, wherein at least one compartment, which is formed by a shell, with an opening that is at least partially covered by an interior cover and an exterior cover as describe in other aspects of the application. In some embodiments, the other compartments of the more than one compartment may be any design and include or not include an interior cover and/or an exterior cover.
- [0161] FIG. 7A and FIG. 7B show cross-sectional schematic diagrams of the pharmaceutical dosage form according to different embodiments of the present application. The pharmaceutical dosage form of the present application may also contain a multi-compartment structure, each of which may be filled with liquid, semi-solid or solid materials that are identical or different from each other.
- [0162] As shown in FIG. 7A, the shell of an exemplary pharmaceutical dosage form 900 defines a compartment 912 with an opening (e.g., a first opening) 911, and the compartment 912 is filled with liquid or semi-solid material. The shell comprises a bottom 913 and a peripheral wall 914. The opening (e.g., first opening) 911 can be covered by an interior cover and exterior cover according to any embodiments provided herein. For simplicity, the interior cover and exterior cover structures used to cover the compartment 912 are not shown in FIG. 7A. The shell further forms a second compartment 915, and the second compartment 915 is filled with solid materials, such as solid drugs, solid excipients, etc. In some embodiments, the second compartment 915 is covered by a second exterior cover 904.
- [0163] FIG. 7B shows an exemplary pharmaceutical dosage form 1000 similar to the pharmaceutical dosage form 900 in FIG. 7A, except that the second compartment 1015 in FIG. 7B is filled with liquid or semi-solid material. The shell of pharmaceutical dosage form 1000 comprises a bottom 1014 and a peripheral wall 1013. The shell defines a first compartment 1012 filled with liquid or semi-solid material and a second compartment 1015 filled with liquid or semi-solid material. Although not shown in FIG. 7B, the second compartment 1015 can be similarly enclosed by any of the interior cover and exterior cover configurations provided herein. Although the first and second compartments shown in FIG. 7A and FIG. 7B are arranged in parallel with each other, the arrangement of the compartments are not limited to this configuration. In other embodiments, a plurality of compartments in a pharmaceutical dosage form may be attached onto each other as layers.
- [0164] In some embodiments, the pharmaceutical dosage form may comprise 2, 3, 4, 5, 6, 7, or 8 compartments. In some embodiments, at least one of the plurality of compartments of the pharmaceutical dosage form is used to contain a liquid or semi-solid material. In some embodiments, at least one of the plurality of compartments of the pharmaceutical dosage form may also be used to contain a solid material, such as a

solid drug, a solid formulation excipient, etc. In some embodiments, a plurality of compartments of the pharmaceutical dosage form are used to contain a liquid material. In some embodiments, a plurality of compartments of the pharmaceutical dosage form are used to contain a semi-solid material. In some embodiments, a plurality of compartments of a pharmaceutical dosage form are used to contain a solid material. In some embodiments, at least one of the plurality of compartments of the pharmaceutical dosage form is covered by any of the interior and exterior covers provided herein. In some embodiments, at least one of the plurality of compartments of the pharmaceutical dosage form is used to contain a liquid material and is covered by any of the interior and exterior covers provided herein. In some embodiments, a plurality of compartments of the pharmaceutical dosage form are used to contain a semi-solid material and are covered by any of the interior and exterior covers provided herein.

[0165] It should be noted that, although the different parts of the dosage form of the drug and the sub-parts of these different parts are mentioned in the detailed description above, this division is only exemplary and not mandatory.

[0166] III. Medical devices

[0167] In some embodiments, the pharmaceutical dosage forms described herein are provided as a medical device, or is comprised within a medical device. In some embodiments, there is provided a medical device, comprising: a bottom formed by a first material; a peripheral wall formed by a second material; wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and the interior cover at least partially covers the opening; a fourth material contained in the compartment; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the interior cover comprises one or more openings in communication with the compartment formed by the shell. In some embodiments, the fourth material contained in the compartment is a liquid or semi-solid. In some embodiments, the interior cover covers the opening of the compartment. In some embodiments, the fourth material contained in the compartment comprises a pharmaceutically acceptable material. In some embodiments, the fifth material comprises a component that is incompatible with a component of the fourth material. In some embodiments, the pharmaceutically acceptable material comprises a heat labile component.

[0168] IV. 3D printing methods

[0169] The present invention in another aspect provides methods for preparing any of the pharmaceutical dosage forms and/or medical devices described herein. The preparation methods comprise but are not limited to 3D-printing or additive manufacturing. In

certain aspects of the methods provided herein, one or more steps of three-dimensional printing or additive manufacturing may be performed by a substitute method, such as injection molding. For example, in some embodiments, the method comprises producing a shell comprising a bottom and a peripheral wall, printing an interior cover, delivering, including via three-dimensional printing, a material comprising a pharmaceutically acceptable material, and printing an exterior cover. Exemplary printing methods can be found in Examples 1 and 2. In some embodiments, the method comprises preparing (e.g., 3D-printing) some components of the pharmaceutical dosage form separately. In some embodiments, the method comprises printing certain components (e.g., the interior cover or exterior cover) separately and cooling down the components before assembling them to form the pharmaceutical dosage form. In some embodiments, the method comprises (1) printing a bottom and a peripheral wall, which together form a shell with a compartment, (2) delivering (e.g., via 3D printing) a material comprising a pharmaceutically acceptable material into the compartment; (3) printing an interior cover at least partially covering the opening of the compartment formed by the shell, and (4) printing an exterior cover. In some embodiments, the pharmaceutical dosage form comprises two or more compartments formed by the shell, and each compartment comprises an opening. Hence in some embodiments, the method comprises delivering (e.g., via three-dimensional printing) a material (can be the same or different) comprising a pharmaceutically acceptable material to one or more (e.g., two or more, or all) compartments through their one or more openings, such as before printing or assembling the interior cover. In some embodiments, the interior cover comprises one or more opening in communication with at least one of the two or more compartments formed by the shell. In some embodiments, the pharmaceutical dosage form comprises two or more interior covers each covering (e.g., at least partially) a compartment of two or more compartments formed by the shell, wherein each interior cover comprises one or more openings in communication with at least one of the two or more compartments. Hence in some embodiments, the method comprises delivering (e.g., via three-dimensional printing) a material (can be same or different) comprising a pharmaceutically acceptable material to one or more (e.g., two or more, or all) compartments through one or more openings of the one or more interior covers, such as after printing or assembling the interior cover (s) . The delivery of the material (can be same or different) into the two or more compartments can be simultaneously (e.g., via multi-channel nozzle) or sequentially (e.g., via one nozzle) .

[0170] In some embodiments, before using the third material to print the interior cover, the method further comprises: i) checking the viscosity of the fourth material to be delivered to the compartment formed by the shell; and/or ii) designing and/or checking the ratio of the area of an opening of the one or more openings (e.g., all of the one or

more openings) of the interior cover to the area of the opening of the compartment formed by the shell.

- [0171] In some embodiments, there is provided a method of printing an interior cover comprising one or more openings (e.g., any of the interior covers described herein), comprising flowing a third material out through a nozzle and depositing the third material to form the interior cover, wherein the movement of the nozzle during the printing the interior cover is set to first print a portion that is relatively far away from each opening of the one or more openings of the interior cover. In some embodiments, each opening of the one or more openings of the interior cover is an elongated opening extending roughly along a second axis, and wherein when printing the interior cover, the angle between the nozzle's moving direction and the second axis is less than 50° (e.g., less than any of 45°, 40°, 30°, 20°, 10°, 5°, 1°, or less).
- [0172] In some embodiments, the preparation methods provided herein further comprises examining the obtained pharmaceutical dosage forms, such as by detecting one or more of loading amount of the fourth material (e.g., by weighing before and after loading the fourth material), surface tension of the fourth material (e.g., via VHX imaging detection), purity or impurity of the pharmaceutically acceptable material in the pharmaceutical dosage form (either before or after storage, such as after 3 days, 5 days, 10 days, 20 days, 1, 2, 3, 6, 12 months or longer storage, e.g., at room temperature, about 0°C to about 18°C, about 30°C to about 50°C, about 38°C to about 42°C, or about 40°C). In some embodiments, the detected property (e.g., value) of the pharmaceutical dosage form is further compared to a quality control.
- [0173] The preparation methods described herein can be carried out in small-scale or in a large-scale (e.g., during a manufacturing workflow or a commercial scale). For example, in some embodiments, the methods disclosed herein may be used to 3D print about 1,000 to about 100,000 pharmaceutical dosage forms per hour. In some embodiments, each drug dosage form of a commercial batch possesses or substantially complies with one or more pre-determined pharmaceutical dosage form characteristics described herein, e.g., printing uniformity, precision of layer thickness (es), precision of layer surface area, precision of opening area, precision of layer active agent (s) mass fraction, precision of pharmaceutical dosage form shape, size, and/or weight, precision of active agent (s) amount, and precision of active agent release profile. In some embodiments, at least about 80%, such as at least about any of 85%, 90%, or 95%, of pharmaceutical dosage forms of a commercial batch possess or substantially comply with one or more pre-determined pharmaceutical dosage form characteristics described herein.
- [0174] Printing Method I

[0175] In certain aspects, provided herein is a method for preparing a pharmaceutical dosage form described herein, wherein the method comprises: producing, such as via three-dimensional printing, a bottom of the pharmaceutical dosage form using a first material; producing, such as via three-dimensional printing, a peripheral wall of the pharmaceutical dosage form using a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; producing, such as via three-dimensional printing, an interior cover attached to the shell using a third material, wherein the interior cover at least partially covers the opening of the compartment; delivering, after the printing of the interior cover (e.g., after the interior cover cools down) , a fourth material to the compartment through the opening of the compartment; and producing, such as via three-dimensional printing, an exterior cover attached to the interior cover and/or shell using a fifth material, such that the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the interior cover comprises one or more openings in communication with the compartment formed by the shell. In certain aspects, provided herein is a method for preparing a pharmaceutical dosage form described herein, wherein the method comprises: producing, such as via three-dimensional printing, a bottom of the pharmaceutical dosage form using a first material; producing, such as via three-dimensional printing, a peripheral wall of the pharmaceutical dosage form using a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; producing, such as via three-dimensional printing, an interior cover attached to the shell using a third material, wherein the interior cover at least partially covers the opening of the compartment, and the interior cover comprises one or more openings in communication with the compartment formed by the shell; delivering, after the printing of the interior cover (e.g., after the interior cover cools down) , a fourth material to the compartment through at least one of the one or more openings of the interior cover; and producing, such as via three-dimensional printing, an exterior cover attached to the interior cover and/or shell using a fifth material, such that the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the exterior cover fully covers all of the one or more openings of the interior cover. In certain embodiments, one or more components of the pharmaceutical dosage form can be produced, such as via three-dimensional printing or other means including injection molding, separately and then attached according to the structural descriptions of the pharmaceutical dosage forms described herein. For example, in some embodiments, the interior cover is printed and then attached to a printed shell according to the structural descriptions of the pharmaceutical dosage forms described herein.

