

[DESCRIPTION]

[Title of Invention]

DOUBLE ODOR MASKING PHARMACEUTICAL COMPOSITION

[Technical Field]

5 The present disclosure relates to a tablet-type pharmaceutical composition featuring a double odor masking coating layer containing a coating agent, an adsorbent, and an encapsulant. More particularly, the present disclosure relates to a tablet as a pharmaceutical composition having an odor masking effect and including a core layer and a coating layer surrounding the core layer, in which the core layer contains a prodrug having a medoxomil group and/or a pharmaceutically
10 acceptable salt thereof, and the coating layer contains a coating agent, an adsorbent, and an encapsulant, thereby absorbing and encapsulating an odor component (diacetyl) generated in the core layer and blocking externally introduced moisture to prevent hydrolysis of the parent drug and the medoxomil to inhibit the generation of an odor component, whereby the coating layer inhibits the odor.

[Background Art]

15 Azilsartan medoxomil is a drug as an angiotensin receptor blocker (ARB) that improves the binding ability and dissociation ability of AT1 (angiotensin 1) receptors, thereby lowering and controlling blood pressure. Prodrug forms, such as Olmesartan medoxomil and Azilsartan medoxomil, are readily separated into an active parent drug and medoxomil, and then medoxomil
20 is hydrolyzed to diacetyl, which, in turn, emits a characteristic unpleasant odor.

 In the related art, methods of reducing unpleasant odors from medoxomil-containing tablets include use of packaging with adsorbents such as silica gel, metal oxides or zeolites, or the use of encapsulating compounds (e.g., *beta*-Cyclodextrin) as formulation additives. However, the methods have disadvantages: in the case where cyclodextrin is used alone, it requires high costs in
25 terms of economics and efficiency; and an encapsulating efficiency is reduced or a large amount

of encapsulants has to be used depending on the molecular weight of materials to be encapsulated.

Edarbi® tablets, a blood pressure medication currently available on the market, has no odor masking technology, which is disadvantageous due to reducing medication adherence in patients. In addition, the hydroxypropyl methyl cellulose (HPMC)-based coating of Edarbyclor® tablets provides some odor masking, but it still reduces medication adherence in patients with a sensitive sense of smell, so there is a need for more effective odor masking.

[Documents of Related Art]

[Patent Document]

(Patent document 1) Korean Patent Application Publication No. 10-2008-0023684

[Non-patent Document]

(Non-patent Document 1) Non-patent Document 1: Reineccius, G. (2007) titled “Controlled release of flavor in food products. Modifying flavor in Food, pp.169-184.”

[Disclosure]

[Technical Problem]

The present disclosure provides a tablet as a pharmaceutical composition including a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof, of which the tablet is characterized by comprising a coating layer containing a coating agent, an adsorbent, and an encapsulant to significantly reduce unpleasant odor generated by diacetyl contained in the prodrug having a medoxomil group.

[Technical Solution]

To improve medication adherence in patients when administered with a medication containing a prodrug having a medoxomil group, the present disclosure provides a tablet as a pharmaceutical composition including a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof, of which the tablet is characterized by comprising a coating layer containing a coating agent, an adsorbent, and an encapsulant. The coating layer significantly

reduces an unpleasant odor caused by diacetyl by reducing disadvantages and improving effects of using each of the coating agent, adsorbent, and encapsulant alone.

One aspect of the present disclosure provides a tablet as a pharmaceutical composition including a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof, of which the tablet is characterized by comprising a coating layer containing a coating agent, an adsorbent, and an encapsulant.

One aspect of the present disclosure provides a tablet as a pharmaceutical composition including Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, of which the tablet is characterized by comprising a coating layer containing hydroxypropyl methyl cellulose (HPMC), magnesium aluminosilicate, and beta-cyclodextrin.

One aspect of the present disclosure provides a tablet as a pharmaceutical composition including Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, in which the tablet comprises a coating layer containing 1% to 10% (w/w) of a coating agent, 0.01% to 0.5% (w/w) of an adsorbent, and 0.05% to 5% (w/w) of an encapsulant, relative to the total weight of the tablet.

One aspect of the present disclosure provides a tablet as a pharmaceutical composition including Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, in which the tablet comprises a coating layer containing 5% to 35% (w/w) of a coating agent, 0.05% to 2.0% (w/w) of an adsorbent, and 1.0% to 20% (w/w) of an encapsulant, relative to the total weight of the Azilsartan medoxomil and/or the pharmaceutically acceptable salt thereof.

[Effects of the Invention]

The tablet-type pharmaceutical composition according to the present disclosure is configured such that the core layer containing a prodrug having a medoxomil group is coated with the coating layer containing a coating agent, an adsorbent, and an encapsulant. The coating layer adsorbs, encapsulates, and removes the odor (diacetyl) generated from the core layer as well as

prevents hydrolysis of the parent drug and the medoxomil by blocking externally-introduced moisture, thereby inhibiting the generation of an odor component to improve the odor masking effect.

The tablets of the present disclosure have an effect of improving medication adherence in patients by masking an odor component generated from the prodrug having a medoxomil group and/or the pharmaceutically acceptable salt thereof.

[Brief Description of the Drawings]

FIG. 1 is a schematic view illustrating one example of a tablet of the present disclosure, in which the tablet is characterized by a coating layer containing a coating agent, an adsorbent, and an encapsulant.

[Detailed Description of Embodiments]

All the terms, as used herein, unless otherwise defined, are used as the same ones understood by the ordinarily skilled in the art. In addition, although preferred methods or samples are described herein, similar or equivalent methods are also included in the scope of the present disclosure.

The term "prodrug having a medoxomil group" in the present disclosure refers to a substance containing medoxomil in the form of a prodrug. The substance is a pharmaceutically active ingredient substance readily separated into an active parent drug and medoxomil. Examples of the prodrug containing a medoxomil group are Olmesartan medoxomil, Azilsartan medoxomil, and so on.

The term "odor masking" in the present disclosure is defined as an activity to remove or reduce an unpleasant odor of pharmaceutically active ingredients, or reduce recognition of the odor.

The present disclosure provides a tablet configured such that a core layer containing a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof is coated

with a coating layer containing a coating agent, an adsorbent, and an encapsulant. The coating layer adsorbs, encapsulates, and removes an odor component (diacetyl) generated from the core layer as well as prevents hydrolysis of the parent drug and the medoxomil by blocking externally-introduced moisture and thereby inhibiting the generation of an odor component to improve the
5 odor masking effect.