- [0176] FIG. 8 shows a flowchart of an exemplary method for preparing pharmaceutical dosage forms by three-dimensional printing according to one embodiment of this application.
- [0177] In order to illustrate the method more clearly, the method 800 for preparing the pharmaceutical dosage form by three-dimensional printing method shown in FIG. 8 will be described below in combination with the structure of the pharmaceutical dosage form shown in FIG. 1A. As shown in FIG. 1A and FIG. 8, when printing the pharmaceutical dosage form 100 shown in FIG. 1A, step S801 comprises printing a bottom 113 using a first material and printing a peripheral wall 114 using a second material. The bottom 113 and the peripheral wall 114 together form a shell. The shell forms (or defines) a first compartment 112 and a first opening 111. In some embodiments, the first material and the second material are identical. In some embodiments, the first material and the second material are different. Subsequently, step S802 comprises printing the interior cover 102 on the shell using a third material such that the interior cover 102 is attached to the peripheral wall 114 of the shell and extends inward from the peripheral wall 114 to at least partially cover the first opening 111. At the same time, a second opening 121 is formed on the interior cover 102. After that, step S803 comprises delivering a fourth material (e.g., API) to the first compartment 112 defined by the shell through the second opening 121. The fourth material can be liquid or semi-solid. When the fourth material is a liquid, during the delivery process of step S803, the interior cover 102 structure located above the first compartment 112 can effectively reduce the influence of the difference between the surface tension and the interfacial tension of the liquid material, and offset the tendency of the liquid material to climb upward along the peripheral wall 114 of the shell, so that the filling of the liquid material can be effectively increased and controlled. Moreover, for the liquid or semi-solid fourth material, the interior cover 102 structure with the second opening 121 prevents liquid or semi-solid material in the first compartment 112 of the pharmaceutical dosage form 100 from directly contacting with a high-temperature exterior cover 103 during the three-dimensional printing process. At least in this way, the stability of the liquid or semi-solid drug or excipients can be improved and the cooling and forming speed of the exterior cover 103 can be optimized.
- [0178] Continuing with reference to FIG. 1A and FIG. 8, after completing the delivery of the liquid or semi-solid fourth material (e.g., API) in step S803, step S804 comprises printing an exterior cover 103 attached to the interior cover 102 or the shell using a fifth material, and the exterior cover 103 is constructed to cover the second opening 121, thereby achieving the closure of the first compartment 112. In some embodiments, the exterior cover 103 is attached to the shell (e.g., see FIG. 1B). In some embodiments, the ratio of the area of the first opening 111 to the second opening 121

is optimized in view of the viscosity of the fourth material of the liquid or semi-solid to be delivered into the first compartment 112 before step S802 (before printing the interior cover 102 attached to the shell using a third material) .

[0179] Printing Method II

[0180] In certain aspects, provided herein is a method for preparing a pharmaceutical dosage form described herein, wherein the method comprises: producing, such as via three-dimensional printing, a bottom of the pharmaceutical dosage form using a first material; producing, such as via three-dimensional printing, a peripheral wall of the pharmaceutical dosage form using a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; delivering a fourth material to the compartment through the opening of the compartment; producing, such as via three-dimensional printing, an interior cover attached to the shell using a third material, wherein the interior cover at least partially covers the opening of the compartment; and producing, such as via three-dimensional printing, an exterior cover attached to the interior cover and/or shell using a fifth material, such that the exterior cover is configured to cover, at least partially, the interior cover. In some embodiments, the interior cover comprises one or more openings in communication with the compartment formed by the shell. In certain embodiments, one or more components of the pharmaceutical dosage form can be produced, such as via three-dimensional printing or other means including injection molding, separately and then attached according to the structural descriptions of the pharmaceutical dosage forms described herein. For example, in some embodiments, the interior cover is printed and then attached to a printed shell according to the structural descriptions of the pharmaceutical dosage forms described herein.

[0181] FIG. 9 shows a flowchart of an exemplary method for preparing pharmaceutical dosage forms by three-dimensional printing according to one embodiment of this application.

[0182] In order to illustrate the method more clearly, the method 900 shown in FIG. 9 will be described in combination with the structure of the pharmaceutical dosage form shown in FIG. 5B. As shown in FIG. 5A and FIG. 9, when printing the pharmaceutical dosage form 500 shown in FIG. 5A, step S901 comprises printing a bottom 513 with a first material and printing a peripheral wall 514 with a second material. The bottom 513 and the peripheral wall 514 together form a shell 512 forming the compartment 512 with an opening (e.g., a first opening) 511. In some embodiments, the first material and the second material are identical. In some embodiments, the first material and the second material are different. Subsequently, step S902 comprises delivering a fourth material to the compartment formed by the shell through the opening 511. Then, step S903 comprises printing the interior cover 502 attached to the shell using

a third material such that the interior cover 502 is attached to the peripheral wall 514 and extends inward from the peripheral wall 514 to at least partially cover the opening 511. In the printing process, the interior cover 502 located above the compartment 512 could prevent the material in the compartment 512 from directly contacting with the high-temperature exterior cover 503 in the three-dimensional printing process, thereby improving stability of the drug or excipients and also reducing material incompatibility between the exterior cover and the drug or excipients.

- [0183] Continuing with reference to FIG. 5A and FIG. 9, after completing the printing of the interior cover 502, step S904 comprises printing an exterior cover 503 using a fifth material, wherein the exterior cover is attached to the interior cover 502, and the exterior cover 503 is constructed to at least partially cover the interior cover 502, thereby realizing the closure of the compartment 512. In some embodiments, the exterior cover 503 is attached to the shell.
- [0184] In order to illustrate the method more clearly, the method 900 for the preparation of the pharmaceutical dosage form by the three-dimensional printing method shown in FIG. 9 will be further described below in combination with the structure of the pharmaceutical dosage form shown in FIG. 5B.
- [0185] In this embodiment, the interior cover 502 can be completed in the form of pre-3D printing. When printing the pharmaceutical dosage form 600 shown in FIG. 5B, in step S901, the bottom 613 is printed with the first material and the peripheral wall 614 is printed with the second material respectively, and the bottom 613 and the peripheral wall 614 together form a shell forming a compartment 612 with the first opening 611. In some embodiments, the first material and the second material are identical. In some embodiments, the first material and the second material are different. Subsequently, in step S902, a fourth material is delivered to the compartment through the first opening 611. Subsequently, step S903 comprises printing the interior cover 602 attached to the shell using a third material. In some embodiments, step S903 comprises printing the interior cover from a point on the peripheral wall 614 and printing inward, such that the printed interior cover could at least partially cover the first opening 611. Optionally, instead of performing step S903, a pre-manufactured interior cover 602 may be attached to the peripheral wall 614 of the shell. Finally, in step S904, the exterior cover 603 is printed using a fifth material, thereby realizing the closure of the compartment 611.
- [0186] Printing Method III
- [0187] In certain aspects, provided herein is a method for preparing a pharmaceutical dosage form described herein, wherein the method comprises: producing, such as via three-dimensional printing, a bottom of the pharmaceutical dosage form using a first material; producing, such as via three-dimensional printing, a peripheral wall of the pharma-

ceutical dosage form using a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; delivering a fourth material to the compartment through the opening of the compartment; and producing, such as via three-dimensional printing, an exterior cover attached to the shell using a fifth material, such that the exterior cover is configured to cover the opening of the compartment. In certain embodiments, one or more components of the pharmaceutical dosage form can be produced, such as via three-dimensional printing or other means including injection molding, separately and then attached according to the structural descriptions of the pharmaceutical dosage forms described herein.

- [0188] The application also provides an exemplary method for printing the dosage form of the drug shown in FIG. 10. Unlike FIG. 8, the pharmaceutical dosage form in FIG. 10 does not comprise the interior cover so step S802 is omitted. Other steps can be the same as in FIG. 8.
- [0189] In some embodiments, there is provided a method of preparing a pharmaceutical dosage form (e.g., any of the pharmaceutical dosage forms described herein), comprising: printing a first surface with a first material along a first preset path; printing a second surface with a second material along a second preset path; wherein the first surface and the second surface together form a compartment; delivering a fourth material to the compartment; and printing a third surface with a fifth material along a third preset path to seal the compartment.
- [0190] In some embodiments, the first preset path extends within a horizontal plane from the starting point. In some embodiments, the third preset path extends within a horizontal plane from the starting point.
- [0191] In some embodiments, the second preset path is not within a horizontal plane. In some embodiments, the end point of the second preset path is vertically higher than the starting point. In some embodiments, printing along the second preset path comprises: (a) printing along a horizontal plane from a starting point then returning to the starting point; (b) repeating path (a) at least once. In some embodiments, the second preset path is printed at a low printing temperature (e.g., less than about any of 100 °C, 80 °C, 60 °C, 40 °C, 30 °C, or at around room temperature). In some embodiments, the low temperature used for printing the second preset path can reduce the heating impact on the fourth material contained in the compartment caused by printing the pharmaceutical dosage form.
- [0192] In some embodiments, the first surface, the second surface, and the third surface may be flat or curved surfaces, and can be arbitrarily set according to the actual needs of the pharmaceutical dosage form.
- [0193] A detailed description of the method is provided below in conjunction with FIG. 11A to FIG. 11C. Step 1101 in FIG. 11A depicts a method for forming a first surface,

and a first material can be discharged along a first preset path from the discharge port by utilizing any kind of apparatus disclosed in the present invention. Starting at the start point shown in FIG. 11A, the first material moves along the first path and returns to the preset boundary until the entire path is complete. In this embodiment, the first preset path extends along the horizontal plane from the starting point, and the starting point and the end point do not coincide. In other embodiments, the printing process can discharge the material from the endpoint along the first preset path to the start point. After completing the preparation of the first surface, any point of the first surface can be selected as the starting point for a second path, so that a second material is discharged along the second preset path 1102. The second preset path comprises one or more path that extends along the horizontal plane and then returns to the starting point. The second preset path in FIG. 11B is combined with the first surface to divide the compartment into a first compartment 1121 and a second compartment 1122. After forming a compartment, the fourth material is filled into the compartment, and the fifth material is discharged along a third preset path 1103 in FIG 11C to seal the compartment.