The present disclosure relates to a pharmaceutical composition containing a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof, of which the pharmaceutical composition is characterized by comprising a coating layer containing a coating agent, an adsorbent, and an encapsulant.

10 In one embodiment of the present disclosure, the pharmaceutical composition may be a tablet or granule. For example, the pharmaceutical composition may be a tablet.

The pharmaceutical composition may be a tablet having a core layer surrounded by a coating layer. For example, the pharmaceutical composition may be a film-coated tablet.

In the film-coated tablet, the coating layer surrounding the core layer containing a
15 pharmaceutically active ingredient contains a coating agent, an adsorbent, and encapsulant.

The core layer may be a single layer, double layer, or multi-layer containing the pharmaceutically active ingredients. The core layer may be a single layer. Alternatively, the core layer may be a double layer.

In one embodiment of the present disclosure, a core layer containing Azilsartan
20 medoxomil and/or a pharmaceutically acceptable salt thereof and Amlodipine and/or a pharmaceutically acceptable salt thereof is surrounded by a coating layer containing a coating agent, an adsorbent, and an encapsulant. Thus, the coating layer adsorbs and removes odor components generated in the core layer, thereby having an odor masking function.

In one embodiment of the present disclosure, there is provided a coating layer composition
25 with an odor masking function. The coating layer composition includes a coating agent, an

adsorbent, and an encapsulant, thereby masking odor by adsorbing and removing odor components generated from a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof.

Composition of coating layer (coating layer composition) having an odor masking
5 **function**

Coating agent

A coating agent is a substance with a specific function that covers the surface of drugs, and may play a role as a mask against a drug exposure, a barrier to moisture, or an antioxidant.

The type of coating agents for the coating layer of the present disclosure is not particularly
10 limited. The coating agent may include one substance or a mixture of two or more substances selected from the group consisting of polyvinyl alcohol (PVA) and water-soluble coating agents belonging to cellulose ether derivatives, such as hydroxypropyl methyl cellulose, hydroxy propyl cellulose, hydroxyethyl cellulose, methyl cellulose, ethyl cellulose, carboxy methyl cellulose, and the like. In one embodiment, hydroxypropyl methyl cellulose may be used as the coating agent. In
15 one embodiment, an Opadry coating agent may be used as the hydroxypropyl methyl cellulose-based coating agent.

The amount of the coating agents may be suitably determined depending on the type of pharmaceutically active ingredients, and depending on the combination and composition of an adsorbent and an encapsulant.

20 In one embodiment of the present disclosure, the coating agent may be included in a range of 1% to 10% (w/w) with respect to the total weight of the tablet. Alternatively, the coating agent may be included in a range of 1% to 8% (w/w). Further alternatively the coating agent may be included in a range of 1% to 5% (w/w). The coating agent may be included as hydroxypropyl methyl cellulose (HPMC).

25 In one embodiment of the present disclosure, the coating agent may be included in a range

of 5% to 35% (w/w) with respect to the weight of the prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof. Alternatively, the coating agent may be included in a range of 7% to 28% (w/w). Further alternatively, the coating agent may be included in a range of 10% to 26% (w/w). The coating agent may be included as hydroxypropyl methyl cellulose (HPMC).

5 **Adsorbent**

An adsorbent is a substance that adsorbs odor-emitting materials, liquids such as moisture, and gaseous materials to be adsorbed. The adsorbent may act as a mask against a certain substance, a barrier to moisture, and so on.

The type of adsorbent included in the coating layer of the present disclosure is not particularly limited. For example, the adsorbent may be selected from inorganic salts and metal silicates. For example, the adsorbent may be a single substance or a mixture of two or more substances selected from the group consisting of magnesium aluminosilicate (trade name: Neusilin[®]), calcium silicate (trade name: Florite[®] R) or colloidal silicon dioxide (trade name: Aerosil[®] 200), or activated carbon or ion exchange resins. For example, magnesium aluminosilicate (Neusilin[®]) may be used as the adsorbent.

The amount of the adsorbent may be suitably determined depending on the amount of diacetyl, which is the odor component and the active ingredient, and depending on the combination and composition of the encapsulant. The ratio of the amount of the adsorbent to the amount of diacetyl produced by the prodrug having a medoxomil group may be 1:1.

20 In one embodiment of the present disclosure, the adsorbent with respect to the total weight of the tablet may be included in a range of 0.01% to 0.5% (w/w). Alternatively, the adsorbent may be included in a range of 0.01% to 0.3% (w/w). Further alternatively, the adsorbent may be included in a range of 0.01% to 0.2% (w/w). The adsorbent may be included as magnesium aluminosilicate.

In one embodiment of the present disclosure, the adsorbent with respect to the total weight of the tablet may be included in a range of 0.01% to 0.05% (w/w).

In one embodiment of the present disclosure, the molar ratio of the prodrug having a medoxomil group and/or the pharmaceutically acceptable salt thereof to the adsorbent may be in a range of from 300:1 to 10:1. For example, the molar ratio may be in a range of 300:1 to 25:1. Alternatively, the molar ratio may be in a range of 300:1 to 50:1. Further alternatively, the molar ratio may be in a range of 300:1 to 100:1.

In one embodiment of the present disclosure, the adsorbent with respect to the total weight of the prodrug having a medoxomil group and/or the pharmaceutically acceptable salt thereof may be included in a range of 0.05% to 2.0% (w/w). For example, the adsorbent may be included in a range of 0.1% to 2.0% (w/w). Alternatively, the adsorbent may be included in a range of 0.1% to 1.0% (w/w). The adsorbent may be included as magnesium aluminosilicate.

Encapsulant

An encapsulant is a substance for complexing and encapsulating various guest molecules. The encapsulant may provide one or more of the following functions: stabilization of the guest molecule against degradation (e.g., hydrolysis, etc.); improvement, or enhancement of the taste, or odor of a marketed product; delayed or sustained release of an odor, or smell.

The type of the encapsulant included in the coating layer of the present disclosure is not particularly limited. Examples of the encapsulant type include alpha-cyclodextrin, beta-cyclodextrin, gamma-cyclodextrin, and the like. In one example, beta-cyclodextrin may be used as the encapsulant.

The amount of the encapsulant may be suitably determined depending on the amount of diacetyl, which is the odor component and is the active ingredient, and depending on the combination and composition of the adsorbents. The ratio of the amount of the encapsulant to the amount of diacetyl produced by the composition may be 1:1.

In one embodiment of the present disclosure, the encapsulant with respect to the total weight of the tablet may be included in a range of 0.05% to 5% (w/w). For example, the encapsulant may

be included in a range of 0.1% to 5% (w/w). Alternatively, the encapsulant may be included in a range of 0.1% to 3% (w/w). The encapsulant may be included as beta-cyclodextrin.

In one embodiment of the present disclosure, the molar ratio of the prodrug having a medoxomil group and/or the pharmaceutically acceptable salt thereof to the encapsulant may be in a range of 200:1 to 10:1. For example, the molar ratio may be in a range of 180:1 to 10:1. Alternatively, the molar ratio may be in a range of 180:1 to 20:1. Further alternatively, the molar ratio may be in a range of 50:1 to 10:1.

In one embodiment of the present disclosure, the encapsulant with respect to the total weight of the prodrug having a medoxomil group and/or the pharmaceutically acceptable salt thereof may be included in a range of 1% to 20% (w/w). For example, the encapsulant may be included in a range of 1% to 15% (w/w). Alternatively, the encapsulant may be included in a range of 2% to 12% (w/w). The encapsulant may be included as beta-cyclodextrin.

In one embodiment of the present disclosure, the weight ratio of the adsorbent and the encapsulant may be in a range of 1:1 to 1:50. For example, the weight ratio may be in a range of 1:1 to 1:40. Alternatively, the weight ratio may be in a range of 1:1 to 1:30. Further alternatively, the weight ratio may be in a range of 1:20 to 1:25.

In one embodiment of the present disclosure, the weight ratio of the adsorbent and the coating agent may be in a range of 1:5 to 1:150. For example, the weight ratio may be in a range of 1:10 to 1:100. Alternatively, the weight ratio may be in a range of 1:30 to 1:80. Further alternatively, the weight ratio may be in a range of 1:25 to 1:62.5. Yet further alternatively, the weight ratio may be in a range of 1:25 to 1:62.5.

In one embodiment of the present disclosure, the weight ratio of the encapsulant and the coating agent may be in a range of 1:1 to 1:30. For example, the weight ratio may be in a range of 1:1 to 1:15. Alternatively, the weight ratio may be in a range of 1:1 to 1:5. Further alternatively, the weight ratio may be in a range of 1:1 to 1:2.5.

In one embodiment of the disclosure, there is provided a tablet in which a core layer containing a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof is coated with a coating layer containing 1% to 5% (w/w) of hydroxypropyl methyl cellulose (HPMC) as a coating agent, 0.01% to 0.2% (w/w) of magnesium aluminosilicate as an adsorbent; 5 and 0.1% to 3% (w/w) of beta-cyclodextrin as an encapsulant, relative to the total weight of the tablet.

In one embodiment of the disclosure, there is provided a tablet in which a core layer containing a prodrug having a medoxomil group and/or a pharmaceutically acceptable salt thereof is coated with a coating layer containing 10% to 26% (w/w) of a coating agent, 0.1% to 1.0% (w/w) 10 of an adsorbent, and 2% to 12% (w/w) of an encapsulant, relative to the total weight of the prodrug and/or the pharmaceutically acceptable salt thereof. In the present disclosure, the coating layer composition containing the coating agent, the adsorbent, and the encapsulant with respect to the total weight of the tablet may be included in a range of 1% to 16% (w/w). For example, the coating layer composition may be included in a range of 1% to 12% (w/w). Alternatively, the coating layer 15 composition may be included in a range of 2% to 8% (w/w), and further alternatively, the coating layer composition may be included in a range of 3% to 5% (w/w).

Active ingredient

The pharmaceutically active ingredients of the tablet according to the present disclosure are contained in the core layer surrounded by the coating layer.

20 In one embodiment of the present disclosure, the active ingredient of the tablet, which is coated with the coating layer, may include a prodrug having a medoxomil group, a pharmaceutically acceptable salt thereof, or both. The examples of the prodrug having a medoxomil group are Olmesartan medoxomil, Azilsartan medoxomil and the like.

In one embodiment of the present disclosure, Azilsartan medoxomil may be included as the 25 active ingredient of a tablet coated with the coating layer.

In one embodiment of the present disclosure, the active ingredient of a tablet coated with the coating layer may include 3% to 30% (w/w) of Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, relative to the total weight of the tablet. For example, the active ingredient may include 5% to 30% (w/w) of Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof. Alternatively, the active ingredient may include 7% to 30% (w/w) of Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof. Further alternatively, the active ingredient may include 10% to 25% (w/w) of Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof.

In one embodiment of the present disclosure, the amount of the Azilsartan medoxomil and/or the pharmaceutically acceptable salt thereof as the active ingredient of the tablet according to the present disclosure may be in a range of 10 mg to 100 mg, a range of 20 mg to 100 mg, a range of 30 mg to 95 mg, or a range of 70 mg to 90 mg.

In one embodiment of the present disclosure, the amount of the Azilsartan medoxomil and/or the pharmaceutically acceptable salt thereof as the active ingredient of the tablet may be 40 mg, 80 mg, or 100 mg.

In one embodiment of the present disclosure, the core layer of the tablet according to the present disclosure may be a single-component composition with a prodrug having a medoxomil group, or a multi-component composition with additional active ingredients. The term “composite tablet” refers to a tablet containing an additional pharmaceutically active ingredient with pharmacologic effects along with the prodrug having a medoxomil group in the core layer.

In one embodiment of the present disclosure, the composite tablet may include Dihydropyridine family and/or a pharmaceutically acceptable salt thereof as an additional active ingredient in addition to the prodrug having a medoxomil group.

In one embodiment of the present disclosure, the composite tablet may include Statin family and/or a pharmaceutically acceptable salt thereof as an additional active ingredient in addition to the

prodrug having a medoxomil group.

In one embodiment of the present disclosure, the composite tablet may include Thiazide family and/or a pharmaceutically acceptable salt thereof as an additional active ingredient in addition to the prodrug having a medoxomil group.