- [0194] The first, second, and fifth materials may be the same or different, and may be one or more of the thermoplastic materials described above. The fourth material can be an active pharmaceutical material and/or excipient, which may be selected from one or more of the active pharmaceutical materials and/or excipients described above.
- [0195] The steps of the 3D printing preparation method for the pharmaceutical dosage forms shown in FIG. 7A and FIG. 7B are approximately same as those for the 3D printing preparation method of the pharmaceutical dosage forms shown in FIG. 1A. The main difference is that the 3D printing method of the pharmaceutical dosage form in FIG. 7A further comprises a step of delivering a solid material in the second compartment 915, which can precede delivery of the liquid or semi-solid material into the first compartment 912. In some embodiments, the step of delivering the solid material may also be carried out after the delivery of the liquid or semi-solid material to the compartment 912 has been completed or during the delivery of the liquid or semi-solid material to the compartment 912. The main difference between the 3D printing method of the pharmaceutical dosage form shown in FIG. 7B and the 3D printing method of the pharmaceutical dosage form shown in FIG. 1A is that, for the dosage form in FIG. 7B, after the printing of the interior cover is completed, a liquid or semi-solid material needs to be delivered to the compartment 1012 and the second compartment 1015 through the second opening and the third opening on the interior cover, respectively.
- [0196] It should be noted that the terms “printing”, “three-dimensional printing”, “3D printing”, “additive manufacturing” or their equivalent expressions shown in this article can be any feasible 3D printing method. In some embodiments, one or more

steps of these methods are performed by the corresponding additive manufacturing system. In some embodiments, “printing”, “three-dimensional printing”, “3D printing”, “additive manufacturing” or their equivalent refers to the process of using a digital design to make a three-dimensional object, such as a pharmaceutical dosage form, layer by layer. The basic process of 3D printing is described in United States Patent No. 5,204,055; 5,260,009; 5,340,656; 5,387,380; 5,503,785; and 5,633,021. Other United States patents and patent applications related to 3D printing include: United States Patent No. 5,490,962, 5,518,690, 5,869,170, 6,530,958, 6,280,771, 6,514,518, 6,471,992, 8,828,411, United States Publication No. 2002/0015728, 2002/0106412, 2003/0143268, 2003/0198677; 2004/0005360. The contents of the above United States patents and patent applications are incorporated herein by reference in their entirety.

[0197] In some embodiments, the material of each step is extruded from the nozzle by a mechanical print head and deposited onto a deposition platform to form the corresponding bottom, peripheral wall, inner or exterior cover structure. The basis of the molten material of this mechanical printhead can be achieved by a single-piston extruder, a single-screw extruder, a twin-screw extrusion, or any combination thereof. Through the movement of the nozzle of the mechanical print head relative to the deposition platform, the different shapes of the bottom, the peripheral wall, the interior cover, the exterior cover, the opening formed by the shell, and the second openings in the interior cover, and the position arrangement between them are realized. FIG. 12A to FIG. 12C show schematic diagrams of different nozzle printing paths of the interior cover shown in FIG. 4E, and FIG. 12D illustrates a schematic diagram of the nozzle printing path of the interior cover of a pharmaceutical dosage form according to one embodiment of this application.

[0198] In some embodiments, the printing temperature (e.g., at nozzle) ranges from about 20°C to about 200°C, such as any of about 20°C to about 60°C, about 40°C to about 50°C, about 50°C to about 180°C, about 80°C to about 150°C, about 100°C to about 150°C, about 100°C to about 200°C, about 20°C to about 100°C, about 130°C, about 40°C, or about 50°C. In some embodiments, the nozzle printing temperature is around room temperature (e.g., about 25°C). The printing temperature (e.g., at nozzle) can be the same or different for the first, second, third, and/or fifth material, which depends on the material components. In some embodiments, the printing temperatures (e.g., at nozzle) for the first, second, third, and fifth materials are the same (e.g., at about 130°C). In some embodiments, the printing temperatures (e.g., at nozzle) for the first, second, third, and fifth materials are different. For example, the first, second, third materials are printed at a first temperature (e.g., at about 130°C), and the fifth material is printed at a second temperature (e.g., at about 50°C). In some embodiments, the printing

temperature (e.g., at nozzle) of the fourth material (e.g., at about room temperature, such as about 25°C) is lower than that for the first, second, third, and/or fifth material (e.g., at about 50°C or at about 130°C). In some embodiments, the fourth material is a semi-solid material printed by extrusion under room temperature.

[0199] As shown in FIG. 12A, when printing the interior cover shown in FIG. 4E, the angle between the direction of movement of the nozzle and the second direction axis of the second opening (as shown in the dotted line in FIG. 4E) is less than 50°. In some embodiments, without bound by any theory, such an angle (less than 50°) is optimized as to achieve a satisfying structural stability, allowing for a uniform drug filling, and also maximizing the printing speed efficiency. In some embodiments, the angle between the direction of movement of the nozzle and the second direction axis of the second opening (dashed line as shown in FIG. 4E) is less than 45°, such as less than about any of 30°. At the same time, the movement trajectory of the nozzle is set to print the part of the interior cover relatively far away from the second opening first. In other embodiments, as shown in FIG. 12B, the angle between the direction of movement of the nozzle and the axis of the second direction is 30 to 60°. In another embodiment, the nozzle may be set to have its print trajectory composed of a plurality of curves, as shown in FIG. 12C, and the nozzle is set to move in arcs until the interior cover is printed with a second opening.

[0200] In some embodiments, the shell material and the drug material can be printed with different and independently selected print heads. For example, in some embodiments, the first to fifth materials are printed by different print heads. In other embodiments, at least two of the first, second, third, and fifth materials may be printed by the same print head.

[0201] In some embodiments, the interior cover can be manufactured in advance. In some embodiments, the interior cover can be manufactured by three-dimensional printing, injection molding, hot press molding, and other subtractive processing. In some embodiments, the method further comprises assembling a pre-manufactured interior cover onto the compartment formed by the shell, thereby covering the opening formed by the shell.

[0202] In some embodiments, the method further comprises designing, in whole or in part, the pharmaceutical dosage form as described herein or its components on a computer system. In some embodiments, the method comprises inputting a target drug release curve and/or dimensions of the pharmaceutical dosage form and/or target dose unit and/or target dosage form precursor into a computer system. In some embodiments, the method comprises inputting one or more target printing parameters, such as target layer surface area, thickness, drug concentration in the fourth material, and/or dissolution rate of various materials. In some embodiments, the designing of the phar-

maceutical dosage form comprises inputting a target drug release curve. In some embodiments, the designing of the pharmaceutical dosage form comprises creating a virtual image of the pharmaceutical dosage form to be printed. In some embodiments, the designing of the pharmaceutical dosage form comprises creating a computer model containing predetermined parameters. In some embodiments, the designing of the pharmaceutical dosage form comprises feeding predetermined parameters to a three-dimensional printer and the method further comprises printing articles according to those predetermined parameters. In some embodiments, the designing of the pharmaceutical dosage form comprises creating a three-dimensional drawing of the article to be printed based on predetermined parameters, wherein the three-dimensional drawing is created on a computer system. In some embodiments, the method further comprises, for example, converting a layered three-dimensional drawing into a three-dimensional printing code, for example, a G-code. In some embodiments, the method comprises using a computer system to execute a three-dimensional printing code such as the dosage form can be printed according to the method described herein.

- [0203] In some embodiments, the methods exemplified in FIG. 8 or FIG. 9 are used to carry out additive manufacturing containing the structure shown in the present application, comprising a 3D printed medical device, a 3D printed human organ or tissue, a 3D printed veterinary drug, etc.
- [0204] In some embodiments, also provided herein is a medical device containing the pharmaceutical dosage forms shown in the present application, optionally printed using the methods exemplified in FIG. 8 or FIG. 9.
- [0205] V. 3D printing equipment
- [0206] The present application in another aspect provides drug production apparatus, which can be used to prepare any of the pharmaceutical dosage forms and/or medical devices described herein, or to carry out any of the preparation methods described herein.
- [0207] In some embodiments, there is provided a drug production apparatus comprising: a first feeding unit, capable of providing a first printing material to a first printing unit; a second feeding unit, capable of providing a second printing material to a second printing unit; a carrying platform capable of moving relative to the first feeding unit and/or the second feeding unit; wherein the first printing unit comprises at least one nozzle, wherein each of the at least one nozzle comprises a feeding channel and a sealing structure, and the sealing structure moves in whole or in part to seal or open the feeding channel; the second printing unit comprises at least one discharging module, a driving device, and a mounting frame, wherein the discharging module comprises a discharging barrel, wherein the driving device drives the discharging of the second printing material from the discharging barrel, and wherein the driving device and the discharging barrel are fixed with the mounting frame; and the first printed material

and/or the second printed material comprises a pharmaceutically active material (e.g., API) . In some embodiments, the driving device comprises a power assembly and a force transmission assembly, wherein the force transmission assembly comprises a push rod and a piston connected with the push rod, and wherein the piston is wholly or partially located inside the discharging barrel. In some embodiments, the force transmission assembly further comprises a screw rod and a fixed block, the screw rod is capable of transmitting the torque of the power assembly, and the fixed block is connected with the screw rod and the push rod, thereby moving the push rod with the rotation of the screw rod. In some embodiments, the mounting frame of the second printing unit comprises a mounting base and a mounting backplate perpendicular to the mounting base, and wherein the discharging barrel is connected with the mounting base or the mounting backplate through a barrel fixing element. In some embodiments, the mounting backplate further comprises a slide rail, and wherein the power assembly of the driving device is connected with the slide rail, and/or the barrel fixing element is connected with the slide rail. In some embodiments, the carrying platform is capable of translationally moving or rotating relative to the first feeding unit and/or the second feeding unit. In some embodiments, the drug production apparatus further comprises a temperature control module.

[0208] FIG. 13 shows a perspective view of an exemplary discharging module 1300 used for delivering the fourth material according to the present application.

[0209] In some embodiments, the delivery of liquid and semi-solid materials of step S803 can be realized through a piston type print head, and the liquid or semi-solid delivery is achieved through a nozzle by the action of a piston. In some embodiments, delivery of liquid and semi-solid materials can also be realized by any other possible delivery mechanism for liquid or semi-solid materials. Examples include, but are not limited to, progressive cavity pumps, axial flow pumps, centrifugal pumps, or structures that simply rely on gravity to allow liquid or semi-solid materials to flow out. As shown in FIG. 13, the discharging module comprises a piston print head, and further comprises a barrel 1301 for holding liquid or semi-solid materials, and a barrel fixing block 1321 for fixing the barrel 1301, a piston push rod 1302 arranged in a barrel and a driving device (e.g., a drive motor component) 1303 for driving a piston push rod 1302 to move along the barrel 1301. In some embodiments, the piston push rod 1302 can also be connected with the lead screw of the driving device (e.g., drive motor component) through the push rod fixed block (not shown in the figure) , so that when the drive motor rotates, the push rod fixed block can be driven to move up and down along the vertical direction, and then the piston push rod 1302 moves along the material barrel 1301. It should be noted that, although the discharging module 1300 shown in FIG. 13 adopts an electric motor to drive the piston push rod, in some embodiments,

the mechanism used for driving the piston push rod may also include one or more of pneumatic actuators, mechanical actuators, electromagnetic actuators or hydraulic actuators.

- [0210] Continue referring to FIG. 13, the discharging module 1300 further comprises a mounting base 1304 and a mounting backplate 1305 that are fixedly connected to each other, wherein the driving device (e.g., drive motor component) 1303 is attached to the mounting backplate 1305, and then is attached to the rest of the three-dimensional printing system through the mounting backplate 1305. At the same time, the barrel 1301 is attached to the mounting backplate 1305 through the barrel fixing block 1321. In some embodiments, the barrel 1301 can be attached to the mounting base 1304 through the barrel fixing block, and then attached to the rest of the three-dimensional printing system through the mounting base 1304. In some embodiments, the driving device (e.g., drive motor component) 1303 can be attached to the mounting backplate 1305 in a way that can move up and down (for example, a slide rail attached to the mounting backplate 1305), so that the driving motor component 1303 can move up and down along the mounting backplate 1305, and the piston push rod 1302 is driven to move along the vertical direction simultaneously. This construction can realize the rapid movement of the piston push rod 1302 relative to the barrel 1301, so that the piston push rod 1302 can be quickly removed from the barrel 1301 to achieve the discharge of liquid or semi-solid material in the barrel 1301.
- [0211] In some embodiments, the three-dimensional printing equipment of the present application further comprises a temperature control module. FIG. 14A through FIG. 14B illustrate a printing device with a temperature control module to keep the temperature of the material to be printed at a lower temperature, such as -20°C to 30°C. As shown in FIG. 14A, one or more semiconductor refrigeration sheets 1322 can be arranged on the barrel 1301, and the target temperature of the temperature control module can be set according to the performance and characteristics of the material to be printed. The inventors found that during the printing of pharmaceutical active materials or excipients for pharmaceutical preparations, it is important to avoid additional moisture entering the pharmaceutical dosage form. In some embodiments, the printing device further comprises a moisture barrier module. In the embodiment of FIG. 14A, the moisture barrier module 1340 is a deflector groove 1340 located on the barrel 1301 and a moisture collection unit positioned at the barrel fixing block or the mounting base 1304 or other positions. Excess moisture attached to the barrel will enter the moisture collection unit along the deflector 1340.
- [0212] In some embodiments, as shown in FIG. 14B, all or part of the discharging module 1300 can be isolated from other printing units, and the ambient temperature control unit is arranged separately. The three-dimensional printing equipment comprises a first

printing unit 1400, a second printing unit 1300 and a carrying platform 1600. The first printing unit 1400 can be used for printing the bottom and/or peripheral wall. In some embodiments, a third printing unit can be arranged to print parts such as peripheral walls to form a shell separately. In some embodiments, the first printing unit 1400 comprises a first feeding unit 1401, a melt extrusion unit 1402, a force transmission assembly 1403, a print head 1404 and a nozzle 1405. In some embodiments, the second printing unit 1300 can be used for printing pharmaceutical active materials or pharmaceutical preparation excipients or mixtures thereof. In some embodiments, the carrying platform 1600 can be moved to the position of the first printing unit and the position of the second printing unit to generate a pharmaceutical dosage form unit 1500. The second printing unit 1300 may further comprise a temperature control unit 1350, such as a glass cover, a plastic cover, etc. In some embodiments, the temperature control unit 1350 comprises an opening 1351, and the size and shape of the opening matches the size and shape of the discharge port tip of the second printing unit 1300. The temperature control unit 1350 includes a temperature control system to ensure that the temperature in the control unit is between -20 °C and 30 °C. The interior of the temperature control unit 1350 may also include a vacuuming system to prevent the ingress of excess moisture into the interior of the pharmacy unit 1500. In some embodiments, the temperature control module of the discharging module 1300 comprises a first temperature control unit and a second temperature control unit. The first temperature control unit is located on or near the peripheral wall of the barrel and is used to control the temperature of the material to be printed. The second temperature control unit is far away from the stage or print head and the temperature is lower than the temperature of the first temperature control unit. Through the heat absorption of the second temperature control unit, the excess moisture in the air is condensed near the second temperature control unit.

[0213] Although the principles of the present invention have been described in conjunction with embodiments, it should be understood that these descriptions are for illustrative purposes only and are not intended to limit the scope of the invention. The contents of this disclosure are for illustrative purposes only and are not exhaustive or limited in a specific form. Many of the adjustments and changes are obvious to those skilled in the art. The contents of the present disclosure have been selected on the basis that the principles and practical applications of the embodiments may be better explained, so that those skilled in the art can understand the various embodiments and adjustments made for specific applications. The scope of this disclosure is limited by the following claims or their equivalents.

[0214] Those skilled in the art will be aware that there may be several embodiments within the scope and spirit of the disclosure of the present application. This disclosure is

further illustrated by the following embodiments, which should not be construed as limiting the scope or spirit of the contents of this disclosure to the specific steps described herein.

[0215] Exemplary Embodiments

[0216] Embodiment 1. A pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, wherein the interior cover at least partially covers the opening of the compartment, and wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover.

[0217] Embodiment 2. The pharmaceutical dosage form of embodiment 1, wherein the pharmaceutical dosage form comprises a volume of gas.

[0218] Embodiment 3. The pharmaceutical dosage form of embodiment 1 or 2, wherein the ratio of the area of an opening of the one or more openings of the interior cover to the area of the opening of the compartment formed by the shell is less than 95%.

[0219] Embodiment 4. The pharmaceutical dosage form of any one of embodiments 1-3, wherein the interior cover is an elongated structure extending roughly along a first axis, each opening of the one or more openings of the interior cover is an elongated opening extending roughly along a second axis, and the angle between the first axis and the second axis is 0°-90°.

[0220] Embodiment 5. The pharmaceutical dosage form of any one of embodiments 1-4, wherein the one or more openings of the interior cover comprises two openings, wherein each of the two openings are formed along an independent axis, and wherein each independent axis is parallel with the other.

[0221] Embodiment 6. The pharmaceutical dosage form of any one of embodiments 1-6, wherein the shape of each opening of the one or more openings of the interior cover is independently selected from the group consisting of circle, square, rectangle, parallelogram, or rhomboid, or a combination thereof.

[0222] Embodiment 7. The pharmaceutical dosage form of any one of embodiments 1-6, wherein each opening of the one or more openings of the interior cover does not comprise a plug.

[0223] Embodiment 8. The pharmaceutical dosage form of any one of embodiments 1-7, wherein the interior cover has a surface area of about 1 mm² to about 300 mm².

- [0224] Embodiment 9. The pharmaceutical dosage form of any one of embodiments 1-8, wherein the interior cover has a thickness of about 0.01 mm to about 2 mm.
- [0225] Embodiment 10. The pharmaceutical dosage form of any one of embodiments 1-9, wherein the third material of the interior cover and the second material of the peripheral wall are monolithic.
- [0226] Embodiment 11. The pharmaceutical dosage form of any one of embodiments 1-10, wherein the shell forms one or more additional compartments.
- [0227] Embodiment 12. The pharmaceutical dosage form of embodiment 11, wherein each of the one or more additional compartments comprises an opening.
- [0228] Embodiment 13. The pharmaceutical dosage form of embodiment 12, wherein the interior cover at least partially covers at least one opening of the one or more additional compartments.
- [0229] Embodiment 14. The pharmaceutical dosage form of embodiment 12, wherein the pharmaceutical dosage form further comprises a second interior cover that at least partially covers at least one opening of the one or more additional compartments.
- [0230] Embodiment 15. The pharmaceutical dosage form of embodiment 14, wherein the second interior cover comprises one or more openings in communication with the at least one opening of the one or more additional compartments.
- [0231] Embodiment 16. The pharmaceutical dosage form of embodiment 14 or 15, wherein the interior cover and the second interior cover comprise the same material.
- [0232] Embodiment 17. The pharmaceutical dosage form of embodiment 14 or 15, wherein the interior cover and the second interior cover comprise different materials.
- [0233] Embodiment 18. The pharmaceutical dosage form of any one of embodiments 1-17, wherein the fourth material is a liquid or semi-solid material.
- [0234] Embodiment 19. The pharmaceutical dosage form of any one of embodiments 1-17, wherein the fourth material is a solid material.
- [0235] Embodiment 20. The pharmaceutical dosage form of any one of embodiments 1-19, wherein the pharmaceutically acceptable material is heat labile.
- [0236] Embodiment 21. The pharmaceutical dosage form of any one of embodiments 1-20, wherein the pharmaceutically acceptable material is incompatible with another component of the pharmaceutical dosage form.
- [0237] Embodiment 22. The pharmaceutical dosage form of any one of embodiments 1-21, wherein the pharmaceutically acceptable material is a pharmaceutically active material, excipient, or an adjuvant.
- [0238] Embodiment 23. The pharmaceutical dosage form of embodiment 22, wherein the pharmaceutically acceptable material is a pharmaceutically active material selected from one or more of a small molecule compound, polypeptide, protein, nucleic acid,

cell-containing hydrogel, probiotic, antibody-drug conjugate, and microbiome, or a combination thereof.