5 The composite tablet may further contain an active ingredient for hyperlipidemia treatment as one of the active ingredients.

In one embodiment of the present disclosure, the composite tablet may contain one or more of Atorvastatin, Rosuvastatin, Ezetimibe, Chlorthalidone, and/or pharmaceutically acceptable salts thereof as additional active ingredients, along with the prodrug having a medoxomil group.

10 In one embodiment of the present disclosure, the active ingredients of the composite tablet coated with the coating layer may include Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, and Amlodipine and/or a pharmaceutically acceptable salt thereof.

In one embodiment of the present disclosure, the active ingredients of the composite tablet coated with the coating layer may include Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, and Atorvastatin and/or a pharmaceutically acceptable salt thereof.

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In one embodiment of the present disclosure, the active ingredients of the composite tablet coated with the coating layer may include Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof; Atorvastatin and/or a pharmaceutically acceptable salt thereof; Ezetimibe and/or a pharmaceutically acceptable salt thereof.

20 In one embodiment of the present disclosure, the active ingredients of the composite tablet coated with the coating layer may include Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, and Rosuvastatin and/or a pharmaceutically acceptable salt thereof.

In one embodiment of the present disclosure, the active ingredients of the composite tablet coated with the coating layer may include Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof, and Chlorthalidone and/or a pharmaceutically acceptable salt thereof.

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In one embodiment of the disclosure, the active ingredients of the composite tablet coated with the coating layer may include Azilsartan medoxomil potassium, and Amlodipine besylate.

In one embodiment of the disclosure, one of the active ingredients of the composite tablet coated with the coating layer may contain 0.05% to 7% (w/w) of Amlodipine and/or a
5 pharmaceutically acceptable salt thereof, relative to the total weight of the tablet. In one example, one of the active ingredients may contain 1% to 5% (w/w) of Amlodipine and/or a pharmaceutically acceptable salt thereof. In another example, one of the active ingredient may contain 1% to 3% (w/w) of Amlodipine and/or a pharmaceutically acceptable salt thereof.

In one embodiment of the present disclosure, the amount of Amlodipine and/or a
10 pharmaceutically acceptable salt thereof may be 5 mg or 10 mg.

Additive

The tablet of the present disclosure may include a diluent, a disintegrant, a binder, a stabilizer, a lubricant, and a colorant as additives in addition to the pharmaceutically active ingredients. The additives may be one or more selected from the group consisting of a diluent, a
15 disintegrant, a binder, a stabilizer, a lubricant, and a colorant.

In one embodiment of the present disclosure, the pharmaceutical composition according to the present disclosure may include a pharmaceutically acceptable diluent, which may be one or more selected from the group consisting of lactose hydrate, starch, sucrose, mannitol, sorbitol, powdered cellulose, microcrystalline cellulose, calcium hydrogen phosphate and the like.

20 In one embodiment of the present disclosure, the pharmaceutical composition according to the present disclosure may include a pharmaceutically acceptable disintegrant, which may be one or more selected from the group consisting of croscarmellose sodium, sodium starch glycolate, gelatinized starch, cross-povidone, low-substituted hydroxypropyl cellulose, alginate, carboxymethyl cellulose calcium or sodium salt, colloidal silicon dioxide, guar gum, magnesium
25 aluminate, methyl cellulose, and sodium alginate.

In one embodiment of the present disclosure, the pharmaceutical composition according to the present disclosure may include a pharmaceutically acceptable binder, which is one or more selected from the group consisting of hydroxypropyl cellulose, low-substituted cellulose, ethyl cellulose polyvinylpyrrolidone, lactose hydrate, starch, talc, and gelatin.

5 In one embodiment of the present disclosure, the pharmaceutical composition according to the present disclosure may include a pharmaceutically acceptable stabilizer, which may include a buffer, a thickener, an antioxidant, a solubilizer, or the like.

In one embodiment of the present disclosure, the pharmaceutical composition according to the present disclosure may include a pharmaceutically acceptable lubricant, which is one or more
10 selected from the group consisting of fatty acid esters, stearic acid, magnesium stearate, glyceryl behenate, calcium stearate, sodium stearyl fumarate, sodium lauryl sulfate, magnesium lauryl sulfate, sodium benzoate, talc, hydrogenated oil, and carnauba wax.

In one embodiment of the present disclosure, the pharmaceutical composition according to the present disclosure may include a pharmaceutically acceptable colorant, which may include iron
15 oxides, natracol iron oxides, carotenoids, and so on.

According to the present disclosure, the tablet containing the prodrug containing Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof may be a tablet prepared by adding and mixing the additives typically used in the related art.

Since the masking of odor produced by a prodrug having a medoxomil group of the present
20 disclosure is not affected by the type and amount of the additives and additional active ingredients other than the prodrug having a medoxomil group, the tablet may be prepared by adding and mixing the additives typically used in the related art.

Film-coated tablet

According to the present disclosure, a core layer containing a prodrug having a medoxomil
25 group and/or a pharmaceutically acceptable salt thereof may be prepared by a conventional method

known in the related art.

In one embodiment of the present disclosure, the pharmaceutical composition including a prodrug having an Azilsartan medoxomil group and/or a pharmaceutically acceptable salt thereof may be prepared using commercially available Edarbi Tab.[®] (lot no. 12127566, Celltrion Pharm
5 Inc.) as a core to prepare the tablet characterized by comprising a coating layer containing a coating agent, an adsorbent, and an encapsulant.

In one embodiment of the present disclosure, the pharmaceutical composition may be a tablet with the core layer containing the pharmaceutically active ingredients surrounded by the coating layer. For example, the pharmaceutical composition may be a film-coated tablet.

10 In one embodiment of the present disclosure, the film-coated tablet may be prepared by the method of: mixing a coating agent, encapsulant, and adsorbent; and obtaining a film-coated tablet by coating the core layer containing a prodrug having a medoxomil group with the mixed coating solution using a coating machine.

In one embodiment of the present disclosure, the preparation method includes obtaining a
15 composite film-coated tablet by coating a double-layered tablet prepared by mixing one or more active ingredients respectively, with the mixed coating solution.

In one embodiment of the present disclosure, the tablet manufacturing method includes mixing, granulation, lubricating, tableting, and the like, which are commonly used tablet manufacturing methods in the related art such as those described in the Korean Pharmacopoeia.