- [0239] Embodiment 24. The pharmaceutical dosage form of embodiment 23, wherein the pharmaceutically active material is a polypeptide selected from the group consisting of an insulin, antidiuretic hormone, calcitonin, calcitonin gene-related peptide, parathyroid hormone, luteinizing hormone, erythropoietin, tissue plasminogen activator, growth hormone, adrenocorticotrophic hormone, interleukin, enkephalin, epinephrine, glucagon-like peptide-1 (GLP-1) receptor agonist, semaglutide, liraglutide, dulaglutide, exenatide, octreotide, teriparatide, vancomycin, linaclotide, pukanatide, vorcyclyde, talterelin, acetaminopressin, marsimorelin, and GLP-2 analogue.
- [0240] Embodiment 25. The pharmaceutical dosage form of embodiment 23, wherein the pharmaceutically active material is a small molecule compound.
- [0241] Embodiment 26. The pharmaceutical dosage form of embodiment 23, wherein the pharmaceutically active material is a protein selected from the group consisting of a blood factor, colony-stimulating factor, interleukin, growth factor, tumor necrosis factor (TNF) , and enzyme.
- [0242] Embodiment 27. The pharmaceutical dosage form of embodiment 23, wherein the pharmaceutically active material is a protein selected from the group consisting of an asparaginase, glutaminase, arginase, arginine deaminase, adenosine deaminase ribonuclease, cytosine deaminase, trypsin, chymotrypsin, papain, epidermal growth factor (EGF) , insulin-like growth factor (IGF) , transforming growth factor (TGF) , nerve growth factor (NGF) , platelet-derived growth factor (PDGF) , bone morphogenetic protein (BMP) , fibroblast growth factor, somatostatin, somatostatin, colony-stimulating factor (CSF) , coagulation factor, tumor necrosis factor, interferon, gastrointestinal peptide, vasoactive intestinal peptide (VIP) , incretin (CCK) , gastrin, secretin, hormone, pancreatic enzymes, superoxide dismutase, thyrotropin-releasing hormone (TRH) , thyroid-stimulating hormone, luteinizing hormone, luteinizing hormone-releasing hormone (LHRH) , tissue plasminogen activator, receptor antagonist (IL-1RA) , leptin, auxin, granulocyte-macrophage colony-stimulating factor (GM-CSF) , adenosine deaminase, uricase, chorionic gonadotropin, heparin, atrial natriuretic peptide, hemoglobin, relaxin, cyclosporine, oxytocin, ankyrin repeat protein, and avidin, or any combination thereof.
- [0243] Embodiment 28. The pharmaceutical dosage form of embodiment 23, wherein the pharmaceutically active material is a nucleic acid comprising oligomers or polymers of at least two linked nucleotides or nucleotide derivatives, a deoxyribonucleic acid (DNA) and a ribonucleic acid (RNA) linked together by phosphodiester bonds, a DNA, a cDNA, or an RNA.

- [0244] Embodiment 29. The pharmaceutical dosage form of embodiment 28, wherein the nucleic acid comprises a DNA molecule and an RNA molecule.
- [0245] Embodiment 30. The pharmaceutical dosage form of embodiment 28, wherein the nucleic acid is single-stranded or double-stranded.
- [0246] Embodiment 31. The pharmaceutical dosage form of embodiment 28, wherein the nucleic acid is cDNA.
- [0247] Embodiment 32. The pharmaceutical dosage form of embodiment 28, wherein the nucleic acid is selected from the group consisting of an antisense nucleic acid, messenger RNA (mRNA), transfer RNA (tRNA), small interfering RNA (siRNA), short hairpin RNA (shRNA), guide RNA (gRNA), small RNA (sRNA), microRNA (miRNA), circular RNA (circRNA), trans-amplifying RNA (taRNA), small activating RNA (saRNA), complementary RNA (cRNA), non-coding RNA, and long RNA, or any combination thereof.
- [0248] Embodiment 33. The pharmaceutical dosage form of embodiment 23, wherein the pharmaceutically active material is a protein, which is an antibody.
- [0249] Embodiment 34. The pharmaceutical dosage form of any one of embodiment 23, wherein the pharmaceutically active material is a probiotic selected from the group consisting of *Bifidobacterium* spp., *Bifidobacterium brevis*, *Bifidobacterium animalis*, *Bifidobacterium lactis*, *Bifidobacterium longum*, *Bifidobacterium bifidum*, *Lactococcus lactis*, *Streptococcus lactis*, *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus kefir*, *Lactobacillus bifidus*, *Lactobacillus brevis*, *Lactobacillus Switzerland*, *Lactobacillus paracasei*, *Lactobacillus rhamnosus*, *Lactobacillus salivarius*, *Lactobacillus campylobacter*, *Lactobacillus Bulgaria*, *Lactobacillus sake*, *Lactobacillus reuteri*, *Lactobacillus lactis*, *Lactobacillus del Brückella*, *Lactobacillus plantarum*, *Lactobacillus johnsonii*, and *Streptococcus thermophilus*, or any combination thereof.
- [0250] Embodiment 35. The pharmaceutical dosage form of embodiment 22, wherein the pharmaceutically acceptable material is an excipient selected from the group consisting of a wetting agent, permeation enhancer, plasticizer, adhesive, developer, filler, and pH adjuster, or any combination thereof.
- [0251] Embodiment 36. The pharmaceutical dosage form of any one of embodiments 1-35, wherein the first material of the bottom and the second material of the peripheral wall are monolithic.
- [0252] Embodiment 37. The pharmaceutical dosage form of any one of embodiments 1-35, wherein the third material of the interior cover, the second material of the peripheral wall, and the first material of the bottom are monolithic.

- [0253] Embodiment 38. The pharmaceutical dosage form of any one of embodiments 1-37, wherein the exterior cover is configured to fully cover all of the one or more openings of the interior cover.
- [0254] Embodiment 39. The pharmaceutical dosage form of any one of embodiments 1-38, wherein the exterior cover is attached to the shell.
- [0255] Embodiment 40. The pharmaceutical dosage form of any one of embodiments 1-39, wherein the exterior cover is attached to the interior cover.
- [0256] Embodiment 41. The pharmaceutical dosage form of any one of embodiments 1-40, wherein the first material is different from the second material.
- [0257] Embodiment 42. The pharmaceutical dosage form of any one of embodiments 1-40, wherein the first material and the second material are the same.
- [0258] Embodiment 43. The pharmaceutical dosage form of any one of embodiments 1-42, wherein the second material is different from the third material.
- [0259] Embodiment 44. The pharmaceutical dosage form of any one of embodiments 1-42, wherein the second material and the third material are the same.
- [0260] Embodiment 45. The pharmaceutical dosage form of any one of embodiments 1-44, wherein the third material is different from the fifth material.
- [0261] Embodiment 46. The pharmaceutical dosage form of embodiment 45, wherein the dissolution rate of the third material is different from that of the fifth material.
- [0262] Embodiment 47. The pharmaceutical dosage form of any one of embodiments 1-44, wherein the third material and the fifth material are the same.
- [0263] Embodiment 48. The pharmaceutical dosage form of any one of embodiments 1-45 and 47, wherein the third material and the fifth material have the same dissolution rate.
- [0264] Embodiment 49. The pharmaceutical dosage form of any one of embodiments 1-48, wherein the shape of the pharmaceutical dosage form is a cylinder, a runway-shaped cylinder, an elliptical cylinder, a cube, a cuboid, a capsule, or a frustum of a cone.
- [0265] Embodiment 50. The pharmaceutical dosage form of embodiment 49, wherein the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the diameter of the cylinder to the height of the cylinder is less than 1, the ratio of the area of all openings of the one or more openings of the interior cover and the area of the opening of the compartment formed by the shell is less than 90%.
- [0266] Embodiment 51. The pharmaceutical dosage form of embodiment 49, wherein the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the diameter of the cylinder to the height of the cylinder is between 1 and 5.5, the ratio of the area of all openings of the one or more openings of the interior cover and the opening of the compartment formed by the shell is less than 90%.
- [0267] Embodiment 52. The pharmaceutical dosage form of embodiment 49, wherein the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the

diameter of the cylinder to the height of the cylinder is more than 5.5, the ratio of all openings of the one or more openings of the interior cover and the opening of the compartment formed by the shell is less than 90%.

- [0268] Embodiment 53. A pharmaceutical dosage form, comprising: a bottom formed by a first material; a peripheral wall formed by a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and wherein the interior cover covers the opening of the compartment; a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and wherein the exterior cover is configured to cover, at least partially, the interior cover.
- [0269] Embodiment 54. The pharmaceutical dosage form of embodiment 53, wherein the fifth material comprises a component that is incompatible with a component of the fourth material.
- [0270] Embodiment 55. The pharmaceutical dosage form of embodiment 53 or 54, wherein the pharmaceutically acceptable material comprises a heat labile component.
- [0271] Embodiment 56. The pharmaceutical dosage form of any one of embodiments 53-55, wherein the third material of the interior cover is an erodible material.
- [0272] Embodiment 57. The pharmaceutical dosage form of any one of embodiments 53-56, wherein the interior cover comprises a mesh.
- [0273] Embodiment 58. A medical device, comprising: a bottom formed by a first material; a peripheral wall formed by a second material; wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; an interior cover formed by a third material, wherein the interior cover is attached to the shell, and the interior cover at least partially covers the opening; a fourth material contained in the compartment; and an exterior cover formed by a fifth material, wherein the exterior cover is attached to the interior cover and/or the shell, and the exterior cover is configured to cover, at least partially, the interior cover.
- [0274] Embodiment 59. The medical device of embodiment 58, wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell.
- [0275] Embodiment 60. The medical device of embodiment 58 or 59, wherein the fourth material contained in the compartment is a liquid or semi-solid.
- [0276] Embodiment 61. The medical device of any one of embodiments 58-60, wherein the fourth material contained in the compartment comprises a pharmaceutically acceptable material.

- [0277] Embodiment 62. The medical device of embodiment 61, wherein the pharmaceutically acceptable material comprises a heat labile component.
- [0278] Embodiment 63. The medical device of embodiment 58, wherein the interior cover covers the opening of the compartment.
- [0279] Embodiment 64. The medical device of embodiment 63, wherein the fourth material contained in the compartment comprises a pharmaceutically acceptable material.
- [0280] Embodiment 65. The medical device of any one of embodiments 62-64, wherein the fifth material comprises a component that is incompatible with a component of the fourth material.
- [0281] Embodiment 66. The medical device of embodiment 64, wherein the pharmaceutically acceptable material comprises a heat labile component.
- [0282] Embodiment 67. A method for preparing a pharmaceutical dosage form by three-dimensional printing, wherein the method comprises: printing a bottom of the pharmaceutical dosage form using a first material; printing a peripheral wall of the pharmaceutical dosage form using a second material, wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening; printing an interior cover attached to the shell using a third material, wherein the interior cover at least partially covers the opening of the compartment, and wherein the interior cover comprises one or more openings in communication with the compartment formed by the shell; delivering, after the printing of the interior cover, a fourth material to the compartment through the opening of the compartment; and printing an exterior cover attached to the interior cover and/or shell using a fifth material, such that the exterior cover is configured to cover, at least partially, the interior cover.
- [0283] Embodiment 68. The method of embodiment 67, wherein the printing the interior cover comprises flowing the third material out through a nozzle and depositing the third material to form the interior cover, and wherein the movement of the nozzle during the printing the interior cover is set to first print a portion that is relatively far away from each opening of the one or more openings of the interior cover.
- [0284] Embodiment 69. The method of embodiment 68, wherein each opening of the one or more openings of the interior cover is an elongated opening extending roughly along a second axis, and wherein when printing the interior cover, the angle between the nozzle's moving direction and the second axis is less than 50°.
- [0285] Embodiment 70. The method of any one of embodiments 67-69, wherein the printing the interior cover comprises depositing the third material to a portion of the shell and extending over the compartment formed by the shell such that at least a portion of the interior cover is suspended over the compartment formed by the shell.
- [0286] Embodiment 71. The method of embodiment 70, wherein the printing the interior cover comprises depositing the third material to a portion of previously printed interior

cover and extending over the compartment formed by the shell such that at least a portion of the interior cover is suspended over the compartment formed by the shell.

- [0287] Embodiment 72. The method of any one of embodiments 67-71, wherein the fourth material is a liquid.
- [0288] Embodiment 73. The method of any one of embodiments 67-71, wherein the fourth material is a semi-solid.
- [0289] Embodiment 74. The method of any one of embodiments 67-73, wherein the fourth material comprises a pharmaceutically acceptable material.
- [0290] Embodiment 75. The method of any one of embodiments 67-74, wherein the three-dimensional printing is a melt extrusion deposition (MED) technique.
- [0291] Embodiment 76. The method of any one of embodiments 67-75, wherein the three-dimensional printing is a semi-solid extrusion technique.
- [0292] Embodiment 77. The method of any one of embodiments 67-76, wherein the method does not comprise a step of extracting powder binder material.
- [0293] Embodiment 78. The method of any one of embodiments 67-77, wherein the method does not comprise a powder binder printing technique.
- [0294] Embodiment 79. A method for preparing a pharmaceutical dosage form, comprising: forming a first surface by a first material along a first preset path; forming a second surface by a second material along a second preset path, wherein the first surface and the second surface together form at least one compartment; forming a third surface by a third material along a third present path to partially enclose the compartment; delivering a fourth material to the compartment; forming a fourth surface by a fifth material along a fourth preset path to seal the compartment via covering any opening defined by the third surface.
- [0295] Embodiment 80. The method of embodiment 79, wherein the first preset path extends along a horizontal plane from a starting point, and/or the third preset path extends along a horizontal plane from a starting point, and/or the fourth preset path extends along aa horizontal plane from a starting point.
- [0296] Embodiment 81. The method of embodiments 79 or 80, wherein in the vertical direction, the end point of the second preset path is higher than the starting point of the second preset path.
- [0297] Embodiment 82. The method of any one of embodiments 79-81, wherein printing along the second preset path comprises: (a) printing along a horizontal plane from a starting point and then returning to the starting point; (b) repeating (a) path at least once.
- [0298] Embodiment 83. A drug production apparatus, comprising: a first feeding unit, capable of providing a first printing material to a first printing unit; a second feeding unit, capable of providing a second printing material to a second printing unit; a

carrying platform capable of moving relative to the first feeding unit and/or the second feeding unit; wherein the first printing unit comprises at least one nozzle, wherein each of the at least one nozzle comprises a feeding channel and a sealing structure, and the sealing structure moves in whole or in part to seal or open the feeding channel; the second printing unit comprises at least one discharging module, a driving device, and a mounting frame, wherein the discharging module comprises a discharging barrel, wherein the driving device drives the discharging of the second printing material from the discharging barrel, and wherein the driving device and the discharging barrel are fixed with the mounting frame; and the first printed material and/or the second printed material comprises a pharmaceutically active material.

- [0299] Embodiment 84. The drug production apparatus of embodiment 83, wherein the driving device comprises a power assembly and a force transmission assembly, wherein the force transmission assembly comprises a push rod and a piston connected with the push rod, and wherein the piston is wholly or partially located inside the discharging barrel.
- [0300] Embodiment 85. The drug production apparatus of embodiment 84, wherein the force transmission assembly further comprises a screw rod and a fixed block, the screw rod is capable of transmitting the torque of the power assembly, and the fixed block is connected with the screw rod and the push rod, thereby moving the push rod with the rotation of the screw rod.
- [0301] Embodiment 86. The drug production apparatus of any one of embodiments 83-85, wherein the mounting frame of the second printing unit comprises a mounting base and a mounting backplate perpendicular to the mounting base, and wherein the discharging barrel is connected with the mounting base or the mounting backplate through a barrel fixing element.
- [0302] Embodiment 87. The drug production apparatus of embodiment 86, wherein the mounting backplate further comprises a slide rail, and wherein the power assembly of the driving device is connected with the slide rail, and/or the barrel fixing element is connected with the slide rail.
- [0303] Embodiment 88. The drug production equipment of any one of embodiments 83-87, wherein the carrying platform is capable of translationally moving or rotating relative to the first feeding unit and/or the second feeding unit.
- [0304] Embodiment 89. The drug production apparatus of any one of embodiments 83-88, wherein the drug production apparatus further comprises a temperature control module.
- [0305] EXAMPLES
- [0306] Example 1. Preparation of exemplary pharmaceutical dosage forms and improvement of drug stability

- [0307] This example illustrates the composition, preparation, and testing of the pharmaceutical dosage forms described herein.
- [0308] Test 1
- [0309] Pharmaceutical Dosage Form 1 and Pharmaceutical Dosage Form 2 were prepared, with the dosage form structures shown in FIG. 15A to FIG. 15D. FIG. 15A and FIG. 15C showed the front views of Pharmaceutical Dosage Form 1 and Pharmaceutical Dosage Form 2, respectively, while FIG. 15B and FIG. 15D showed the top view of Pharmaceutical Dosage Form 1 and Pharmaceutical Dosage Form 2, respectively.
- [0310] The printing steps for Pharmaceutical Dosage Form 1 were as follows: The bottom and the peripheral wall were printed separately to form the shell. The interior cover with an opening was printed and attached to the shell. The pharmaceutical material was delivered into the compartment formed by the shell through the opening in the interior cover. Finally, the exterior cover was printed.
- [0311] The printing steps for Pharmaceutical Dosage Form 2 were as follows: The bottom and the peripheral wall were printed separately to form the shell. The pharmaceutical material was delivered into the compartment formed by the shell. Finally, the exterior cover was printed.
- [0312] The printing temperatures for each part are shown in Table 1-1.
- [0313] Table 1-1. Printing temperature of components of pharmaceutical dosage forms

Pharmaceutical Dosage Form 1	Printing temperature at nozzle
Exterior Cover/Interior cover/Shell	130°C
Material in the compartment	Semi-solid printed by extrusion under room temperature
Pharmaceutical Dosage Form 2	Printing temperature at nozzle
Exterior Cover/Shell	130°C
Material in the compartment	Semi-solid printed by extrusion under room temperature

- [0314] The composition and dimensions of the Pharmaceutical Dosage Forms 1 and 2 are shown in Table 1-2 below.
- [0315] Table 1-2. Compositions and dimensions of pharmaceutical dosage forms

	Pharmaceutical Dosage Form 1	Weight/ mg	Pharmaceutical Dosage Form 2	Weight/ mg	Dimensions		
					W/mm	L/mm	H/mm
Exterior cover	HPC SSL	50.90	HPC SSL	49.39	W4=8.8	L4=17.8	H4=0.4
	TEC	5.66	TEC	5.49			
Material in compartment	Semaglutide	2.99	Semaglutide	2.94	W2=7.0	L2=16	H2=4.8
	Span 80	477.6	Span 80	470.4			
Interior cover	HPC SSL	44.55	N/A	N/A	W3=7.8; W5=2.6	L3=16.8; L5=5.6	H3=0.4
	TEC	4.95					
Shell	HPC SSL	227.50	HPC SSL	220.61	W1=8.8	L1=17.8	H1=5.6
	TEC	25.25	TEC	24.48			

- [0316] After printing, high-performance liquid chromatography (HPLC) was used to test the impurities and drug content of different pharmaceutical formulations immediately after printing.