20 In one embodiment of the present disclosure, there is provided a pharmaceutical composition including Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof in which the pharmaceutical composition is a tablet including: a core layer containing 5% to 30% (w/w) of Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof relative to the total weight of the tablet; and a coating layer containing 1% to 10% (w/w) of hydroxypropyl methyl cellulose
25 (HPMC), 0.01% to 0.5% (w/w) of magnesium aluminosilicate, and 0.05% to 5% (w/w) of beta-

cyclodextrin, relative to the total weight of the tablet.

In one embodiment of the present disclosure, there is provided a pharmaceutical composition including Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof. The pharmaceutical composition is a table including: a core layer containing 5% to 30% (w/w) of Azilsartan medoxomil and/or a pharmaceutically acceptable salt thereof relative to total weight of the tablet; and a coating layer containing 0.5% to 7% (w/w) of Amlodipine and/or a pharmaceutically acceptable salt thereof, 1% to 10% (w/w) of hydroxypropyl methyl cellulose (HPMC), 0.01% to 0.5% (w/w) of magnesium aluminosilicate and 0.05% to 5% (w/w) of beta-cyclodextrin, relative to the total weight of the tablet.

Hereinafter, the present disclosure will be described in more detail with reference to examples and experimental examples below. However, the following examples and experimental examples are presented to illustrate the present disclosure and are not intended to limit the scope of the present disclosure.

Example 1. Tablets containing Azilsartan medoxomil depending on types of adsorbent and encapsulant, and the odor masking effects thereof

Uncoated (core) tablet of Azilsartan medoxomil (Edarbi Tab.[®])

Experiments were carried out with Edarbi Tab.[®] (lot no. 12127566, Celltrion Pharm Inc.) purchased on the market.

Examples 1-1 to 1-4

As shown in Table 1, film-coated tablets were obtained by adding an adsorbent and an encapsulant to a coating agent with the use of the purchased Edarbi Tab.[®]. First, as shown in the combination of Examples 1-1, 1-2, 1-3, and 1-4 in Table 1 below, either of 6 g of alpha-cyclodextrin (Cavamax W6, Ashland) or beta- cyclodextrin (Cavamax W7, Ashland) as an encapsulant, and either of 0.6 g of calcium silicate (Florite-R, Tomita) or magnesium aluminosilicate (Fuji Chem.) were dissolved in 270 g of purified water in order. Next, a hydroxypropyl methyl cellulose-based

coating agent (Opadry 03A640040 Pink, Colorcon with hydroxypropyl methyl cellulose in amount of 78% of the total) was dissolved. Afterwards, the prepared coating solution was used to coat the 360 mg core tablets by using a coating machine (KC65FC, Keumsung), and then film-coated tablets in the weight of 370 mg per tablet were obtained.

5 **Comparative Example 1**

Film-coated tablets in the weight of 367.8mg per tablet were prepared in the same manner as in Example 1 except that the coating layer contains Opadry only, which is a hydroxypropyl methyl cellulose-based coating agent, as shown in Comparative Example 1-1 in Table 1 below.

10 **Experimental Example 1. Measurement of amounts of diacetyl detected from Azilsartan medoxomil tablets containing coating agent, adsorbent, and encapsulant to select the types of adsorbent and encapsulant**

15 An amount of diacetyl detected from Azilsartan medoxomil tablets containing a coating agent, an adsorbent, and an encapsulant prepared in Example 1 was measured over time by using a GC-based electronic nose. The prepared coated tablets were vacuum-dried at a temperature of 40°C and at a pressure of 2.0 mbar for 12 hours. The tablets along with a 1 g silica gel were sealed in an aluminum bag, and loaded in a test chamber. After the test chamber loading, the amount of diacetyl was measured through unloading in Week 1 (1W).

Method of detecting amounts of diacetyl with the use of electronic nose

20 A chromatogram was obtained by using a GC-based electronic nose (Heracles-II, Alpha-Mos) to measure amounts of detected diacetyl. Five tablets prepared in each example were put in 50ml vials and loaded on the electronic nose. Each vial was incubated at a temperature of 40°C for 20 minutes, and 5ml of the gases in the upper portion were collected and injected in the GC. Two columns, MXT-1701-FID (slightly polarized) and MXT-5-FID (non-polarized) were used, and the peak shown at about 27-28.5 seconds (RT) on the MXT-5-FID (non-polarized) column was
25 identified as the peak of diacetyl in the Arochem library of the electronic nose. All the samples of

Example 1 exhibited differences within the range of the peak only, and showed similarity in the rest of the peaks outside the range, thereby the difference of odor among the examples may be seen as a result of the difference in the amounts of detected diacetyl. The amounts of diacetyl were detected by calculating the corresponding peak area of the chromatogram, and expressed as a percentage based on the initial amounts of detected diacetyl of Comparative Example 1-1.

[Table 1]

Amounts of detected diacetyl of Azilsartan medoxomil tablets depending on types of adsorbents and encapsulants

Experimental example 1	Coating agent	Adsorbent	Encapsulant	Amounts of detected diacetyl (relative to Initial amount of Comparative example 1-1, %)	
	7.8 mg	0.2 mg	2 mg	Initial	1 W
Example 1-1	Opadry	Florite-R	alpha – CD	63.5	108.1
Example 1-2	Opadry	Neusilin	alpha – CD	45.0	149.3
Example 1-3	Opadry	Florite-R	beta – CD	44.1	120.9
Example 1-4	Opadry	Neusilin	beta – CD	29.5	72.1
Comparative Example 1-1	Opadry	-	-	100.0	155.5

According to the result of Experimental Example 1, Examples 1-1 to 1-4 containing all of a coating agent, an adsorbent, and an encapsulant exhibited a smaller amount of detected diacetyl than that of Comparative Example 1-1, and Example 1-4, wherein magnesium aluminosilicate and beta-cyclodextrin (beta - CD) were used as an adsorbent and an encapsulant respectively, exhibited the smallest amount of detected diacetyl among the groups.

Example 2. Odor masking effects of Azilsartan medoxomil tablets depending on the amount of adsorbent and encapsulant

Experiments were conducted as below to figure out the optimal amount of coating agent, adsorbent, and encapsulant and the odor masking effects thereof, each of which were selected based on the result of Example 1 and Experimental Example 1.