[0317] Chromatography conditions: The instrument used was an Agilent 1260. The column used was a Phenomenex Kinetex C18 (4.6mm*150mm, 2.6um) . The wavelength was set to 214nm. Eluent A consisted of 0.1%TFA/H₂O (v/v) , and Eluent B consisted of 0.09%TFA/ACN (v/v) . The mobile phase ratio was Eluent A (%) : Eluent B (%) = 55:45. The results are shown in Table 1-3 below.

[0318] Table 1-3. Purity of Semaglutide in pharmaceutical dosage forms

Pharmaceutical Dosage Form	Impurity Content	Drug Content
Pharmaceutical Dosage Form 1	2.39%	97.61%
Pharmaceutical Dosage Form 2	6.25%	93.75%

[0319] The results indicated that the impurity content of Pharmaceutical Dosage Form 1 was significantly lower than that of Pharmaceutical Dosage Form 2, and the drug (Semaglutide) content of Pharmaceutical Dosage Form 1 was higher than that of Pharmaceutical Dosage Form 2, suggesting that the interior cover could significantly reduce the impact of high temperature on the material stability in the compartment.

[0320] Test 2

[0321] Pharmaceutical Dosage Form 3 and Pharmaceutical Dosage Form 4 were prepared, with the dosage form structures shown in FIG. 16A to FIG. 16D. FIG. 16A and FIG. 16C showed the front views of Formulation 3 and Formulation 4, respectively, while FIG. 16B and FIG. 16D showed the cross-sectional views from the bottom of Pharmaceutical Dosage Form 3 and Pharmaceutical Dosage Form 4, respectively.

[0322] The printing steps for Pharmaceutical Dosage Form 3 were as follows: The bottom and the peripheral wall were printed separately to form the shell. The API material was delivered into the compartment formed by the shell. The interior cover was printed separately and cooled, and then, the interior cover was attached to the shell. Finally, the exterior cover was printed.

[0323] The printing steps for Pharmaceutical Dosage Form 4 were as follows: The bottom and the peripheral wall were printed separately to form the shell. The material was delivered into the compartment formed by the shell. Finally, the exterior cover was printed.

[0324] Additionally, Intermediate 3-1 and Intermediate 4-1 were prepared, which only had the shell, interior cover (only for Pharmaceutical Dosage Form 3) , and materials in the compartments of Pharmaceutical Dosage Form 3 and Pharmaceutical Dosage Form 4, respectively, with the same dimensions as the compartments of Pharmaceutical Dosage Form 3 and Pharmaceutical Dosage Form 4.

[0325] The printing temperatures for each part are shown in Table 1-4.

[0326] Table 1-4. Printing temperature of components of pharmaceutical dosage forms

Pharmaceutical Dosage Form 3	Printing temperature at nozzle
Exterior Cover	50°C
Interior cover/Shell	130°C
Material in the compartment	Semi-solid printed by extrusion under room temperature

Pharmaceutical Dosage Form 4	Printing temperature at nozzle
Exterior Cover	50°C
Shell	130°C
Material in the compartment	Semi-solid printed by extrusion under room temperature

[0327] The composition and dimensions of the Pharmaceutical Dosage Forms 3 and 4 are shown in Table 1-5 below.

[0328] Table 1-5. Compositions and dimensions of pharmaceutical dosage forms

	Pharmaceutical Dosage Form 3	Weight/mg	Pharmaceutical Dosage Form 4	Weight/mg	Dimensions		
					W/mm	L/mm	H/mm
Exterior cover	HPC SSL	208.28	HPC SSL	198.07	W4=8.8	L4=17.8	H4=0.4
	Glycerol	52.12	Glycerol	49.57			
Material in compartment	Semaglutide	3.06	Semaglutide	2.91	W2=7.0	L2=16.0	H2=4.8
	Sodium Caprate	30.60	Sodium Caprate	29.10			
	Span 80	153.00	Span 80	145.50			
	SNAC	306.00	SNAC	291.00			
Interior cover	HPC SSL	45.90	N/A	N/A	W3=7.8	L3=16.8	H3=0.4
	TEC	5.10					
Shell	HPC SSL	234.40	HPC SSL	222.91	W1=8.8	L1=17.8	H1=5.6
	TEC	26.01	TEC	24.74			

[0329] Pharmaceutical Dosage Form 3, Pharmaceutical Dosage Form 4, Intermediate 3-1, and Intermediate 4-1 were stored in a storage chamber at 40°C (temperature 40±2°C, humidity 70±5%) for 10 days. High-performance liquid chromatography (HPLC) was used to test the changes in impurity and drug content (Semaglutide) before and after storage. The testing method was the same as in Test 1 in this example. The results are shown in Table 1-6.

[0330] Table 1-6. Impurity level of the drug (Semaglutide) before and after storage

		Impurity Level	Drug Level
Pharmaceutical Dosage Form 3	Day 0	Not detected	100%
	Day 10	26.81%	73.19%
Pharmaceutical Dosage Form 4	Day 0	Not detected	100%
	Day 10	46.51%	53.49%
Intermediate 3-1	Day 0	Not detected	100%
	Day 10	26.94%	73.06%
Intermediate 4-1	Day 0	Not detected	100%
	Day 10	26.91%	73.09%

[0331] The results indicated that there was no increase in impurities in Pharmaceutical Dosage Form 3 before and after storage, while there was a significant increase in impurities in Pharmaceutical Dosage Form 4 after storage, suggesting that the interior cover could effectively reduce the material incompatibility between the exterior cover and the material in the compartment, thereby improving the stability of the material in the compartment.

[0332] Example 2: Filling rate improvement by interior cover

[0333] Intermediate 1, intermediate 2, intermediate 3 and intermediate 4 were prepared respectively, and FIG. 17A to FIG. 17D show cross-sectional front view schematic diagrams of intermediates of pharmaceutical dosage forms according to different embodiments of this application. Weighing tests and VHX imaging detection tests were carried out. The structural dimensions of intermediates 1 and 2 are shown in Table 2.

[0334] Table 2 Structural dimensions of intermediates 1 and 2

	Intermediate 1 (mm)		Intermediate 2 (mm)
W1	8	W2	8
H1	2.8	H2	2.8
T11	0.8	T21	0.8
T12	0.8	T22	0.8

[0335] Test 1: Weighing test

[0336] Before printing the exterior cover and filling the liquid, intermediate 1 and intermediate 2 without exterior cover were prepared respectively by the same method as in Example 1 (the schematic diagram of the structure of intermediate 1 and intermediate 2 is shown in FIG. 17A and FIG. 17B).

[0337] Then, intermediate 1 was placed on the balance, and the balance was reset to zero. The compartment of intermediate 1 was filled with water containing methylene blue to the maximum extent so that there was still room for printing the exterior cover, thereby forming intermediate 3 (FIG. 17C shows a schematic diagram of the structure of intermediate 3). The printed intermediate 3 was placed on the balance and weighed.

[0338] Intermediate 2 was also placed on balance and the balance was reset to zero. The compartment of intermediate 2 was filled with water containing methylene blue to the maximum extent so that there was still room for printing the exterior cover, thereby forming intermediate 4 (FIG. 17D shows the schematic structure of intermediate 4). The printed intermediate 4 was placed on the balance and weighed.

[0339] Following similar steps, two other samples (Sample 2 and Sample 3) were prepared as intermediate 3 and intermediate 4, respectively. Their weight increase after water filling was recorded and shown below.

[0340] Table 3 Weight increase for intermediates 3 and 4

	Intermediate 3 (mg)	Intermediate 4 (mg)
Sample 1	81.55	64.64
Sample 2	81.90	63.82
Sample 3	82.25	65.87
Average value	81.90	64.78

[0341] The results show that the setting of the interior cover can effectively improve the filling rate of liquid or semi-solid materials in the compartment.

[0342] Test 2: VHX imaging detection

[0343] The intermediate 3 and the intermediate 4 were imaged and detected by a digital microscope (model: VHX7000) . Under room temperature environment, VHX three-dimensional imaging X20 was used to carry out 3D molding. 6 points and 5 points were selected in the 3D diagram of the intermediate 3 and intermediate 4 respectively, and the height of each point from the center to the outer edge of the intermediate relative to the datum level was measured. The measurement results are shown in Table 4 and in FIG. 18A and FIG. 18B.

[0344] Table 4. The height of each point in the intermediate from the stage

Intermediate 3	Height of each point from the stage (μm)	Intermediate 4	Height of each point from the stage (μm)
1	3132.525	1	3717.378
2	1428.876	2	3569.166
3	1842.500	3	2047.373
4	1102.849	4	1443.052
5	4058.755	5	661.482
6	3558.564		

[0345] The results show that the distance between the center point 5 of intermediate 4 and the stage was significantly shorter than that of the center point 4 of intermediate 3 and the stage, and the filling of liquid materials of intermediate 3 and intermediate 4 was consistent with the schematic diagram of FIG. 2A and FIG. 2B, which further confirms that the setting of the interior cover can effectively improve the filling rate of liquid or semi-solid materials in the compartment.

Claims

- [Claim 1] A pharmaceutical dosage form, comprising:
a bottom formed by a first material;
a peripheral wall formed by a second material,
wherein the bottom and the peripheral wall together form a shell
forming a compartment comprising an opening;
an interior cover formed by a third material,
wherein the interior cover is attached to the shell,
wherein the interior cover at least partially covers the opening of the
compartment, and
wherein the interior cover comprises one or more openings in commu-
nication with the compartment formed by the shell;
a fourth material in the compartment, wherein the fourth material
comprises a pharmaceutically acceptable material; and
an exterior cover formed by a fifth material,
wherein the exterior cover is attached to the interior cover and/or the
shell, and
wherein the exterior cover is configured to cover, at least partially, the
interior cover.
- [Claim 2] The pharmaceutical dosage form of claim 1, wherein the ratio of the
area of an opening of the one or more openings of the interior cover to
the area of the opening of the compartment formed by the shell is less
than 95%.
- [Claim 3] The pharmaceutical dosage form of any one of claims 1-2, wherein the
interior cover is an elongated structure extending roughly along a first
axis, each opening of the one or more openings of the interior cover is
an elongated opening extending roughly along a second axis, and the
angle between the first axis and the second axis is 0°-90°.
- [Claim 4] The pharmaceutical dosage form of any one of claims 1-3, wherein the
one or more openings of the interior cover comprises two openings,
wherein each of the two openings are formed along an independent
axis, and wherein each independent axis is parallel with the other.
- [Claim 5] The pharmaceutical dosage form of any one of claims 1-4, wherein
each opening of the one or more openings of the interior cover does not
comprise a plug.
- [Claim 6] The pharmaceutical dosage form of any one of claims 1-5, wherein the
interior cover has a surface area of about 1 mm² to about 300 mm².