Examples 2-1 to 2-5

In Example 2, Edarbi Tab.[®] purchased in Example 1 was also used to prepare film-coated tablets. In specific, first, magnesium aluminosilicate (Neusilin, Fuji Chem.) and beta-cyclodextrin (beta-CD; Cavamax W7, Ashland) were dissolved in a purified water in order in the same amounts as those of adsorbents and encapsulants shown in Table 2. Next, a 10 mg hydroxypropyl methyl cellulose-based coating agent (Opadry 03A640040 Pink, Colorcon) was dissolved. Afterwards the film-coated tablets of Examples 2-1, 2-2, 2-3, 2-4 were obtained to have the total amount as shown in Table 2 by coating 360 mg of the core tablets with the prepared coating solution by using a coating machine (KC65FC, Keumsung).

Comparative Examples 2-1 to 2-4

Preparations were carried out according to the method of Example 2 to obtain film-coated tablets with the amount and combinations as shown in Comparative Examples 2-1, 2-2, 2-3, 2-4 in Table 2 below. Comparative Example 2-4 used Edarbi Tab.[®] purchased as in Example 1.

[Table 2]

Compositions of Azilsartan medoxomil tablets with coating layer containing coating agent, adsorbent, and encapsulant according to Example 2.

	Azilsartan medoxomil (mg)	Coating agent (Opadry) (mg)	Adsorbent (Magnesium Aluminosilicate) (mg)	Encapsulant (beta-Cyclodextrin) (mg)	Total tablet amount (mg)
Example 2-1	80	10	0.2	2	372.2
Example 2-2	80	10	0.4	2	372.4
Example 2-3	80	10	0.2	4	374.2
Example 2-4	80	10	0.4	4	374.4
Comparative Example 2-1	80	10	0	2	372
Comparative Example 2-2	80	10	0.2	0	370.2
Comparative Example 2-3	80	10	0	0	370
Comparative Example 2-4	80	0	0	0	360

Experimental example 2-1. Measurement of amounts of detected diacetyl of Azilsartan medoxomil tablets depending on the amount of adsorbent and encapsulant

Amounts of detected diacetyl were measured over the course of time by using a GC-based electronic nose for the Azilsartan medoxomil tablets with a coating layer containing a mixture of Opadry, magnesium aluminosilicate, and beta-cyclodextrin as shown in Example 2 or Table 2.

The prepared film-coated tablets were vacuum-dried at a temperature of 40°C and at a pressure of 2.0 mbar for 12 hours, sealed in an aluminum bag, and loaded in a test chamber. After the test chamber loading, the amount of detected diacetyl was measured through unloading in Week 1 (1W).

A GC-based electronic nose was used to measure amounts of detected diacetyl in the same manner as in Example 1. The amounts of detected diacetyl were expressed as a percentage based on the initial amount of detected diacetyl of Comparative Example 2-3. The results were described in Table 3 below.

[Table 3]

Measurement of amounts of detected diacetyl of Azilsartan medoxomil tablets depending on the amount of adsorbent and encapsulant

Experimental example 2-1	Amounts of detected diacetyl (relative to Initial amount of Comparative example 2-3, %)	
	Initial	1W
Example 2-1	51	121
Example 2-2	41	427
Example 2-3	42	60
Example 2-4	31	413
Comparative Example 2-1	59	541
Comparative Example 2-2	69	1331
Comparative Example 2-3	100	2,135
Comparative Example 2-4	316	12,508

According to the results of Table 3, the amounts of detected diacetyl in all of Examples 2-1 to 2-4, wherein an adsorbent and encapsulant were co-contained in addition to a coating agent, were significantly reduced compared to those of comparative examples, regardless of the change in the amount of the adsorbent and encapsulant. The experiments suggested that a combination of the components co-containing an adsorbent and encapsulant in addition to a coating agent exhibits excellent effects, and that a suitable amount of the combination of the three components must be adjusted to significantly minimize the amount of detected diacetyl.

Example 3. Long-term odor masking effects of Azilsartan medoxomil tablets depending on the amount of coating agent, adsorbent, and encapsulant

Examples 3-1 to 3-11

Edarbi Tab.[®] purchased as in Example 1 was used. Film-coated tablets of Examples 3-1 to 3-11 were obtained by using Edarbi Tab.[®] which added an adsorbent and an encapsulant to a coating agent as shown in Table 4 below. In specific, first, magnesium aluminosilicate (Neusilin, Fuji Chem.) and beta-Cyclodextrin (Cavamax W7, Ashland) were dissolved in a purified water in order in the same amounts as those of a coating agent, an adsorbent, and an encapsulant shown in Table 4. Next, a Hydroxypropyl methyl Cellulose-based coating agent (Opadry 03A640040 Pink, Colorcon) was dissolved in the same amounts as those shown in Table 4. Afterwards, film-coated

tablets were obtained by coating 360 mg of the core tablets with the prepared coating solution by using a coating machine (KC65FC, Keumsung) to have the total weight as shown in Table 4.

Comparative Example 3-1

Comparative Example 3-1 used Edarbi Tab.[®] purchased as shown in Example 1.

5 [Table 4]

Compositions of Azilsartan medoxomil tablets depending on the amount of coating agent, adsorbent, and encapsulant according to Example 3

	Azilsartan medoxomil (mg)	Coating agent (Opadry) (mg)	Adsorbent (Magnesium Aluminosilicate) (mg)	Encapsulant (beta-cyclodextrin) (mg)	Total tablet amount (mg)
Example 3-1	80	12.5	0.5	5	378
Example 3-2	80	12.5	0.5	1	374
Example 3-3	80	12.5	0.2	5	377.7
Example 3-4	80	7.5	0.5	5	373
Example 3-5	80	12.5	0.2	1	373.7
Example 3-6	80	7.5	0.5	1	369
Example 3-7	80	7.5	0.2	5	372.7
Example 3-8	80	7.5	0.2	1	368.7
Example 3-9	80	10	0.35	3	373.4
Example 3-10	80	10	0.35	3	373.4
Example 3-11	80	10	0.35	3	373.4
Comparative Example 3-1	80	0	0	0	360

Experimental Example 3-1: Measurement of amounts of detected diacetyl of Azilsartan medoxomil tablets depending on the amount of coating agent, adsorbent, and encapsulant

Amounts of detected diacetyl were measured over the course of time by using a GC-based electronic nose for the Azilsartan medoxomil tablets coated with a coating layer containing a mixture of Opadry, magnesium aluminosilicate, and beta-cyclodextrin as shown in Example 3 and Table 4.

The prepared film-coated tablets were vacuum-dried at a temperature of 40°C and at a pressure of 2.0 mbar for 12 hours, sealed in an aluminum bag, and loaded in a test chamber. After the test chamber loading, the amount of detected diacetyl was measured through unloading in Week 4.

5 A GC-based electronic nose was used to measure amounts of detected diacetyl in the same manner as in Example 1. The amounts of detected diacetyl were expressed as a percentage based on the initial amount of detected diacetyl of Comparative example 3-1. The results were described in Table 5 below.

[Table 5]

10 Measurement of amounts of detected diacetyl of Azilsartan medoxomil tablets depending on the amount of coating agent, adsorbent, and encapsulant

Experimental example 3-1	Amounts of detected diacetyl (relative to Initial amount of Comparative example 3-1, %)	
	Initial	4W
Example 3-1	11.50	52.46
Example 3-2	19.26	211.04
Example 3-3	7.97	50.50
Example 3-4	22.10	251.90
Example 3-5	22.63	210.74
Example 3-6	29.00	601.10
Example 3-7	18.12	230.88
Example 3-8	37.29	592.79
Example 3-9	31.20	360.79
Example 3-10	22.62	365.30
Example 3-11	24.05	324.93
Comparative Example 3-1	100.00	1,651.77

According to the results of Table 5, the amounts of detected diacetyl in all of Examples 3-1 to 3-11, wherein an adsorbent and encapsulant were co-contained in addition to a coating agent, were significantly reduced compared to the amount of comparative example 3-1, regardless of the change
15 in amount levels of the adsorbent and encapsulant.

In particular, although the samples of Experiment Examples 3-1 and 3-3 in Table 5 were

under 4-week of long-term testing condition, the amount of detected diacetyl was about 33 times smaller than that of Week 4 sample of Comparative Example 3-1 with no coating, and thereby excellent odor masking effects of the components were identified.

Experimental example 3-2. Measurement of odor intensity of Azilsartan medoxomil tablets depending on the amount of coating agent, adsorbent, and encapsulant through survey

A survey was conducted to 16 adults on the odor intensity of Azilsartan medoxomil tablets according to Example 3 based on the four scales listed in Table 6 (1. Not perceived, 2. Faintly perceived, 3. Strongly perceived, 4. Perceived to the extent that it interferes with taking). Based on the analysis result of the GC-based electronic nose, the samples with the smallest coating amount shown in Examples 3-3, 3-7, and 3-9 were selected among the samples in Table 4, and the selected samples and the sample of Comparative example 3-1 were surveyed based on the four scales of odor intensity listed in Table 6. The results are shown in Table 6 below as a percentage of the total headcount.

[Table 6]

Survey scores of odor intensity of tablets depending on the amount of coating agent, adsorbent, and encapsulant

Experimental example 3-2	Survey scores of odor intensity (Percentage of total headcount %)				
	Not perceived	Faintly perceived	Strongly perceived	Perceived to the extent that it interferes with taking	p-value
Example 3-3	50.0	43.8	6.3	0.0	0.006
Example 3-7	6.3	56.3	37.5	0.0	0.004
Example 3-9	6.3	31.3	62.5	0.0	0.001
Comparative Example 3-1	0.0	25.0	75.0	0.0	0.000

A significant difference in the odor masking effects depending on the amount of coating was identified, and better effects were shown in all the Examples compared to that of Comparative example 3-1. Statistical significance was determined by a Chi-square test with a confidence interval

of 95% or greater (p-value < 0.05). Greater than or equal to 50% of the survey participants did not perceive odor at all in the result of Example 3-3, and around 94% did not or very slightly perceived the odor, thereby showing a remarkable effect. Therefore, excellent odor masking effects of the compositions were determined through the survey.

5 **Example 4. Odor masking effects of composite tablet containing Azilsartan medoxomil and Amlodipine, or a pharmaceutically acceptable salt thereof depending on the amount of coating agent, adsorbent, and encapsulant**

Method of preparing Azilsartan medoxomil layer

853.6 g of Azilsartan medoxomil potassium, 1058.2 g of mannitol 1058.2 g, 1058.2 g of
10 microcrystalline cellulose, 360.0 g of croscarmellose sodium, 36.0 g of fumaric acid, 18.0 g of sodium hydroxide, and 180.0 g of hydroxypropyl cellulose were granulated using a fluidized bed granulator (Unilab L, Bosch). 36.0 g of magnesium stearate was added to it, and all the substances were mixed and stirred in a mixer (FTMF 50 MCG, Muller).

Method of preparing amlodipine layer

15 138.89 g of Amlodipine besylate, 1331.11 g of silicified microcrystalline cellulose, 400.00 g of calcium phosphate anhydrous, 20.00 g of colloidal silicon dioxide, and 100.00 g of crosspovidone were mixed in a mixer (FTMF 50 MCG, Muller). 10.00 g of magnesium stearate was added to it, and all the substances were lubricated.

Method of preparing double-layered tablet

20 The Azilsartan medoxomil mixture and the Amlodipine besylate mixture were tableted by using a bi-layer tablet press machine (EP200L, Parle). In the tableting process, 360 mg of Azilsartan medoxomil layer and 200 mg of Amlodipine layer were made respectively, to have a total of 560 mg per tablet by using a 14.5 x 8.0 mm oblong punch.

Method of preparing film-coated and double-layered tablet

25 As shown in Example 2 or 3, film-coated tablets may be obtained using the double-layered

tablets prepared above by adding an adsorbent and encapsulant to a coating agent. Afterwards, film-coated tablets were obtained by using a coating machine (KC65FC, Keumsung) to coat the double-layered tablets with the prepared coating solution as shown in Table 7.

Example 4-1

In specific, first, 0.632 g of beta-cyclodextrin (beta-CD; Cavamax W7, Ashland) and 15.820 g of magnesium aluminosilicate (Neusilin, Fuji Chem.) were dissolved in a purified water in order. Next, 39.548 g of hydroxypropyl methyl cellulose-based coating agent (Opadry 03A640040 Pink, Colorcon) was dissolved. Afterwards, as shown in Table 7, film-coated tablets in the weight of 588 mg per tablet were obtained by coating 560 mg double-layer (core) tablets with the prepared coating solution by using a coating machine (KC65FC, Keumsung).