- [Claim 7] The pharmaceutical dosage form of any one of claims 1-6, wherein the interior cover has a thickness of about 0.01 mm to about 2 mm.
- [Claim 8] The pharmaceutical dosage form of any one of claims 1-7, wherein the third material of the interior cover and the second material of the peripheral wall are monolithic.
- [Claim 9] The pharmaceutical dosage form of any one of claims 1-8, wherein the shell forms one or more additional compartments.
- [Claim 10] The pharmaceutical dosage form of any one of claims 1-9, wherein the fourth material is a liquid or semi-solid material.
- [Claim 11] The pharmaceutical dosage form of any one of claims 1-9, wherein the fourth material is a solid material.
- [Claim 12] The pharmaceutical dosage form of any one of claims 1-11, wherein the pharmaceutically acceptable material is heat labile.
- [Claim 13] The pharmaceutical dosage form of any one of claims 1-12, wherein the pharmaceutically acceptable material is incompatible with another component of the pharmaceutical dosage form.
- [Claim 14] The pharmaceutical dosage form of any one of claims 1-13, wherein the pharmaceutically acceptable material is a pharmaceutically active material, excipient, or an adjuvant.
- [Claim 15] The pharmaceutical dosage form of claim 14, wherein the pharmaceutically acceptable material is a pharmaceutically active material selected from one or more of a small molecule compound, polypeptide, protein, nucleic acid, cell-containing hydrogel, probiotic, antibody-drug conjugate, and microbiome, or a combination thereof.
- [Claim 16] The pharmaceutical dosage form of claim 15, wherein the pharmaceutically active material is a polypeptide selected from the group consisting of an insulin, antidiuretic hormone, calcitonin, calcitonin gene-related peptide, parathyroid hormone, luteinizing hormone, erythropoietin, tissue plasminogen activator, growth hormone, adrenocorticotrophic hormone, interleukin, enkephalin, epinephrine, glucagon-like peptide-1 (GLP-1) receptor agonist, semaglutide, liraglutide, dulaglutide, exenatide, octreotide, teriparatide, vancomycin, linacotide, pukanatide, vorcyclide, talterelin, acetaminopressin, marsimorelin, and GLP-2 analogue.
- [Claim 17] The pharmaceutical dosage form of claim 14, wherein the pharmaceutically acceptable material is an excipient selected from the group consisting of a wetting agent, permeation enhancer, plasticizer, adhesive, developer, filler, and pH adjuster, or any combination thereof.

- [Claim 18] The pharmaceutical dosage form of any one of claims 1-17, wherein the first material of the bottom and the second material of the peripheral wall are monolithic.
- [Claim 19] The pharmaceutical dosage form of any one of claims 1-17, wherein the third material of the interior cover, the second material of the peripheral wall, and the first material of the bottom are monolithic.
- [Claim 20] The pharmaceutical dosage form of any one of claims 1-19, wherein the exterior cover is configured to fully cover all of the one or more openings of the interior cover.
- [Claim 21] The pharmaceutical dosage form of any one of claims 1-20, wherein the exterior cover is attached to the shell.
- [Claim 22] The pharmaceutical dosage form of any one of claims 1-21, wherein the exterior cover is attached to the interior cover.
- [Claim 23] The pharmaceutical dosage form of any one of claims 1-22, wherein the first material and the second material are the same.
- [Claim 24] The pharmaceutical dosage form of any one of claims 1-23, wherein the second material and the third material are the same.
- [Claim 25] The pharmaceutical dosage form of any one of claims 1-24, wherein the dissolution rate of the third material is different from that of the fifth material.
- [Claim 26] The pharmaceutical dosage form of any one of claims 1-24, wherein the third material and the fifth material have the same dissolution rate.
- [Claim 27] The pharmaceutical dosage form of any one of claims 1-26, wherein the shape of the pharmaceutical dosage form is a cylinder, a runway-shaped cylinder, an elliptical cylinder, a cube, a cuboid, a capsule, or a frustum of a cone.
- [Claim 28] The pharmaceutical dosage form of claim 27, wherein the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the diameter of the cylinder to the height of the cylinder is less than 1, the ratio of the area of all openings of the one or more openings of the interior cover and the area of the opening of the compartment formed by the shell is less than 90%.
- [Claim 29] The pharmaceutical dosage form of claim 27, wherein the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the diameter of the cylinder to the height of the cylinder is between 1 and 5.5, the ratio of the area of all openings of the one or more openings of the interior cover and the opening of the compartment formed by the shell is less than 90%.

- [Claim 30] The pharmaceutical dosage form of claim 27, wherein the shape of the pharmaceutical dosage form is a cylinder, and when the ratio of the diameter of the cylinder to the height of the cylinder is more than 5.5, the ratio of all openings of the one or more openings of the interior cover and the opening of the compartment formed by the shell is less than 90%.
- [Claim 31] A pharmaceutical dosage form, comprising:
a bottom formed by a first material;
a peripheral wall formed by a second material,
wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening;
an interior cover formed by a third material,
wherein the interior cover is attached to the shell, and
wherein the interior cover covers the opening of the compartment;
a fourth material in the compartment, wherein the fourth material comprises a pharmaceutically acceptable material; and
an exterior cover formed by a fifth material,
wherein the exterior cover is attached to the interior cover and/or the shell, and
wherein the exterior cover is configured to cover, at least partially, the interior cover.
- [Claim 32] The pharmaceutical dosage form of claim 31, wherein the fifth material comprises a component that is incompatible with a component of the fourth material.
- [Claim 33] The pharmaceutical dosage form of claim 31 or 32, wherein the pharmaceutically acceptable material comprises a heat labile component.
- [Claim 34] The pharmaceutical dosage form of any one of claims 31-33, wherein the third material of the interior cover is an erodible material.
- [Claim 35] The pharmaceutical dosage form of any one of claims 31-34, wherein the interior cover comprises a mesh.
- [Claim 36] A medical device, comprising:
a bottom formed by a first material;
a peripheral wall formed by a second material;
wherein the bottom and the peripheral wall together form a shell forming a compartment comprising an opening;
an interior cover formed by a third material,
wherein the interior cover is attached to the shell, and the interior cover at least partially covers the opening;

a fourth material contained in the compartment; and
an exterior cover formed by a fifth material,
wherein the exterior cover is attached to the interior cover and/or the
shell, and the exterior cover is configured to cover, at least partially, the
interior cover.

[Claim 37] The medical device of claim 36, wherein the interior cover comprises
one or more openings in communication with the compartment formed
by the shell.

[Claim 38] The medical device of claim 36 or 37, wherein the fourth material
contained in the compartment is a liquid or semi-solid.

[Claim 39] The medical device of any one of claims 36-38, wherein the fourth
material contained in the compartment comprises a pharmaceutically
acceptable material.

[Claim 40] The medical device of claim 39, wherein the pharmaceutically ac-
ceptable material comprises a heat labile component.

[Claim 41] The medical device of claim 36, wherein the interior cover covers the
opening of the compartment.

[Claim 42] The medical device of claim 41, wherein the fourth material contained
in the compartment comprises a pharmaceutically acceptable material.

[Claim 43] The medical device of any one of claims 40-42, wherein the fifth
material comprises a component that is incompatible with a component
of the fourth material.

[Claim 44] The medical device of claim 43, wherein the pharmaceutically ac-
ceptable material comprises a heat labile component.

[Claim 45] A method for preparing a pharmaceutical dosage form by three-di-
mensional printing, wherein the method comprises:
printing a bottom of the pharmaceutical dosage form using a first
material;
printing a peripheral wall of the pharmaceutical dosage form using a
second material,
wherein the bottom and the peripheral wall together form a shell
forming a compartment comprising an opening;
printing an interior cover attached to the shell using a third material,
wherein the interior cover at least partially covers the opening of the
compartment, and
wherein the interior cover comprises one or more openings in commu-
nication with the compartment formed by the shell;

delivering, after the printing of the interior cover, a fourth material to the compartment through the opening of the compartment; and printing an exterior cover attached to the interior cover and/or shell using a fifth material, such that the exterior cover is configured to cover, at least partially, the interior cover.

- [Claim 46] The method of claim 45, wherein the printing the interior cover comprises flowing the third material out through a nozzle and depositing the third material to form the interior cover, and wherein the movement of the nozzle during the printing the interior cover is set to first print a portion that is relatively far away from each opening of the one or more openings of the interior cover.
- [Claim 47] The method of claim 46, wherein each opening of the one or more openings of the interior cover is an elongated opening extending roughly along a second axis, and wherein when printing the interior cover, the angle between the nozzle's moving direction and the second axis is less than 50°.
- [Claim 48] The method of any one of claims 45-47, wherein the printing the interior cover comprises depositing the third material to a portion of the shell and extending over the compartment formed by the shell such that at least a portion of the interior cover is suspended over the compartment formed by the shell.
- [Claim 49] The method of claim 48, wherein the printing the interior cover comprises depositing the third material to a portion of previously printed interior cover and extending over the compartment formed by the shell such that at least a portion of the interior cover is suspended over the compartment formed by the shell.
- [Claim 50] The method of any one of claims 45-49, wherein the fourth material is a liquid.
- [Claim 51] The method of any one of claims 45-49, wherein the fourth material is a semi-solid.
- [Claim 52] The method of any one of claims 45-51, wherein the fourth material comprises a pharmaceutically acceptable material.
- [Claim 53] The method of any one of claims 45-52, wherein the three-dimensional printing is a melt extrusion deposition (MED) technique.
- [Claim 54] The method of any one of claims 45-53, wherein the three-dimensional printing is a semi-solid extrusion technique.
- [Claim 55] The method of any one of claims 45-54, wherein the method does not comprise a step of extracting powder binder material.

[Claim 56]

The method of any one of claims 45-55, wherein the method does not comprise a powder binder printing technique.