Comparative Examples 4-1 to 4-2

Preparations were carried out according to the method of Example 4, to obtain film-coated tablets with the amount and combinations as shown in Comparative Examples 4-1 and 4-2 in Table 7.

[Table 7]

	Azilsartan medoxomil (mg)	Amlodipine (mg)	Coating agent (Opadry) (mg)	Adsorbent (Magnesium Aluminosilicate) (mg)	Encapsulant (beta-cyclodextrin) (mg)
Example 4-1	80	10	19.774	0.316	7.91
Comparative Example 4-1	80	10	0	0	0
Comparative Example 4-2	80	10	19.774	0	0

Experimental example 4. Measurement of amounts of detected diacetyl of composite tablets containing Azilsartan medoxomil and Amlodipine depending on the amount of coating agent, adsorbent, and encapsulant

Amounts of detected diacetyl from Azilsartan medoxomil tablets coated with a coating layer containing Opadry, magnesium aluminosilicate, and beta-cyclodextrin, as shown in Example 4 and Table 7, were measured over the course of time by using a GC-based electronic nose.

The prepared film-coated tablets were vacuum-dried at a temperature of 40°C and at a pressure of 2.0 mbar for 12 hours, sealed in an aluminum bag, and loaded in a test chamber. After the test chamber loading, the amount of detected diacetyl was measured through unloading in Week 4 (4W).

A GC-based electronic nose was used to measure amounts of detected diacetyl in the same manner as in Example 1. The amounts of detected diacetyl were expressed as a percentage based on the initial amount of detected diacetyl of Comparative Example 4-2. The results were described in Table 8 below.

[Table 8]

	Amounts of detected diacetyl (relative to Initial amount of Comparative example 4-2, %)	
	Initial	4W
Example 4-1	53	160
Comparative Example 4-1	228	7,210
Comparative Example 4-2	100	762

According to the results of Table 8, the amount of detected diacetyl in Example 4-1, wherein an adsorbent and encapsulant were co-contained in addition to a coating agent, was significantly reduced compared to those of Comparative Examples 4-1 and 4-2.

In particular, although the sample of Example 4-1 was under 4-week of long-term testing condition, the amount of detected diacetyl of the sample was about 5 times smaller than that of the Week-4 sample of Comparative example 4-2 coated with a coating agent only, and thereby excellent odor masking effects of the components were identified in a composite tablet as well.

[Claims]

[Claim 1]

A tablet as a pharmaceutical composition comprising a prodrug having a medoxomil group or a pharmaceutically acceptable salt thereof, of which the tablet is characterized by
5 comprising a coating layer containing a coating agent, an adsorbent, and an encapsulant.

[Claim 2]

The tablet of claim 1, wherein the coating agent in the coating layer is in a range of 1% to 10% (w/w) relative to the total weight of the tablet.
10

[Claim 3]

The tablet of claim 1, wherein the adsorbent of the coating layer is in a range of 0.01% to 0.5 % (w/w) relative to the total weight of the tablet.

[Claim 4]

The tablet of claim 1, wherein the encapsulant of the coating layer is in a range of 0.05% to 5% (w/w) relative to the total weight of the tablet.

[Claim 5]

The tablet of claim 1, wherein the coating layer comprises 5% to 35% (w/w) of the coating agent, 0.05% to 2.0% (w/w) of the adsorbent, and 1% to 20% (w/w) of the encapsulant, relative to the total weight of the prodrug having a medoxomil group or the pharmaceutically acceptable salt thereof.
20

25

[Claim 6]

The tablet of claim 1, wherein a weight ratio of the adsorbent and the encapsulant is in a range of 1:1 to 1:50.

5 [Claim 7]

The tablet of claim 1, wherein a weight ratio of the adsorbent and the coating agent is in a range of 1:5 to 1:150.

[Claim 8]

10 The tablet of claim 1, wherein a weight ratio of the encapsulant and the coating agent is in a range of 1:1 to 1:30.

[Claim 9]

15 The tablet of claim 1, wherein a molar ratio of the prodrug having a medoxomil group or the pharmaceutically acceptable salt thereof to the adsorbent is in a range of 300:1 to 10:1.

[Claim 10]

The tablet of claim 1, wherein a molar ratio of the prodrug having a medoxomil group or the pharmaceutically acceptable salt thereof to the encapsulant is in a range of 200:1 to 10:1.

20

[Claim 11]

The tablet of claim 1, wherein the coating agent is any one or a mixture of two or more selected from the group consisting of hydroxypropyl methyl cellulose, hydroxy propyl cellulose, hydroxyethyl cellulose, methyl cellulose, ethyl cellulose, and carboxy methyl cellulose.

25

[Claim 12]

The tablet of claim 1, wherein the adsorbent is any one or a mixture of two or more selected from the group consisting of magnesium aluminosilicate, calcium silicate or colloidal silicon dioxide, activated carbon, and ion exchange resins.

5

[Claim 13]

The tablet of claim 1, wherein the encapsulant is any one or a mixture of two or more selected from the group consisting of alpha-cyclodextrin, beta-cyclodextrin, and gamma-cyclodextrin.

10

[Claim 14]

The tablet of claim 1, wherein the coating layer comprises hydroxypropyl methyl cellulose as the coating agent, magnesium aluminosilicate as the adsorbent, and beta-cyclodextrin as the encapsulant.

15

[Claim 15]

The tablet of claim 1, wherein the coating layer comprising the coating agent, the adsorbent, and the encapsulant is in a range of 1 to 16 w/w% relative to the total weight of the tablet.

20

[Claim 16]

The tablet of claim 1, wherein the prodrug having a medoxomil group is Azilsartan medoxomil.

25

[Claim 17]

The tablet of claim 1 as a composite tablet further comprising an additional pharmaceutically active ingredient in addition to the prodrug having a medoxmil group.

5 [Claim 18]

The composite tablet of claim 17, wherein the additional pharmaceutically active ingredient comprises one or more selected from Amlodipine, Atorvastatin, Rosuvastatin, Ezetimibe, Chlorthalidone, or pharmaceutically acceptable salts thereof.